

S3 Leitlinie Lagerungstherapie und Mobilisation von kritisch Erkrankten auf Intensivstationen

# Evidenztabellen

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#001 Klem 2021 PMID: 34047169 DOI: 10.4045/tidss kr.20.0351 Specification of study: systematic review with meta-analysis	17 RCTs (1805 pts) from 2006 to 2020 <sup>1-17</sup> Inclusion criteria: - ICU patients > 18 years with MV in an ICU - oral intubation or tracheostomy Exclusion criteria: - injury or disease-specific muscle wasting -passive or almost exclusively passive intervention -non relevant outcome measures -other publication years -non-English or Scandinavian language -high risk of bias		- respiratory muscle training -active or active- assisted exercises for the extremities - mobilization to the edge of the bed or sitting in a chair -mobilization to a standing or ambulatory position - in-bed cycle ergometry	different treatment or no treatment	Primary endpoints: -duration of MV -weaning time from ventilator -mortality in the hospital, at 1–3 months, 1–6 months and after 1 year Secondary Outcomes: -ICU LOS -hospital LOS -patient safety -adverse events	Significant differences between groups in: -duration of MV (EM-intervention, n=4, 335 pts): -1.43 days; 95 % CI -2.68 to -0.18, p = 0.02 - ICU LOS (EM-intervention, n=7, 143 pts): - 1.08 days; 95 % CI -1.95 to -0.21, p = 0.02 - hospital mortality (EM-intervention): OR 0.90 (0.61 to 1.33) - 1–3-month mortality (n=1, 200 pts.): OR 0.51 (0.14 to 1.80) - 1-6-month mortality (n=3, 723 pts.): OR 0.95 (0.54 to 1.65) No significant differences between groups in: - duration of MV (IMT-intervention, n=2, 146 pts): -0.11 days; 95 % CI -1.76 to 1.53, p = 0.89 - 79 adverse events over the course of 5 675 training sessions (incidence rate of 1.4 %)	1

EM = early mobilization, ICU = Intensive Care Unit, IMT = inspiratory muscle training, LOS = length of stay, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial

#### Early mobilization led to a reduced duration of mechanical ventilation and length of stay in the ICU.

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Reference, Study Type	(Partici Charact	d Controls ipant #, eristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#002 Das 2021 PMID: 34045809 DOI: 10.5005/jp- journals-10071- 23789 Specification of study: Non randomized controlled study	50 pts Inclusion/e criteria: not Purposive s method was Per B	t provided. ampling		Graded early mobilization protocol: - for 10 sessions (multiple within a day) Phase 1: critically ill; goal: sitting at the edge of bed and initiate standing Phase 2: acute/ subacute phase; initiate re-education of gait with the walker Phase 3: acute/ subacute phase; able to actively participate; independent transfer training with a walker and provide progressive walking re-education Phase 4: subacute phase; promote progressive transfers and walking independence	not further defined	Primary endpoints: -FIM -GAD-7 -ICU LOS	Primary endpoints: - FIM score: 65.7 ± 12.2 vs. 17.4 ± 4.9; p > 0.001 - GAD-7 score: 7.5 ± 2.6 vs. 19.50 ± 2.7; p > 0.001 - ICU-LOS: 3.1 ± 0.6 vs. 5.6 ± 1.1; p>0.001	4 (downgraded from 3)

FIM = functional independence measure scale, GAD-7 = 7 point generalized anxiety depression scale, ICU = intensive care unit; LOS = length of stay, Pts = patients

Early mobilization seems to have a benefit in relation to FIM, GAD-7 and ICU length of stay.

Reference, Study Type	(Partio Charac	nd Controls cipant #, cteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#005 Jouffroy 2021 PMID: 33990007 DOI: 10.1016/j.jcrc.2021 .04.014 Specification of study: monocentric retrospective observational study.	20 and A 2020	19 d to ICU I February		<b>SBPP</b> at least 3 h 2x/day	Standard of care	Primary endpoints: -mortality (ICU/Hospital) -intubation -28 days survival	Primary endpoints: - ICU mortality 4 (13.3%) vs 94 (32.4%), p= 0.05 - In-hospital mortality: 5 (16.7%) vs 98 (41.4%), p= 0.02 - risk of invasive ventilation: sHR 0.96; 95% Cl 0.49; 1.88 - survival at day 28: HR 0.51, 95% Cl 0.16-1.16	3

COVID-19 = Corona Virus Disease 2019, ICU = Intensive Care Unit, SBPP = spontaneously breathing prone position

#### SBPP in COVID-19 patients reduced ICU and hospital mortality. It had no effect on intubation risk and mortality at day 28.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#006 Paton 2021 PMID: 33967203 DOI: 10.1097/CCM.00 0000000005058 Specification of study: Post hoc Secondary Analysis of a Prospective Cohort Study	<ul> <li>194 ICU pts from 2 tertiary ICUs</li> <li>Inclusion criteria: <ul> <li>pts of "The impact of disability in survivors of critical illness" trial</li> <li>all pts admitted to the 2 main tertiary hospitals</li> <li>MV &gt; 24 hours</li> <li>survivor of critical illness</li> </ul> </li> <li>Exclusion criteria: <ul> <li>age &lt; 18 years</li> <li>English language barrier</li> <li>proven or suspected acute primary brain process likely to result in global impairment of consciousness or cognition</li> <li>second or subsequent ICU admission for the hospital stay</li> </ul> </li> </ul>	9 pts (n = 8: records not obtainable n = 1: incomplete outcomes )	Measurement of dosage of mobilization in during the ICU stay (using IMS) Measurement of number of active mobilization sessions performed during the ICU stay.	No	<ul> <li>Primary endpoints: <ul> <li>change in health</li> <li>status from</li> <li>preadmission to 6-</li> <li>months following ICU</li> <li>admission (the EQ-5D-</li> <li>5L utility score)</li> </ul> </li> <li>Secondary outcome: <ul> <li>change in the EQ-5D-</li> <li>5L mobility domain</li> <li>from preadmission to</li> <li>6-months following</li> <li>ICU admission</li> </ul> </li> </ul>	<ul> <li>Significant differences between groups in:</li> <li>EQ-5D-5L utility scores, with every increase in IMS level increasing the EQ-5D-5L utility score by 0.045 (p &lt; 0.0001)</li> <li>effect higher in those with a lower health status pre-admission than those with higher health status pre admission (β = 0.046 [CI, 0.012–0.08] vs. 0.026 [CI, 0.007–0.045], respectively)</li> <li>health status 6 months following ICU admission (Multivariate analysis; β = 0.022 [CI, 0.002–0.042]; p = 0.033)</li> <li>EQ-5D-5L mobility domain score 6 months from ICU admission (β = 0.127 [CI, 0.049–0.205]; p = 0.001)</li> </ul>	4

EQ-5D-5L= euro-quality of life-5D-5 Level, ICU = intensive care unit, IMS= intensive care mobility scale, MV = mechanical ventilation, pts = patients

#### A higher IMS level increased quality of live 6 months after ICU admission.

Reference, Study Type	(Participant	and Controls #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#008 Nydahl 2021 PMID: 33946128 DOI: 10.1111/nicc.1 2638 Specification of study: pilot RCT	<ul> <li>expected to spen</li> <li>ICU</li> <li>Exclusion criteria:</li> <li>expectation of de</li> <li>no informed cons</li> <li>pre-existing immode</li> <li>contraindication a</li> <li>delirium before r</li> <li>positive pregnance</li> <li>participation in a</li> <li>the outcome of de</li> </ul>	ponsive d for delirium nobilized out of bed nd at least 1 night in the eath < 72 hours sent for the study obility against mobilization recruitment cy test competitive study with		<b>Mobilization</b> - to the edge of the bed - between 9pm and 11pm	Usual care	Primary endpoint: -safety Secondary Outcomes: -duration and incidence of delirium -mortality -duration of MV -hospital LOS for 28 days follow-up	Primary endpoint: -adverse events: 16.7% (n = 9) without serious consequences - most common event - deviation of systolic blood pressure > 20% (n = 4, 7.4%) -no pts. required re-/insertions of lines or tubes, or cardiopulmonary resuscitation. Secondary Outcomes: - duration of delirium, median (IQR) of intervention group: 1.5 (1-2.7) vs. control group: 2 (1-2) days, p = 0.860 - incidence of delirium OR 0.37 (95%CI 0.11-1.26), p = 0.133) - no other significant differences	2

ICU = Intensive Care Unit, LOS = length of stay, MV = mechanical ventilation, OR = odds ratio, pts = patients, RASS = Richmond Agitation Sedation Score, RCT = randomized controlled trial

Mobilization in the evening is feasible and safe.

Reference, Study Type	Cases and (Particiț Characte Tot	pant #, eristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#009								
Moran								
2021							Mortality at 28-30 days: PP 1057 vs SP	
PMID: 33942659 DOI: 10.1177/08850	8 RCTs (2001-2013) with 2607 ARDS pts <sup>1-8</sup>			Prone position in moderate-severe ARDS: -PP>12 h -PP<12 h	SP	<b>Endpoints:</b> Mortality at 28-30 days, 2-3 months and 6-months	1004 RR: 0.84 (0.65-1.09), I <sup>2</sup> = 69%, p<0.01 Mortality 2-3 months: PP 1088 vs. SP 1031 RR: 0.85 (0.70-1.03), I <sup>2</sup> = 64%, p<0.01 Mortality 6 months: PP 320 vs. SP 326	1
666211014479	Per Br	anch					RR: 0.99 (0.84-1.17), I <sup>2</sup> = 30%, p=0.23	
Specification of study: Multivariate meta-analysis	PP 1357	SP 1250					Mortality: ≥12 hours vs <12 hours PP (RR: 0.75, 95%Cl: 0.65, 0.86, P < 0.001)	

ARDS = Acute Respiratory Distress Syndrome, pts = patients, PP = prone positioning, SP = supine positioning

#### Prone positioning does not reduce mortality when compared to supine positioning.

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Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#011 Waldauf 2021 PMID: 339315 70 DOI: <u>10.1136/t</u> horaxjnl-2020- 215755 Specification of study: RCT	150 pts Inclusion criteria: ≥18 years -MV -predicted ICU lengt Exclusion criteria: -primary systemic neud disease/spinal cord lest -severe lower limb inju- -bedridden premorbic -imminent death or we treatment < 24 h -pregnancy -external fixator or me lower limb -open wounds/skin ab application points -presence of pacemak defibrillator or another electronic medical dev - unable to receive first session < 72 hours of a - transferred from another hours of MV - other conditions prevent FESCE or considered us study Per Ba randomised: n = 75 analysed: n = 42	aromuscular sion at admission ury/amputation d state ithdrawal of medical etallic implants in orasions at electrode er, implanted er implanted vice st rehabilitation admission other ICU after > 24 venting the use of unsuitable for the	Intervention: n = 33 / 44% Reasons: - death (n=18 until discharge; n=15 after ICU discharge) Control: n = 29 / 39% Reasons: - death (n=16 until discharge; n=13 after ICU discharge)	Progressive mobility program -start the day after randomization - until ICU discharge or day 28 -aiming for 90 minutes of active exercise per day - incorporating functional electrical stimulation and in-bed cycling	Standard physiotherapy -2x/day - 6 days a week - when requested by the treating physician	Primary endpoint: -SF-36 Physical Component Score 6 month after discharge Secondary outcomes: -PFIT -CSD -MRC -NB -VFD at day 28 -NDI -ICP elevations per day of ICP measurement Not prespecified outcome: -SF-36 MCS 6 month after discharge -6-Month survival	Primary endpoint: -SF-36 score, Median [IQR]: intervention 50 [21 – 69] vs control 49 [26 – 77], p = 0.261 Secondary outcomes: P-FIT, median[IQR]: intervention 9.4 [8.0 – 10.8] vs control 9.6 [8.3 – 10.9], p = 0.77 -CSD as difference from baseline (cm), Median [IQR]: intervention -11 [-17 – -6] vs control: -13 [-19 – -7], p = 0.64 -MRC, median [IQR]: intervention 42.4 [39.2 – 45.6] vs control: 39.4 [36.5 – 42.4], p = 0.13 -NB (gN/m2/day), median [IQR]: intervention: Median [IQR] -2.7 [-3.1 – -2.4] vs control -3.4 [-3.7 – -3.0], p = 0.004 -VFD, median [IQR]: intervention 9.3 [6.5 – 12.0] vs control 11.0 [8.2 – 13.8], p = 0.33 -NDI: none -ICP, median [IQR]: intervention: 1.5 [0.2 – 2.9] vs control 0, p = 0.018 Not prespecified outcome: -MCS, median [IQR]: intervention 54.8 [37.1 – 69.6] vs control 70.2 [51.5 – 81.3] p = 0.00 -6-month survival, intervention n = 42 (56%) vs control n=46 (61%), p = 0.46	2

CSD = muscle cross sectional diameter, ICU = Intensive Care Unit, ICP = intracranial pressure, MCS = mental component score, MRC = medical research council score, MV = mechanical ventilation, NB = nitrogen balance, NDI = number of dialysis interruptions, PFIT = physical fitness in intensive care test, RCT = randomized controlled trial, SF-36 = 36 item short form survey, VFD = ventilator free days

#### Functional electrical stimulation and cycle ergometry do not improve physical function 6 months after discharge.

Reference, Study Type	(Participant #,	d Controls Characteristics) ttal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#012 Barker 2021 PMID: 33931557 DOI: <u>10.1136/p</u> ostgradmedj- 2020-139631 Specification of study: Retrospective cohort study	<ul> <li>(type 1) req</li> <li>severe acut syndrome-c</li> <li>(SARS-CoV- PCR on nase swab</li> <li>findings of r ground-glas and/or cons imaging</li> <li>Exclusion criterit</li> <li>not Covid-1</li> <li>previous AP</li> <li>intubated b</li> </ul>	a: piratory failure piratory failure puiring oxygen e respiratory coronavirus 2 2) detected by opharyngeal multifocal as opacities solidation on a: 9	none	<b>Prone position</b> - with spontaneous breathing between 30 min and 2 h	Supine position or as usual	<b>Primary endpoints:</b> - 28-day mortality - ISARIC 4C mortality scores - non- invasive ventilation and IMV No sample size calculation (retrospective)	Significant differences between groups in: -ICU-LOS, APP group median number of days: 22, IQR 16– 41; control: 7, IQR 4–14, p=0.02 -for APP: SpO2/FiO2 most likely to PO2 increase after first episode (before median: 152, IQR 135–185; after: median 192, IQR 156–234, p=0.04) No significant differences between groups in: -number of pts requiring non- invasive ventilation and IMV -28-day mortality, APP group: 1; control: 4, p=0.12	4

APP = awake prone position, IMV = invasive medical ventilation, LOS = length of stay, pts = patients

Prone positioning reduces ICU-LOS and respiratory parameters.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#013 Ponnapa 2021 PMID: 33927120 DOI: <u>10.1097/CCM.</u> 000000000005086 Specification of study: Systematic review (SR)	25 observational studies <sup>1-25</sup> Inclusion criteria: - hypoxemic laboratory- confirmed COVID-19 - adult patients (≥ 18 years) requiring supplemental oxygen - received PP and reported on oxygenation variables (Pao2/Fio2, Pao2, or Spo2) Exclusion criteria: - narrative reviews - not reported oxygenation variables - case reports or case series with fewer than five patients Per Branch		<b>Prone position</b> with spontaneous breathing		Primary endpoint: - Improvement in oxygenation variables Secondary endpoints: - Serious adverse events - Intubation rate - mortality	Significant outcomes: - improvement in P/F ratio (39), in the ratio of Pao2 to Fio2 (mean difference, 39; 95% CI, 25-54) - PaO <sub>2</sub> (mean difference, 20 mmHg; 95% CI, 14-25), and peripheral oxygen saturation (mean difference, 20 mmHg; 95% CI, 14-25). - respiratory rate decreased after prone position (mean difference, - 3.2 breaths/min; 95% CI, -4.6 to - 1.9) - intubation and mortality rates were 24% (95% CI, 17-32%) and 13% (95% CI, 6-19%) - no serious adverse events were recorded in the small subgroup of studies that reported them.	1 → 2 (not only RCTs included)

Prone positioning was associated with improvement in oxygenation variables without any reported serious adverse events.

#### References

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Reference, Study Type	(Participant #	nd Controls , Characteristics) otal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
015 Scaramuzzo 2021 PMID: 33900484 DOI: 10.1186/s1361 3-021-00853-1 <b>Specification of</b> <b>study:</b> Retrospective cohort study	who participat prospective stu 15 intensive ca hospitals betw and 4 May 202 Exclusion criteri - NIV	ria: RS-CoV-2 eiving invasive ntilation ysis of patients ed in a previous udy conducted in re units of Italian een 22 February 0.		<b>PP</b> in COVID- ARDS: <u>1. Responders:</u> P/F increase when returning to SP > the median response of the population <u>2. non- Responders:</u> P/F increase less than the median response of the population		<ul> <li>Primary endpoint: <ul> <li>ICU VFD</li> <li>ICU mortality</li> <li>likelihood of liberation from MV at D28 after ICU admission</li> </ul> </li> <li>Secondary endpoints <ul> <li>tracheostomy</li> <li>attempted extubation</li> <li>plateau pressure during the first 5 days</li> <li>higher static compliance</li> <li>duration of PP</li> <li>duration of MV</li> <li>reintubation following weaning failure</li> <li>VAP</li> <li>steroid use</li> <li>non pulmonary infections</li> <li>cardiovascular complications</li> <li>neurologic complications</li> <li>renal replacement therapy</li> <li>veno-venous ECMO</li> </ul> </li> </ul>	<ul> <li>Significant differences between groups in: <ul> <li>tracheostomy 46 (47.9%) vs. 67 (70.5%), p = 0.008</li> <li>attempted extubation 33 (34.4%) vs. 6 (6.3%), p &lt; 0.001</li> </ul> </li> <li>VFD at D28 (Mean ± SD) 6.3 ± 8.1 vs. 2.7 ± 5.6, p &lt; 0.001</li> <li>ICU mortality 32 (33.3%) vs 51 (53.7%), p = 0.006</li> <li>plateau pressure 25 cmH2O vs 26 cmH2O (p=0.04) during the first 5 days</li> <li>higher static compliance 37 vs 33 ml/cmH2O (p=0.005) during the first 5 days</li> </ul> <li>No significant differences between groups in: <ul> <li>duration of prone positioning (Median [IQR]) 16 [16- 16.7] vs. 16 [16-17], p = 0.757</li> <li>duration of MV (Median [IQR]) 18 [10-27] vs. 18 [12-29], p = 0.432</li> <li>reintubation following weaning failure: 17 (17.7%) vs 5 (5.3%), p = 0.093</li> <li>VAP: 53 (55.2%) vs. 52 (54.7%), p = 0.885</li> <li>steroid use 72 (75%) vs. 61 (64%), p = 0.083</li> <li>non pulmonary infections: 37 (38.5%) vs. 35 (36.8%), p = 0.333</li> <li>digestive complications 5 (5.2%) vs. 3 (3.2%), 0.721</li> <li>neurologic complications 9 (9.4%) vs. 8 (8.4%), p = 1.0</li> <li>renal Replacement Therapy: 22 (22.9%) vs. 21 (22.1%), p = 1.0</li> <li>veno-venous ECMO 0 (0%) vs 3 (3.2%), p = 0.121</li> <li>ICU length of stay (Median [IQR]) 22 [15-35] vs. 21 [14-</li> </ul></li>	4

ARDS = acute respiratory distress syndrome, ECMO = extra-corporal membrane oxygenation, ICU = intensive care unit, NIV = non-invasive ventilation, P/F = PaO<sub>2</sub>/FiO<sub>2</sub>ratio, PP = prone positioning, pts = patients, SD = standard deviation, VAP = ventilator associated pneumonia, VFD = ventilator-free days; SP=supine position; MV= mechanical ventilation; LOS= length of stay

## Sustained oxygenation improvement after first PP session is independently associated to improved survival and reduced duration of mechanical ventilation in critically ill COVID-19 patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
#017 Tan 2021 PMID: 33888007 DOI: 10.1177/1753466 6211009407 Specification of study: meta analysis	16 studies (6 cohort studies, 10 case series) with 243 pts <sup>1-16</sup> Inclusion criteria: - cohort studies or case series - 18 years or older with AHRF or ARDS in waking state - PP combined with non-invasive respiratory support (non-invasive mechanical ventilation -high flow nasal canula, venturi mask, conventional oxygen therapy - outcomes including at least one of following measures: aggregated mortality rate, intubation rate, tolerability, prior to and following difference of PaO2/FiO2 ratios, peripheral oxygen saturation (SpO2) and respiratory rate Exclusion criteria: - not in English or commentaries, reviews, duplicate publications - data could not be extracted by the statistical methods or non-targeted outcomes	Prone positioning	Supine positioning	Primary endpoints: - intubation rate - mortality rate - improvement of PaO2/FiO2 ratio - improvement in SpO2 - changes in respiratory rate - intolerance rate	Significant differences between groups: - aggregated intubation rate and mortality rate were 33% [95% CI: 0.26–0.42, I2 = 25%] and 4% (95% CI: 0.01–0.07, I2 = 0%), resprectively - the intolerance rate was 7% (95% CI: 0.01–0.12, /2 = 5%) - prone positioning increased PaO2/FiO2 [mean difference (MD) = 47.89, 95% CI: 28.12–67.66; p < 0.00001, I2 = 67%] and SpO2 (MD = 4.58, 95% CI: 1.35–7.80, p = 0.005, I2 = 97%) - prone positioning reduced respiratory rate (MD = -5.01, 95% CI: $-8.49$ to $-1.52$ , p = 0.005, I2 = 85%) - subgroup analyses: rate of shorter duration prone ( $\leq$ 5 h/day) and longer duration prone (>5 h/day) were 34% and 21%, and mortality rate of shorter duration prone ( $\leq$ 5 h/day) and longer duration prone (>5 h/day) were 6% and 0%	$1 \rightarrow 2$ (non RCTs included)

AHRF = Acute Hypoxemic Respiratory Failure, ARDS = Acute Respiratory Distress Syndrome, CI = confidence interval, PP = prone position, pts = patients

Prone positioning may improve oxygenation and respiratory rate in patients with AHRF or ARDS.

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Reference, Study Type	Cases and Con (Participant #, Chara Total		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#018 Güner 2021 PMID: 33884691 DOI: 10.1111/nicc.12 633 Specification of study: RCT	60 pts. analyzed (87 randomized) Inclusion criteria: - ≥18 years of age - admitted to the ICU following orotr in the clinics or the ICU of the study   Exclusion criteria: - history of endotracheal intubation i - intubation in different hospital beforestudy site - hemodynamic instability (mean artifor 30 min, resistant to colloid therages support) - obligatory supine position (following surgery) - post- abdominal surgery - presence of surgical drains (might of positioning) - diagnosis of VAP before admission for - obesity (body mass index [BMI] >30 - pregnancy Per Branct <30° group (n=20) 30° group (n=20)	hospital in previous 30 days ore being admitted to cerial pressure < 60 mm Hg py or with inotropic ng trauma or spinal cause difficulty in to ICU D)	< 30°: lost to follow-up (exitus) (n= 5) 30°: lost to follow-up (exitus) (n=4), discontinued intervention (extubation) (n=5), (reintubation) (n=2) 45°: lost to follow-up (exitus) (n=5)	30° and 45° HOB elevation	<30° HOB elevation	Primary outcomes: - occurrence of VAP - timing of VAP	Primary outcomes: - frequency of VAP was significantly lower in the 45° compared with the <30° group (p= 0.022) - no significant differences between the <30° and 30°(p=0.053) as well as the 45° and 30° (p=0.705) groups - the timing of the VAP (early or late) was not dependent on the degree of HOB elevation (p=0.703)	2

HOB = head of bed, ICU = intensive care unit, pts = patients, RCT= randomized controlled trial, VAP = ventilator associated pneumonia

Placing and keeping the mechanically ventilated patients in semi recumbent position as close to 45° as possible can help prevent VAP.

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#020 Samimian 2021 PMID: 33870210 DOI: 10.22037/aaem.v9i1.106) Specification of study: Cohort study	Total         76 pts admitted to ICU         Inclusion criteria:         age > 18 years         RASS score equal to -4 or -5         MV for at least 24h         no spinal cord damage         normal intracranial pressure         without recent bladder surgery         without nasogastric tube and         Foley catheter         Exclusion criteria:         - intolerance to HOB elevation		IAP measurement was performed every 8 hours for 24 hours using the KORN method in three different degrees of the head of bed (HOB) elevation (0°, 15°, 30°)	No control group	Primary endpoints: - IAP measuring in relation to HOB	<ul> <li>Primary outcome:</li> <li>prevalence of intra-abdominal hypertension = 18.42%</li> <li>mean ± standard deviation (SD) of IAP</li> <li>8.44 ± 4.02 mmHg for HOB angle 0°,</li> <li>9.58 ± 4.52 for HOB angle 15°, 11.10 ± 4.73 for HOB angle 30°(p = 0.0001)</li> <li>mean IAP = 8.44 ± 4.02 mmHg in 0°,</li> <li>9.58 ± 4.52 mmHg in 15°, and 11.10 ± 4.73mmHg in 30° of HOB (p &lt; 0.001)</li> <li>normal IAP prevalence = reduced from 0° (81.6%) to 15° (65.8%) and 30°(57.9%), grade III IAH prevalence was increased from 0° to 30° (3.9%)</li> </ul>	

HOB = head-of-bed, IAH = intra-abdominal hypertension, IAP = intra abdominal pressure, ICU = intensive care unit, MV = mechanical ventilation, pts = patients, RASS = Richmond Agitation Sedation Scale

Elevation of HOB angle from 0° to 30° significantly increases IAP.

Reference, Study Type	Cases and C (Participant #, Ch Total	aracteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#026 Tonelli 2022 PMID: 33824084 DOI: 10.1016/j.pul moe.2021.03. 002 Specification of study: Retrospective 2-centre cohort study	114 COVID patients wi between March 1 <sup>st</sup> and Inclusion criteria: - 18 - 80 years - RR > 30 - SaO <sub>2</sub> <93% - PaO <sub>2</sub> /FiO <sub>2</sub> < 300mmH - Lung infiltrates > 50% Exclusion criteria: - intubation within 24H - no maximal therapy - DNI - missing core data Per Bran 38	d June 1 <sup>st</sup> ,2020. Hg 6 of lung n		Self-pronation with assistance for 3h for 1-4x/day + standard care	Standard care	Primary outcome:         - ETI rate         Secondary outcomes:         - in-hospital mortality         - time to ETI         - tracheostomy rate         - length of RICU and hospital stay         Power analysis:         Estimated ETI rate of 70% and presumed reduction by 40% in those receiving pronation α = 0.05, power 80% and an enrollment ratio of 1:2 = 93 pts.	Significant differences between groups: - ETI rate: HR = 0.59 95% CI [0.3–0.94], p = 0.03 - VFD: PP 15 (2–22) vs. SP 20 (2–24), p= 0.03 - LOS in RICU: PP 15 (3–26) vs. SP 10 (3–21), p= 0.02 - hospital LOS: PP 24 (3–45) vs. SP 20 (3–41), p= 0.03 No significant differences between groups: - in-hospital mortality - rate of tracheostomy	4

ARDS = acute respiratory distress syndrome; DNI = do not intubate; ETI = endotracheal intubation; ICU = intensive care unit; LOS = length of stay; pts = patients; RICU = respiratory intensive care unit, RR= respiratory rate; VFD = ventilator-free days

## Awake prone positioning reduces the rate of intubation, length of stay in ICU and hospital and increases the ventilator free days.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#027 Langer 2021 PMID: 33823862 DOI: 10.1186/s130 54-021- 03552-2 Specification of study: Retrospective multicenter	1057 ventilated CC between February 2020. Inclusion criteria: - laboratory confirminfection - ICU admission for Exclusion criteria: - < 18 years - pts. treated for n disease - missing data on F Per Br	OVID-19 pts 22 and June 14, med SARS-CoV-2 r ARDS on-respiratory		<b>PP</b> at least once during ICU stay	SP	Primary outcomes: - ICU mortality - hospital mortality - ICU-LOS - hospital LOS - duration of invasive MV	<ul> <li>Significant differences between the groups:</li> <li>ICU mortality: PP 262 (41%) vs SP 112 (28%), p&lt; 0.001</li> <li>Hospital mortality: PP 278 (45%) vs SP 127 (33%), p&lt; 0.001</li> <li>ICU-LOS: PP 16 (11–28) vs. SP 12 (7–21), p &lt; 0.001</li> <li>Hospital LOS: PP 30 (17–49) vs. SP 26 (16–40), p=0.008</li> <li>duration of invasive MV: PP 16 (10–30) vs. SP 10 (6–19), p &lt; 0.001</li> </ul>	4
cohort study	648	409						

ARDS = Acute Respiratory Distress Syndrome, ICU = Intensive Care Unit; LOS = length of stay, MV = mechanical ventilation, PP = prone positioning, pts= patients, SP = supine positioning

Patients receiving at least one PP session during their ICU stay have a higher ICU and hospital mortality and longer ICU and hospital stay as well as a longer duration of mechanical ventilation.

#028       B0 pts         #028       Inclusion criteria: - prolonged MV (>72 h) - stable orgens starution, fraction of inspired oxgens55%, and positive end expiratory pressure 36 mH2O - ods et dopammen: Dug/Kg/min and dose of epinephrine - dod healing pressure 35 mig and unine outputs 1 mL/kg/h - good healing of the indicis and there surgery - normal cognitive function - no history of chronic mental illness or chronic obstructive pulmonary disease       Rehabilitation therapy from day 2 until day 4 included six levels of rehabilitation exercises. - Level 0, turning over once every 2 h, for unconscious pts with unstable viral signs - Level 1, maintaining joint range of motion - strendopulmonary disease       Primary endpoint: - DE - DTF         PMID: 33781 259 DOI: 10.1186 (s12890-021 0161-2 0161-	Reference, Study Type	(Participant #,	nd Controls , characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Dong 2021 PMID: 33781 259 DOI: <u>10.1186</u> /s12890-021- 01461-2 Specification of study:	Inclusion criteria: - prolonged MV (>72 h) - stable oxygen saturation, frac and positive end expiratory pro- - dose of dopamine<10 μg/kg/ < 0.4 μg/kg/min - mean arterial pressure>75 m - good healing of the incision a - normal cognitive function - no history of chronic mental in pulmonary disease Exclusion criteria: - inability to perform physical a - long-term MV prior to admiss - neurological comorbidities in - irreversible disorders with a 6 according to APACHEII) - unsound limbs - administration of glucocortical corticosteroid dose equivalent prior to admission - cardiopulmonary resuscitatio - radiotherapy or chemotherap - presence of comorbidities, in venous thrombosis/embolism, - unstable fractures	essure ≤8 cmH2O (min and dose of epinephrine Hg and urine output>1 mL/kg/h after surgery illness or chronic obstructive activities sion ivolving muscles 6-month mortality rate of>50% oids (prednisone or other ts>20 mg/day) for at least 20 days on before admission to the ICU py within the previous 6 months iccluding acute myocarditis, deep , and cerebrovascular accident		day 2 until day 4 included six levels of rehabilitation exercises. - Level 0, turning over once every 2 h, for unconscious pts with unstable vital signs - Level 1, maintaining joint range of motion - Level 2, sitting in bed for 20 min 3 times a day - Level 3, additionally sitting on the edge of the bed - Level 4, additional standing up or sitting in a chair for at least 20 min a day - Level 5, pts actively moved from the bed and walked to		endpoint: - DE - DTF Secondary outcomes: - time on MV - intubation	<ul> <li>DE at day 1: 1.43 ± 0.47 vs.</li> <li>1.41 ± 0.59, p= 0.851</li> <li>DE at day 4: 1.33 ± 0.39 vs.</li> <li>1.27 ± 0.48, p= 0.541</li> <li>DTF in rehabilitation vs.</li> <li>control group, 0.15 vs 0.12</li> <li>p=0.008</li> <li>decrease of DTF:</li> <li>rehabilitation 0.017 vs control</li> <li>0.034 p = 0.026</li> </ul> Secondary Outcomes: <ul> <li>time on MV: 7.49±2.59 days</li> <li>vs. 9.41±5.32 days, p-value=0.045</li> <li>duration of intubation:</li> <li>8.31±2.80 days vs. 10.37±5.32</li> </ul>	2

APACHE II = Acute Physiology and Chronic Health Evaluation II, DE = diaphragmatic excursion, DTF = diaphragmatic thickening fraction, LOS = length of stay, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial

#### Early rehabilitation has a positive effect on the diaphragmatic thickening fraction but not on the diaphragmatic excursion.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#030 Rodriguez-Huerta 2022 PMID: 33725746 DOI: 10.1111/nicc. 12606 Specification of study: Retrospective cohort study	44 consecutive pts. Inclusion criteria: - COVID-19 ARDS - undergoing MV - ≥1 PP session during ICU stay Per Branch		<b>PP</b> without standardized protocol		Primary endpoints: - total number of PP maneuvers - total number of PP maneuvers per patient - duration of each PP session (hours) - total cumulative number of hours spent in PP per patient Secondary outcome: - AEs		4

AEs = adverse events, ARDS = Acute Respiratory Distress Syndrome, COVID-19 = Corona Virus Disease 2019, ICU = intensive care unit, MV = mechanical ventilation, PP = prone positioning; pts = patients

Despite the large number of maneuvers and the long time spent in the PP, no serious AEs occurred. Time spent in PP and number of PP sessions was associated with a higher risk for skin lesion.

Reference, Study Type	Cases and C (Participant #, Ch Tota	naracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#032 Sryma 2021 PMID: 33686973 DOI: 10.4103/lungi ndia.lungindi a_794_20 Specification of study: Prospective study	45 pts with COVID- hypoxemic respirat receiving non-invas therapy Inclusion criteria: - nasopharyngeal sy RT-PCR-confirmed - room air pulse oxy (SpO2) <94% Exclusion criteria: - hypercapnic respi hemodynamic insta - altered sensorium - immediate trache of hypoxia - hospitalization for - BMI >30 kg/m2 - PaO2/FiO2 <100 - on NIV/HFNC - intolerance to PP Per Bra 30	tory failure sive oxygen wab COVID-19 ygen saturation ratory failure, ability n tal intubation r > 12 h		Prone position	Supine positio n	Primary outcome: - rate of intubation Secondary outcomes: - ROX index 30min after start of PP - ROX index at 12h - days to recovery of hypoxia (SpO <sub>2</sub> > 93% at room air) - mortality	Primary outcome: - rate of intubation: PP 2 (6.7 %) vs. SP 5 (33.3%), p=0.02 Secondary outcomes: - ROX index 30 min before PP: PP 10.7 ± 3.8 vs. SP 6.7 ± 2.6, p<0.001 - ROX index after 12h: RR 12.4 (4.5) vs. SP 6.4 (3.0), p< 0.001 - days to recovery: n.s mortality: PP 2 (6.7%) vs. SP 4 (26.7%), p=0.06	3 → 4 Bias in group allocation (definitions missing)

HFNC = high flow nasal cannula, NIV = non-invasive ventilation, PP = prone position, ROX = respiratory rate - oxygenation, SP = supine position

Prone positioning seems to reduce the rate of intubation and mortality but has no effect on the time to recovery.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#033 Patterson 2021 PMID: 33675753 DOI: 10.1016/j.ajo.2021. 02.019 Specification of study:	11 RCTs with 2247 patients <sup>1-11</sup> Inclusion criteria: - >18 years - hospital inpatients in critical care (Level 2 in National Health Service Critical Care Service Framework) - English language - published between January 1, 1990 and July1, 2020 Exclusion criteria: - conference abstracts		РР	SP	Primary outcome: - incidence of ocular injuries	Primary outcome:         - incidence of ocular injuries (across all studies) <sup>1-11</sup> : OR: 1.02 (95% CI: 0.82–1.26), I <sup>2</sup> = 0%         - incidence of ocular injuries (only studies with low risk of bias) <sup>2,3,5</sup> : OR: 0.79 (95% CI: 0.11–44)	1
Systematic review with meta-analysis	Per Branch	-					

PP = prone positioning, RCT = randomized controlled trial, SP = supine positioning

#### Prone positioning does not seem to increase the incidence of ocular injury.

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Reference, Study Type		Cases and Controls ipant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#036 Nauka 2021 PMID: 33615236 DOI: 10.1097/CCE.0 0000000000 348 Specification of study: Retrospective case-control study	respiratory insufficient Inclusion criteria: -> 18 years - laboratory-confirm Exclusion criteria: - DNI Cases= pts that met mortality Controls = pts that wet time (death or intuk gender, admission of LOS.	the endpoint IMV or in-hospital vere alive and not intubated at index pation of case), matched 2:1 by age, late (within 2 weeks) and hospital <b>Per Branch</b>		nPP	No nPP	Primary outcomes: - risk of invasive MV - inhospital mortality adjusted for Charlson comorbidity index, BMI, worst S/F ratio and SOFA score.	<b>Primary outcome:</b> - risk of invasive MV: nPP: unadjusted HR 2.57; 95% Cl 1.17–5.64; p = 0.02 adjusted HR 0.92; 95% Cl 0.34–2.45; p = 0.86 - in-hospital mortality: adjusted HR 0.92; 95% Cl 0.90–0.94; p < 0.001	4
	Cases: n=200	Controls: n=400						

BMI = Body Mass Index, COVID-19 = Corona Virus Disease 2019, DNI = do not intubate, IMV = invasive mechanical ventilation, MV = mechanical ventilation, nPP = non-intubated PP, PCR = Polymerase Chain Reaction, PP = prone positioning, pts = patients S/F= SpO<sub>2</sub> / FiO<sub>2</sub>, SOFA = Sequential Organ Failure Assessment

COVID-19 patients receiving non-intubated prone positioning did not have a significantly higher risk of mechanical ventilation and had a significantly lower in-hospital mortality when adjusting for BMI, oxygenation and disease severity.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#037 Wiart 2021 PMID: 33653912 DOI: 10.4187/respc are.08461 Specification of study: Retrospective 2-center cohort study	39 consecutive pts with a total of 113 PP sessions Inclusion criteria: - >18 years - moderate and severe ARDS - PP > 12h during first 72h of admission No exclusion		ARDS related to COVID-19	ARDS unrelated to COVID-19	Not defined	Significant differences between the groups: - duration of MV: COVID-19: 26 days (13– 43) vs. non-COVID-19: 13 days (6–23), p=0.01 - ICU-LOS: COVID-19: 27.5 days (15–70) vs. non-COVID-19: 18 days (9–28), p=0.02 - number of PP sessions in PSV: COVID-19: 45 (66) vs. non-COVID-19: 39 (87), p=0.01 - number of PP sessions/ subject: COVID- 19: 4 (2–4) vs. non-COVID-19: 2 (1–4), p=0.02 No significant differences between the groups: - 28d-mortality - ICU mortality - VFD on day 28	4

ARDS = Acute Respiratory Distress Syndrome, COVID-19 = Corona Virus Disease 2019, ICU = Intensive Care Unit, LOS = length of stay, MV = mechanical ventilation, PP = prone position, PSV = pressure support ventilation, pts = patients, VFD = ventilator-free days

## COVID-19 patients receiving at least one prone session have a longer duration of mechanical ventilation and longer stay in the ICU and received fewer prone sessions on PSV and per patient.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#038 Simioli 2021 PMID: 33646105 DOI: 10.5152/TurkT horacJ.2021.20 158 Specification of study: single-center case-control study		11 pts (no complaints to PP)	Prone position with spontaneous breathing for approx. 10 h/d	Usual care	Primary Endpoints: - consolidation/atelectasis - P/F-ratio - duration of respiratory failure	Significant differences between groups in: - P/F during PP increased compared with noncompliant controls (288 vs. 202; p=0.0002) - Total duration of respiratory failure was shorter in pts with PP (14 vs. 21 days; p=0.002)	4

COVID-19 = Corona Virus Disease 2019, NIV = noninvasive ventilation, P/F = pO2/FiO2 ratio, PP = prone position, pts = patients

#### PP has a documented substantial effect on pO2/FiO2 ratio when started early and for at least 10 h/d.

Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#043 Mathews 2021 PMID: 33595960 DOI: 10.1097/CCM.000 000000004938 Specification of study: Large retrospective COVID-19 cohort study	2338 of critically ill adults w 2019 admitted to 68 U.S. h Inclusion criteria: - admitted to an ICU betwe 15 2020 - proning used for least one - adult pts(≥ 18 years old) - moderate-to-severe hypo Pao2/Fio2 ratio ≤ 200 mm I - within the first 2 days of IC - receiving invasive MV Exclusion criteria: - Pao2/Fio2 ratio less than of the first 2 days of ICU admi - pts who received ECMO o - experienced cardiac arres ICU day 1 - pregnancy Per Br n = 702 prone positioning < 48 h	ospitals een March 4 2020 and May e STOP-COVID patient xemia (Berlin criteria: Hg) CU admission or equal to 200 mm Hg in ssion in ICU day 1 t or severe arrhythmia on		<b>Prone</b> <b>position</b> Within the first 2 days of ICU	Usual Care	Primary outcome: - mortality - time to in- hospital death - censored at hospital discharge - last follow-up	<ul> <li>Primary outcome : <ul> <li>mortality HR : 0.84 (95% Cl, 0.73–</li> <li>0.97)</li> </ul> </li> <li>proned patients had a higher occurrence of shock on ICU day 1 vs. non-proned patients (114 [26.2%] vs. 208 [12.7%])</li> <li>total of 1.017 patients (43.5%) were discharged alive; 1.101 (47.1%) died (327 of pp pts., 46,6%; 774 of usual care pts., 47.3), 220 (9.4%) remained hospitalized at last follow-up (unadjusted HR, 0.89 [95% Cl, 0.79–1.02])</li> <li>median follow-up patients was 34 days (IQR, 25–46 d) and 30 days (IQR, 22–43 d) overall</li> </ul>	4 → 3 (large cohort)

ECMO= extracorporeal membrane oxygenation, HR= hazard ratio, ICU = Intensive Care Unit, pp= prone positioning, pts = patients, STOP-COVID= Study of the Treatment and Outcomes in Critically III Patients with Coronavirus Disease

## In-hospital mortality was lower in mechanically ventilated hypoxemic patients with coronavirus disease 2019 treated with early proning compared with patients whose treatment did not include early proning.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#044 Lai 2021 PMID: 33590997 DOI: 10.1097/CCM.0000 00000004849 Specification of study: Prospective monocentric study	22 ventilated pts with ARDS Inclusion criteria: -presence of ARDS - decision taken by the attending physicians to perform PP and monitoring of CI with calibrated pulse contour analysis Exclusion criteria: - ≤ 18 years old - extracorporeal membrane oxygenation - impossibility to perform EEXPO test Per Branch		РР	SP	<b>Primary</b> <b>outcome</b> hemodynamic effects of PP (measurements taken before and 15 min after PP maneuver)	Significant differences between measurements in SP and PP in preload responsive patients: - cardiac index L/min/m <sup>2</sup> : PP 3.5 (3.3–4.5) vs. SP 2.9 (2.7–3.5), p<0.05 - global end-diastolic volume index mL/m <sup>2</sup> : PP 780 (648–840) vs. SP 649 (556–754), p<0.05 - Pms mmHg: PP 34 (28–39) vs. SP 16 (15–21), p<0.05 - CVP mmHg: PP 14 (10–18) vs. SP 8 (8–12) - Pms – CVP mmHg: PP 19 (17–23) vs. SP 8 (6–12) - Rvr mm Hg/min/L: PP 3.0 (2.6–3.7) vs. SP 1.7 (1.5–1.9) - IAP mmHg: 15 (14–17) vs. 10 (9–15) No significant differences: - PaO <sub>2</sub> /FiO <sub>2</sub> - respiratory system compliance - total positive end-expiratory pressure - plateau pressure - heart rate - arterial pressure	4

CO = cardiac output, CVP = central venous pressure, EEXPO = end-expiratory occlusion, IAP = intra-abdominal pressure, Pms = mean systemic pressure, PP = prone positioning, Rvr = resistance to venous return, SP = semirecumbent positioning

Prone positioning induces an increase in cardiac index, global end-diastolic volume index, mean systematic pressure, central venous pressure, and intra-abdominal pressure.

Reference, Study Type	(Participant #,	l Controls Characteristics) tal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#045 Ohbe 2021 PMID: 33561986 DOI: 10.3390/jcm100 40618 Specification of study: observational study	30568 eligible pt Inclusion criteria - underwent CAE - admitted to the consecutive days of CABG Exclusion criteria - aged <18 years - received cardio resuscitation wit their CABG Per B	s a: a: b ICU > 3 s from the date a: pulmonary hin 3 days of ranch		<b>any rehabilitation</b> <b>program</b> within 3 days of CABG	usual care	Primary Endpoint: - Barthel Index score at discharge Secondary Outcomes: - in-hospital mortality - ICU LOS - hospital LOS - total hospitalization costs	Significant differences between groups in:         - Barthel Index scores at discharge in the early rehabilitation group were significantly higher than usual care group (difference: 3.2; 95% confidence interval: 1.5–4.8); <0.001	4 → 3 (upgrade, large cohort and consistent results)
	17418	13150					- hospital LOS (difference: -3.7 (Cl 95% : -5.2 to -2.2); p<0.001)	

CABG = coronary artery bypass grafting, CI= confidence interval, ICU = Intensive Care Unit, LOS = length of stay, pts = patients

An early rehabilitation program seems to have a benefit in relation to the Barthel score, in-hospital mortality, ICU LOS and hospital LOS in CABG patients.

Reference,	Cases and Controls (Participant #, Characteristics)		Drop -out	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	То	tal	Rate					Grade
#050 Ozyemisci Taskiran 2021 PMID: 33448757 DOI: 10.23736/S1973- 9087.21.06551-5	35 pts Inclusion criter - admission to I diagnosis of AR Berlin definitior COVID-19 ->18 years old	CU with a DS according to		Rehabilitation program - began ≥5 days of the ICU stay and ≥10 days after the onset of COVID symptoms - passive and active ROM	Standard ICU care	Primary endpoints: - duration of MV - ICU LOS - mortality rates - handgrip strength - MRC score - range of joint motion	Primary endpoints: - no significant differences in all outcomes	3
Specification of study: observational study	<b>Per B</b>	ranch 17	-	NMES (Compex Rehab 400, Compex, Ecublens, Switzerland)		- health-related quality of life was assessed with 36- item Short Form Survey		

ARDS = Acute Respiratory Distress Syndrome, ICU = Intensive Care Unit, LOS = length of stay, MRC = Medical Research Council Scale, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, pts = patients, ROM = range of motion

#### A late rehabilitation program including NMES showed no difference in relation to the predefined outcomes.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#051 Ibarra 2020 PMID: 33446462 DOI: 10.1016/j.bjps. 2020.12.057 Specification of study: Monocentric case-control study	polymerase chain - invasive mecha - treated with PP <b>Exclusion criteria</b> - noninvasive ver - patients not tre	herapy <b>:</b> base confirmed by n reaction nical ventilation therapy <b>a:</b> ntilation		Recording the pressure damage cases were defined as those who presented prone- positioning pressure sores (PPPS) such as ulcers on the forehead, cheek, ala nasi, lip, chin, chest, knee, leg or toe	controls were classified as those who met inclusion criteria but <b>did not</b> <b>present any PP</b> <b>pressure injuries</b>	<b>Primary endpoints:</b> presence, location, and severity of PPPS over bony prominences, as well as the injuries related to a medical or other device	(69%)	4

PP = prone positioning, PPPS = prone-positioning pressure sores, pts = patients

PPPS are related to the characteristics of the maneuver and the previous nutritional state. The implementation of improved positioning protocols may enhance results in critical patient caring.

Reference, Study Type	(Participant #,	d Controls Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#053 Clarke 2021 PMID: 33422143 DOI: 10.1186/s13104- 020-05426-2 Specification of study: prospective monocentric cohort study	20 COVID-ARDS pt ventilation Inclusion criteria: - > 18 years of age - confirmed SARS-( - invasively ventila - met the Berlin cri diagnosis of ARDS - underwent PP as management	CoV-2 infection ted in the ICU iteria for the	1 patient (treated in an area without an electronic health record system)	<b>PP</b> (16 h)	Supine position (before PP)	Primary endpoints: - ICU free days and ventilator free days (VFDs) - PaO2/FiO2 ratio before and after PP Secondary endpoints: - 28-day-mortality - compliance	<ul> <li>- median improvement in the PaO2/FiO2 ratio of 132 in the prone position compared to the supine position (IQR 67–228)</li> <li>- no significant difference in respiratory system static compliance</li> <li>- 28-day mortality rate of 15%</li> <li>- median number of ventilator free days at 28 days: 16 (IQR, 0–21)</li> <li>- median number of ICU free days at 28 days: 14.5 (IQR, 0–20)</li> </ul>	3

ARDS = Acute Respiratory Distress Syndrome, COVID = Corona Virus Disease, ICU = intensive care unit, PP = prone positioning, pts = patients

Prone positioning should be considered in patients with SARS-CoV-2 ARDS.

Reference, Study Type	(Participant #,	d Controls Characteristics) ttal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#054 Scheffenbichler 2021 PMID: 33416257 DOI: 10.1097/CCM.0 000000000048 08) Specification of study: International, multicenter, prospective cohort study	<ul> <li>&gt; 48 h</li> <li>- lower extremity a</li> <li>- comfort care</li> <li>- high risk of persis</li> <li>(motor componen and traumatic brainers)</li> <li>- pregnancy</li> <li>- neurodegenerational</li> <li>- paraplegia</li> <li>- tetraplegia</li> </ul>	0 < 48 h prior to her hospitals, long n facilities or th a preceding stay amputation stent brain injury t of the GCS < 5 in injury)	- n = 2 ICU follow up incomplete - n = 2 tissue edema rectus femoris muscle	none		<ul> <li>Primary outcome: <ul> <li>adverse discharge</li> <li>dispositions (loss of the ability to live independently)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>association between dose of mobilization and ICU length of stay, hospital length of stay, and 30-day mortality.</li> <li>association between dose of mobilization and mmFIM</li> <li>effect of dose of mobilization on DASI 3 months after hospital discharge.</li> </ul> </li> <li>Sample size calculation: <ul> <li>Estimated correlation between dose of mobilization and discharge disposition of 0.25, thus a sample size of 150 patients provides a power of 0.88 to identify a significant effect (alpha error of 0.05) for the primary outcome.</li> </ul></li></ul>	pts divided in low dose (LD) of mobilization (MQS ≤ 6.5) and high dose (HD) of mobilization (MQS > 6.5) Primary outcome: - adverse discharge: LD 55 (74%) vs. HD 37 (51%), p< 0.001 Secondary outcomes: - ICU-LOS: aIRR 0.72; 95% CI 0.57- 0.92; p=0.009 - hospital LOS: aIRR 0.79; 95%CI 0.64-0.98; p=0.035 - 30-day mortality: aOR 0.14; 95%CI 0.05-0.40; p<0.001 - mmFIM at ICU discharge: aIRR 2.45; 95%CI 1.94-3.08; p<0.001 - mmFIM at hospital discharge: aIRR 1.92; 95%CI 1.52-2.43; p<0.001 - DASI at 3-month FU: coefficient 9.82; 95%CI 3.88-15.75; p=0.001	3

CI = confidence interval, DASI = Duke Activity Status Index, GCS = Glasgow Coma Scale, ICU= Intensive Care Unit, IRR = incidence rate ratio, mmFIM = minimal modified functional independence measure, MQS = Mobilization Quantification Score, OR = odds ratio

High dose mobilization protects patient's ability to live independently after discharge.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#056 Menges 2021 PMID: 33407707 DOI: 10.1186/s13 054-020- 03446-9 Spezification of study: systematic review with meta- analysis	<ul> <li>- 12 RCTs <sup>1-12</sup></li> <li>Inclusion criteria: <ul> <li>studies conducted in</li> <li>adult ICU pts</li> <li>-aged ≥ 18 years</li> <li>requiring invasive or</li> <li>non-invasive MV at</li> <li>enrollment or during the</li> <li>ICU stay</li> </ul> </li> <li>Exclusion criteria: <ul> <li>studies that enrolled</li> <li>relevant proportions (≥</li> <li>10%) of pts with burn</li> <li>injuries, neurological</li> <li>conditions or transplant</li> <li>pts,</li> <li>postoperative pts</li> <li>requiring MV for &lt; 24 h on</li> <li>average</li> </ul> </li> </ul>		Systematic early mobilization - any physical or occupational therapy targeting muscle activation - initiated within 7 days after ICU admission - with a clearly defined protocol or specific clinical criteria	Late mobilization - initiated 7 days or more after ICU admission Standard early mobilization - initiated within 7 days but less systematically No mobilization - sham intervention or no rehabilitative intervention	Primary endpoints: 1) MRC-SS 2) ICUAW 3) Function Secondary outcomes: - quality of life - mortality - LOS - safety	<ul> <li>Significant differences between groups in:</li> <li>SF-36 PFS at 6 months after hospital discharge (MD 12.3; 95% CI 3.9–20.8; p = 0.004; one study; very low certainty)</li> <li>improvement in SF-36 PCS when comparing systematic early to late mobilization (MD 3.4; 95% CI 0.01-6.8; p=0.050)</li> <li>No significant differences between groups in:</li> <li>SF-36 PCS compared to standard early mobilization (MD -2.4; 95% CI -6.1 to 1.3; p=0.20)</li> <li>MRC-SS at ICU discharge (MD 5.8; 95% CI -1.4 to 13.0; p=0.12)</li> <li>incidence of ICUAW (RR 0.62; 95% CI 0.38-1.02; p=0.06)</li> <li>no conclusive evidence for quality of life, cognitive and mental health outcomes, length of ICU or hospital stay, duration of MV or in-hospital or post-discharge mortality</li> <li>Adverse effects n.s.</li> </ul>	1

ICU-AW = ICU-acquired weakness, ICU = intensive care unit, LOS= length of stay, MRC-SS = Medical Research Council Sum Score, n.s. = not significant, , pts = patients, SF-36 PCS = SF-36 physical health component score, SF-36 PFS = SF-36 physical function domain score

## Systematic early mobilization seems to have a benefit for the functional outcome compared to late mobilization (>7 d) but not standard early mobilization.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#057 Douglas 2021 PMID: 33405409 DOI: 10.1097/CCM.000 000000004818 Specification of study: Retrospective single-center study	61 pts with COVID-19 between March 1, 2020 and May 30, 2020 Inclusion criteria: - COVID-19 pneumonia/ARDS - requiring intubation - MV - PP Exclusion criteria: - No ICU admission - Not intubated Per Branch PP = 61		РР		Primary endpoint: - pressure wounds by grade (1-4) Secondary outcomes: - rate of facial and limb edema - hospital-acquired infection - device displacement - LOS	Primary endpoint- Pressure ulcers grade 1-3: 38 (71.7%)- Pressure ulcers grade 4:2 pts.Secondary outcomes- rate of facial and limbedema: "common" nocalculations- hospital-acquiredinfections: 3 (4.9%)- device displacement:not stated- ICU-LOS in survivors:16.5 d (10–25.8 d)- hospital-LOS insurvivors: 28 days(18–42 d)	

ARDS = Acute Respiratory Distress Syndrome, ICU = Intensive Care Unit, LOS = length of stay, MV = mechanical ventilation, PP = prone positioning, SP = supine positioning

Patients in prone position were likely to develop pressure ulcers.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#058 Gutiérrez-Arias 2021 PMID: 33402382 DOI: 10.4187/respcare. 08363 Specification of study: Systematic Review	<ul> <li>12 RCTs with 530 pts Meta analysis for 10 RCTs<sup>1-10</sup></li> <li>Inclusion criteria: <ul> <li>RCTs</li> <li>adult subjects</li> <li>invasive MV</li> <li>no restrictions regarding admission diagnosis ICU type or language</li> <li>neuromuscular or functional electrical stimulation compared to no intervention (i.e., usual care or physical therapy) or placebo of neuromuscular or functional electrical stimulation</li> </ul> </li> <li>Exclusion criteria: <ul> <li>published only in conference proceedings</li> <li>applied another intervention to only 1 of the 2 groups</li> </ul> </li> </ul>		Neuromuscul ar or functional electrical stimulation	No intervention or Placebo stimulation	Primary endpoint: - duration of invasive MV in days Secondary outcomes: - adverse events	Significant differences between groups in: - duration of MV, mean difference (95%CI): -2.68 (-4.35 1.02), p = 0.002 adverse events: no meta-analysis	1

CI = confidence interval, ICU = intensive care unit, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial

## Neuromuscular electrical stimulation reduces duration of mechanical ventilation in a meta-analysis including 2 out of 12 studies in this systematic review.

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Reference, Study Type	(Participant #,	l Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#059 Shearer 2021 PMID: 33389768 DOI: 10.1002/lary. 29374	263 patients Inclusion criteria: - age > 18 years - diagnosed with CO <sup>V</sup> - requiring intubation			pp	Supine positioning	Primary endpoints: - developing facial injuries - average duration of prone positioning	Primary outcome: - pp group: n=68 (47.6%) developed pressure injuries (head and neck) -supine group: n=2 (1.2%) with pressure injury - average duration of prone positioning for patients that developed pressure injuries was significantly longer (6.79 days vs. 3.64 days, P < .001)	4
Specification of study:	Per B	ranch					- mean duration of proning : 5.14	
Retrospective 2-centre cohort study	Prone position n=143	Supine position N=120					days (4.27%) (range: 1-26), with pressure injury: 6.79 days (4.87%), without pressure injury: 3.64 days (2.96.%)	

ICU = intensive care unit, pp = prone positioning, pts = patients

Longer duration of prone positioning was correlated with the development of pressure injuries, but early supination may not be a feasible option.

261 pts       261 pts         061 Shelhamer       Inclusion criteria:         2021       ->17 years of age         ->17 years of age       ->intubated         -not undergone PP       -met criteria for PP (PaO2: FiO2 < 150 mm Hg, PEEP ≥ 10 cm of water and FiO2 ≥ 0.6)         001:       10.11777/088506662         0980399)       -confirmed SARS-CoV-2 infection by real-time reverse transcription-polymerase chain nasal swab         - from March 25 through May 2, 2020         001         002         0030399         Prospective Cohort Study         0980399         Prospective Cohort Study         0980399         Prospective Cohort Study         0980399         Prospective Cohort Study         0980399         0980399         Prospective Cohort Study         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399         0980399	Reference, Study Type	(Participant #, 0	d Controls Characteristics) Ital	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	061 Shelhamer 2021 (PMID: 33380236 DOI: 10.1177/088506662 0980399) Prospective Cohort	Inclusion criteria: ->17 years of age - intubated - not undergone PP - met criteria for PP mm Hg, PEEP ≥ 10 cr FiO2 ≥ 0.6) - confirmed SARS-Cc real-time reverse tra polymerase chain na - from March 25 thr	(PaO2: FiO2 < 150 m of water and oV-2 infection by anscription- asal swab ough May 2, 2020		by a specialized		outcome: in-hospital	<ul> <li>- unadjusted SHR (95%CI): 0.51 (0.39 – 0.66), p &lt; 0.005</li> <li>- multivariate adjusted SHR (95%CI): 0.57 (0.42 – 0.76), p&lt; 0.005</li> <li>- stabilized doubly robust IPTW SHR</li> </ul>	3

IPTW = inverse probability treatment weight, PEEP = positive end expiratory pressure, PP = prone position, pts = patients, SHR = sub-distribution hazard ratio

Prone positioning may reduce in-hospital mortality in COVID-19 patients. Limited significance due to baseline differences and insufficient adjustment.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
065 Cao et al 2020 (PMID: 33343939 DOI: 10.1155/2020/ 4973878) Systematic Review with Meta-Analysis	12 publications (RCTs) <sup>1-12</sup> Inclusion Criteria: - adults with ARDS - intervention: prone position - control: supine position - outcomes: efficacy outcomes including mortality, mechanical ventilation duration, and ICU stays, and the safety outcomes, including any adverse events reported ≥2 studies - study design: RCT Per Branch		PP	SP	Primary outcomes: - mortality - duration of MV - ICU LOS - adverse events	Significant outcomes: - mortality - subgroup lung protective ventilation, RR (95%CI): 0.77 (0.63 – 0.93), p = 0.006 - mortality - <70% male pts, RR (95%CI): 0.70 (0.58 – 0.85), p < 0.001 - pressure sores, RR (95%CI): 1.23 (1.07–1.42), p = 0.003 Non-significant outcomes: - morality, RR (95%CI): 0.87 (0.75 – 1.00), p= 0.055 - ICU LOS, mean difference (95%CI): -0.39 (-2.70 – 1.91), p = 0.738 - duration of MV, mean difference (95%CI): -0.22 (-3.14 – 2.70), p = 0.883 - displacement of tracheal tube, RR (95%CI): 1.35 (0.47–3.84), p = 0.579 - displacement of a thoracotomy tube, RR (95%CI): 3.14 (1.02– 9.69), p = 0.047 - unplanned extubation, RR (95%CI): 1.02 (0.73–1.43), p = 0.906 - selective intubation, RR (95%CI): 2.64 (0.26–26.73), p = 0.411 - endotracheal tube obstruction, RR (95%CI): 2.45 (1.42–4.24), p = 0.001 - loss of venous access, RR (95%CI): 1.52 (0.22–10.26), p = 0.669 - hemoptysis, RR (95%CI): 0.71 (0.40–1.26), p = 0.245 - pneumothorax, RR(95%CI): 0.71 (0.40–1.26), p = 0.471 - ventilator-associated pneumonia, RR (95%CI): 1.34 (0.65–2.76), p = 0.427	1 → 2 high risk of bias

CI = confidence interval, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, PP = prone position, pts = patients, RCT = randomized controlled trial, RR = risk ration, SP = supine position

Overall, prone positioning in comparison to supine position could not show a benefit regarding mortality, duration of mechanical ventilation or length of ICU stay. Beneficial effect in terms of lower mortality in subgroups and the high heterogeneity as well as publication bias in the funnel plots warrant further large-scaled RCTs.

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Reference, Study Type	Cases and ( (Participant #, Ch Tota	haracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
068 Hernandez- Rubio 2020 (PMID: 33326484 DOI: 10.1371/journal.po ne.0243968) Prospective cohort study	70 pts Inclusion criteria: - adult pts - positive PCR for COV - admission to the ICU of the following: RR > breaths/minute, seve accessory muscles or despite FiO2 >0.5 oxy Exclusion criteria: - pts transferred from undergo weaning Per Bra 32	J with at least one 30 are dyspnea, use of SpO2 <92% agen therapy		Self-/Awake- proning	Usual care	<b>Primary endpoint:</b> incidence of endotracheal intubation	<b>Primary outcome:</b> - Cox proportional hazard model for incidence of endotracheal intubation, adjusted OR (95%CI): 0.05 (0.005 – 0.54, p = 0.00)	3

ICU = intensive care unit, OR = odds ratio, PCR = polymerase chain reaction, pts = patients, RR = respiratory rate

Awake prone positioning reduced risk for endotracheal intubation.

Reference, Study Type	(Partic Charac	d Controls Sipant #, teristics) Dtal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
069 Berney 2020 (PMID: 33323480 DOI: 10.1136/tho raxjnl-2020- 215093) Specificatio n of study: multicentre RCT	criteria - primary neur diagnosis - not expected discharge	ere sepsis require MV > J stay > 4 days eria: not meet safety	6: Intervention 5, Control 1 (withdrew consent or developed exclusion criteria after randomisation)	60 min of FES- cycling >5days/week while in ICU + Standard care	Standard care	Primary outcomes: - quadriceps muscle strength at hospital discharge - cognitive impairment at 6-month follow-up Secondary outcomes: - all-cause mortality - incidence and duration of delirium - hand grip strength - PFIT - FSSI - SPPB - 6-MWT - Katz Index - LIAODL - HADS - SF-36 - EQ-5D	Primary outcomes: - quadriceps muscle strength at hospital discharge (Nm): 57.3 (SD: 21.6) vs. 53.1 (SD: 24.1) MD: 4.7 (95% Cl: -4.7 to 14.1) - cognitive impairment at 6-month follow-up: 9 (41%) vs 6 (40%), OR 1.1 95% Cl 0.30 - 3.8) p= 0.929 Secondary outcomes: - PFIT: 6.4 (SD: 2.4) vs. 5.1 (SD: 3.0) MD 1.3 (95% Cl 0.4 to 2.3) - FSSI: 20.4 (SD 9.7) vs. 15.9 (SD 10.0) MD 4.5 (95% Cl 1.1 to 8.0) - all-cause mortality: n.s. - incidence of delirium: no calculation - duration of delirium: n.s. - hand grip strength: n.s. - SPPB: n.s. - 6-MWT: n.s. - Katz Index: n.s. - LIAODL: n.s. - HADS: n.s. - SF-36: n.s	2

EQ-5D = european quality of life 5 dimensions, FES-cycling= functional electrical stimulation-assisted cycling, FSSI = functional status score for ICU, HADS = hospital anxiety and depression scale, ICU= intensive care unit, LIAODL = Lawton's instrumental activities of daily living, PFIT = physical function in ICU-Test, SF-36 = short form health survey 36, SPPB = short physical performance battery, 6-MWT= 6-minute walking test

#### Additional FES-cycling does not improve quadriceps muscle strength or cognitive impairment.

Reference, Study Type	(Partici Charact	d Controls ipant #, eristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
070 Chaplin 2021 (PMID: 33303317 DOI: 10.1016/j.aucc. 2020.10.011) Retrospective cohort study	72 patients or based on whe received perio positioning du ECMO run Inclusion crite - adults who re vvECMO at CV Auckland,NZ, I 1 2014 an July Exclusion crite -lung transplat Per B prone positioning n= 13	ther they ods of prone iring the eceived /ICU in between July 9 2019		<b>PP</b> values were recorded immediately before pronation, immediately before the end of the pronation episode, and 4-6 h after the end of the pronation episode	Supine position	Primary outcomes: - alive at 6 months - duration of ECMO (hours) Secondary outcome: - significant differences	Primary outcomes: - ECMO outcome (alive after 6 month): proned n=9 (69.2), nonproned n=41 (69.5) - pts in prone position: longer ECMO treatment than supine group with a median (IQR) time of 599 h (522±738) vs 230 h (133±404), respectively (p < 0.0002) Secondary outcome: Significant differences in PaCO2, MABP, VT: - before proning: PaCO2= 43.5 (40.7±46.9), before deproning: paCO2= 43.2 (40.5±46.3), 4-6h after supination: paCO2= 42 (39.8±46.3) (p-value < 0.0001) - before proning: MABP (mmHg)= 70 (65±75), before deproning: MABP= 75 (65±83.8), 4-6h after supination: MABP = 70 (65±75) (p- value<0.03) - before proning: VT (ml/kg)= 102 (33±120), before deproning: VT= 97.5 (48.8±138), 4-6h after supination: VT= 86 (32±138) <0.0001	4

CVICU= cardiothoracic and vascular intensive care unit, ECMO = extra corporeal membrane oxygenation, MABP= mean arterial blood pressure, PaCO2 (in mmHG) = partial carbon dioxide pressure, PP = prone position, pts = patients, VT = tidal volume, vvECMO = venous venous extra corporeal membrane oxygenation

Proning patients on ECMO appears to incur no further complications. Whether it has a clinical benefit needs further investigation.

DOI:     - prognosticated lethal outcome     3 pts     unilateral       withdrew     neuromuscular       consent     electrical	Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Per Branch	Segers 2021 (PMID: 33285371 DOI: 10.1016/j.jcrc. 2020.11.018) Specification	<ul> <li>Inclusion criteria:</li> <li>18 years or older</li> <li>≥ 48 hours but ≤ 96 hours since ICU admission</li> <li>predicted ICU LOS ≥7 days</li> <li>Exclusion criteria:</li> <li>transfer from another ICU or other hospital</li> <li>re-admission to the ICU</li> <li>prognosticated lethal outcome</li> <li>presence of a pacemaker</li> <li>pregnancy</li> <li>pre-existing neurological or neuro- muscular disease</li> <li>intracranial pressure &gt; 20cmH<sub>2</sub>O</li> <li>abnormal musculoskeletal and skin conditions that could interfere with the stimulation (e.g., femur fracture, burn injury on the thigh, skin disease)</li> </ul>	withdrew	physiotherapy and early mobilization + unilateral neuromuscular electrical stimulation for 60 minutes daily for 7 days (M. vastus medial; M. vastus	physiotherapy and early	thickness of the M. rectus femoris via ultrasound Secondary outcomes: - MRC - quadriceps	<pre>muscle and unstimulated muscle of the same patient:  Primary outcome: - average decline in intervention vs. control: 0.13 cm (95% CI 0.04 - 0.22), p = 0.007  Secondary outcomes: - MRC Median [IQR], Control: 4 [4–5] vs Intervention: 4 [4–5], p = 0.317 - HHD: Mean ± SD: control 101 ± 62 vs intervention 106 ± 72, p =</pre>	2 → 3 Intraindividual only

HHD = handheld dynamometry, ICU = intensive care unit, LOS = length of stay, MRC = medical research council score, pts = patients, RCT = randomized controlled trial

Neuromuscular electrical stimulation reduced loss of muscle mass.

Reference, Study Type	(Partici Charact	d Controls ipant #, :eristics) ital	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
075 Braune-Olsen 2020 (PMID: 33259044 DOI: 10.1186/s13613 -020-00776-3) prospective observational study	ill patients on Inclusion crite pts treated wit severe circulat respiratory fail	<b>ria:</b> th ECLS for cory and/or	-	Active mobilisation (IMS ≥ 3)	No active mobilisation (IMS < 3)	Primary outcome: - ECLS-associated complications during Secondary outcomes: - length of ECLS treatment - ICU-LOS - Hospital-LOS - ICU-mortality	332 active mobilisation sessions <b>Primary outcome:</b> - circuit malfunction: blood flow <2l/min: 3 (0.9%) - blood flow < 0,5l/min: 1 (0.3%) - SpO <sub>2</sub> < 85%: 63/ 332 (19%) - MAP < 50mmHg: 25/332 (7.5%) - HR > 140/min: 19/332 (5.7%) - bleeding from cannula: 3/43 (6.9%) vs. 11/72 (15.3%) - cannula displacement: 1/332 (0.3%)	3

ECLS = extracorporeal life support, HR = heart rate, IMS = ICU mobility scale, LOS = length of stay, MAP = mean arterial pressure, SpO<sub>2</sub>= peripheral oxygen saturation

Active mobilisation of critically ill patients on ECLS is feasible and safe.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
076 Liang 2020 (PMID: 33250403 DOI: 10.1016/j.aucc. 2020.10.004) Systematic review and meta-analysis	34 studies with 7159 pts (10 RCTs, 8 controlled clinical trials, 16 before-and- after studies) studies on early mobilisation n= 7 <sup>1-7</sup> Inclusion criteria: - ICU patients > 18 years Exclusion criteria: - studies including patients with history of a neurologic condition such as dementia, traumatic brain injury, stroke, or hepatic encephalopathy or who had undergone neurosurgery Per Branch		Early mobilisation	Standard care	Outcomes: - incident of delirium - duration of delirium - ICU-LOS - mortality - psychological outcomes (level of anxiety, quality of recovery) - family satisfaction of care provided	Outcomes: - incidence of delirium <sup>1,2,5-7</sup> : OR 0.33 95% Cl 0.24 - 0.46, p<0.0001, l <sup>2</sup> =24% - duration of delirium <sup>3-</sup> <sup>6</sup> : MD: -1.24 95% Cl - 1.431.04, p<0.0001, l <sup>2</sup> =0% - ICU-LOS <sup>3,4</sup> : MD: -1.02 95% Cl -2.88 - 0.84 p= 0.28, l <sup>2</sup> =54%	1 → 2 (downgraded as not only RCTs are included)

ICU = intensive care unit, LOS = length of stay, RCT = randomized controlled trial

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
077 Goldfarb 2021 (PMID: 33247593 DOI: 10.1093/ageing/afa a253) Before/after QI project to implement nurse- driven mobility program on a cardio-surgical ICU	412 pts Inclusion criteria: - ≥ 80 years Exclusion criteria: - incomplete data and cardiac surgery during hospital admission Per Branch N= 234 N= 178		nurse-driven <b>EM program</b> - twice daily mobilization activities - based on level of function, 0=immobile, 5 = able to walk > 20 m)	- usual mobility care	Primary endpoint: - discharge home Secondary outcomes: -LOS - in-hospital mortality - emergency room visits after discharge within 30 days - hospital readmission within 30 days of discharge	Primary outcome -return home 74.4%(n=234) vs. 65.7%(n=178), p = 0.047 -lower mortality in hospital 6.4%(n=234) vs. 14.6%(n=178), p = 0.006 Secondary outcome - LOS in days: n=234 3.0 ± 2.4, n=178 2.7 ± 3.4, p-value = 0.43 - in-hospital-death: Intervention= 15 (6.4%), Control=26 (14.6%), p-value= 0.006 - ER visits: Intervention = 45 (19.2%), Control= 39 (21.9%), p-value= 0.50 -readmission: Intervention= 21 (9.0%), control= 21 (11.8%), p-value=0.35	4

EM = early mobilization, ER = emergency room, ICU = intensive care unit, LOS = length of stay, pts = patients, QI = quality improvement

#### A nurse-driven EM program seems to have a benefit in relation to return home and a lower in hospital mortality

Reference, Study Type	Cases and (Particip Characte Tota	pant #, eristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
079 Scheffenbichler 2020 (PMID: 33239045 DOI: 10.1186/s1305 4-020-03346-y) prospective observational study	200 pts <b>Classified int</b> <b>groups:</b> Low acuity = <13 Moderate ac APACHE II 14 High acuity = >21 <b>Per Bra</b> 104	APACHE II uity = -20 APACHE		Early goal- directed mobilization	Standard care	Primary outcome: - functional independence at hospital discharge (defined at mmFIM score of 8) Secondary outcome: - speed of mobility progress (change in SOMS level)	Primary results         High acuity:         - intervention n= 10 (31%)         - control n= 8 (26%)         P=0.632         Moderate acuity:         - intervention n= 14 (41%)         - control n= 3 (11%)         P=0.001         Low acuity:         - intervention n= 20 (53%)         - control n= 14 (39%)         P=0.234         Secondary results:         • not significantly higher in intervention group p=0.18         • Moderate acuity: significantly higher speed in intervention group p=0.018         • Low acuity: not significantly higher in intervention group p=0.30	4

mmFIM = minimal modified functional independence measure, pts = patients, SOMS = speed of mobility scale

Early, goal-directed mobilization is a resource-intensive intervention that cannot be applied to all ICU patients. Focusing time and effort on patients benefitting most is probably more cost-effective.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
080 Nieto-García 2021 (PMID: 33236855 DOI: 10.1111/iwj.1 3516) A systematic review and meta-analysis	7 publications , prospective or retrospective two-group comparative and pre-post quasi-experimental research, n= 7520 patients Inclusion criteria - edited in English or Spanish - assessment of the effects of an EMP in an ICU - included PI rates - published in a peer-reviewed journal - involving adult pts(≥18 years old) - hospitalised in the ICU - implemented early mobility protocol - EM compared to usual care - prospective or retrospective observational studies or clinical trials Exclusion criteria - pediatric pts - languages other than English or Spanish - data from editorials, letters to editors, reports of expert committees, and opinions of respected authorities Per Branch		Early mobilization protocol/pr ogram	Usual care	Primary endpoint: effect of early mobilization in the prevention of hospital- acquired pressure injuries	Primary outcomes - five quasi- experimental studies were significantly heterogeneous (p = 0.02 for Q test and 66% for I <sup>2</sup> ), odds ratio = 0.97 (95% CI: 0.49-1.91) with a non- significant statistical difference between both groups (p = 0.9)	1 → 2 (not only RCTs)

EM = early mobilization, EMP = early mobility program, HAPI = hospital-acquired pressure injury, ICU = intensive care unit, LOS = length of stay, pts = patients

## The effect of an implementation of an early mobility program on the incidence of pressure injuries in critically ill patients remains inconclusive.

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Reference, Study Type	(Participant #,	d Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
082 Gatty 2020 (PMID: 33228448 DOI: 10.1080/095 93985.2020. 1840683) non- randomized controlled trial	for physiotherap Exclusion criteri - unstable fractu injuries - deep vein throu - seizure disorde - myocardial infa - severe LV dysfu admission	or older referred by a: res or any other mbosis ers arction		Structured early mobilization protocol	Usual mobilization	Primary endpoint - Perme ICU mobility score Secondary outcomes: - ICU LOS - MV duration	Primary endpoint - significant increase from the first day of rehabilitation to the last day of rehabilitation between groups (23; 12) (p < .001) Secondary outcomes: - no significant differences for other outcomes	3

ICU = intensive care unit, LOS = length of stay, LV = left ventricle, MV = mechanical ventilation, pts = patients

A structured early mobilisation protocol in a general population of critically ill patients showed a benefit in relation to the Perme ICU mobility score.

Study Type	Total	out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
083 Yagi 2021 (PMID: 33213824 DOI: 10.1016/j.ap mr.2020.09.3 89) Retrospective cohort study	<ul> <li>29.982 pts with EM</li> <li>Inclusion criteria:         <ul> <li>aged 20 years and older</li> <li>admitted to an ICU within 2 days of hospital admission</li> <li>started MV within 2 days of admission</li> <li>started rehabilitation within 3 days of starting MV</li> <li>discharged hospital from April 2010 to March 2016</li> <li>continued MV for ≥3 days</li> </ul> </li> <li>Exclusion criteria:         <ul> <li>missing data on rehabilitation, diagnosis, or hospital information</li> <li>patients who discharged from hospital within 5 days of admission</li> <li>pts who were liberated from MV within 5 days of admission</li> </ul> </li> <li>Per Branch         <ul> <li>N= 22237</li> </ul> </li></ul>		Intensive rehabilitation - ≥1 unit/day	Less intensive rehabilitation <1 unit/day	<b>Primary endpoint:</b> in-hospital mortality <b>Secondary outcomes:</b> liberation from MV	Primary outcome - in-hospital mortality after propensity score matching (risk difference: - 3.4%;95%Cl, -4.9 to -1.9%; p<0.001) Secondary outcome - median of time to liberation from MV (14.0d [range, 8.0-26.0d] vs 13.0d [range, 8.0-25.0d], p<0.001) - higher proportion of liberation from mechanical ventilation (subdistribution hazard ratio, 1.08; 95% Cl, 1.03-1.13) compared to control group	4 → 3 large cohort

CI = confidence interval, d = days, EM = early mobilization, ICU = intensive care unit, MV = mechanical ventilation, pts=patients

## Intensive rehabilitation may offer a benefit in relation to in-hospital mortality and liberation from MV in a general population of critically ill patients.

Reference, Study Type		cases and Cor ipant #, Char Total		Drop- out Rate	Interv	ention	Control	Optimal Population	Primary Results	Evidence Grade
085 Matsuki 2020 (PMID: 33163685 DOI: 10.2490/prm.2 0200027) Specification of study: Retrospective Cohort Study	emergency l July 2014 to underwent i Exclusion cr - orthopedic - central ner - acute myo - those who cardiovascul - mental illn - patients re	June 2018 ar rehabilitation iteria: disease vous system cardial infarct had undergo ar surgery ess quiring pallia tation indicat italization g ICU stay Per Branc	than 48 h from nd who in the ICU disease tion ne elective tive care ted, - bedridden		Re- habilitation protocol group with dedicated PT	Re- habilitation protocol group without dedicated PT	Usual Care	<b>Outcomes:</b> - ICU and hospital LOS - MRC-score - FSS-ICU - incidence of delirium - duration of MV - discharge to home - FIM score	Significant differences between groups in: PT + Protocol group vs. Usual care: - ICU LOS (d) 4.5±3.9; 9.4±6.3; p<0.05 - hospital LOS (d) 38.5; 67.1; p=0.028 - MRC score at ICU discharge 49.7; 20.9; p=0.001 - FSS-ICU at ICU discharge 16.7; 7.7; p=0.001 Protocol vs. Usual care: - MRC score at ICU discharge 48.1; 20.9; p=0.001 - FSS-ICU at ICU discharge 15.4; 7.7; p=0.003 No significant differences between groups in: - incidence of delirium - duration of MV	4
	Protocol: n=32	Protocol and PT: n=37	Usual care: n=18						<ul> <li>discharge to home</li> <li>FIM at hospital discharge</li> </ul>	

d = days, FIM = functional independence measure, FSS-ICU = functional status score for the intensive care unit, h = hours, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, PT = physical therapist

# A rehabilitation protocol group with and without dedicated therapist (PT) seems to have a benefit in relation to ICU and hospital LOS, MRC and FSS-ICU scores.

Reference,		d Controls Characteristics)	Drop- out	Intervention	Control	Optimal	Primary Results	Evidence
Study Type	То	otal	Rate			Population		Grade
088 Jonkman 2020	40 pts in pooled Inclusion criteria -≤ 72h after intu	a:		Expiratory muscle functional			Primary endpoint: - non-serious AEs in control: 3 (2.9% of sessions) vs intervention: 13 (7.7% of sessions) - compliance rate = 91.1%	
(PMID: 33126902	Exclusion criteria - expected durat	<b>a:</b> ion of MV < 72h		electrical stimulation: - 30 minutes 2x	Sham	Primary endpoint: feasibility	Secondary outcomes: pooled analysis	3
DOI: 10.1186/s130 54-020- 03352-0) RCT + pooled analysis with another trial with a similar	<ul> <li>congenital myoneuropathies</li> <li>cardiac pacema</li> <li>refractory epile</li> <li>abdominal surgiveeks</li> <li>BMI &gt; 35 kg/m<sup>2</sup></li> <li>inadequate conresponse to NMI</li> </ul>	aker epsy gery in the last 4 2 htractile		<ul> <li>daily 5 days per</li> <li>week</li> <li>the first 5 days</li> <li>consecutively until</li> <li>weaning from MV</li> <li>or week 6</li> <li>and</li> <li>standard weaning</li> <li>protocols</li> </ul>	stimulation + standard weaning protocol	Secondary outcomes: - abdominal expiratory muscle thickness - duration of MV - ICU LOS	<ul> <li>abdominal expiratory muscle thickness (mm), Mean difference (95%Cl): 2.25 (0.34 – 4.16), p=0.02</li> <li>duration of MV (days) median, control: 52 vs intervention: 10, p=0.07</li> <li>duration of MV for those successfully extubated in the ICU n.s.</li> <li>ICU LOS (days) median, control: 54 vs intervention: 12, p=0.03</li> </ul>	(down grade from 2 due to pooled analysis)
intervention protocol	Per B	Franch					<ul> <li>ICU LOS for those successfully extubated and discharged alive from the ICU n.s.</li> </ul>	
protocol	Intervention n = 20	Control n = 20					- ICU mortality n.s.	

AE = adverse event, BMI = body mass index, ICU = intensive care unit, IQR = interquartile range, LOS = length of stay, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, pts = patients, RCT = randomized controlled trial, VI = confidence interval

#### Electrical muscle stimulation of the expiratory muscles is safe.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
091 Ribeiro 2021 (PMID: 33103326 DOI: 10.1002/pri.1882) RCT	49 pts undergoing CABG Inclusion criteria: - score of 15 on the Glasgow (C - musculoskeletal and cardiop suitable for accomplishment (C - absence of neurological sequ neurodegenerative diseases Exclusion criteria: - previous cardiac surgeries - hemodynamic instability tha performance - breathing discomfort - invasive ventilatory support - oxygen saturation below 90% - coagulation disorders - infections in any of the syste -nonperformance of the who Per Br N=33	ulmonary conditions of the proposed activities uelae and/or t prevented protocol % ms le protocol		Early mobilisation on POD 1-3: (n=16) -usual care + cycle ergometer exercises and ambulation or EM+ virtual reality on POD 1-3: (n=17) - Nintendo Wii games for upper and lower limbs	Usual care: - on POD 1-3 - respiratory physiotherapy - foot and ankle exercises	Primary outcomes - heart rate variability - hospital and ICU LOS - MV duration	Primary outcomes - hospital LOS (days): EM (10.2±3.5) vs. VR (8.1±1.6) ; CG (16±7.3), p=0.03 - ICU-LOS: EM = 2.5 ± 1.8 vs VR =4.3 ±1.4 , control =4.1 ± 2.3 , p=0.25 - MV duration (in h): EMG= 11.2 ±5.5, VRG = 11.2 ± 5.5, control= 9.3± 3.1, p- value= 0.10	2 → 3 (high risk of bias)
	IN=33	IN=TO						

CABG = Coronary artery bypass grafting, CG = control group, EM = early mobilization, EMG= early mobilization group, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, POD = postoperative day, pts = patients, VR = virtual reality, VRG= virtual reality group

#### Early mobilization and virtual reality in postoperative CABG patients seem to shorten hospital LOS.

10.1016/j.auneurological impairments- in-hospital- in-hospital- ICU-LOS in days : intervention =cc.2020.07.0- any current cancer or chemotherapy- pre-existing mobility impairment- pre-existing cognitive impairment- minimum time of 20 min for passive and 30 min for active exercise- in-hospital- ICU-LOS in days : intervention =secondary- language barrier- inminent death- inminent death- ICU and hospital LOS- hospital-LOS: intervention = 41.9d (34.3-56.4) vs control=34.4d (29.3- 87.2), p = 0.85 - ventilation days: intervention =RCT (#3121)- physiotherapist was unavailable- pre-existing cognitive impairment- informative passive and 30 min for active exercise- informative passive and 30 min for active exercise- inclusion days - ventilation days - ventilation days - ventilation days: intervention =RCT (#3121)- physiotherapist was unavailable- pre-existing cognitive impairment - passive and 30 min for active exercise- informative - ventilation days: intervention =08)- informative - passive and 30 min for active exercise- informative - ventilation days:- informative - ventilation days:08)- informative - passive and 30 min for active exercise- informative - ventilation days:- informative - ventilation days:08)- pre-existing cognitive impairment - pre-existing cognitive impairment - informative - ventilation days:- informative - ventilation days:- informative - ventilation days:08)- pre-existing cognitive - passive- in	Reference, Study Type	(Participant #,	d Controls Characteristics) ttal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
N=7 N=8	2021 (PMID: 33039302 DOI: 10.1016/j.au cc.2020.07.0 08) secondary analysis of	Inclusion criteria: - pts aged 18 y or olde - anticipated ECMO du Exclusion criteria: - > 72 h on ECMO or 5 recruitment - preexisting musculos neurological impairme - any current cancer o - pre-existing mobility - pre-existing cognitive - language barrier - imminent death - physiotherapist was Per B	uration of > 24 h 6 d in the ICU before skeletal or ents or chemotherapy r impairment e impairment s unavailable granch		rehabilitation: - up to 1 hour per day - minimum time of 20 min for passive and 30 min for active		<ul> <li>time for exercising</li> <li>Secondary outcomes:         <ul> <li>in-hospital mortality</li> <li>ventilation days</li> <li>ICU and hospital</li> </ul> </li> </ul>	<ul> <li>time for exercising (n = 7 vs. n = 8): mean = 28.7 vs. 4.2 min, p &lt; 0.0001)</li> <li>Secondary outcomes <ul> <li>in-hospital mortality:</li> <li>intervention=3(42.9)vs.</li> <li>Control=1(12.5), p = 0.46</li> <li>ICU-LOS in days : intervention =</li> <li>12.9 d (7.2-16.7) vs. Control =</li> <li>21.4d (15.538.5), p = 0.05</li> <li>hospital-LOS: intervention= 41.9d</li> <li>(34.3-56.4) vs control=34.4d (29.3- 87.2), p = 0.85</li> <li>ventilation days: intervention =</li> </ul> </li> </ul>	4

ECMO = extracorporeal membranous oxygenation, d = days, h = hours, ICU = intensive care unit, IMS = incidental medical services, LOS = length of stay, pts = patients, RCT = randomized controlled trial, y = years

## Early intensive rehabilitation in (veno-venous, veno-arterial) ECMO patients seems to be safe in terms of physiological parameters.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
096 Ferrando 2020 (PMID: 33023669 DOI: 10.1186/s130 54-020- 03314-6) Prospective multicenter cohort study	199 COVID-19 patients with acute respiratory failure Inclusion criteria: - age ≥ 18 years - confirmed SARS-CoV-2 infection - no previous invasive MV or NIV use before starting HFNO - peripheral oxyhemoglobin saturation (SpO2) < 93% with a non-rebreather face mask at 15 L/min Exclusion criteria: - non-confirmed SARS-CoV-2 infection - no data on ventilation strategies Per Branch N= 55 N= 144		HNFO + Awake Prone Positioning	HNFO	Primary outcomes: - ICU LOS - 28-day mortality - risk of intubation	No significant differences between groups in: - ICU LOS (days) median [IQR]: control= 7.5 [4-14] vs. intervention=8 [5-14], $p = 0.276$ - 28-day mortality, hazard ratio (95%CI): 2.411 (0.556 – 10.442), p = 0.23 - intubation, hazard ratio (95%CI): 1.002 (0.531 – 1.890), $p$ = 0.60 - trend for delay in intubation: Intervention group vs. Control group: [median 1 (interquartile range, IQR 1.0–2.5) vs 2 IQR 1.0– 3.0] days ( $p = 0.055$ ), but awake- PP did not affect 28-day mortality [RR 1.04 (95% CI 0.40–2.72), $p =$ 0.92]	3

ARF= acute respiratory failure, CI = confidence interval, HFNO = high-flow nasal oxygen, ICU = intensive care unit, IQR = interquartile range, LOS = length of stay, MV = mechanical ventilation, NIV = non-invasive ventilation, PP=prone position, pts = patients

Awake proning in COVID-19 patients receiving HFNO did not reduce ICU length of stay, mortality or need for intubation. In patients with COVID-19 ARF treated with HFNO, the use of awake-PP did not reduce the need for intubation or affect mortality.

Reference, Study Type	Cases and Con (Participant Characteristi Total	#, Drop-	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
098 Collinsworth 2020 (PMID: 33003078 DOI: 10.1097/CCM.00000 0000004609) <b>Specification of</b> <b>study:</b> prospective observational multicenter study	<ul> <li>awaiting a transfe a non-ICU bed</li> <li>primary diagnosis tumor</li> <li>mental disorder</li> <li>stroke</li> <li>intracranial injury- intoxication</li> <li>hospital stay &gt; 30</li> </ul>	une 2015 4 h d < 14 d r order to of brain - days	ABCDE bundle ≥ 60%	ABCDE bundle adherence ≤ 60%	Primary endpoint: - in-hospital mortality Secondary outcomes: - LOS - home discharge ´ - direct costs of hospital care (cost difference) - costs and QALYs for pts 1 year follow up	Primary endpoint - In-hospital mortality (%) : control =684 (54.7) vs. intervention= 318 (18.4) , Adjusted (95% CI) OR 0.28 (0.24–0.34); P< 0.001 Secondary outcomes: - LOS (days): mean (sd) control= 9.9 (7.0) vs. intervention= 12.3 (6.8), Adjusted (95% CI) 0.57 (0.45–0.69); p< 0.001 - discharge (%): control= 206 (16.5) vs. Intervention= 637 (37.3); Adjusted (95% CI) OR=2.46 (2.02–2.89); p < 0.001 - Cost difference (\$) n (%): control= 25.685 (26.370) vs. Intervention = 31.170 (33.109), adjusted (95% CI) 4.067 (989– 7.144); p< 0.001 - 1 year follow up: control= \$34.181 (cost per patient), 0.2237(Inpatient Survival Rate), \$152.799 (Cost/ Effectiveness) - intervention= \$39.130 (cost per patient), \$4.949 (incremental cost), 0.3412 (inpatient survival rate), 0.1175 (Incremental Effectiveness), \$115.088 (Cost/ Effectiveness Ratio)	3 → 4 (mobilization evaluated as part of bundle)

ABCDE= awakening and breathing, coordination, delirium monitoring/management, early exercise/mobility, CI= confidence interval, ICU= intensive care unit, LOS = length of stay, MV= mechanical ventilation, OR= odds ratio, pts= patients, QALY= quality-adjusted life-years, SD= standard deviation

#### The ABCDE bundle appears to be a cost-effective means to reduce in-hospital and 1-year mortality for patients in the ICU.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
099 Mayer 2020 (PMID: 33001619 DOI: 10.1097/CCM. 00000000000 4526) Systematic Review	15 publications <sup>1-15</sup> including 437 patients Inclusion criteria: - adult pts (≥ 18 years old) explicitly receiving CRRT located in the ICU - received physical therapy or occupational therapy, physical rehabilitation, active mobilization, or exercise while on CRRT - data on AEs or "potential safety events" - reasons for early termination of activity or presafety screening were reported Exclusion criteria: - review articles, conference abstracts, and non–peer-reviewed articles Per Branch		Physical therapy, occupational therapy, active mobilization or exercise while on CRRT		Primary endpoint: - AEs per total number of rehabilitation sessions - feasibility measured by implementation rate and level of physical activity/mobilisat ion achieved.	Primary endpoint: no meta- analysis	1 → 2 (downgraded due to inclusion of non-RCTs)

AE = adverse events, CRRT = continuous renal replacement therapy, ICU = intensive care unit, pts = patients

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
109 Deng 2020 (PMID: 32919363 DOI: 10.1016/j.jcrc.2020.08.019) Specification of study: Systematic review and meta-analysis	<ul> <li>n = 26 studies included in the meta analysis (n = 7035 pts)<sup>1-14</sup></li> <li>Inclusion criteria: <ul> <li>RCTs or cohort studies</li> <li>pts &gt;18 years</li> <li>admitted to an ICU</li> <li>non-pharmacological interventions for prevention of ICU delirium</li> <li>peer-reviewed</li> <li>assessment of incidence of delirium, delirium duration, ICU LOS or hospital mortality</li> </ul> </li> <li>Exclusion criteria: <ul> <li>case reports</li> <li>protocol study</li> </ul> </li> </ul>		EP	Standard of Care	<ul> <li>delirium incidence</li> <li>delirium duration</li> <li>hospital mortality</li> <li>ICU length of stay</li> </ul>	Significant differences between groups in:         -       delirium incidence:         ○       CHI (RR 0.55, 95% CI 0.34-0.89, p < 0.001)	1 → 3 (downgraded for imprecision, heterogeneity/ risk of bias, not exclusively RCTs)

CHI = cerebral hemodynamic improving, CI = confidence interval, EP = exercise program, FP = family participation, HR = hazard ratio, ICU = intensive care unit, LOS = length of stay, MD = mean difference, MLT = multicomponent studies, PEI = physical environment intervention, pts = patients, RCT = randomized controlled trial, RR = risk ratio, SR = sedation reducing, SUCRA = surface under the cumulative ranking curve

Physical exercise in an ICU-environment leads to improved delirium incidence and survival.

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Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
111 Yang 2021 (https://pub med.ncbi.nlm .nih.gov/3290 0917/) Specification of study: systematic review	<ul> <li>- 24 studies<sup>1-24</sup></li> <li>Inclusion criteria: <ul> <li>no study type restrictions</li> <li>original studies</li> <li>&gt;18y, admitted to ICU and MV for &gt;24h</li> </ul> </li> <li>Exclusion criteria: <ul> <li>articles with only active in-bed mobilization and no out-of-bed mobilization</li> </ul> </li> </ul>		- early mobilization	- usual ICU care	<b>Primary Endpoints:</b> - safety assessment criteria	Primary Results: - safety assessment criteria: 17 variables and 48 parameters - 4 criteria included in flow diagram: - consciousness: S5Q ≥3; RASS -2 - +2 or SAS 3-4 - cardiac reserve: heart rate: 40-130 beats/min; blood pressure: MAP 65- 110mmHg and SBP 90-200 mmHg, <20% fluctuation; low/medium level of single vasoactive medication and no increase in the past 2h - respiratory reserve: F <sub>i02</sub> ≤0.6 and PEEP ≤10; 5-40 breaths/min; S <sub>p02</sub> ≥88% and fluctuation <4%; P <sub>a02</sub> /F <sub>i02</sub> ≥200; No ventilator dysynchrony - muscle strength: upper limbs: MRC ≥III or Lovett >3; Bilateral quadriceps strength: MRC ≥III or Lovett ≥2	1 → 3 (not only RCTs, no metanalysis)

y=years; ICU=Intensive care unit; h=hours; S5Q=standardized 5 ques-tions for cooperation; RASS=Richmond Agitation Sedation Scale; SAS=Sedation-Agitation Scale; MAP=mean arterial pressure; SBP=systolic blood pressure; MRC=Medical Research Council

Yang et al defined safety criteria for early mobilization based on their systematic review.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
112 Nakanishi 2020 (PMID: 32897665 DOI: 10.1097/CCM. 00000000000 4522) <b>Specification</b> of study: Multicenter RCT	42 ptsInclusion criteria:- expected to be MV $\geq$ 48 h- expected stay in the ICU $\geq$ 5 daysExclusion criteria:- <18 years	Intervention: 4 pts (14%) (1 died before day 5; 2 no muscle contraction; 1 withdrawn due to pain) Control: 2 pts (died before 5 <sup>th</sup> day)	Neuromuscular electrical stimulation: - 30 min for 5 days and - standardized progressive mobilization	Standardized progressive mobilization	Primary endpoint: - muscle thickness via ultrasound Secondary outcomes: - cross sectional area via ultrasound - muscle strength MRC score - ICU mobility scale - hospital LOS - ventilator-free days - ICU-free days - ICU-free days - IMS at ICU discharge	Primary endpoint: -muscle thickness M. biceps brachii (difference in % between day 1 and 5, mean $\pm$ SD), control -11.2 $\pm$ 2.1 vs intervention -1.9 $\pm$ 2.4, p = 0.007 Secondary outcomes: - muscle cross sectional area M. biceps brachii (difference in % between day 1 and 5, mean $\pm$ SD), control -10.0 $\pm$ 1.5 vs intervention -2.7 $\pm$ 2.6, p = 0.03 - muscle thickness M. rectus femoris (difference in % between day 1 and 5, mean $\pm$ SD), control -14.7 $\pm$ 2.7 vs intervention -0.9 $\pm$ 3.1, p = 0.003 - muscle cross sectional area M. rectus femoris (difference in % between day 1 and 5, mean $\pm$ SD), control -10.4 $\pm$ 2.8, intervention -1.7 $\pm$ 2.9, p = 0.04 - MRC score day 5(median [IQR]), control 52 [35 – 59] vs intervention 55 [50 – 58], p = 0.53 - hospital LOS (median [IQR]), control 40 [26 – 64] vs intervention 23 [19 – 34], p = 0.04 - ventilator-free days (median [IQR]), control 22 [10 – 24] vs intervention 23 [19 – 25], p = 0.45 - ICU-free days, median [IQR], control 20 [9 – 23] vs intervention – median [IQR]: 21 [12 – 23], p = 0.97 - IMS (median [IQR]), control 2 [1 - 3] vs intervention 3 [1 - 4], p = 0.42	2

ICU = intensive care unit, IMS = ICU mobility scale, IQR = interquartile range, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial

Neuromuscular electrical stimulation decreased muscle thickness loss between day 1 and 5.

Reference, Study Type	Cases and (Partici Charact	pant #, eristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
122 Chin-Ming 2019 (PMID: 32767475 DOI: 10.1111/nicc.1 2530) Specification of study: retrospective, observational, before-and- after outcome study	173 pts Inclusion cri - ICU patient years	<b>teria:</b> ts > 18 dmitted to a ter ICU in		Implementation of quality improvement program: multidisciplinary team performed ABCDE bundle Mobilization: - EM within 72 hours of MV - twice daily (each 30 min), 5 days/ week in co- operation with family members - 4-step mobilization program: Level I (passive extremities movement for unconscious pts), Level II (active extremities movement), Level III (sitting on edge of bed) Level IV (chair)	Pts on ICU on MV before implemention of ABCDE - not further defined (Standard of care)	Primary endpoints: - duration of ICU and hospital LOS - duration of MV - intra-hospital mortality - costs before and after ABCDE bundle care Secondary outcome: -APACHE II sample size calculation: no power calculation reported	Primary endpoints: - intervention group had lower mean ICU LOS (8.0 vs 12.0 days) - similar MV duration (170.2 vs 188.1 hours) and hospital stay (21.1 vs 23.3 days) - intervention group caused lower costs (22.1 vs 31.7x10 <sup>4</sup> New Taiwan Dollars) and intra-hospital mortality (8.3 vs 36.6%). Secondary outcome: Apache Score II before intervention 23.4+/- 9.4 vs after intervention 19.8+/-6.9 p=0.004 adverse events: n/a	4

ABCDE bundle = daily awakening, breathing trial, drug co-ordination, delirium survey and treatment, early mobilization, APACHE II = acute physiology and chronic health evaluation II, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients

The ABCDE care bundle improved the outcome of acute renal failure patients with MV, especially shortening ICU stays, lowering medical costs and hospital mortality.

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total				-		
124 Worraphan 2020 (PMID: 32750371 DOI: 10.1016/j.apmr.2020. 07.004)) Specification of study: Systematic Review with Network-Meta analysis	18 RCTs investigating the effect of IMT, EM, or CPT on MV duration and the weaning duration in patients with MV (934 patients) Inclusion criteria: - aged > 18 years - received MV via an endotracheal or tracheostomy tube Exclusion criteria: - had a successful simple weaning process - received combined intervention treatments (EM and IMT) - presence of neurologic conditions - previous musculoskeletal conditions		EM or CPT + IMT or IMT	СРТ	Primary outcomes: - duration of MV - weaning duration	Primary outcome -MV duration, EM was more effective than CPT (MD; 95% CI) (-2.00; -3.57 to -0.44) -MV duration (-2.01; - 3.81 to -0.221), (P=0.45) - IMT+CPT significantly reduced the weaning duration compared to CPT (mean difference; 95% confidence interval) (-2.60; -4.76 to -0.45), (P=0.02)	1

CPT = conventional physical therapy, EM = early mobilization, IMT = inspiratory muscle training, MD= mean difference, MV = mechanical ventilation, NMA = network-metaanalysis, pts = patients, RCT = randomized controlled trial

#### EM shows a benefit for MV duration.

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Reference, Study Type	(Partic Charact	d Controls ipant #, teristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
127 Semsar- kazerooni 2021 (PMID: 32739452 DOI: 10.1016/j.cjca .2020.03.038) <b>Specification</b> of study: Retrospective cohort study	1.489 pts adm Inclusion crite - consecutive p admitted to th February 1, 20 30, 2019 Exclusion crite - incomplete d - pts undergoi surgery during Per B N= 852	eria: patients ne CICU from 018, to June eria: data ng cardiac		Nurse-driven EM program	Historic control before implementation of EM program	Primary outcome - discharge home Secondary outcomes - CICU and hospital LOS - in-hospital mortality - emergency room (ER) visit and hospital readmission within 30 days of discharge	Primary outcome - discharge home: $83.9\%$ (n= $852$ ) vs 78.3%(n= $637$ ), P < 0.007 Secondary outcome - in-hospital mortality 36 (4.2%), 43 (6.8%); p= $0.04$ - no difference in CICU or hospital length of stay between the groups (P = $0.63$ and P = $0.54$ , respectively) - ER visit: intervention= 144 (13.5%) vs. Control=122 (19.2%), p= $0.003$ - hospital readmission: Intervention= 55 (6.5%) vs. Control= 56 (8.8%), p= $0.14$	4

CICU = cardiovascular intensive care unit, EM = early mobilization, ER = emergency room, ICU= intensive care unit, LOS = length of stay, pts = patients

#### A nurse-driven EM program resulted in lower in-hospital mortality in cardiac ICU patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
128 Wang 2020 (PMID: 32736250 DOI: 10.1016/j.ijnur stu.2020.10370 8) Specification of study: Systematic Review with meta analysis	Total 39 RCTs with a total of 3837 pts <sup>1-39</sup> Inclusion criteria: - RCTs - age >18 years - pts in ICU - intervention: EM and rehabilitation - control: daily nursing care		EM and rehabilitation - including a range of active or passive physical exercises	Daily nursing care - no exercise intervention or only respiratory PT treatment)	Primary endpoints: - ICUAW rate - duration of MV - ICU LOS - ICU mortality Secondary outcomes: - MRC score - handgrip strength (kg) - Barthel index score - delirium rate - hospital LOS - mortality - ventilator-associated pneumonia rate (VAP) - DVT rate Pressure sore rate past begnital	Significant differences between groups in: - ICU-AW (RR 0.49 [0.32, 0.74]; p=0.0008, I <sup>2</sup> >50%) - length of MV (MD -2.10 [-2.47, -1.73]; p<0.001; I <sup>2</sup> >50%) - ICU LOS (MD -2.74 [-3.52, -1.97]; p<0.001, I <sup>2</sup> >50%) - MRC Score (MD 5.99 [3.22, 8.76]; p<0.001, I <sup>2</sup> >50%) - MRC Score (MD 5.99 [3.22, 8.76]; p<0.001, I <sup>2</sup> >50%) - Barthel index score (MD 12.78 [2.71, 22.85]; p=0.01, I <sup>2</sup> >50%) - hospital LOS (MD -3.71 [-5.70, -1.71]; p=0.0003, I <sup>2</sup> >50% - VAP (RR 0.68 [0.49,0.94]; p=0.02) - DVT (RR 0.16 [0.06, 0.47]; p= 0.0007) - pressure sore rate (RR 0.17 [0.06,0.49] p=0.001) No significant differences between groups in: - ICU mortality (RR 0.003 [-0.08, 0.03]; p=0.36) - hospital mortality n.s.	1
					<ul> <li>post-hospital</li> <li>discharge</li> </ul>	<ul> <li>delirium rate n.s.</li> <li>handgrip strength n.s.19.</li> </ul>	

DVT = deep vein thrombosis, EE = effect estimate, ICU = intensive care unit, ICU-AW = ICU- acquired weakness, LOS = length of stay, MD = mean difference, MRC = medical research council score, MV = mechanical ventilation, n.s. = not significant, PT = physio therapy, pts = patients, RCT = randomized controlled trial, RR= relative risk, VAP = ventilator-associated pneumonia

# Early mobilization and rehabilitation seems to have a benefit in relation to ICU-AW, length of MV, ICU LOS, MRC score, Barthel Index and hospital LOS.

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Reference, Study Type	Cases and Cont (Participant #, Charad Total		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
130 Bento 2020 (PMID: 32695996 DOI: 10.1097/CCE.00000 0000000131) Specification of study: retrospective observational cohort study		ent unit		CRRT + PT		<b>Primary endpoint:</b> - therapy data (IMS, Number of PT sessions) - safety and feasibility of PT	<ul> <li>Primary endpoints: <ul> <li>IMS median 5</li> <li>1517 PT sessions, 377 included ambulation</li> <li>ambulation mean of 4,83/d; daily average of 150,61 feet</li> <li>in-hospital mortality highest for pts. with no therapy (73,53%) and lowest for pts. who ambulated (17,95%)</li> <li>one safety event (0,0007% of all PT sessions)</li> </ul> </li> </ul>	4

CRRT = continuous renal replacement therapy, CVIVU = cardiovascular ICU, IMS = ICU mobility scale, PT = physical therapy, SICU = surgical ICU

Physical therapy, including ambulation, while on CRRT is feasible and safe.

No detailed assessment was carried out further because higher-quality evidence is available on this topic.

Reference, Study Type	(Participant #	nd Controls ‡, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
131 Miguel 2020 (PMID: 32695988 DOI: 10.1097/CCE. 0000000000 00119) Specification of study: Comparative effectiveness cohort study	2014-2015 - critical ill patient group 3 or 4 (3:red > 96h + major ope procedure; 4: trac with MV >96h) <b>Exclusion criteria:</b> - imminent death, - active bleeding c - emergent vitals s	rs with MV within ts (diagnosis-related quiring ECMO or MV erating room cheostomy placement		Included patients in 2014	Included patients in 2015	Primary endpoints: - average LOS for diagnostic related group 3,4 coded pts - days until initiation of physical therapy Secondary outcome: - no. of physical therapy follow-up consults	Significant differences between groups in: - mean ICU LOS (34.4d control vs. 30.5d; p < 0.05) - overall LOS (52.7d vs. 43.3d; p < 0.002) - days until initiation of physical therapy (20.09d vs. 14.78d; p<0.001) - increased no. of physical therapy follow-up consults 6.14 vs. 7.7; p<0.05)	4

ECMO = extracorporeal membrane oxygenation, HTN = hypertension, ICU = intensive care units, LOS = length of stay, MV = mechanical ventilation, pts = patients

Mobilizing individuals in an intensive care setting decreases length of stay and hospital costs.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics Total	) Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
132 Liu et al. 2020 (PMID: 32685621 DOI: 10.1016/j.ijnss. 2020.03.002) Systematic Review + MA	11 RCTs with 576 pts         Inclusion criteria:         - ICU pts         - ≥ 18 and < 85 years of age	11 included studies in total, for some endpoints only 2-6 included in the analysis	NMES	Sham NMES or routine care	Primary endpoints: - MRC duration of MV - ICU LOS - total LOS Secondary outcomes: - Barthel index - FSS-ICU - MIWD - GCS Not prespecified outcomes: - mortality	Significant differences between groups in: - MRC, MD (95%Cl):1.78 (0.44 – 3.12), p = 0.009 - MV duration, MD (95%Cl): -0.65 (-1.03 0.27) p<0.001 - ICU LOS, MD (95%Cl): -3.41 (-4.58 2.24), p<0.001 - total LOS, MD (95%Cl): -3.97 (-6.89 1.06), p = 0.008 - Barthel index, MD (95%Cl): 0.09 (0.45 – 1.35), p<0.001 - FSS-ICU, MD (95%Cl): 9.14 (-1.14 – 19.43), p = 0.08 - MIWD, MD (95%Cl): 239.03 (179.22 – 298.85), p <0.001 - GCS, MD 0.78 (-0.07 – 1.62), p = 0.07 No significant differences between groups in: Mortality, RR (95%Cl): 1.07 (0.62 – 1.84), p = 0.80	1

ICU = intensive care unit, LOS = length of stay, MD = mean deviation, MRC = medical research council, MV = mechanical ventilation, NMES = neuromuscular electric stimulation, pts = patients, RCT = randomized controlled trial

Neuromuscular electrical stimulation increased muscle strength, reduced duration of mechanical ventilation, ICU length of stay and total length of stay in a meta-analysis including 3 to 6 out of 11 studies.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
135 Takaoka 2020 (PMID: 32628501 DOI: 10.1513/Ann alsATS.20200 1-059OC) Specification of study: Systematic Review and Meta- analysis	<ul> <li>- 14 publications (12 randomized, 2 non-randomized, 926 pts)<sup>1-14</sup></li> <li>Inclusion criteria:         <ul> <li>examining critically ill pts</li> <li>&gt;18 y, admitted to an ICU for at least 24h</li> <li>leg-cycle ergometry in the ICU</li> <li>compared with no leg-cycle ergometry</li> </ul> </li> <li>Per Branch</li> </ul>		Leg-cycle ergometry	No leg-cycle ergometry	<b>Primary outcomes:</b> - physical function - duration of MV - LOS - mortality - QoL	No significant differences between groups in: - hospital discharge: 3 RCTs; n = 225; standardized MD, 0.07 [95% Cl, 20.38 to 0.53]; very low certainty - MV duration: 9 RCTs; n = 676; MD, 0.01 [21.04 to 1.07] days; moderate certainty - ICU LOS: 10 RCTs; n = 511; MD, 0.23 [21.44 to 1.89] days; moderate certainty - hospital LOS :7 RCTs; n = 393, MD 20.07 [23.87 to 3.73] days; moderate certainty - QoL at 6 months after hospital discharge: 2 RCTs; n = 103; MD, 9.13 [13.80 to 32.05] points higher; very low certainty - hospital mortality: 7 RCTs; n = 710; RR 1.09 [0.82 to 1.46]; moderate certainty	2 (downgraded due to inclusion of non-RCTs)

LOS = length of stay, MD = mean difference, MV = mechanical ventilation, pts = patients, QoL = quality of life, Y = years

#### Leg-cycling could not show a benefit in relation to physical function, duration of MV, LOS, mortality, QoL, muscle strength.

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	Tot	haracteristics) al	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
136 Nickels 2020 - (PMID: E: 32585438 - DOI: m 10.1016/j.j - crc.2020.0 - 5.008) - Specificati on of - study: -	74 pts nclusion criteria: • expected to be MV for • recruited within 96h a • expected to remain in Exclusion criteria: • <18y old • pre-existing condition mobility • neurological disorder • injuries precluding in- • >135kg body weight • pregnant • uncontrolled seizures • unlikely to survive the admission Per Br 37	after ICU admission h the ICU for > 48h h that impaired -bed cycling c or status epilepticus e current hospital	Intervention group: 6 (1 did not receive allocated intervention; 1 died, 4 discharged from acute hospital prior to assessment) Control group: 6 ( 1 excluded as ineligible; 1 died, 4 discharged from acute hospital prior to assessment)	Daily assessment of routine physiotherapy + 30 minutes in-bed cycling -once daily (MOTOmed Letto2 (RECK- Technik GmbH & Co. KG, Betzenweiler, Germany)	Daily assessment of routine physiotherapy	Primary outcome: - muscle atrophy in RF <sub>CSA</sub> at day 10 post-study enrolment Secondary outcomes: - RFT and VIT thickness - MRC <sub>SUM</sub> - HGS - functional status score - 6MWT - ICU mobility score - functional milestones - delirium incidence - EQ5D-5L Sample size calculation: - 68 pts (34 per group)	Primary endpoint: - no significant between- group differences (p=0.52) Secondary outcomes: - no significant between- group differences in any secondary outcome	3 (dowgraded as under- powered)

H = hours, HGS = handgrip strength, ICU = intensive care unit, MRC<sub>SUM</sub> = medical research council sum score, pts = patients, RCT = randomized controlled trial, RF<sub>CSA</sub> = rectus femoris cross-sectional area, RFT = rectus femoris thickness, VIT = vastus intermedius thickness, y = years, 6MWT = six-minute walk test

#### In-bed cycling in addition to early mobilization showed no benefit in relation to muscle atrophy. The study was underpowered.

Reference, Study Type	(Participant #, cha Total	· · ·	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Jochmans 2020 (https://pubmed .ncbi.nlm.nih.go v/32449068/) Specification of study: Prospective cohort study	103 patients perform sessions Inclusion criteria: - PP was indicated in moderate-to severe with PaO2/FiO2 < 15 PEEP of at least 10 c use of NMBA Exclusion criteria: - severe hemodynam or withdrawal of life treatments Per Bran 103	n case of hypoxemia 50 despite a set mH2O and the nic instability sustaining	- severe hemodynamic compromise ( <i>n</i> =5), missing data at inclusion ( <i>n</i> =3), therapeutic limitation decision ( <i>n</i> =1)	Prone position		Primary Endpoint: - time sufficient to obtain the maximum improvement in several physiological respiratory parameters in the first PP session and in all PP sessions Secondary Endpoint: - physiological parameters related to patient survival in PP	Primary Result: - pooled responder sessions showed beneficial physiological effect continued after 16 h of PP and at least up to 24 h Secondary Result: Before PP vs 2h after PP Increase in: - pH 7.26 $\pm$ 0.1 vs 7.29 $\pm$ 0.1 (p<0.05) - static compliance 39 $\pm$ 16 vs 40 $\pm$ 15 [mL/cmH2O] (p>0.05) - PaO2/FiO2 129 $\pm$ 52 vs 189 $\pm$ 79 (p<0.05) - PaO2 77 $\pm$ 32 vs 99 $\pm$ 60 [mmHg] (p<0.05) Decrease in: - PaCO2 54 $\pm$ 13 vs 51 $\pm$ 15 [mmHg] (p<0.05) - decrease in $\Delta P$ was the only parameter significantly associated with an increase in PaO2/FiO2 > 50%	3

PP=prone position; ICU=intensive care unit; PEEP=positive endexpiratory pressure; NMBA=neuromuscular blocking agents; h=hours

PP sessions should be prolonged at least 24 h and be extended if the PaO2/FiO2 ratio at 24 h remains below 150, especially since no criteria can predict which patient will benefit or not from it.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
150 Boyd 2020 (PMID: 32349888 DOI: 10.1016/j.aucc .2020.02.004) Specification of study: a prospective observation	20 patients after cardiac surgery who were receiving vasoactive therapy Inclusion criteria: - > 18 years - undergoing elective open-heart surgery - postoperatively receiving low, moderate, or high levels of vasoactive support Per Branch N=20		Positional changes: - supine - high sitting (60 degrees) - sit on the edge of bed - standing - marching on the spot - sit on the edge of bed - high sitting (60 degrees) - supine 1-minute-per-position		Primary endpoints: - cardiac output - cardiac index - stroke volume Secondary outcomes: - heart rate - rhythm, - arterial systolic and diastolic blood pressure - mean arterial pressure - respiratory rate, - oxygen saturation - adverse events	<ul> <li>Primary outcome:</li> <li>mean arterial pressure, upright positioning caused significant increases (p=0.018) values increasing from baseline (supine) from 72.31 (11.91) mmHg to 77.44 (9.55) mmHg when back in supine.</li> <li>No significant differences in: <ul> <li>cardiac output, heart rate, stroke volume, or cardiac index with upright positioning</li> </ul> </li> </ul>	3 → 4

pts = patients

Low-level exercise in patients after cardiac surgery receiving vasoactive medication was well tolerated with a low incidence of adverse events and led to significant increases in MAP. Upright positioning and low-level exercise appeared safe and feasible in this patient cohort.

No detailed assessment was carried out further because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
151 Waldauf 2020 (PMID: 32345834 DOI: 10.1097/CCM.00 000000000438 2) Systematic Review mit MA	43 studies (RCTs) with 3.548 pts Inclusion criteria: - RCTs - critically ill pts Per Branch		Rehabilitation - protocolized physical rehabilitation - neuromuscular electrical stimulation - supine cycling	No intervention or Placebo stimulation	<b>Outcomes:</b> - ICU mortality - end of study mortality - duration of MV - ICU LOS - hospital LOS - long-term functional outcome	Significant differences between groups in: ICU LOS Mean difference: $(95\%CI)$ : -1.2 (-2.5 – 0.0) PPR - mean difference $(95\%CI)$ : -2.02 (-3.49 0.56) NMES - mean difference $(95\%CI)$ : -0.23 (-2.45 – 1.98) Cycling - mean difference $(95\%CI)$ : 1.10 (-1.59 – 3.80) effect influenced by exposure to the intervention early initiation of the therapy had no effect duration of mechanical ventilation mean difference: $(95\%CI)$ : -1.7 (-2.50.8 PPR - mean difference $(95\%CI)$ : -2.0 (-3.30.7) NMES - mean difference $(95\%CI)$ : -2.1 (-3.70.6) cycling - mean difference $(95\%CI)$ : -0.1 (-2.1 – 1.8) effect influenced by ICU length of stay measured as duration of mechanical ventilation <b>No significant differences between groups in:</b> - ICU mortality, OR (95%CI): 1.02 (0.84 – 1.24) - mortality end of study, OR (95%CI): 0.94 (0.79 – 1.12) -hospital LOS, MD: (95%CI): -1.6 (-4.3 – 1.2) - SF-36 Physical Component Score, MD: (95%CI): 1.5 (-2.1 – 5.1)	1

ICU = Intensive care unit, LOS = length of stay, MV = mechanical ventilation, NMES = neuromuscular electric stimulation, RCT = randomised controlled trial, pts = patients

Rehabilitation interventions in critically ill patients do not influence mortality and are safe. Protocolized physical rehabilitation significantly shortens time spent on mechanical ventilation and in ICU, but this does not consistently translate into long-term functional benefit. Stable patients with lower Acute Physiology and Chronic Health Evaluation II at admission (<20) and prone to protracted ICU stay may benefit most from rehabilitation interventions.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
155 Franca 2020 (PMID: 32294698 DOI: 10.1590/1414 - 431X2020877 0) <b>Specification</b> of study: RCT	35 pts         Inclusion criteria:         - ≥21 years         - intubated ≥ 24 h         - adequate cardiac reserve (demonstrated by variability o20% heart rate at rest)         - systolic blood pressure between 90 and 180 mmHg         - normal electrocardiogram         - peripheral capillary oxygen saturation > 90%         - fraction of inspired oxygen < 60%         - respiratory rate < 25 bpm         - hemoglobin > 7 g/dL         - platelets > 20,000 cells/mm³         - without sepsis         Exclusion criteria:         - unable to walk without assistance before ICU         - pregnant         - BMI > 35 kg/m²         - preexisting neuromuscular disease, vascular disease or stroke         - skin lesions at electrode locations         - unconsolidated fracture         - pacemaker         - signs of low or high blood pressure         - clot at blood collection site         Per Branch         PCE = 9         FES = 9       control = 10         PCE + FES = 7	Interventio n: 4 pts (did not receive allocated interventio n) Control: 3 (did not receive allocated interventio n)	3 Intervention groups: - NMES: - M. rectus femoris/vast us lateralis 20 min - PCE: 20 min - NMES+PCE	Physio- therapy	<b>Outcomes:</b> - ICU LOS - duration of MV	Outcomes: - ICU LOS (days), mean ± SD: control 4.7 ± 2.45 vs NMES 7.22 ± 5.91, NMES+PCE 4.57 ± 1.27, PCE 7.78 ± 3.96, p = 0.108 - duration of MV (days), mean ± SD: control 4.90 ± 2.80 vs NMES 5.67 ± 3.35, NMES+PCE 4.29 ± 1.38, PCE 6.44 ± 3.64, p = 0.174	2 → 3 (high risk of bias)

ICU = intensive care unit, FES = Functional electrical stimulation, LOS = length of stay, MV = mechanical ventilation, NMES = neuromuscular electric stimulation, PCE = passive cycle ergometry, RCT = randomized controlled trial, pts = patients

Neuromuscular electrical stimulation and passive cycle ergometry did not influence ICU length of stay or duration of mechanical ventilation.

Reference, Study Type	(Partic Charac	d Controls ipant #, teristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
156 Schujmann 2020 (PMID: 32205595 DOI: 10.1097/CC M.0000000 00004181) Specification of study: RCT	<ul> <li>contraindica mobilization</li> <li>cognitive impaninability to commands an tests</li> </ul>	of 100 in the 2 CU admission eria: ospitalized at ls lterations ys in the ICU oon admission tions for pairment with understand	intervention: n= 18 (7 died; 1 discharge before evaluation, 10 discharge ICU before 3 days) control: n= 18 (11 died; 2 discharge before evaluation; 5 discharge ICU before 3 days)	- PPR - NMES - Cycling all patients in intervention groups started physical therapy care within 48 hours of ICU admission	conventional physiotherapy	Primary endpoint: - functional status (BI scores) after ICU discharge Secondary outcomes: - respiratory, muscular, and physical activity - ICU and hospital LOS	Primary endpoint:- Barthel Index at discharge $97\pm5$ ; $76\pm20$ ; $p<0.001$ - ICU Mobility Scale in discharge moment $9.8\pm0.4$ ; $7\pm2$ ; $p<0.001$ Secondary outcomesPhysical activity (% of the time)- inactive $92.3\pm2.8$ ; $95.7\pm2$ ; $p<0.001$ - light $6.4\pm2.4$ ; $3.85\pm1.9$ ; $p<0.001$ - moderate $1.012\pm0.6$ ; $0.3\pm0.2$ ; $p<0.001$ - intense $0.15\pm0.10$ ; $0.03\pm0.02$ ; $p=0.002$ Muscular function- sit and stand (repetitions) $8\pm3$ ; $5\pm3$ ; $p<0.001$ - timed up and go (s) n.s handgrip strength (kgf) n.s.ICU LOS (days)-5 (4-7); $8(5-12)$ ; $p=0.003$ Hospital LOS n.s functional independence (using BI) at 3 months afterdischarge $39(97,5\%)$ VS. $29(74,4\%)$ , $p = 0.03$ - no adverse events that would require intervention werereported	2

d = days, ICU = intensive care unit, LOS = length of stay, NMES = neuromuscular electrical stimulation, n.s. = not significant, PPR = protocolized physical rehabilitation, RCT = randomized controlled trial

# An early and progressive mobility program seems to have a benefit in relation to Barthel Index, ICU Mobility Score, physical activity and shortens the ICU length of stay.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
159 Kim 2019 (PMID: 32166241 DOI: 10.1097/CCE.00000 0000000060) Specification of study: Retrospective cohort study	183 pts Inclusion criteria: <ul> <li>ICU pts</li> <li>&gt; 18 years</li> <li>receiving EM</li> <li>admitted to hospital from home</li> </ul> Exclusion criteria: <ul> <li>ineligible ICU admission (discharged to hospice or transferred to another hospital)</li> <li>LOS &gt; 45d, NICU LOS &gt; 21 d</li> <li>history of limb amputation</li> <li>no surviving until hospital discharge</li> </ul> Per Branch 183		<b>None</b> ICU-related and mobilization-related factors were tested for their association with discharge home		Primary endpoint: -discharge home Secondary endpoint: - adverse events Sample size calculation: no power calculation reported	Primary endpoint: - incremental increase in the maximum level of mobility was associated with 46% greater odds of discharge home (odds ratio, 1.46; 95% Cl, 1.13-1.88). - increased age was associated with 5% decreased odds (odds ratio, 0.95) and each additional day of hospitalization with a 5% decrease (odds ratio, 0.94) was associated with decreased odds of discharge home Adverse events: n/a	4

ICU = intensive care unit, LOS = length of stay, pts = patients

Among medical ICU patients who resided at home prior to their ICU admission, the maximum level of mobility achieved in the medical ICU was the factor most strongly associated with discharge back home.

No detailed assessment was carried out further because higher-quality evidence is available on this topic.

Reference, Study Type	(Participant	nd Controls #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
160 Yu 2019 (PMID: 32156142 DOI: 10.21037/ap m.2020.02.12 ) Spezification of study: RCT	arrhythmia, blood p and ECMO assist	for final analysis fter admission dmission cause of ICU before admission 10	- 5 (due to being transferred to another hospital due to the change in disease condition or discharge from the hospital)	Routine ICU treatment + in-bed cycling - (MOTOmed letto2, Germany) with upper limb passive joint activity - passive and active cycling	Routine ICU treatment	<b>Outcomes:</b> - ICU-AW - adverse events - MV time - ICU LOS - Barthel Index	Outcomes: - ICU LOS [d] (11.87±2.00, 13.24±2.32, p = 0.001) - MV time [h]( 200.57±25.97, 248.10±39.43, p<0.001) - Barthel Index (41.04±7.016, 33.70±8.81, p<0.001) - incidence of ICU-AW (16 (30.2%), 32 (59.3%), p=0.003) - no serious adverse events in both groups	2 → 3 (downgrade: high risk of bias in RoB)

ARF = acute respiratory failure, y = years, APACHE II score = acute physiology and chronic health score, d = day, GCS = Glasgow coma scale, h = hours, ICU-AW = intensive care unit acquired weakness, ICU LOS = intensive care unit length of stay, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial

In-bed cycling seems to have a benefit on ICU-AW, MV time, ICU LOS and Barthel Index in relation to usual ICU care.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
162 Anekwe 2020 (PMID: 32135387 DOI: 10.1016/j.p hysio.2019. 12.004) Specificatio n of study: systematic review	9 publications (RCTs) including 948 pts Inclusion criteria: - conducted in the ICU - RCTs - adult pts - evaluated the effect of EM or NMES - reported the incidence of ICUAW or assessed muscle strength using the MRC Exclusion criteria: - pts already diagnosed with ICUAW Per Branch		EM and/or NMES	Usual care	Primary endpoint: - incidence of ICUAW measured at any time point after initiation of intervention Secondary outcomes: - length of time spent on MV(ventilator-free days and duration of MV) - discharge location - ICU and hospital LOS - acute mortality (defined as death in the ICU or hospital)	Primary outcome - random effect model OR 0.63 (95% CI: 0.43 to 0.92) (screened population) 0.71(95% CI: 0.53 to 0.95) (total population randomized) - the fixed effect model had the same results. significantly more pronounced effect of EM in patients with longer ICU-LOS. -NMES had a greater effect on ICUAW than EM (0.71 vs. 0.26) -EM <72h is more effective than EM >72h (0.7 vs. 0.75) Secondary outcomes - acute mortality: no difference between groups (OR 1.19; 95% CI: 0.79 to1.80) - ICU LOS no meta analysis - MV Duration no meta analysis - discharge home OR 1.69 (95% CI: 1.04 to 2.75) in favour of rehabilitation for being discharged home - only two studies favoring discharge home in the intervention group (p = 0.06 and 0.0007)	1

EM = early mobilization, ICU-AW = ICU-acquired weakness, ICU = intensive care unit, LOS = length of stay, MRC = medical research council scale, NMES = neuromuscular electrical stimulation, pts = patients

EM and/or NMES shows a benefit in relation to the incidence of ICU-AW.

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Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
170 Ding 2020 PMID: 32000806 DOI: 10.1186/s1305 4-020-2738-5 <b>Specification of</b> <b>study</b> : a multi-center prospective cohort study	20 pts. Between January 2018 and April 2019 Inclusion criteria: - Non-intubated moderate to severe ARDS patients - arterial blood gas analysis after a PEEP of 5 cmH2O supported by NIV (CPAP/BiPAP mode) with FiO2 0.5 for at least 30 min → PaO2/FiO2 was less than 200 mmHg Exclusion criteria: -signs of respiratory fatigue (RR > 40/min, PaCO2 > 50 mmHg/pH < 7.30, and obvious accessory respiratory muscle use) - immediate need for intubation (PaO2/FiO2 < 50 mmHg, unable to protect airway or change of mental status) - inability to collaborate with PP with agitation or refusal		Interventions: (1) <u>HFNC</u> , high-flow nasal cannula support alone. (2) <u>HFNC+PP</u> , high-flow nasal cannula therapy combined with prone positioning. (3) <u>NIV</u> , non-invasive ventilation support alone. (4) <u>NIV+PP</u> , non-invasive ventilation combined with prone positioning.		No sample size calculation Primary endpoints: - rate of avoidance for intubation. Secondary endpoints: - increase in PaO2/FiO2 from HFNC alone to HFNC+PP, to NIV alone, and to NIV+PP - threshold of PaO2/FiO2 for successful PP cases - time duration (tolerance) for each PP therapy session	Primary endpoints: - 11/20 pts, 55% avoided intubation → success group. -9/20 intubated, 3 needed ECMO, 1 died → failure group Secondary endpoints: -PaO2/FiO2 showed a trend of increase in transitions from HFNC to HFNC+PP, to NIV, and to NIV+PP (no p value) -in the success group: <ul> <li>PaO2/FiO2 higher in HFNC+PP than in HFNC (130 ± 35 mmHg vs 95 ± 22 mmHg, P = 0.016).</li> <li>PaO2/FiO2 upward trend when PP was added to NIV (166 ± 12mmHg vs 140 ± 30 mmHg, P = 0.133)</li> <li>-in the failure group:</li> <li>PaO2/FiO2 were significantly higher in NIV+PP compared to NIV (111 ± 20 mmHg vs 77 ± 14 mmHg, P = 0.011)</li> <li>PaO2/FiO2 in those evaluated on HFNC+PP was significantly higher in the success group than in the failure group (125 ± 41 mmHg vs 119 ± 19 mmHg, P = 0.043)</li> <li>No significant difference in total days, frequency, and duration of PP between the successful and the failure groups was demonstrated</li> </ul>	3 → 4

Pts. =patients; ARDS= acute respiratory distress syndrome; PEEP= end-expiratory positive airway pressure; NIV=non-invasive ventilation; HFNC= high-flow nasal cannula; PP=prone position

Early application of PP with HFNC, especially in patients with moderate ARDS and baseline SpO2 > 95%, may help avoid intubation.

Reference, Study Type		and Controls #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
171 Gama Lordello 2020 (PMID: 31994405 DOI: 10.1177/0 269215520 901763) Specificati on of study: RCT	<ul> <li>either elective revascularization by median stere extracorporeal</li> <li>Exclusion critee</li> <li>difficulty und activities</li> <li>motor or neu- that would pre- using a cycle en- walking independent - discontinued</li> </ul>	ria: cardiac surgery e myocardial on or valve surgery motomy with circulation ria: erstanding the rological impairment event them from rgometer or from endently the protocol on the	6 pts, return to ICU: 3 interventions, 3 control)	Rehabilitation program: -start 6 to 8 hours after extubation - twice in a 24-hour period using only the cycle ergometer (Delta- Sport Handelskontor GmbH Nr. AT-2154, version 08/2015; Hamburg, Germany) - 10 minute sessions	Standard mobilization: -6 to 8 hours after extubation - 10 minutes sessions - active exercises for lower and upper limbs - each movement repeated 10 times in an open kinetic chain	Primary endpoint: - difference in total number of steps recorded on pedometer over 3 days of use Secondary outcomes: - mobility - reasons that prevented pts from walking during phase I cardiac rehabilitation Sample size calculation: - 216 pts, 108 in each group	<ul> <li>Primary endpoint: <ul> <li>no significant</li> <li>difference (p=0.167)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>higher motivation to</li> <li>walk in intervention</li> <li>group (37,6%, 25,2%, p=0.04)</li> <li>no significant</li> <li>differences in other</li> <li>outcomes</li> </ul> </li> </ul>	2
	114	120						

ICU = intensive care unit, pts = patients, Y = years

In-bed cycling seems to have no benefit in relation to number of steps on pedometer after intervention.

173 Windmoller 202042 pts enrolled, 31 analyzedI 11pts (6 Inter- vention, 5 Control; 6 for arhythmia, 111pts (6 Inter- vention, 5 Control; 6 for arhythmia, 1Primary endpoint: - 6MWTPrimary endpoint: - 6MWT0/VID: 31988253- underwent myocardial revascularization surgery11pts (6 Inter- vention, 5 Control; 6 for arhythmia, 1 for surgical reinter- vention, 2 not respiratoryStep program in immediate postoperative period arhythmia, 1Physiotherapeutic program (step program): 2 daily session with a average duration of 5tudy: RCTPrimary endpoint: - 6MWT, no significant difference (p=0.16)Primary endpoint: - 6MWT, no significant difference (p=0.16)10.4187/resp care.06919Exclusion criteria: - unable to understand and follow the research procedures postoperative postoperative gostoperative postoperative gostoperative postoperativePrimary endpoint: - 6MWT, no significant difference (p=0.16)Specification of study: RCT- unable to understand and follow the research procedures and 2 for death- for deathNot respectication of study: RCTPer Branch- we have a set of the 4th postoperative day- no significant differences in other outcomes- no significant differences in other outcomes- no significant differences in other outcomes	Reference, Study Type	Cases and Cont (Participant #, Chara Total		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
21 21 and control)	Windmoller 2020 (PMID: 31988253 DOI: 10.4187/resp care.06919) Specification of study:	Inclusion criteria: - 40–70 years - underwent myocard revascularization surg Exclusion criteria: - unable to understand follow the research pr - had complications postoperative Per Branch	dial gery nd and rocedures <b>h</b>	(6 Inter- vention, 5 Control; 6 for cardiac arrhythmia, 1 for surgical reinter- vention, 2 not reassessed and 2 for	immediate postoperative period + cycle ergometer with CPAP: 1 daily session from the 2 <sup>nd</sup> to the 4 <sup>th</sup>	<pre>program (step program): 2 daily sessions with an average duration</pre>	<ul> <li>- 6MWT</li> <li>Secondary outcomes: <ul> <li>respiratory muscle</li> <li>strength</li> <li>lower limbs muscle</li> <li>resistance</li> <li>MV time</li> <li>ICU LOS</li> <li>hospital LOS</li> </ul> </li> <li>Sample size <ul> <li>calculation:</li> <li>30 (15 intervention</li> </ul></li></ul>	<ul> <li>- 6MWT, no significant difference (p=0.16)</li> <li>Secondary outcomes: <ul> <li>- significantly lower ICU</li> <li>LOS [d] (2.5±0.5, 2.9 ± 0.7, p=0.05)</li> <li>- no significant differences</li> </ul> </li> </ul>	2

CPAP = continuous positive airway pressure, d = days, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial, 6MWT = 6 minute walk test

#### In-bed cycling with CPAP seems to have a small benefit on ICU LOS in comparison to a standard physiotherapeutic program.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
174 Coles 2020 (PMID: 31972758 DOI: 10.1097/TA. 000000000 002588) <b>Specification</b> of study: retrospective pre-post study	526 critically ill trauma p Inclusion criteria: - adult trauma pts (>18 y - admitted to ICU at a Le over a 2-year period prive EMP implementation (w period) - admitted during study Exclusion criteria: - pediatric pts(<18 years - any trauma pts admitted the transition period (Ap , 2015) Per Br 234 post-EMP	years old) evel I trauma center or to and following vith a 1-year transition v period. s) ed to ICU during pril 1, 2014 to March 3		Multidisciplinary, stepwise approach to patient mobilization with a new Early Mobilization Protocol - ICU clinicians evaluate pts readiness for participation in mobilization activities using a 4-level system - for unconscious pts mobility sessions consist of passive ROM activities	Usual care - prior to EMP implemen tation	Primary endpoint: - in-hospital mortality Secondary outcomes: - ICU mortality - ICU LOS - hospital LOS - ventilator-free days	Significant differences between groups in: - in-hospital mortality, n (%): 41 (17.5); 74 (25.3); p=0.031 - ICU mortality n (%) 30 (12.8); 63 (21.6); p=0.009 No significant differences between groups in: - ICU LOS n.s. - hospital LOS n.s. -ventilator-free days n.s.	4

EMP = early mobilization protocol, ICU = intensive care unit, LOS = length of stay, n.s. = not significant, pts = patients, ROM = range of motion

# A multidisciplinary, stepwise approach to patient mobilization seems to have a benefit in relation to in-hospital and ICU mortality.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Recommendations
176 Aquim 2019 (PMID: 31967216 DOI: 10.5935/010	<ul> <li>28 publications (16 RCTs, 3 SRs, and 9 prognostic cohort studies)</li> <li>Inclusion criteria: <ul> <li>adult pts ≥ 7 days hospitalized in the ICU</li> <li>receiving MV</li> <li>early mobilization</li> <li>full texts available</li> <li>RCTs</li> <li>prognostic cohort studies</li> <li>SRs with or without meta-analysis</li> </ul> </li> </ul>	<ol> <li>Early mobilization is safe. Adverse events are mainly related to hemodynamic and/or respiratory changes, are low-frequency and are reversible with the interruption of the intervention. Adverse events are not frequent or severe, and early mobilization is considered safe</li> <li>Early mobilization is indicated for adults in the ICU, preferably those under spontaneous breathing, who cooperate and who do not have intracranial hypertension. Mechanical ventilation and noncooperation may be considered limitations for early mobilizations, but not contraindications.</li> <li>Early mobilization is contraindicated for terminal patients with systolic hypertension (systolic blood pressure &gt; 170mmHg) or intracranial hypertension, unstable fractures, recent acute myocardial infarction and open abdominal wounds.</li> <li>The appropriate dose of early mobilization is defined by clinical efficacy and individual tolerance. The doses are as follows:         <ul> <li>passive mobilization: approximately 10 to 20 mobilizations per selected joint, up to two times/day.</li> </ul> </li> </ol>
3- 507X.201900	Definition of EM	- active exercises: 1 hour per day, up to two 30-minute sessions.
84) Specification of study: National Guideline	<b>Early physical therapy</b> - for critically ill pts - starting in the first 48 hours after the institution of MV	<ul> <li>The following constitute positioning and progression: <ul> <li>assisted verticalization with an orthostatic board: up to 1 hour per day, up to twice a day.</li> <li>passive ergometer cycling: 20 minutes, 20 cycles/minute.</li> <li>active ergometer cycling: two 10-minute sessions per day.</li> </ul> </li> <li>The care and safety criteria for early mobilization do not require specific monitoring, and hemodynamic and respiratory stability characterize a safe intervention model.</li> <li>The prognostic indicators include an assessment of the risk of functional decline, weight, functional range, muscle strength, hemodynamic instability, respiratory dysfunction, recent extubation, protective factors, sedation, length of stay in the ICU and duration of mechanical ventilation.</li> </ul>

Reference, Study Type	(Partic	d Controls ipant #, teristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Тс	otal	nate					
177 Mayer 2019 (PMID: 31922059 DOI: 10.1016/j.ekir.2019. 10.003) Specification of study: A quality Improvement Study	N = 67 Inclusion crit - adult pts - requiring CF Exclusion crit - RASS > 2 or - high ventila (FiO2 > 70%, - 2+ vasopres - hemodynan Per E 112 complete rehabilitation sessions	RRT ≤ 2 tion settings PEEP >8) sors		Mobility progression scheme of early rehabilitation: Level 1 & 2 (PT or OT): Level 1: passive activity in bed Level 2: active activity in bed Monitor CRRT access/return pressure alarms Level 3 (PT, OT and RN) Edge of Bed activity Monitor CRRT access/ return pressure alarms Level 4 (PT, OT & RN (RT if MV)): Standing and Transfer CRRT fluid removal paused for 15- 20 minutes Level 5 (PT, OT, & RN (RT if MV)): Ambulation CRRT machine in recirculation mode if filter life < 36h	No control group	Primary outcomes: - feasibility - safety Secondary outcome: - clinical outcomes	Primary outcomes: feasibility: - 112 rehabilitation sessions were performed of 152 attempts (74% completion rate) Safety: - no major adverse events Secondary outcome: Clinical outcomes: - patients achieving higher levels of mobility were more likely to be alive at discharge (p = 0.076). - number of completed rehabilitation sessions directly correlated with MV days, hospital LOS, ICU LOS, and CRRT days (r % 0.392, 0.254, 0.384, 0.467)	4

\*CRRT = continous renal replacement therapie, MV = mechanical ventilation, OT = occupational therapie, PT = physical therapy, RN = registered nurse, RT = respiratory therapist

The provision of early rehabilitation in critically ill patients requiring CRRT is safe and feasible.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
181 Okada 2019 (PMID: 31867111 DOI: 10.1186/s40560- 019-0413-1) Specification of study: systematic review	11 publications 1322 pts <sup>1-11</sup> <b>Inclusion criteria</b> - RCTs - adult pts ≥18 y admitted to ICU		<b>Early mobilization</b> - physical and/or occupational therapy - start within 1 week of ICU admission, - initiated earlier than usual care or control	Usual care or mobilization - started later than the intervention	<ul> <li>Primary endpoints: <ul> <li>in-hospital mortality</li> <li>ICU/hospital LOS</li> <li>SF-36 or EQ-5D</li> </ul> </li> <li>Secondary outcomes: <ul> <li>physical function</li> <li>cognitive function</li> <li>mental disorders such as depression or anxiety</li> <li>all adverse events</li> </ul> </li> </ul>	Significant outcomes: - in-hospital mortality: OR (95% CI: 0.80 to 1.58) - ICU-LOS: OR -1.54 (95% CI: -3.33 to -0.25) - hospital LOS: OR -2.86 (95% CI -5.51 to -0.21, I 2 = 85%) - MRC: MD 4.84 (95% CI: 0.36-9.31) Not significant outcomes: - PFIT, handgrip and AE n.s. - SF-36 PF: MD 4.65 (95% CI: -16.13 to -25.43) - EQ-50: MD 0.29 (95% CI: - 11.19 – 11.78)	1

AE = adverse events, EQ-5D = EuroQol 5 dimension, ICU = intensive care unit, LOS = length of stay, MRC = Medical Research Council Scale for Muscle Strength, n.s. = not significant, PFIT = physical function in ICU Test, pts = patients, QOL = quality of life, RCT = randomized controlled trial, SF-36 = short form health survey 36-item, y = years

#### Early mobilisation seems to have a benefit in relation to a shorter length of hospital stay and muscle strength.

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Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
https://doi.org/10. 1053/j.jvca.2019.1 0.055	1 institutional database between October 2016 and October 2018→ 24 pts., 6 pts. undergoing PP during ECMO therapy. Inclusion criteria: -PP for the treatment of ARF after cardiac surgery Exclusion criteria: -not stated Per Branch 6		<b>PP</b> Data before, after (6h), at the end of PP and after SP (6h)	Patients acted as their own control	No sample size calculation (retrospective study) <b>Outcomes:</b> - respiratory conditions (e.g., HI) - ECMO support	<b>Results:</b> -increase in HI at the end of PP (p < 0.001) as well as 6h after SP (p < 0.001) -a significant reduction of ECMO support from 3.0 (2.2-5.6) liters/min to 2.5 (2.0-4.6) liters/min (p = 0.023) in pts. undergoing PP and ECMO	4

PP=Prone position; pts=patients; ARF=acute respiratory failure; ECMO= extracorporeal membrane oxygenation; SP=supine position; HI=Horowitz index

PP can be considered for the treatment of ARF after cardiac surgery to improve short-term respiratory conditions and possibly facilitate ECMO weaning.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, o To	characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#185 Lucchini 2020 (PMID: 31789984 DOI: 10.1097/DCC.00000000 00000393)	Exclusion criteria: - Patients with noninv Per Bi	position in a general m January 2008 – undergoing invasive n in prone position rasive ventilation	- none	Prone Position maneuvers (patients with pressure sores)	maneuvers (patients without pressure	- incidence of pressure	Results - 23 (14%) of pts developed pressure sores - 31 pressure sores related to PP on these 23 pts Significant differences - difference in the PaO <sub>2</sub> /FiO <sub>2</sub> mmHg ratios observed in 4 time frames (before PP: 109mmHg (IQR 80-148, after 1h: 144mmHg (IQR 96-200), before placed in supine position: 158mmHg (110-213), after 1h supine position: 131mmHg (95-175); p<0.0001)	4
	170							

ARDS = acute respiratory distress syndrome ; ICU = intensive care unit; pts = patients; PP = prone position

#### The overall incidence of pressure sores under PP was low. The PaO<sub>2</sub>/FiO<sub>2</sub> mmHg ratio could positively influenced by PP.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, C Tota	haracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
186 Schieren, 2020 (PMID: 31757469 DOI: 10.1016/j.i njury.2019. 11.009) retrospecti ve matched- pair cohort study	60 pts Inclusion criteria: - ≥18 y, ventilated v trauma (abbreviate (AIS)Thorax ≥3) Exclusion criteria - no/minor chest (AISThoraxA 2) - secondary hospi >24 hours from a - duration of mec ventilation <72 ho Per Bra	with thoracic ed injury scale : trauma ital admission ccident hanical ours anch	Exclusion during data collection (16 patients) (incomplete/illeg ible records (8 patients), exclusion of corresponding partners (8 patients))	<b>CLRT:</b> - with a rotational arc of up to 124°	<b>Conventional</b> <b>therapy:</b> - manually turning pts from side-to- side in 2-4 h intervals with the head of the bed elevated	Outcomes: - depth of sedation - level of agitation - pneumothorax/ pleural infusion/ pulmonary infiltrates on X-ray - Lung injury score - paO2/FiO2 ratio - incidence in pneumonia, sepsis, liver or kidney failure - ICU and hospital LOS	Significant differences between groups: - deeper Sedation in control (RASS -3.6 vs. 4.0, p = 0.01) - more agitation (RASS ≥2) after intervention (41% v. 9%, p = 0.01) No significant differences between groups in: - visibility of pneumothoraxes or pulmonary infiltrates or pleural effusion on chest X-Ray - change in Lung Injury Score - development of severe respiratory dysfunction - paO2/FiO2 ratio - incidence in pneumonia, sepsis, liver or kidney failure - ICU and hospital LOS	4
	30	30						

CLRT = continuous lateral rotation therapy, ICU = intensive care unit, LOS = length of stay, pts = patients

In this well-matched sample, the use of CLRT did not seem to translate into relevant clinical benefits in patients with thoracic trauma in the setting of modern ICU care with the widespread implementation of lung protective ventilation. Agitation was more likely in the CLRT group. *No detailed assessment was carried out because higher-quality evidence is available on this topic.* 

Reference, Study Type	(Parti Charao	nd Controls cipant #, cteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
189 Kim 2019	im 19 Inclusion criteria: - adults (≥18 years) with /IID: sepsis						Comparison between low skeletal mass and non-low skeletal mass groups	
(PMID: 31700866 DOI: 10.21037/at m.2019.08.1 17) Specification of study: case control Study	- adults (≥18 years) with		-	Rehabilitation - 30 minutes daily - stretching, strengthening exercises, NMES, dysphagia therapy for pts with swallowing difficulty,	No Rehabilitation	Primary Endpoints: - hospital stay - ICU stay - in-hospital mortality - discharge	<ul> <li>hospital mortality: no significant difference between groups</li> <li>6-months mortality higher in the low skeletal muscle mass group(44.9% vs. 26.3%, p=0.001)</li> <li>1-year mortality higher in the low skeletal muscle mass group (50.1% vs. 32.6%, p=0.002)</li> <li>rate of discharge to home lower in the low skeletal muscle mass group(39.4% vs. 58.9%, p=0.001)</li> <li>Low skeletal mass group, rehabilitation vs control:</li> <li>urinary tract infection higher in the rehabilitation group (15.3% vs. 7.8%, p=0.015)</li> <li>mean hospital LOS higher in the rehabilitation group (73.2</li> </ul>	4
	Low skeletal muscle mass: n = 421 (Interventi on: 215, Control: 206)	Non-low skeletal muscle mass: n = 95				to home - 6-month mortality - 1 year mortality	<ul> <li>vs. 35.5 days, p&lt;0.001)</li> <li>mean ICU LOS higher in the rehabilitation group(22.5 vs. 15.9 days, p=0.004).</li> <li>hospital mortality lower in the intervention group (26% vs. 39.8%, p=0.003)</li> <li>6-month mortality lower in the rehabilitation group(38.6% vs. 51.5%, p=0.008)</li> <li>rate of discharge to home higher in the rehabilitation group (43.3% vs. 35.4%, p=0.011)</li> <li>no differences in the non-low skeletal muscle mass group.</li> </ul>	

CT = computer tomography, ICU = intensive care unit, LOS = length of stay, NMES = neuromuscular electric stimulation, pts = patients

ICU rehabilitation was independently associated with reduced 1-year mortality from sepsis among low skeletal muscle mass patients, but not among non-low skeletal muscle mass patients. Therefore, the delayed initiation of ICU-rehabilitation should be avoided, especially in low skeletal muscle mass patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out – Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
190	155 pts selected from an ICU						
Shimogai 2019	Inclusion criteria: - ≥ 20 y - rehabilitation was performed					Significant outcomes: - age (p=0.001, OR= 1.06	
(PMID: 31698814	- medical patients admitted to ICU		- data collection - evaluating ADL		Primary outcomes: - factors affecting	95%CI=1.02 – 1.09) - APACHE II score	
DOI: 10.3390/ijerph 16224324)	<ul> <li>Exclusion criteria:</li> <li>rehabilitation started in general ward</li> <li>rehabilitation was prescribed in the ICU but was not performed while the patient was in the ICU</li> <li>death</li> </ul>		before admission - assessment of muscle strength - assessment of		discharge to home from ICU (Age, APACHE-II-Score, Independence at home before	<ul> <li>(p=0.002, OR=1.12, 95%CI= 1.04 - 1.20)</li> <li>independence at home before admission</li> <li>(P=0.008, OR=7.10, 95%CI=1.65 - 30.44)</li> </ul>	4
Specification of study: Retrospective	<ul> <li>cerebrovascular disease</li> <li>patient declined rehabilitation</li> <li>missing data in the variable of interest</li> </ul>		disability		admission, standing within 5 days of admission)	<ul> <li>95%CI=1.65 - 30.44)</li> <li>standing within 5 days of admission (p&lt;0.001, OR=6.58, 95% CI=2.60</li> </ul>	
cohort study						- 16.61)	
	155						

ADL = activities of daily life, CI = confidence interval, ICU= intensive care unit, OR = odds ratio, Pts = patients, y = years

Independence of home life before admission and early start of standing were identified as factors strongly related to discharge to home. The degree of independence in living before hospital admission and progress toward early mobilization are helpful when considering an ICU patient's discharge destination.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	(Participant #	nd Controls ‡, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
194 Ding 2019 (PMID: 31589642 DOI: 10.1371/jour nal.pone.022 3151) Specification of study: systematic review with network meta-analysis	Chinese Exclusion criter - abstracts, lette non-RCTs, expe reviews, repeat - did not specify mobilization ini outcomes	ia: years e MV d in English and ia: ers, case reports, rt opinions, ed literature		<b>Early mobilization</b> - initiated at various time points, as follows: within ≤ 24h, 24–48h, 48–72h, 72–96h, and > 96 h of MV, and > 5 and > 7 days after ICU admission	Usual nursing care	<b>Outcomes:</b> - ICU-AW (MRC ) - duration of MV - ICU LOS	Significant differences between groups between: - incidence of ICU-AW, in mobilization within 72–96 h and 24–48 h of MV, with the former leading to a greater reduction in ICU-AW - duration of MV, in mobilization within $\leq$ 24 h, 48–72 h, > 96 h, and 24–48 h of MV, with shorter durations for pts mobilized at $\leq$ 24h, 48–72h, and > 96 h relative to 24– 48 h - mobilization within $\leq$ 24 h or > 96 h of MV and > 5 days after ICU admission, with $\leq$ 24 h or > 96 h leading to shorter durations No significant differences between groups in: - ICU LOS among the 7 initiation times	1

ICU-AW = ICU-acquired weakness, ICU = intensive care unit, MRC = medical research council, MV = mechanical ventilation, NMA = network meta-analysis, pts = patients, RCT = randomized controlled trial

Mobilization within 48–72 h of mechanical ventilation may be optimal for improvement of clinical outcomes.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
195 Zhang 2019 (PMID: 31581205 DOI: 10.1371/journ al.pone.02231 85) Specification of study: systematic review	<ul> <li>- 23 publications<sup>1-23</sup></li> <li>Inclusion criteria: <ul> <li>English publications</li> <li>pts ≥18y</li> <li>RCTs</li> </ul> </li> <li>Exclusion criteria: <ul> <li>pts with neurological conditions</li> <li>inclusion of ineligible interventions, such as, NMES, continuous lateral rotation of the bed, lateral positioning in bed, inspiratory muscle training / diaphragmatic electrical stimulation/breathing exercises, chest physiotherapy/airway clearance, massage therapy, and stroke rehabilitation <ul> <li>exercises performed after ICU discharge</li> <li>pediatric, animal or cell-based studies</li> </ul> </li> </ul></li></ul>		Early mobilization	Standard of care	Outcomes: - muscle strength - functional mobility capacity - duration of MV - ventilator-free days - mortality rates (28-day, ICU, and hospital) - discharged-to- home rate - adverse events	Significant differences between groups in: - ICUAW at hospital discharge (RR: 0.60, 95% CI [0.40, 0.90]; $p = 0.013$ , $I2 = 0.0\%$ ) - number of ventilator-free days (SMD: 0.17, 95% CI [0.02, 0.31]; $p = 0.023$ , $I^2 = 35.5\%$ ) - discharged-to-home rate (RR: 1.16, 95% CI [1.00, 1.34]; $p = 0.046$ ) No significant differences between groups in: - no change in MRC (n.s.) - ICUAW at ICU discharge n.s. - MV duration n.s. (SMD -0.33; 95% CI: -0.66 to -0.00; $p = 0.051$ ; $I^2 = 89.1\%$ ) - handgrip force n.s. - quadriceps force n.s. - no meta-analysis on functional mobility capacity	1

CI = confidence interval, EM = early mobilization, ICU-AW = ICU-acquired weakness, ICU = intensive care unit, MV = mechanical ventilation, NMES = neuromuscular electric stimulation, pts = patients, RCT = randomized controlled trial, RR = relative risk, SMD = standardized mean difference, y = years

Early mobilization seems to have a benefit in relation to muscle strength, ventilator free days and discharge to home rate.

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Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop-out - Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
198 Nakamura 2019 (PMID: 31544949 DOI: 10.2340/165 01977-2594) RCT	<ul> <li>multiple-drug-resis</li> <li>lower extremity events</li> <li>pacemaker</li> <li>neuromuscular dise</li> <li>CT not performed of</li> <li>do not attempt ressioned to obtain in</li> <li>included in other clipse</li> </ul>	cted discharge from s co our ICU ed pregnant mbrane oxygenation tant bacteria ent eases on the first day uscitation formed consent	N = 57 (60,6%) NMES: 26 (6 died, 18 discharged early, 2 CT unable) Control: 31 (7 died, 17 discharged early, 7 CT unable)	Early rehabilitation: - for 20 min per day NMES: - lower extremities 20 min per day until day 10	<b>Early</b> <b>rehabilitation:</b> - for 20 min per day	Primary endpoint: - femoral muscle volume cia CT Secondary outcomes: - ICU LOS - hospital LOS - 28-day survival - duration of MV - Barthel index	Primary endpoint: - femoral muscle volume change day 1 to 10 (%), control – MD (95%Cl): -17.7 (-11.9 – -23.5) vs intervention - MD (95%Cl): -10.4 (-5.8 – 15.1), p = 0.04 Secondary outcomes: - ICU LOS, control: Mean $\pm$ SD: 10.6 $\pm$ 4.7 vs intervention: Mean $\pm$ SD: 9.9 $\pm$ 5.7, p = 0.71 - hospital LOS, control: Mean $\pm$ SD: 20.6 $\pm$ 8.9 vs intervention: Mean $\pm$ SD: 17.4 $\pm$ 9.9 p = 0.32 - duration of MV (days), control: Mean $\pm$ SD: 8.5 $\pm$ 4.5 vs intervention: Mean $\pm$ SD: 29.0 $\pm$ 18.8 vs intervention: Mean $\pm$ SD: 29.0 $\pm$ 18.8 vs intervention: Mean $\pm$ SD: 50.4 $\pm$ 31.6, p = 0.16 - 28-day survival, control: %: 51.5 vs intervention: %: 49.2, p = 0.63	2 → 3 (downgraded due to high drop-out rate)

CT = computer tomography, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation

Belt electrode electrical muscle stimulation reduces muscle loss in the ICU.

Reference, Study Type	(Participant #	nd Controls , Characteristics) Fotal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
199 Pang 2019 (PMID: 31537777 DOI: 10.12659/M SM.916210) Specification of study: RCT	injury - APACHE II score ≥: - age 18–80 y - onset of disease for - signed informed c <b>Exclusion criteria:</b> - long-term inability independently prior - advanced stage of underwent radiother chemotherapy of tu months - imperfect limbs ar - long-term MV due diseases - heart rate exceeder allowable for age - family members d	or the first time onsent y to move r to onset of disease malignant tumors or erapy or umors within the last 6 and new fracture to neuromuscular ed the 70% maximum		Early rehabilitation therapy: - performed at 2 days after the pts became stable - once daily, 6 times per week for 10 days - awaking therapy, hyperbaric oxygen therapy , comprehensive sensory stimulation therapy, and fastigial nucleus stimulation , therapeutic exercise (such as intelligent rehabilitation training system for lower limbs , passive activity training/active assistant activity training), and electrical stimulation therapy	<ul> <li>monitored for respiratory functions and blood oxygen</li> <li>provided nutritional support therapy</li> <li>placed in supine position or lateral decubitus position.</li> <li>bed sores were prevented by turning over, slapping the back, and massaging skin, and sputum was drained to avoid asphyxia.</li> <li>rehabilitation in usual care</li> </ul>	Derived endpoints: - incidence rates of ICU-AW - incidence rate of DVT/pneumonia - APACHE II scores/MRC scores prior to and after treatments - MV time - hospital stay in ICU - total hospital stay no power analysis	Derived outcomes: - APACHE II after treatment (8.90±2.07; 10.24±2.19; p<0.05) - MRC post treatment (52.95±3.99; 50.10±4.21; p<0.05) - improved GCS (GCS>9; 86% vs 76%; p<0.05, GCS>12; 48% vs 24%; p<0.05, GCS=15; 24% vs 9.5%; p< 0.05) - incidence of complications (ICUAW, DVT, pneumonia) 19%; 43%; p<0.05 - ICU- LOS (11.76±2.63; 14.00±2.19; p<0.05) - hospital stay (31.38±4.006; 35.24±5.059; p<0.05) - MV duration (3.00±0.71; 5.17±0.75; p<0.05)	2 → 4 (downgraded due to high risk of bias and and low number of pts)

APACHE II = acute physiology and chronic health evaluation, DVT = deep vein thrombosis, DVT = deep venous thrombosis, GSC = Glasgow coma scale, ICU-AW = intensive care unit – acquired weakness, ICU = intensive care unit, IV = intravenous, LOS = Length of stay, MRC = medical research council, MV = mechanical ventilation, pts = patients, y = years,

Early rehabilitation therapy seems to have a benefit in relation to APACHE II, MRC, consciousness rate, adverse events, ICU and hospital length of stay and MV time compared to Control Group.

Reference, Study Type	(Participant #,	d Controls characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Seo 2019 PMID: 31522973 https://doi.org /10.1016/j.auc c.2019.07.005 <b>Specification</b> of study: Retrospective study		for at least three ved more than one session e medical record plantation		< 65 years of age	≥ 65 year of age	No sample size calculation (retrospective study) Endpoints: - rehabilitation characteristics (activity level) - functional recovery - AM-PAC scores - safety events	<b>Results:</b> - Activity level of session (Level II (AROM): 59 (17.6); 38 (8.5), Level III (sitting): 145 (43.3); 189 (42.5), Level IV (standing): 84 (25.1); 162 (36.4), Level V (walking <10m): 13 (3.9); 12 (2.7), Level VI (walking - no significant differences in functional recovery were seen between the age groups - AM-PAC scores increased from the beginning of rehabilitation to the time of ICU discharge (from $11.6 \pm 0.4$ to $13.9 \pm 0.4$ , p < 0.01) - AM-PAC scores increased in both age groups (from $12.4 \pm 4.9$ to $14.8 \pm 4.9$ in those aged < 65 years and from 111.1 $\pm 4.1$ to $13.1 \pm 4.8$ in those aged $\ge 65$ years) -During the 780 rehabilitation sessions, 23 potential safety events (3.0%), most common dyspnoea (n = 7), patient refuel (n = 4), and tachyaerdia (n = 2)	4
	68	89					refusal (n = 4), and tachycardia (n = 3)	

SICU = surgical intensive care unit; pts = patients; AROM = active range of motion; pts. =patients; AM-PAC= Activity Measure for Post-Acute Care

Active rehabilitation in critically ill surgical is feasible and sage regardless of age.

21 pts admitted to two ICUs within the Charité – Universitätsmedizin Berlin receiving NMES were considered in this sub-analysis branched into Responders and Non-Responders       Amitted to two ICUs within the Charité – Universitätsmedizin Berlin receiving NMES were considered in this sub-analysis branched into Responders and Non-Responders       Non-Responders       Primary Endpoint: - Significantly greater proportion of stimulations leading to an adequate contractile response in responders         201       Non-Responders       Non-Responders       Sample Size calculation: None for sub-analysis son-responders       Significantly greater proportion of stimulations leading to an adequate contractile response in responders         2019       - Admitted to the ICU < 72h Exclusion criteria: - Admitted to the ICU < 72h Exclusion criteria: - Prior hospital treatment for longer than 7 days - lillness prohibiting early mobilization - pre-existing neuromuscular disease - insulin-dependent diabetes mellitus Secondary analysis of RCT       - Prior hospital treatment diabetes mellitus Body Mass Index > 35 kg/m2 - not ambulating before admission - poor prognosis with a high likelihood of death within the next hours       - none Per Branch       - None Per Branch       - None Per Branch       - None NES during the itervention       - SOFA score - necessary electrical intervention       - SOFA score - necessary electrical intervention	Reference, Study Type	Cases and (Participant #, c Tot	haracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	201 Grunow 2019 PMID: 31506074 https://doi.org/10.1186 /s13054-019-2540-4 <b>Specification of study:</b> Secondary analysis of	Charité – Universitätsr receiving NMES were of sub-analysis branched Non-Responders Inclusion criteria: - ≥ 18 y - SOFA Score ≥ 9 - Admitted to the IO Exclusion criteria: - Prior hospital treat than 7 days - illness prohibiting - pre-existing neuro - insulin-dependent - Body Mass Index 3 - not ambulating be - poor prognosis wi of death within th	nedizin Berlin considered in this into Responders and CU < 72h atment for longer early mobilization pmuscular disease t diabetes mellitus > 35 kg/m2 efore admission th a high likelihood ie next hours	- none	Defined as >50% contractile response to NMES during the first 7 days of the study	with ≤ 50% contractile response to NMES during the first 7 days of the study	Sample Size calculation: None for sub-analysis Endpoints: -contractile response -SOFA score -necessary electrical current	<ul> <li>Significantly greater proportion of stimulations leading to an adequate contractile response in responders vs non-responders</li> <li>Significant difference:</li> <li>Significantly higher SOFA score in non-responders.</li> <li>The electrical current necessary for a muscle contraction in responders was significantly lower (38.0 [32.8/42.9] vs. 54.7 [51.3/56.0] mA, p&lt; 0.001). Muscle strength showed higher values in the upper extremities of responders at ICU discharge (4.4 [4.1/4.6] vs. 3.3 [2.8/3.8] MRC</li> </ul>	4

ICU = Intensive Care Unit; NMES = Neuromuscular electrical stimulation SOFA = Sepsis-related organ failure assessment; MRC=Medical Research Council; ICU=intensive care unit

# Patients show a differential contractile response to NMES, which appears to be dependent on the severity of illness and also relevant for potential outcome benefits.

No detailed assessment was carried out because higher-quality evidence is available on this topic

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
203 de Figueiredo 2020 PMID: 31466922 DOI: 10.1016/j.burn s.2019.07.037 <b>Specification of</b> <b>study</b> : Prospective cohort study	74 pts. From April 2014 to March 2015 → 32 pts. Evaluated at hospital discharge Inclusion criteria: -older than 16 years admitted to the burn ICU Exclusion criteria: no data on admission - ICU death - refusal of performing tests - discharge before evaluation - Transference Per Branch	N=28 (ICU death); n=14 (excluded from post-ICU analysis) due to refused to perform all the tests (n=4); discharge before evaluation (n=9); transference (n=1)	Routine physiotherapy care: -respiratory therapy (airway clearance maneuvers, lung expansion techniques, oxygen therapy and NIMV -mobility therapy (20 min of positioning, general limb (passive, active or resistive) and trunk exercises, SOEOB, SOOB, standing up and walking away from the bed)	-	No sample size calculation <b>Primary endpoints:</b> -MRCS -6MWT -handgrip <b>Secondary</b> <b>endpoints:</b> -mobility practice -barriers -addition of a mobility session (12h-shift v. 24h- shift) -mobility level and outcomes (IMS)	Primary endpoints:         - no improvement in the MRCS scores at hospital discharge compared to the MRCS scores at ICU discharge (57.5 [9] vs 55 [7]; p = 0.368).         - positive relationship between the 6MWT and handgrip strength (r = 0.555; p = 0.04)         - negative correlation between length of hospital stay and handgrip strength (r =0.444; p = 0.03).         Secondary endpoints:         -mobility therapies (3088 sessions)         ○ IMS=0 1048/3088 (34%)         ○ IMS=0 1048/3088 (51%)         ○ IMS>4 444/3088(14%)         -barriers:         ○ hemodynamic instability in 71 events (2% of sessions)         ○ limited time for assistance in 49 events (1% of sessions)         ○ addition of a mobility session:         ○ no difference founded in any clinical (ICU LOS, MV duration and mortality) or functional outcomes (6MWD, handgrip strength, maximum mobility level)         - mobility level and outcome:         ○ association between IMSmax and mortality (p < 0.001 OR: 0.5, 95%CI: 0.36–0.68)	3

ICU = intensive care unit ; LOS = length of stay ; MRCS = Medical Research Council Scale ; TBSA = total burn surface area; 6MWT= 6-minute walking test; SOEOB= sitting on the edge of the bed; SOOB= sitting out of bed; NIMV= noninvasive mechanical ventilation;

Mobilization therapy of patients with burns in the ICU was characterized by a low mobility level during MV with a low functional status at hospital discharge

Reference <i>,</i> Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
209 Griffiths 2019 https://doi.org/1 0.1136/bmjresp- 2019-000420 <b>Specification of</b> <b>study:</b> National Guidelines	14 publications from 1999-2015 (14 systematic reviews, 12 with meta-analysis) <sup>1-14</sup> (number of pts., inclusion criteria, intervention and control not specified) Inclusion criteria: Systematic reviews comparing prone positioning to standard of care in <u>ARDS</u> patients Per Branch		РР	Standard of Care	<ul> <li>No primary endpoint defined</li> <li>Endpoints extracted: <ul> <li>Mortality (n = 8 studies with 2141 patients)</li> <li>Treatment harms</li> <li>a. Pooled analysis (n = seven studies with 7377 participants)</li> <li>b. Subgroup analysis of cardiac events (n = three studies with 1599 participants)</li> <li>c. Subgroup analysis of endotracheal tube displacement (n = five studies with 1597 participants)</li> <li>d. Subgroup analysis of ventilator-associated pneumonia (n = four studies with 1007 participants)</li> <li>e. Subgroup analysis of pressure sores (n = two studies with 1095 participants)</li> <li>f. Subgroup analysis of incidence of pneumothorax (n = four studies with 1160 participants)</li> <li>g. Subgroup analysis of loss of venous access (n = two studies with 646 participants)</li> </ul> </li> </ul>	<ul> <li>Results:</li> <li>Mortality (defined as overall mortality at the longest available follow-up) was reduced by PP (RR 0.9; 95% CI 0.82 – 0.96)</li> <li>a. Subgroup analysis based on lung-protective ventilation (low tidal volume, 6-8 ml/kg/body weight): PP in combination with lung-protective ventilation reduced mortality RR 0.73; 95% CI 0.62 – 0.86) compared to PP without lung-protective ventilation (RR 1.01; 95% CI 0.9 – 1.13)</li> <li>b. Subgroup analysis based on the duration of intervention: PP &gt; 12 hours reduced mortality (RR 0.75; 95% CI 0.65 – 0.87) compared to PP &lt; 12 hours (RR 1.03, 95% CI 0.91 – 1.17)</li> <li>Treatment Harms</li> <li>a. Pooled risk of adverse events was increased by PP (RR 1.10; 95% CI 1.01 – 1.12)</li> <li>b. PP increases the risk of cardiac events (RR 1.01; 95% CI 0.87 – 1.17)</li> <li>C. PP increases the risk of ventilator-associated pneumonia (RR 0.88, 95% CI 0.71 – 1.17)</li> <li>e. PP increases the incidence of pressure sores (RR 1.23; 95% CI 1.07 – 1.41)</li> <li>f. PP reduces the incidence of pneumothorax (RR 0.87; 95% CI 0.59 – 1.30)</li> <li>g. PP increases the incidence of loss of venous access (RR 1.98; 95% CI 1.11 – 3.55)</li> </ul>	1

Pts = patients, ARDS = acute respiratory distress syndrome, PP = prone positioning, RR = risk ratio, CI = confidence interval, P/F ratio = partial pressure of oxygen in relation to fraction of inspired oxygen

Use of prone positioning for at least 12 hours per day is strongly recommended for patients with moderate and severe ARDS (P/F ratio ≤ 20 kPa).

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
210 Zang 2020 (PMID: 31219229 DOI: 10.1111/nic c.12455) <b>Specificatio</b> <b>n of study:</b> systematic review	15 publications <sup>1-15</sup> incl. Chinese database, 1.914 pts Inclusion criteria: - RCTs - adult pts admitted to the ICU - paper outcomes: ICU- AW, mortality rate, length of ICU stay, hospital LOS, MRC score, Barthel Index score, ventilator-free days, handgrip strength, deep vein thrombosis, VAP, and pressure sores Per Branch		Early mobilization or rehabilitation	Standard physical care or daily nursing care	Derived outcomes - ICU-AW - ICU mortality rate - length of ICU stay - length of hospital stay - handgrip strength - MRC score - ventilator free days - Barthel Index - VAP - deep vein thrombosis - pressure sores	Significant differences between groups in:         - incidence of ICU-AW (RR = 0.49, 95% CI: 0.26, 0.91; p =         0.025), I <sup>2</sup> = 89.8%         - ICU LOS (WMD = -1.82 days, 95% CI: -2.88, -0.76; p =         0.001), I <sup>2</sup> = 95.9%         - length of hospital stay (WMD = -3.90 days, 95%         CI-5.94, -1.85; p < 0.001), I <sup>2</sup> = 10.4%         - MRC score (WMD = 4.47, 95% CI: 1.43, 7.52; p = 0.004),         I <sup>2</sup> = 10.4%         - Barthel Index score at hospital discharge (WMD =         21.44, 95% CI: 10.97, 31.91; p < .001)	1

ICU-AW = ICU-acquired weakness, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, n.s.= not significant, RCT = randomized controlled trial, RR = risk ratio, pts = patients, VAP = ventilator-associated pneumonia; WMD = weight mean difference

# Early mobilization showed a benefit in relation to ICU-AW, length of ICU and hospital stay, MRC score, Barthel Index, deep vein thrombosis and pressure sores.

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Reference, Study Type	Cases and (Partici Charact To	eristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
211 Liu 2019 (PMID: 31162197 DOI: 10.1097/CCM .000000000 003850) Specification of study: Retrospective before-after cohort study	391 pts Inclusion criter - admitted to 10 - 18 years or ol Exclusion criter - acute cardiov disease - acute cerebro disease - progressive ne disease - post cardiopu arrest syndrom - condition lim mobilization in unstable pelvic - discharged from within 48 hours Per Bi 187	CU der ria: ascular ovascular euromuscular lmonary ne iting cluding fractures om the ICU s		The Maebashi EM Protocol: progressive goal-directed EM program	Historical control with <b>routine</b> <b>care</b> , not well defined	Primary endpoint: - hospital mortality - total hospital costs Secondary outcomes: - % of pts who achieved each rehabilitation level - days from ICU admission to achievement of each rehabilitation level - adverse effects - duration of MV - ICU and hospital LOS - % of pts who ambulate at hospital discharge - discharge destination - functional independence measure value - SOFA Score and subscores at ICU admission, maximum during the ICU stay and at ICU discharge, the change between ICU admission and maximum, ICU admission and ICU discharge	Primary endpoints:- hospital mortality: was reduced in intervention group (adjusted hazard ratio, 0.25; 95% CI, 0.13– 0.49; $p < 0.01$ ), declined from 24% to 11%- mean hospital costs : (from \$29,220 to \$22,706), estimated effect of the intervention was \$–5,167 per patient (95% CI, 1,069–8,304; $p = 0.02$ )Secondary outcomes: Significant differences - intervention group: 78% of pts could get out of bed within 3 days (median, 2.0 d; IQR, 1.3–2.9 d) - length of MV decreased by 40%, and the ICU LOS decreased by 17% - hospital LOS reduced by 17% - SOFA score at ICU discharge significantly decreased after introduction of the protocol (3.0 vs 2.0; $p < 0.01$ )No significant difference between : - SOFA score and subscores at admission and at maximum - functional independence measure sum and motor values at hospital discharge improved	4

CI = confidence interval, EM = early mobilization, ICU = intensive care unit, IQR = interquartile range, LOS = length of stay, MV = mechanical ventilation, pts = patients, SOFA = sequential organ failure assessment

# This single-center historical quality comparison study shows that hospital mortality and total hospital costs are significantly decreased after the introduction of a progressive EM program in the ICU.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
212 Zayed 2020							
(PMID: 31160215	6 publications <sup>1-6</sup> 718 pts				Primary outcome: - MRC	No significant differences between groups in: - MRC, MD (95%CI): 0.45 (-2.89 – 3.80), p = 0.79	
DOI: 10.1016/j.aucc.201 9.04.003)	Inclusion criteria: - RCTs - ICU pts		Neuromuscular electrical stimulation	Usual care	Secondary outcomes: - ICU mortality	- ICU Mortality, RR: (95%Cl): 1.30 (0.95 – 1.78), p = 0.10 - ICU LOS, MD: (95%Cl): -3.06 (-9.79 – 3.68), p = 0.18	1
Specification of study:	$- \ge 18$ years of age				- ICU LOS - duration of MV	- duration of MV, MD: (95%Cl): -2.07 (-5.06 – 0.92), p = 0.37	
Systematic Review with Meta-Analysis							

ICU = intensive care unit, LOS = length of stay, MD = mean difference, MRC = medical research council, MV = mechanical ventilation, pts = patients, RCT = Randomized controlled trial

# Neuromuscular electrical stimulation had no effect on muscle strength, ICU mortality, ICU length of stay or duration of mechanical ventilation

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Reference, Study Type	(Partici Charact	d Controls ipant #, eristics) tal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
214 Nydahl 2019 (PMID: 31125163 DOI: 10.1111/nicc .12438) <b>Specification</b> of study: cluster- randomized pilot study	mobilization pr Exclusion crite - palliative stat - had an immo - mobilisation v documented	v and order for resent ria bility order	2 (interven tion group; lost to follow up)	period of usual care and a protocol for <b>early mobilisation</b> intervention in a stepwise manner, based on ICU mobility scale	Usual care	<ul> <li>Primary endpoint: <ul> <li>percentage of pts with at least one active out-of-bed mobilization, defined as ≥ level 3 on the ICU Mobility Scale</li> </ul> </li> <li>Secondary outcomes <ul> <li>presence/duration of MV</li> <li>delirium, ICU / hospital LOS</li> <li>adverse events</li> </ul> </li> <li>Power analysis: <ul> <li>using five ICUs and steps with 12 included pts per prevalence survey and per ICU</li> <li>(=360 pts overall), and with an assumed intra-class correlation coefficient 35 of 0.05, the pilot study would have a power of 50% to find significant results.</li> </ul> </li> </ul>	<ul> <li>Primary endpoint: <ul> <li>no significant difference</li> <li>in relation to percentage</li> <li>of out-of-bed mobilization</li> <li>(p = 0.106)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>no significant differences</li> <li>adherence to the</li> <li>protocol was &gt;90%</li> <li>unwanted safety events</li> <li>were rare</li> </ul> </li> </ul>	4

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, y = years

Implementation of a protocol for early mobilization seems to have no benefit in relation to percentage of out of bed mobilization.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, 0 To		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
215 Ferreira 2018 (PMID: 31090853 DOI: 10.5935/010 3- 507X.20190 017) <b>Specificatio</b> <b>n of study:</b> Systematic Review	<ul> <li>hospitalized in ICL</li> <li>underwent PT usin protocols (respirato electrophysical inte including light, sour electrical stimulatio</li> </ul>	e control, case es including ese & Spanish, 317 dies (cohort, cross- trol, case report, or rs Js on ECMO ng multimodal ory, motor, and/or erventions, nd, thermal, or on) during ECMO omparison uese and Spanish		Physical therapy during ECMO support	Usual care (no PT) during ECMO support	Primary endpoint: - safety of PT (evaluated according to the mortality rate, adverse events, oxygen perfusion characteristics, hemodynamic stability) Secondary outcomes: - the length of MV - length of ECMO support - ICU LOS - hospital LOS	<ul> <li>Primary outcome <ul> <li>8 studies provided data on the number of deaths, which ranged from 1-16</li> <li>mortality in patients: IG vs. CG (odds ratio, 0.19; 95% confidence interval, 0.04 - 0.98), (IG=1, CG=7)</li> </ul> </li> <li>Secondary outcome <ul> <li>length of MV:</li> <li>3 studies reported significant differences (IG vs. CG), length of MV in IG &gt; CG</li> <li>(Rehder et al.) mean MV times in IG= 1.75 and CG= 0.77 days</li> <li>(Munshi et al.)reported significant differences: IG vs. CG (median [interquartile range] of 3 [0.87 - 7.00] and 1.16 [0.33 - 4.00] days</li> <li>(Bain et al) IG= 12days (5 - 15) vs. CG= 1 (1 - 5) day</li> </ul> </li> <li>hospital LOS /ICU LOS: <ul> <li>(10 studies) IG=8 [6 - 22] vs. CG=45 [34 - 56] days</li> <li>(2 studies) PT reduced hospital LOS</li> <li>(Rehder et al.) mean total hospitalization time IG= 22 days (n = 10) and 60 days in the CG (n = 3), mean length of ICU stay : IG= 11 days , CG= 45 - (Keibun) mean total hospitalization time IG= 22 days (n = 10) and 60 days in the CG (n = 13), mean ICU stay IG= 14 days vs. CG= 42 days</li> </ul> </li> <li>length of ECMO support(in days): <ul> <li>(Bain et al.) IG= 12, CG=30</li> <li>(Rehder et al.) IG= 12, CG=30</li> <li>(Rehder et al.) IG= 8.75, CG= 2.17(mean)</li> <li>(8 studies) 5-125</li> </ul> </li> </ul>	1 → 5 (no RCTs, no meta- analysis)

CG = control group, ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit, IG = intervention group, LOS = length of stay, MV = mechanical ventilation, PT = physical therapy, pts = patients

This review demonstrated that physical therapy using respiratory techniques, early progressive mobilization (standing and ambulation), and functional electrical stimulation cycling is feasible and safe for patients on extracorporeal membrane oxygenation support regardless of the type of cannulation used.

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Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
217 McWilliams, 2014 (PMID: 25316527 DOI: 10.1016/j.jcrc.20 14.09.018) Specification of study: quality	582 pts Inclusion criteria: - invasively ventilated for Exclusion criteria: - significant neurologic i - orthopedic injury with mobilize - significant burn - poor preadmission mo reported by the pts fam	njury a contraindication to bility levels (<10 yards)		invasively ventilated for at least 5 days in the previous 12 months	ventilated for at least 5 days in the 12 months after the introduction of the rehabilitation team	Primary endpoints: - mobility level at ICU discharge (assessed via the Manchester Mobility Score) - mean ICU LOS - post-ICU LOS - ventilator days	Primary outcome - MMS on ICU discharge, median (IQR): Intervention(n=202) = 3 (2- 5), control group(n=225) = 5 (3-6), p=0.05 Significant differences between groups in: - ICU LOS (16.9 vs 14.4 days, p=0.007) - ventilator days (11.7 vs 9.3 days, P <0.05) - total hospital LOS (35.3 vs 30.1	4
improvement	Per Branch						days, p< 0.001)	
project	n=290					- in-hospital mortality	- in-hospital mortality (39% vs 28%, p<0.05)	

ICU = intensive care unit, IQR = interquartile range, LOS = length of stay, MMS= Manchester mobility score, pts= patients

The implementation of a new rehabilitation team with a focus on early and enhanced rehabilitation was associated with a significant reduction of mortality, ICU and hospital LOS and increase of mobility at discharge.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
218 Wollersheim 2019 (PMID: 31016887 DOI: 10.1002/jcsm .12428) <b>Specification</b> of study: randomized controlled trial	50 pts Inclusion criteria: - pts on MV ≥18 yea - sepsis related MOI sepsis-related orgar - assessment (SOFA the first 72 h after lo Exclusion criteria: - pre-existing neuro illness prohibiting ea - insulin-dependent prior treatment for longer than 7 da - body mass index > - not ambulating be - with a poor prograve - prone to die within Per Br 33	DS indicated by a n failure ) score ≥9 within CU admission muscular disease, arly mobilization diabetes mellitus, NS • 35 kg/m2 fore admission osis n the next hours		Muscle activating measures such as: <b>NMES and/or</b> <b>WBV</b> - in addition to <b>protocol-</b> <b>based</b> <b>physiotherapy</b>	Protocol- based physiotherapy	Derived endpoints: - muscle strength evaluated by MRC score and handgrip dynamometry on the 1 <sup>st</sup> day the pts became awake, at ICU discharge, at a 12 month in-hospital follow-up - FIM at ICU discharge and at a 12-month follow-up - 6 min walking test at the 12 month in-hospital follow-up up	Significant differences between groups in: - muscle strength from the 1 <sup>st</sup> day pts became sufficiently awake until ICU discharge (control group p=0.008, intervention group = 0.009) No significant differences between groups in: - MRC score, handgrip Strength, FIM score at ICU discharge - MRC score and function (minimal modified FIM) compared with common physiotherapeutic practice - 6 min walking test at 12 month follow up	2

FIM = Functional Independence Measurment, ICU = intensive care unit; MODS = multiple organ dysfunction syndrome, MRC = medical research council, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, WBV = whole-body vibration

In patients with sepsis at high risk for ICU-acquired weakness, muscle activating measures in addition to early protocol-based physiotherapy did not improve muscle strength or function at first awakening, ICU discharge, or 12-month follow-up.

Reference, Study Type	(Partici Charact	d Controls pant #, eristics) tal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
219 Hsieh 2019 (PMID: 30985390 DOI: 10.1097/CC M.0000000 00003765) <b>Specification</b> of study: Prospective cohort study	1.855 pts Inclusion c - on MV - ≥18 years - admitted Per B 1.036	5		<b>Full bundle ICU:</b> - Baseline: B - Period 1: A + D - Period 2: E + C	<b>Partial bundle ICU:</b> - Baseline: B - Period 1:A + D	Primary endpoint: -hospital LOS Secondary outcomes: - ICU-LOS - duration of MV Cost outcomes: - total hospital and ICU cost Clinical quality outcomes: - ICU restraint use, prevalence of ICU- acquired pressure ulcers	Significant differences between groups in: -implementation of the full (B-AD-EC) reduced hospital LOS (-7.8%, 95% CI -8.7% to -6.9%, p=0.006) - MV duration (-22.3%, 95% CI -22.5% to -22.0%, p <0.001) in full bundle - ICU LOS (-10.3%, 95% CI -15.6% to -4.7%, p=0.028) in full bundle - total ICU and hospital cost reduced by 24.2% (95% CI -41.4% to -2.0%, p=0.03) and 30.2% (95% -46.1% to -9.5%, p=0.007) - ICU-acquired pressure ulcers and physical restraint use decreased (period 1 vs 2: 39% vs 23% of pts; 30% vs 26% pts days, respectively, p<0.001 for both)	3

ABCDE-Bundle = awakening, breathing trials, coordination, delirium, early mobilization, CI = confidence interval, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients

The implementation of (E)arly Mobilization and (C)oordination in addition to spontaneous (B)reathing trials, (A)wakening and (D)elirium management can have a positive impact on hospital and ICU LOS, duration of MV and costs.

Reference, Study Type	(Participant #,	d Controls Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
222 Defosse 2019 (PMID: 30923850 DOI: 10.1007/s00 063-019- 0565-8) <b>Specification</b> of study: retrospective cohort study	D	2005 : Thorax ≥3) ted : days after injury al trauma center		CLRT	Conventional therapy	Retrospective – no determination of primary endpoint Derived endpoints, rates of: - organ and multi-organ dysfunction - incidence of sepsis - ICU and hospital LOS - duration of MV - ventilation-free days - discharge to home or rehabilitation facility - hospital mortality - duration of CLRT	Significant differences between groups:         - less secondary relocation in CLRT (%11.3;         17.6 p<0.016)	4

AIS = abbreviated injury scale, CLRT = continual-lateral rotation therapy, ICU= intensive care unit, LOS= length of stay, MV= mechanical ventilation

#### In thoracic trauma CLRT has no clinical benefit but but duration of ventilation and ICU length of stay) in a retrospective analysis.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
225 Jahani 2018 (PMID: 30894882 DOI: 10.25122/jml -2018-0028) <b>Specification</b> of study: single group clinical trail	58 pts in single group trial Inclusion criteria: <ul> <li>ARF</li> <li>18 – 60 y</li> <li>tracheal intubation &gt; 6h</li> <li>synchronized intermittent mechanical ventilation</li> <li>hemodynamically stable</li> <li>no pressure ulcers</li> <li>no ICP</li> </ul> Exclusion criteria: <ul> <li>HR &lt; 60 or &gt; 100</li> <li>blood pressure &gt; 140 or &lt; 60</li> <li>SpO<sub>2</sub> &lt; 80%</li> <li>ventricular tachycardia</li> <li>asystole</li> <li>ventricular fibrillation</li> <li>need for variation of ventilation mode</li> </ul>	4 (HR > 100, removal of MV equipment, RR = 32, hypotension)	<b>prone</b> <b>position</b> for 2h repeated for 3 days	<b>supine</b> <b>position</b> for 2h repeated for 3 days	<b>Outcome:</b> - Physiological signs after 1h and 2h - ABG at 2h	Significant differences: - SpO <sub>2</sub> : Day 1: PP: 93.76 $\pm$ 7.56 vs. SP: 95.46 $\pm$ 7.33; p< 0.05 Day 2: PP: 97.82 $\pm$ 7.49 vs. SP: 95.69 $\pm$ 7.48; p< 0.05 Day 3: PP: 99.45 $\pm$ 7.83 vs. SP: 97.73 $\pm$ 7.74; p < 0.05 - PaO <sub>2</sub> : Day 1: PP: 92.24 $\pm$ 2.008 vs. 93.74 $\pm$ 1.82; p < 0.05 Day 2: PP 95.40 $\pm$ 1.23 vs. SP: 93.92 $\pm$ 1.46; p < 0.05 Day 3: PP: 96.72 $\pm$ 1.12 vs. 95.27 $\pm$ 1.17; p < 0.05 <b>No Significant differences:</b> - Systolic blood pressure - Diastolic blood pressure - Respiratory rate	4

ABG = arterial blood gas, ARF = acute respiratory failure, HR = heart rate, ICP = intracranial pressure, MV = mechanical ventilation, PP = prone positioning, SP = supine positioning

Prone positioning improved SpO<sub>2</sub> and PaO<sub>2</sub> on day 2 and 3 compared to supine positioning.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
226 Bonizzoli 2019 (PMID: 30871301 DOI: 10.23736/S03 75- 9393.19.1328	n = 101 Inclusion criteria: - adults with refractor ECMO support - admitted to an ICU referral center - submitted to physi - 2016 Per B	of a tertiary ECMO otherapy from 2009		Early PT		Primary endpoint: - ICU mortality Secondary outcomes: - LOS	Primary outcome:ICU mortality (early physiotherapy (within the first week) vs. delayed physiotherapy) 12 vs 14 (p>0.05)Multivariable logistic regression analysis: BMI was an independent predictor of in- ICU mortality (OR 0.899, 95% CI 0.823 – 0.981, p = 0.017)Secondary outcomes: Time from ECMO start to first physiotherapy session showed a significant	4→5
9393.19.1328 7-7) Specification of study: Retrospective observational study	n = 33 Time from ECMO start to first physiotherapy session within the first week	Time from ECMOTime from ECMOstart to firststart to firstphysiotherapyphysiotherapyession within thesession after the				- LOS - duration of MV	physiotherapy session showed a significant relation with LOS: 12 (7.25-21) days vs 25 (18.75-36.25) (r <sup>2</sup> = 0.48, p < 0.001) Duration of MV: 11 (5-17.75) vs 23 (13.75-33.25) (P=0.001)	

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, SAPS II = simplified acute physiology score, T = physiotherapy, vvECMO = veno-venous extracorperal membrane oxygenation

In patients with VV-ECMO support, physiotherapy is feasible and safe and the early physiotherapy, initiated within the first week from ECMO start, is associated with shorter duration of ECMO support and ICU length of stay.

Reference <i>,</i> Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
227 Chiarici 2019 (PMID: 30796918 DOI: 10.1016/j.apmr .2019.01.015) <b>Specification</b> of study: Observational prospective cohort study, with retrospective controls	275 pts Inclusion criteria: - admitted to ICU Exclusion criteria: - died/transferred within 24 hours of admission Per Branch 152 133		Rehabilitation care pathway based on: - interdisciplinary teamwork - early customized and goal-oriented rehabilitation - daily functional monitoring and treatment revision - agreed discharge policy - continuity of care - treatment was customized to pts' clinical condition in terms of training content and duration	Usual care	Primary endpoint: - ICU LOS - proportion of ventilator-free days out of the total ICU stay Secondary outcomes: - feasibility - safety Power analysis: the number of pts who should be included is 126 for each group (with alpha error <0.05 and beta error <0.10	<ul> <li>Significant differences between groups in:</li> <li>proportion of ventilator free days: increased from 30% to 48% (p&lt;0.0006) in the total sample and from 30% to 62% (p&lt;0.0001) in those who underwent rehabilitation</li> <li>ICU LOS in postoperative subgroups, decrease from 22.9±12.9 to 7.0 ± 7.9 (p&lt;0.0001) in retrospective group and from 55.3±15.4 to 21.2±16.6 (p=0.01) in prospective group</li> <li>No significant differences between groups in:</li> <li>adverse effects</li> <li>ICU LOS, comparison of the total retrospective and prospective cohorts(p=0.089)</li> <li>Skewed evidence: The rehabilitation team assessment was performed in 100% of cases in the prospective group p&lt;0.0001)</li> </ul>	4

ICU = intensive care unit, LOS = length of stay, pts = patients

An early interdisciplinary rehabilitation in the ICU reduces the hospital LOS and increases ventilator-free time with greater benefits for postoperative patients.

Reference, Study Type	(Partici Charact	l Controls pant #, eristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
228 Chou 2018 (PMID: 30789023 DOI: 10.1177/147 99731188203 10) <b>Specification</b> of study: Retrospective case control study	Per B	nitted at ICU nvasive MV racheal tube		<b>Early rehabilitation:</b> - within 72 hours of MV in hemodynamically and respiratory stable pts - provided twice daily, 5 days per week.	Matched pts with <b>no early</b> <b>rehabilitation</b>	<b>Primary endpoints:</b> - duration of MV - ICU and hospital LOS - medical costs	Primary endpoint: - MV duration (hours): intervention = 137.3 ± 136.9, control = 160.1 ± 125.7; p= 0.396 - ICU stays (days): intervention= 5.8 ± 6.1, control = 9.2 ± 8.3, p= 0.033 - hospital LOS (days): intervention= 17.9 ± 14.6, control= 25.4 ± 24.0; p= 0.095 - medical costs (x \$10.000): intervention= 15.2 ± 13.6, control = 22.9 ± 21.7; p=0.058	4

COPD = chronic obstructive lung disease, ER = early rehabilitation, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients

#### Early rehabilitation for patients in the ICU with COPD with acute respiratory failure shortened the duration of their MV.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
234 Trethewey 2019 PMID: 30673625 https://doi. org/10.101 6/j.jcrc.201 9.01.008 Specificatio n of study: Systematic review	22 RCTs (n = 2792 pts) <sup>1-22</sup> Inclusion criteria: -RCTs investigating interventions to preserve muscle mass and/or function in critically ill patients -pts. admitted to a HDU or ICU for level 2 or level 3 care		improving or maintaining muscle mass/size and/or muscle function (strength or performanc e) Subgroups: 1. NMES 2. Exercise- based 3. nutrition- based 4. combined	usual care or placebo /sham interven tion	-ICU/hospital	<ul> <li>Primary Endpoint:         <ul> <li>measure of muscle</li> <li>mass/size and muscle function</li> <li>NMES: MRC-Score, HGS, Quadriceps MLT, Leg and thigh circumference, ankle joint movement, leg or arm circumference, bicep thickness, quadriceps muscle fibre CSA; Quadriceps CSD, quadriceps muscle volume</li> <li>1 study: greater preservation of muscle strength (MRC-Score) (median [range]: 58points [33-60 points] vs. 52 points [2-60 points], p=0.04)</li> <li>EB: no study assessed muscle mass/size; 6MWT; incremental shuttle walk Test; quadriceps force; Functional Independence Measure; maximum walking distance; IMS Scale; PFIT; Functional Status Score in ICU test; SPPB, HGS</li> <li>1 study: daily cycle ergometer sessions until ICU discharge had greater 6MWT (median [range]: 196m [126-329m] vs.143m [37–226m], p&lt;0.05) and improved self-reported physical performance (median [range]: 21 points [18–23 points] vs. 15 points [14–23 points], p&lt;0.01)</li> <li>1 study: daily physical and occupational therapy greater return to independent functional status (number [%]: 29 [59%] vs. 19 [35%], p=0·02), greater maximum walking distance at hospital discharge (median [range]: 33·4m [0–91·4m] vs. 0m [0–30·4m], p=0·004)</li> <li>NB: HGS, femoral volume, FEV1; FVC; maximal inspiratory pressure, Mid-arm muscle circumference; muscle wasting and fat loss (subjective)</li> <li>1 study: Greater impairment of post-op FEV1 and FVC in intervention group. (no p-value)</li> <li>1 study: Increased return to independent functional status, maximum walking distance (no p value)</li> <li>1 study: Faster initial rate of improvement ti nuddriceps force at hospital discharge in the intervention group (no p value)</li> <li>1 study: NMES and early, targeted physical rehabilitation improvement in HRQOL in the domains of 'physical role' (mean score ±5D: 61.4 ±43.8 vs. 17.1 ±34.4, p=0.005) measured at</li></ul></li></ul>	1 → 2 (no meta- analysis)

Secondary Endpoints:
-ICU/hospital LOS
<ul> <li>NMES: no difference mentioned</li> </ul>
<ul> <li>EB: 1 study 2x daily intensive physical therapy resulted in shorter ICU LOS (no p-</li> </ul>
value)
<ul> <li>NB: no difference mentioned</li> </ul>
<ul> <li>CINT: 1 study: Shorter ICU LOS in the exercise + placebo group (no p-value)</li> </ul>
-days with MV
<ul> <li>NMES: 1 study shorter duration of weaning from MV (median [range]: 1 day [0-16 days] vs. 4 days [0-44 days], p=0.003) and a shorter time off MV (median [range]: 4 days [0-16 days] vs. 6 days [0-41 days], p=0.003)</li> <li>EB: 1 study: daily physical and occupational therapy greater number of ventilator-</li> </ul>
free days (median [range]: 23·5 days [7·4–25·6 days] vs. 21·1 days [0·0–23·8 days], p=0·05)
<ul> <li>NB: 1 study: early parenteral nutrition (starting day 1 of ICU admission) continued until ICU discharge compared with usual care resulted in a shorter duration of invasive mechanical ventilation (number of days, adjusted for duration of ICU stay: 7.26 vs. 7.73 days per 10 patient x ICU days, p=0.01)</li> <li>CINT: no difference mentioned</li> </ul>
-rate of hospital readmission
<ul> <li>NMES: no difference mentioned</li> </ul>
<ul> <li>EB: no difference mentioned</li> </ul>
<ul> <li>NB: no difference mentioned</li> </ul>
<ul> <li>CINT: no difference mentioned</li> </ul>
-mortality
<ul> <li>NMES: no difference mentioned</li> </ul>
• EB: no difference mentioned
<ul> <li>NB: no difference mentioned</li> </ul>
<ul> <li>CINT: no difference mentioned</li> </ul>

RCT=randomized controlled trial; pts. =patients; HDU=high dependency unit; ICU=intensive care unit; LOS=length of stay; MV=mechanical ventilation; MRC=Medical Research Council; MLT=muscle layer thickness; HGS=hand grip strength; 6MWT=6-minute walking test; TUAG= timed up-and-go test; HRQoL= health related quality of life; EB=exercise-based; SPPB=short physical performance battery; NB=nutrition-based; CINT=combined intervention; ACIF= acute care index of function; PFIT=physical function ICU test; CSA= cross sectional area; CSD= cross sectional diameter; IMS= ICU Mobility Scale

NMES and exercise-based interventions may preserve muscle mass and function in patients with critical illness, but there is a lack of consistency seen in the effects of these interventions.

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200 pts on MV       Primary outcome       Primary outcome         Inclusion criteria:       - ≤ 18 years       - functional       - immediate postrandomization         - MV < 48 h and expected to require MV for > 24       h at the time of screening       - functional independence at hospital       GCS had no effect on the         236 Schaller       - functional independent at baseline with a	
2019       -functional independent at baseline with a Barthel Index Score 270 at 2 weeks before admission to the surgical ICU 30666366       Secondary outcome admission to the surgical ICU admission to the hospital > 5 days before screening       Inter- admission to the hospital > 5 days before screening       Inter- vention: 7       SOMS- guided mobility       Standard treatment with a facilitator       Standard for Stady:       - average achieved mobility level during the interaction GCS × intervention)       - EM significantly increased the functional independence at hospital discharge hospital discharge         001: 34-019- 05528-x)       - motor component of the immediate post-injury 34-019- 05528-x)       Inter- vention: 7       Standard freatment mortality of > 50%       Standard freatment mortality of > 50%       Standard independence at hospital discharge       Hospital discharge hospital discharge       Hospital discharge	3

EM = early goal directed mobilization, GCS= Glasgow coma scale, ICU = intensive care unit, ICP = intracranial pressure, MV= mechanical ventilation, SOMS = surgical optimal mobilization score

Early, goal-directed mobilization in patients with an impaired initial conscious state (GCS≤8) is not harmful but effective.

Reference, Study Type		es and Cont int #, Chara Total		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
237 Young 2019 (PMID: 30659467 DOI: 10.1007/s120 28-019-00670- 2) <b>Specification</b> of study: prospective observational cohort study with historical control	the Neuro quaternar center fro - patients perimeser for whom hospice ca were not i <b>Phase 1 a</b> prospectiv	cephalic SA comfort me re were init ncluded <b>nd phase 2</b> : rely enrollec exclusion cr	medical 014 H or those asures or iated	not reported	<b>Phase I:</b> use of a PT/OT- driven protocol. Mobilization during formal PT/OT sessions with continuous presence of both the therapist and the bedside nurse <b>Phase II:</b> nurse-driven protocol	Phase 0: retrospectiv ely enrolled control either Phase 0 or Phase 1 depending on analysis	Primary endpoint: - frequency of patient mobilization Secondary outcomes - ICU and hospital length of stay - rate of tracheostomy and ventriculoperitoneal shunt placement - discharge disposition - ventilator days - Safety outcomes: elevation of ICP, acute onset of headache during mobilization, and acute focal/worsening of neurologic deficits No power analysis was conducted	<ul> <li>Primary results: <ul> <li>Phase I (n=24), first mobilization occurred 14 days earlier (hospital day 6 versus hospital day 20; p &lt; 0.0001)</li> <li>Phase II mobilization occurred on average 1 day earlier than with the therapy-driven protocol (p=0.099).</li> </ul> </li> <li>Secondary results concerning safety: <ul> <li>four sessions in Phase I were aborted mid-session due to pain, increased ICP, and hypotension. In Phase II, one session was stopped mid-session due to elevated ICP.</li> <li>no falls, incidental medical device dislodgement, acute hypoxia, new onset arrhythmias, prolonged elevated ICP, or neurologic changes occurred in association with early mobilization.</li> </ul> </li> <li>No significant differences in secondary outcomes (Table 2)</li> </ul>	4

ICP = intracranical pressure, OT = occupational therapy, PT = physical therapie, SAH = subarachnoid haemorrhage

Nurse-driven mobilization for patients with EVDs is safe, feasible, and leads to more frequent ambulation compared to a therapy-driven protocol. Nurse-driven mobilization may be associated with improved discharge disposition, although exact causation cannot be determined by these data.

Reference, Study Type		and Controls #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
238 Ragland 2019 (PMID: 30642773 DOI: 10.1016/j.iccn .2018.12.005) Specification of study: Retrospective before-after	failure with IHD, E Exclusion criteria: - in process of wit - not passing the s - ordered transfer - RRT patients afte evaluation remain than a week	DVVH, or CRRT DVVH, or CRRT hdrawing care safety screening out of ICU er first mobility hing on ICU for longer		<b>Mobility plan</b> following introduction of a stepwise <b>mobility</b> <b>protocol</b>	before implement ation of <b>mobility</b> <b>protocol</b>	Primary outcome: - compliance to the mobility plan Secondary outcomes: - safety/adverse advents	Primary outcome: compliance to mobility before vs after introduction of the protocol: 12.5% vs 62.5% (overall increase of 400%) Secondary outcome: adverse events: no adverse events during the project	4
cohort study	31	Post protocol 25						

CRRT = continuous renal replacement therapy, DVVH = daily venonenous filtration, ICU = intensive care unit, IHD = intermittent heamodialysis, pts = patients, RRT = renal replacement therapy

The use of a step-wise mobility protocol was an effective and safe strategy to increase mobility in the renal replacement therapy patient population.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evide nce Grade
242 Yatabe 2018 PMID: 30541003 https://doi.org/10 1159/000495213 Specification of study: A Multicenter Observational Study	13 hospitals in Japan (10 university hospitals and 3 public hospitals) between April 2015 and March 2016 -> 389 pts. Inclusion criteria: -MV for at least 24 h -in the ICU for >72 h Exclusion criteria: -aged <20 years -on their second or subsequent readmission to the ICU during the study period -refused the use of their data 223 GG: 105 PG: 118	n=107 (ICU < 7days)	No intervention (observational study) <u>Divided for</u> <u>analysis of</u> <u>secondary</u> <u>endpoint by</u> <u>physical status:</u> GG: more than end sitting. PG: bed rest and sitting.	/	Sample Size calculation: - minimum of 240 pts., because number of potential factors that affected physical status=10 → 360 pts., predicted that two thirds of all pts. remained in the ICU for ≥7 day Primary Endpoint: - calorie and protein intake in the ICU on days 3 and 7, and at ICU discharge Secondary Endpoints: - physical status at ICU discharge in patients who remained in the ICU for ≥7 days	Primary Endpoint: -Day 3, 44% pts. received EN, 86% PN and median amount of protein intake via EN and PN: 0.2 (0–0.5) g/kg/day -Day 7, 66% pts. received EN, 10% PN and median amount of protein intake via EN and PN: 0.4 (0.1–0.8) g/kg/day -ICU discharge, median amount of protein intake via EN and PN: 0.3 (0–0.7) g/kg/day Secondary Endpoint: -CIN on day 3 in the PG higher than in GG (10.1 [5.8, 16.2] vs. 5.2 [1.9, 12.4] kcal/kg/day, p < 0.001). - pts. received higher rehabilitation in the GG than in the PG (92 vs. 63%, p < 0.001) -orally fed on day 7 and at ICU discharge in GG higher than in PG (21%, 6%; p = 0.001 and 42%, 16%; p < 0.0001, respectively) multivariate analysis: - CIN (day 3) and rehabilitation in ICU, use of ventilator at ICU discharge as independent factors that affect physical status (OR 1.19; 95% CI 1.05-1.34; p = 0.005 and OR 0.07; 95% CI 0.01-0.34; p = 0.001 and OR 20.4; 95% CI 4.36–95.2; p < 0.001, respectively); -initiation of rehabilitation during ICU stay and oral intake at ICU discharge, independent factors affecting physical status (OR 0.07; 95% CI 0.02–0.29; p < 0.0001 and OR 0.20; 95% CI 0.06–0.74; p = 0.02, respectively)	

Pts.=patients; MV=mechanical ventilation; ICU=Intensive Care Unit; GG=Good Group; PG=Poor group; EN=enteral nutrition; PN=parenteral nutrition; CIN=caloric intake; CI= Confidence interval

Critically ill patients might benefit from low caloric intake (less than 10 kcal/kg/day) until day 3 and rehabilitation during ICU stay.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total			Intervention	Control	Optimal Population	Primary Results	Evidence Grade
244 Chohan 2018	was carried out in an hospital in an urban Inclusion criteria: - responsive to verba commands	al stimulation and obeying				No sample size calculation	<b>Results:</b> - reliability of 87% (median) was achieved	
PMID: 30515467 https://doi.org /10.1136/bmjo q-2018- 000339	<ul> <li>PEEP &lt; 8 and FiO2 &lt;50% an CV stable</li> <li>Vasopressor/Inotrope Infusions have not increased in the last 2 hours</li> <li>no active volume resuscitation</li> <li>controlled arrhythmias</li> <li>no active myocardial ischemia</li> </ul> Exclusion criteria:			Achieve 95% reliability with a standardized mobilization process.	No population	(retrospective study) Endpoints: - Reliability - Delirium Rates -Length of stay and adverse events	<ul> <li>PDSA (Plan, Do, Study, Act) cycles allowed development of the process and achieved a median of 87% reliability</li> <li>Delirium rates fell from 54,1% to 28,8%</li> <li>no change in average</li> </ul>	4 → 5
Specification of study: Retrospective study	<ul> <li>bony/soft tissue injury requiring immobilization</li> <li>abdominal compartment syndrome</li> <li>Vac dressing or Sengstaken tube</li> <li>BMI &gt; 45</li> <li>Difficult Airways</li> </ul> Per Branch						length of stay and adverse events	
	Not specified	Not specified						

AE = adverse events ; BMI = body mass index ; CAM-ICU = confusion assessment method for the ICU ; CV = cardiovascular ; ICU = intensive care unit ; LOS = length of stay ; PDSA = Plan, Do, Study, Act

# Team learning from Plan, Do, Study, Act (PDSA)cycles, as well as feedback from both staff and patients, allowed us to develop the process and achieve a median 87% reliability.

No detailed assessment was carried out because higher-quality evidence is available on this topic

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
nal.pone.020 7428)	115 pts Inclusion criteri - adults 18 years - expected stay ≥72h - had been inde before the onse illness Exclusion criteri - previous musc - contraindicatio - enrolment in a intervention stu - palliative care - admission diag excluding possifi walking at hosp - did not unders or French Per Br 58	s on MV for pendent it of critical ia: le weakness ons to cycling inother idy gnosis pility of ital discharge itand German	Total 9 pts: intervention: 4 lost to follow up control: 5 lost to follow-up	Early endurance (motor-assisted bed-cycle) and resistance training combined with mobilization	Standard physiotherapy including early mobilization	Primary endpoint: - functional capacity (6- MWD) Secondary outcome: - FIM and muscle strength at ICU discharge Sample size determination was based on the 6MWD to show a difference of 54m and a mean walking distance of 301m (SD 81). A statistical power of 80% and an α-level of 0.05 required a sample size of 72 pts in total(36 per group).	Primary endpoints: - 6-MWD (experimental 123m (IQR 25–280) vs control 100m (IQR 0–300); p = 0.542 - or functional independence (98 (IQR 66–119) vs 98 (IQR 18–115); p = 0.308 Secondary endpoints: - no differences found, except a trend towards improved mental health in the experimental group after 6 months (84 (IQR 68–88) vs 70 (IQR 64–76); p = 0.023 - adverse events: rare (0.6%) and without consequences	2

FIM = functional independence measurement, ICU = intensive care unit, IQR = interquartile range, MV= mechanical ventilation, pts = patients, SD = standard deviation, 6-MWD = 6-minute walking distance

Early endurance and resistance training in mechanically ventilated, intensive care patients does not improve functional capacity or independence at hospital discharge compared to early standard physiotherapy but may improve mental health 6-months after critical care discharge.

11     Not     conventional     Secondary Endpoints:       11     Exclusion criteria:     specified     physical       Secondary Endpoints:     - incidence of histologically diagnosed     (high riteria)	Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
38 42	247 Koutsioumpa 2018 ( <u>https://doi.org/1</u> 0.4037/ajcc20183 <u>11</u> ) <b>Specification of</b> <b>study:</b> prospective, open-	Inclusion criteria: -aged 18 years or older -ICU stay of 96h or more -MV for 96h or more Exclusion criteria: -known vasculopathies if these conditions had induced myopathy Per Branch		conventional physical therapy +	conventional physical	calculation specified <b>Primary Endpoint:</b> - incidence of histologically diagnosed myopathy on the 14th ICU day <b>Secondary Endpoints:</b> - incidence of histologically diagnosed myopathy on the 4th ICU day -MRC-Score on the 14 <sup>th</sup> ICU day -ICU LOS	<ul> <li>- incidence of histologically diagnosed myopathy on the 14th ICU day (P=0.3)</li> <li>Secondary Endpoints: <ul> <li>- incidence of histologically diagnosed myopathy on the 4th ICU day (P=0.6)</li> <li>-MRC-Score on the 14<sup>th</sup> ICU day (P&lt;0.001)</li> <li>-ICU LOS (P=0.01)</li> </ul> </li> </ul>	2 → 3 (high risk of bias)

Pts.=patients; ICU=Intensive Care Unit; MV=Mechanical Ventilation; TENMS=transcutaneous electrical neuromuscular stimulation; MRC=Medical Research Council Score; LOS=Length of stay; n.s.=not significant

TENMS had no significant impact on myopathy in the critically ill patients in this study.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
249 Yataco 2018 PMID: 30357597 DOI: 10.1007/s1 2028-018- 0632-7 <b>Specificatio</b> <b>n of study:</b> Retrospecti ve study	NSICU at Mayo Clinic in Jacksonville, Florida between 1. January 2013 and May 16. 2016. →153 pts. Inclusion criteria: - all patients in NSICU who underwent placement of an EVD - hemodynamically and medically/neurosurgically stable Exclusion criteria: - femoral sheath or recent removal of femoral vascular sheath - hemodynamic instability, active bleeding or angioedema - heart rate greater than 120 beats per minute - ICP higher than 25 mm Hg or as deemed unstable by the treating NSICU/neurosurgery team - a cerebral perfusion pressure lower than 50 mm Hg - resting heart rate of 50% age-predicted maximum or less, - systolic blood pressure lower than 90 or higher than 180, diastolic blood pressure higher than 105 - peripheral oxygen saturation of 90% or less - marked diaphoresis, facial pallor, intense anxious or painful facial expression (especially in patients who were aphasic) - active bleeding from lines, catheters, or wounds		patients received EVD	Populati on was its own control	No sample size calculation (retrospective study) Endpoints: - principal diagnosis - survival to discharge - LOS - discharge disposition - mobilized or reason not mobilized - completed mobilization activities - time from EVD placement to first mobilization - degree of required mobility assistance - AE with mobilization	Results: - SAH was the most common diagnosis (61.4%) - 127 survived to discharge - median LOS was 18 days (range, 2-106) - 117 patients were mobilized and median time from EVD placement to initial mobilization was 38h (range 4-537) - mean time from EVD placement to initial mobilization was 83h - 36 patients not mobilized: most common reason was decreased patient responsiveness (23 – 63%) - The highest level of patient mobility activity achieved by the group was ambulation for 51 patients (43.6%), followed by transferring from supine to sitting for 36 patients (30.8%), from bed to a chair for 20 patients (17.1%), and from sitting to standing for 10 patients (8.5%). The peak distance mobilized during ambulation was 120 feet (range, 1–1080) - only 6.9% of patients experienced any sort of AE	4
	153	-					

AE = adverse events; EVD = external ventricular drain; ICP = intracranial pressure; LOS = length of stay; NSICU = Neurosurgical intensive care unit; LOS=length of stay;

Reference, Study Type	Cases and (Participant #, C Tota	haracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
251 Dos Santos 2020 (PMID: 30321084 DOI: 10.1080/09593 985.2018.14903 63) <b>Specification of</b> <b>study:</b> RCT	51 pts Inclusion criteria: - ≥ 18 years of age 18 - MV < 72 h - no known neuromus Exclusion criteria: - cardiopulmonary arr - end stage malignanc - Increased ICP - obstacles that did no NMES - prolonged MV (> 21 Per Bra Ex: 13 NMES: 11 NMES+Ex: 12	ecular disease est y ot allow the use of days)	N=18 (35%) Died	NMES: 2x daily for 55 min Exercise (Ex): structured assisted/active exercise program	Usual care	Sample size calculation: calculated (G*power version 3.1.4, Franz, Universitat Kiel, Germany) based on the first RCT about early physical therapy in ICU patients (Schweickert et al. 2009), resulting in a total sample size of 52 patients ( $\alpha = 0.05$ , $\beta =$ 0.80) Primary endpoints: - duration of MV Secondary endpoints: -duration of sedation -ICU LOS	Primary endpoints: - overall comparison, duration on MV was significantly shorter ( $p = 0.007$ ) in the NMES + EX group ( $5.7 \pm 1.1$ days) and NMES group ( $9.0 \pm$ 7.0 days) in comparison to CG ( $14.8 \pm 5.4$ days) Secondary endpoints: - duration of sedation, statistical significance only survival's analysis in comparisons among NMES + EX ( $0.6 \pm 1.0$ ) and EX ( $0.4 \pm 0.5$ ) groups with CG ( $5.83 \pm 5.1$ ) -ICU LOS mean Standard deviation: NMES+EX:11.4 ( $9.8$ ), EX:10.3( $8.7$ ), NMES: 13.8 ( $6.9$ ) and CG: 14.2 ( $9.7$ ) ( $p=0.03$ )	2 → 3 (high risk of bias)

ICP = intracranial pressure, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation

Neuromuscular electrical stimulation reduced duration of mechanical ventilation. The impact on ICU mortality and ICU length of stay is not clear.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
252 Kang 2018 PMID: 30300863 https://doi.org /10.1016/j.jcrc. 2018.09.032 Specification of study: systematic review and meta-analysis	35 publications from 2007 - 2016 (11 RCTs, 20 cohort studies, one CBA study and one CCT with n = 25283 pts) <sup>1-35</sup> (one article divided in two substudies) <sup>19,20</sup> Inclusion criteria: - age ≥ 18 years - ICU treatment - non- pharmacological intervention for delirium prevention compared to usual care and assessed for occurrence or duration of delirium - English language - published in a journal between 2007 and 2016 Exclusion criteria: - case reports - protocol studies - non-accessible studies		Non- pharmacological interventions for delirium prevention: - multicomponent intervention - physical environment intervention - daily interruption of sedation intervention	Standard of Care	Endpoints: - occurrence of delirium - duration of delirium - ICU LOS - ICU mortality	<ul> <li>15 articles included in meta-analysis.</li> <li>5ignificant differences between groups:         <ul> <li>total-effect-size-analysis:</li> <li>a. occurrence of delirium is reduced by non-pharmacological interventions             (OR 0.65, 95% CI 0.50 – 0.86, p = 0.002).</li> <li>b. duration of delirium is reduced by non-pharmacological interventions             (OR 0.41, 95% CI 0.10 – 0.94, p = 0.039).</li> <li>effect-size-per-intervention-analysis: effects of multicomponent intervention on delirium occurrence were significant             (OR 0.48, 95% CI 0.35 – 0.65, p &lt; 0.002).</li> </ul> </li> <li>essnitutiva manksis: effect size of the included studies investigating duration of delirium occurrence were significant         (OR 0.48, 95% CI 0.35 – 0.65, p &lt; 0.002).</li> <li>essnitutiva manksis: effect size of the included studies investigating duration of delirium moccurrence were significant         (OR 0.47, 95% CI 0.55 – 0.93) &gt; 10% and therefore with possible impact on validity of the findings)</li> <li>Non-significant differences between groups:         <ul> <li>total-effect-size-analysis:</li>             a. (CU LOS (OR 0.85, 95% CI 0.67 – 1.09, p = 0.194)</ul></li>             b. (CU mortality (OR 0.92, 95% CI 0.83 – 1.01, p = 0.138)             effects are unitcomponent intervention on duration of delirium (OR 0.20, 95% CI 0.04 – 1.14, p = 0.071) <li>effects of multicomponent intervention on delirium occurrence             (OR 0.77, 95% CI 0.68 – 1.16, p = 0.38)</li> </ul> <li>effect size of dali interruption of sedation intervention on delirium occurrence             (OR 0.89, 95% CI 0.68 – 1.16, p = 0.38)</li> <li>subgroup analysis:             <ul> <li>effect sizes of multicomponent and physical environment interventions were not different between studies using             delirium occurrence as the outcome variable (OR 0.45 vs. 0.83, p = 0.418)&lt;</li></ul></li>	1

Pts = patients, RCT = randomized controlled trials, CBA = controlled before and after, CCT = controlled clinical trial, ICU = intensive care unit, LOS = length of stay, SCCM = Society of Critical Care, CAM-ICU = Confusion Assessment Method for the Intensive Care Unit, ICDSC = Intensive care Delirium Screening Checklist

Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
256 Barbalho 2019 (PMID: 30246555 DOI: 10.1177/0269 215518801440 ) <b>Specification</b> of study: a within- patient randomized trial	partial pressure of o inspired oxygen (Pa oxygen saturation < systolic blood press arterial blood press arterial blood press diastolic 50–120 mr respiratory rate of u minute, absence of electrocardiogram a <b>Exclusion criteria:</b> - not meeting inclus - declined to partici - death	from September to assive mobilization ollowing parameters: oxygen/fraction of O2 / FiO2) > 300, 140 bpm, ure 90–180 mmHg, ure <60 bpm, ure (PaO2) >90%, nHg, up to 30 breaths per uncontrolled arrhythmias	n=14 excluded (11 not meeting inclusion criteria, 3 death)	Experimental blood flow restriction in one limb	Limb with no blood flow restriction	Primary endpoints: - thigh muscle thickness and circumference	Primary outcomes - muscle thickness: within-subjects analysis showed significant differences (F = 334.6, $\eta^2 = 0.90, p < 0.001$ ) between-subjects analysis showed no significant difference (F = 0.22, $\eta^2 = 0.01,$ P = 0.64) - thigh circumference: significant differences in within-subject analysis (F = 257.81, $\eta^2 = 0.87, p < 0.001$ ) between-subjects analysis showed no significant difference (F = 0.23, $\eta^2 = 0.01,$ P = 0.63)	4

ICU = intensive care unit

The use of blood flow restriction did not present adverse effects and seems to be a valid strategy to reduce the magnitude of the rate of muscle wasting that occurs in intensive care unit patients.

Reference, Study Type	(Participant #, (	l Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
258 Whelan 2018	26 patients							
(PMID:	- adult pts admitted	into trauma ICU						
30214949	- surgical pts admitte			<b>CPAx tool</b> as part of physiotherapy patient		Primary	Primary endpoint:	
DOI:	Non-inclusion criter	ia:		assessment	Historical control	endpoint:	- no significant difference	
10.4102/sajp.v	- bedbound prior to	admission		- CPAx tool assesses pts	group: part of standard	ICU LOS	in median ICU LOS in days	4
74i1.450)	- traumatic brain injure received for other ne			functional ability - rehabilitation goals	, physiotherapy		between groups (intervention 3.7 [2.3–5.4];	
Specification	conditions			were modified according	practice		control 2.7 [IQR 1.1–5.2]; p	
of study:	- placed on bedrest in ICU as a result of			to their CPAx score			= 0.27).	
historically	complex orthopedic	or spinal injuries						
controlled	Per B	ranch						
interventional trial	26	26						

CPAx = Chelsea critical care physical assessment, ICU = intensive care unit, LOS = length of stay

Problem-oriented patient rehabilitation informed by the CPAx tool resulted in improvement of physical function but did not reduce ICU or hospital LOS.

Reference Study Type		ases and Con nt #, Charact Total		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
264 Leite 2018 (PMID: 30123586 DOI: 10.1155/201 8/4298583) <b>Specification</b> of study: Pilot study	<ul> <li>pregnan</li> <li>BMI &gt; 35</li> <li>neuromu</li> <li>brain des</li> <li>peripher</li> <li>bone fra</li> <li>use of in</li> <li>fixators</li> <li>skin lesio</li> <li>end-stag</li> <li>pacemal</li> <li>spinal in</li> </ul>	criteria: namic instabi cy is kg/m <sup>2</sup> uscular diseas ath al vascular di ctures ternal or exter ons e cancer ser jurie to receive Mi	se sease ernal RC score	12: 7 QG (4 death, 3 cognitive state), 5 DG (2 death, 3 cognitive state)	DG: conventional physical therapy 1x/d + 1x/d session of diaphragm NMES (Neurodyn Multicorrentes <sup>™</sup> ) QG: conventional physical therapy 1x/d + 1x/d quadriceps NMES	Conventional physical therapy 2x/d	Outcomes: - MIP at discharge - MRC at discharge - MV time - Hospital LOS - FSS-ICU	Outcomes: - MIP (mmHg): QG: $-40.4 \pm 8.71$ vs. DG: $-37.9 \pm 10.31$ vs. CG: $-25.9 \pm 9.59$ ; p= 0.00003 - MRC: QG: $48.2 \pm 11.48$ vs. DG $41.8 \pm 11.14$ vs. CG: $43.4 \pm 6.45$ ; n.s. - MV time: QG: $23.3 \pm 10.61$ vs. DG: $27.5 \pm 12.16$ vs. CG: $15.8 \pm 5.75$ ; p=0.0001 - Hospital LOS: QG: $18.2 \pm 11.28$ vs. DG: $29.3 \pm 13.59$ vs. CG: $25.4 \pm 12.04$ ; p= 0.0031 - FSS-ICU: QG: $29.1 \pm 12.38$ vs. DG: $21.5 \pm 10.16$ vs. CG $14.6 \pm 8.01$ ; p=0.001	3

BMI = body mass index, CG = control group, DG = diaphragm group; FSS-ICU = functional status score for the ICU, LOS = length of stay, MIP = maximal inspiratory pressure, MRC = medical research council, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, QG = quadriceps group

NMES of the diaphragm does not improve MRC, MIP, duration of mechanical ventilation or hospital LOS compared to conventional physical therapy. But NMES of the quadriceps exeeds both diaphragmatic NMES and conventional physiotherapy in all the before mentioned outcomes except MRC.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
265 Devlin 2018 (PMID: 30113379 DOI: 10.1097/CCM.00 000000000329 9) <b>Specification of</b> <b>study:</b> Guideline for pain, agitation/ sedation, delirium, immobility and sleep	<ul> <li>16 RCTs</li> <li>Inclusion criteria: <ul> <li>range of motion</li> <li>mobilisation, including in bed mobility, transfers out of bed, and walking</li> <li>physical and occupational therapy</li> <li>interventions, including exercises, transfer</li> <li>training, sitting, and ambulation</li> <li>in-bed cycle ergometry</li> <li>neuromuscular electrical stimulation</li> </ul> </li> <li>Exclusion criteria: <ul> <li>continuous lateral rotation of bed</li> <li>lateral positioning in bed</li> <li>inspiratory muscle training/diaphragmatic</li> <li>electrical stimulation/breathing exercises</li> <li>chest physiotherapy/airway clearance</li> <li>massage therapy</li> <li>stroke rehabilitation</li> <li>any intervention conducted in a long-term acute care hospital or similar facility since</li> </ul> </li> </ul>		See inclusion criteria	Usual care, a different rehabilitation / mobilization intervention, placebo, or sham intervention	<b>Derived</b> <b>outcomes:</b> - mortality - duration of MV - quality of life	Duration of mechanical ventilation: (11 RCTs, 1.128 patients) Significant reduction by 1.31 days (95% CI, -2.44 to -0.19; low quality evidence) (406-409, 411, 413-416) Quality of life: (measured using 36-item short form health survey instrument) no statistically significant improvement p>0.05 (SMD, 0.64 [95% CI, -0.05 to 1.34]) Mortality: no effect on hospital mortality was observed	1

MV = mechanical ventilation, RCT = randomized controlled trial

The guideline offeres recommendations to improve pain, agitation/sedation, delirium, immobility and sleep in critically ill patients.

Reference, Study Type		l Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
268 Taito 2018 (PMID: 30048540 DOI: 10.1371/journal.po ne.0201292) <b>Specification of</b> <b>study:</b> Systematic review and meta-analysis	sepsis	a: unpublished s ≥18 years) with a: cord injury ires probable		Protocolised rehabilitation: - neuromuscular stimulation - passive range of motion exercise, - active exercises - designed to either commence earlier and/or be more intensive than the care received by the control group	Usual care	Primary endpoints: - QoL - ADL - ICU mortality Secondary outcomes: - ICU LOS - Hospital LOS - MRC score - AEs	<ul> <li>QoL very low evidence</li> <li>21.10 [6.57–35.63] and 44.40</li> <li>[22.55–66.05] (n=1 RCT)</li> <li>ICU mortality (RR 2.02 [95% CI: 0.46–8.91], I2 = 0%; (n = 2 RCT) (p&gt;0.05)</li> <li>ICU LOS/ hospital LOS and muscle strength no meta-analysis.</li> <li>no meta-analysis for QoL or ADL</li> <li>no adverse events (n=2 RCT)</li> </ul>	1→2

ADL = activities of daily living, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, pts = patients, QoL = quality of life, RCT = randomized control trial

#### Earlier or more intensive rehabilitation did not have a significant impact on ICU mortality in sepsis patients.

#### References

- 1. Kayambu G, Boots R, Paratz J. Early physical rehabilitation in intensive care patients with sepsis syndromes: a pilot randomised controlled trial. Intensive Care Med. 2015; 41(5):865–74. https://doi.org/10. 1007/s00134-015-3763-8 PMID: 25851383
- 2. Shen SY, Lee CH, Lin RL, Cheng KH. Electric Muscle Stimulation for Weaning from Mechanical Ventilation in Elder Patients with Severe Sepsis and Acute Respiratory Failure—A Pilot Study. Int J Gerontol. 2017; 11(1):41–5.

a.2018.9592 ) crebral disease requiring deep sedation for at least 72 hours - acute polyradiculoneuropathy (Guillain-Barré syndrome) - myasthenia - advanced dementia - deep venous thrombosis or pulmonary embolism treated for ≤ 48 hours - contraindication to EMS or leg cycling for musculoskeletal, dermatological, or surgical reasons - contraindication to standing or transfer to a chair <b>Per Branch</b> - corebral disease requiring deep sedation for at least 72 hours - acute polyradiculoneuropathy (Guillain-Barré syndrome) - myasthenia - advanced dementia - contraindication to EMS or leg cycling for musculoskeletal, dermatological, or surgical reasons - contraindication to standing or transfer to a chair <b>Per Branch</b> - contraindication to standing or transfer to a chair <b>Per Branch</b> - contraindication to standing or transfer to a chair <b>Per Branch</b> - thickness of the M. rectus - 50 min NMES - 50	Reference, Study Type	Cases and C (Participant #, Cha Total	aracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	2018 (PMID: 30043066 DOI: 10.1001/jam a.2018.9592 ) Specification of study:	Inclusion criteria: - ≥18 years or older - admitted to the ICU ≤ 72 hours - deemed to need ≥ 48h of care - independent walking ability w admission - Barthel Index ≥ 55 within 15 d Exclusion criteria: - pregnant - cardiac arrest was the cause o - cardiac arrest before screening - pacemaker or implantable car - cerebral disease requiring dee hours - acute polyradiculoneuropathy syndrome) - myasthenia - advanced dementia - deep venous thrombosis or put treated for ≤ 48 hours - contraindication to EMS or leg musculoskeletal, dermatologica - contraindication to standing o	e in the ICU vithin 15 days before ICU days before ICU admission of ICU admission og rdioverter-defibrillator ep sedation for at least 72 y (Guillain-Barré ulmonary embolism g cycling for al, or surgical reasons or transfer to a chair	(one patient in each group	early rehabilitation: - weekdays - 15 min leg cycling exercise	early rehabilitation	- MRC Secondary outcomes: - ICU mobility scale - Katz Index of independence - Barthel Index - duration of MV (Number of ventilator-free days until day 28) - SF-36 - thickness of the M. rectus femoris via ultrasound	- MRC, MD (95%Cl): -3.0 (-7.0 – 2.8) p = 0.28 Secondary outcomes: - ICU mobility scale, MD (95%Cl): 0 (-1 – 2), p = 0.52 - Katz Index of Independence, MD (95%Cl): 0.3 (-1.0 – 1.3), p = 0.57 - Barthel Index at 6-months, MD (95%Cl): 0 (-5 – 5), p = 0.90 - duration of MV, MD (95%Cl): 1.0 (-2.0 – 3.0), p = 0.24 - SF-36 n.s - thickness of the M. rectus femoris MD (95%Cl): -0.5 (-1.0 – 2.4), p = 0.17 - adverse events (7/4159	2

CI = confidence interval, EMS = electrical muscle stimulation, MD = median difference, MRC = medical research council score, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, n.s. = not significant, SF-36 = short form 36

Neuromuscular electrical stimulation + in-bed cycling did not increase muscle strength, howeverthe study was underpowered for the primary endpoint.

Reference, Study Type	(Participant #,	d Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
272 Lucchini 2018 (PMID: 30037534 DOI: 10.1016/j.icc n.2018.04.00 2) Specification of study: Retrospective cohort study	45 pts in PP partly with retrospective analysis - admitted in general I 2009 to November 20 - supported by VV-ECN - experienced at least Per B 14	of pts: ICU from November 14 MO		PP and vv-ECMO	PP without ECMO	Primary endpoint: - modification on PaO2/FiO2 ratio Secondary endpoint: - safety and feasibility	Primary outcome: - pre- vs end-prone position (113 mmHg vs 147 mmHg) (p=0.034) Secondary outcome: - 45 prone positioning manoeuvres performed (median 8 hours IQR 6-10) - no AEs	4

AE = adverse event, PP = prone position, (vv-)ECMO = (veno-venous) ectracorporeal membrane oxygeation

The application of prone position during VV-ECMO has shown to be a safe and reliable technique when performed in a recognised ECMO centre with the appropriately trained staff and standard procedures.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
DOI:	30 pts. in a NCU of a university hospital in Istanbul between August 2013 and December 2016 Inclusion criteria: -aged 18 years or older -undergone EVD and/or ICP monitoring -intra-arterial catheters -granted permission by a legally authorized representative. Exclusion criteria: -neurologically and hemodynamically unstable -do not tolerate a position change (ICP>25 mmHg for 5 minutes after positioning) -diagnosed with brain death -no or irregular ICP waves -undergoing craniotomy in the NCU where the study was conducted Per Branch	N=16	HOB positions: -15°,30°,45° supine; -15°,30°,45° left lateral; -15°,30°,45° - right lateral	Patients acted as their own control	Sample Size calculation: Difference between mean pre-and post-positioning (right lateral position HOB 15°) ICP score averages (2.93), Power of 80% and an alpha of 0.05. Endpoints: - pre-and post-positioning ICP and CPP values - impact on ICP and CPP in patients with different GCS scores	Significant differences between groups: - 15° left lateral position, increased ICP in patients with a GCS score of 13-15 (p=0.024); decreased CPP with GCS score of 3-8 compared to GCS score of 9-12 (p=0.034) - 15° right lateral position, increased ICP in patients with a GCS score of 3-8 (p=0.04), CPP decreased (p=0.007) -right lateral position, HOB 45° with GCS score 9-12 and 13-15 CPP decreased (P=0.018) No significant differences between groups in: - Supine positions, left lateral and right lateral with HOB elevations differences were n.s.	3 → 4

NCU=neurocritical care units; pts. = patients; EVD= external ventricular drainage; ICP = intracranial pressure; HOB=head of bed; CPP=cerebral perfusion pressure; GCS=Glasgow Coma Scale; n.s. =not significant

Different positions (HOB degree of 15, 30, and 45) led to slight insignificant changes in ICP and CPP.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
278 Sanchez 2018 (PMID: 29958844 DOI: 10.1016/j.en fi.2018.03.0 01) <b>Specificatio</b> <b>n of study:</b> SR	<ul> <li>primary studies published from 30/04/2009 until present</li> <li>retrospective observational studies, prospective studies or full text clinical trials performed on critically ill patients in the ICU, aged &gt;15 years, with MV and whose outcome</li> </ul>		Early mobilisation via PT/Ergo or Electrical stimulation or Early mobilisation together with insulin therapy / euglycemic management	Standard of care	<b>Outcomes:</b> - duration of ventilation - ICU length of stay - mortality	No meta-analysis statistically significant (p<0.05) relationship was observed between ICUAW and - failure in ventilator disconnection - mortality - increase in ICU stay - time that the patients required mechanical ventilation	1 → 4 (downgraded as no meta- analysis and not only RCTs)

ICU = intensive care unit, ICUAW = intensive care unit acquired weaknes,s PT = physiotherapie

This systematic review showed a significant relashionship between ICUAW and duration of ventilation, ICU length of stay and mortality. All of this improved in this type of patients with the application of a rehabilitation therapy.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
79 Hickmann 2018 (PMID: 29957714 DOI: 10.1097/CC M.00000000 00003263) Specification of study: RCT	21 pts Inclusion criteria: - adults with septic shock within 72 hours after ICU admission Exclusion criteria: - pre-existing cognitive abnormalities -malnutrition or cachexia - inability to walk independently - leg amputation - fractures -ongoing chemotherapy - long-term corticoid treatment	3 (died before 2nd muscle biopsy - 1 intervention group - 2 before group allocation)	intervention with two daily (7/7 days) sessions of both <b>manual</b> <b>mobilization</b> and 30 minutes each <b>passive/ active</b> <b>cycling therapy</b> (1 h/d)	manual mobilization once a day (5/7 days)	Primary endpoint: regulation of protein degradation / synthesis pathways during the 1 <sup>st</sup> week following the onset of septic shock Secondary outcome: - preservation of the muscle fiber CSA - presence of exercise- induced muscle Inflammation - restoration of neuromuscular function by measuring electrophysiology values and muscle strength - safety - tolerance of the intervention by monitoring hemodynamic/ respiratory values - pts perception	<ul> <li>Primary endpoints: <ul> <li>catabolic ubiquitin proteasome pathway: no significant difference for</li> <li>a. MARbx: -7.3% ± 138.4% in control vs -56.4% ± 37.4% in intervention group; p = 0.23</li> <li>b. MURF-1: -30.8% ± 66.9% in control vs -62.7% ± 45.5% in intervention group; p = 0.15)</li> <li>autophagy-Lysosomal System better control at D7</li> <li>a. ULK1 Ser-757: IG 30% ± 59% vs. CG -16% ± 33%, p = 0.01</li> <li>b. ULK1 Ser-317: IG 20% ± 148% vs. CG 311% ± 703%, p = 0.03</li> <li>c. LC3b mRNA: IG -21% ± 18% vs. CG 5% ± 47%, p = 0.16</li> <li>d. Bnip3 mRNA: IG -59% ± 23% vs. CG 27% ± 198%, p = 0.003</li> <li>e. GabarapL1: IG -16% ± 85% vs. CG 73% ± 174%, p = 0.09</li> <li>f. unchanged: Cathepsin-L, p62 mRNA, LC3bII/I ratio, p62 protein levels, co-staining LC3b-p62</li> <li>g. LAMP2/p62 colocalization was decreased at D7 in IG and increased in CG (p = 0.007)</li> <li>anabolic Akt-mTOR pathway</li> <li>a. Akt(Ser-473) increased D7 in IG (p = 0.04)</li> <li>b. m-TOR downstream unchanged</li> </ul> Secondary results: <ul> <li>CSA (µm2) was preserved by exercise (all fibers, Type 1 fibers, Type-IIa and Type-IIb fibers all p &lt; 0.05)</li> <li>markers of inflammation were not modified by the intervention</li> <li>electrophysiology: too few data to compare</li> <li>muscle strength: Paucity of data did not allow any comparison between the two time points by groups</li> <li>safety: 1 reversible hypotension in intervention</li> </ul></li></ul>	2

CG = control group, CSA = cross sectional area, IG = intervention group, ICU = intensive care unit, LAMP = lysosomal-associated membrane protein, MARbx = muscle ubiquitin ligases (E3-ligases) muscle atrophy F-box, MURF = muscle ring finger-1, pts = patients, ULK = Unc-51 like kinase

#### Early physical therapy during the first week of septic shock is safe and preserves muscle fiber cross-sectional area.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
280 Goldfarb 2018 (PMID: 29879568 DOI: 10.1016/j.jcrc.2018. 05.013) <b>Specification of</b> <b>study:</b> retrospective analysis frail vs non- frail	- EM but no frailty assessment - neither EM nor frailty assessment		<b>Early</b> <b>mobilisation</b> in frail pts	<b>Early mobilisation</b> in non-frail pts	<b>Primary outcomes:</b> mean change in LOF at discharge	<b>Primary outcomes:</b> - mean LOF improvement was 0.5 ± 0.8 and did not differ based on frailty status - mean LOF increased by 0.37 in frail patients compared to 0.52 in non- frail patients ( <i>p</i> =0.15)	4

CICU = cardiovascular ICU, EM = early mobilization, LOF = level of function

Functional status improved in both frail and non-frail older adults.

Reference, Study Type	(Participant #,	l Controls Characteristics) tal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
283 Shah 2018 (PMID: 29747562 DOI: 10.1177/0885066 616677507) <b>Specification of</b> <b>study:</b> Prospective QI project	90 pts with a total of 185 were recorded over a 12- Inclusion criteria: - pts with EVD - SAH: - awake and followir - Lindegaard ratio <3 - MCA mean flow ve - MAP> 80 mm Hg - ICP consistently <20 - ICH: - stable CT scan after - ICP consistently <20 - others (TBI, hydrocepha consistently <20 mm Hg Exclusion criteria: - pts were delirious using intubated	patient encounters month period. ag commands 3.0 locity <120 cm/s, 0 mm Hg r 24h 0 mm Hg alus, tumor,): ICP		<b>Evaluation by PT</b> + <b>Standardised early mobilisation</b> (30-60 min ranging from PROM to walking)		<b>Outcome:</b> adverse events	AEs: 4 AEs (2.2%)	4
	Per B	ranch	-					

CAM-ICU = confusion assessment method for ICU, ICP = intracranial pressure, ICH = intracranial hemorrhage, MAP = mean arterial pressure, MCA = middle cerebral artery, PT = physical therapist, PROM = passive range of motion, QI = quality improvement, SAH = subarachnoid hemorrhage, TBI = traumatic brain injury

#### Early mobilisation is safe in patients with EVD.

Reference, Study Type	(Participant #,	l Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
284 Fuke 2018 (PMID: 29730622 DOI: 10.1136/bmjope n-2017-019998) <b>Specification of</b> <b>study:</b> Systematic review and meta-analysis	6 RCTs with 709 Inclusion criteria - adult pts admit Exclusion criteria - traumatic brain - stroke - did not fulfill th Per B 298	<b>i:</b> ted to ICU <b>a:</b> i injury		<b>Early</b> <b>rehabilitation</b> - start earlier than usual care or - start within 7 days of ICU admission	Standard care or no early rehabilitation	Primary endpoints: - short-term physical related outcome assessed during hospitalization - cognitive related outcomes - mental status related outcomes Secondary outcomes (long term): - HRQL (EQ5D) - S F-36 for physical function	Significant differences between groups in: - ICUAW (OR 0.42, 95% CI 0.22 to 0.82, p=0.01, I <sup>2</sup> = 0% - MRC score (SMD): 0.38, 95% CI 0.10 to 0.66, p=0.009) I <sup>2</sup> = 0% No significant differences between groups in: - delirium-free days n.s - HADS n.s - EQ5D n.s. - SF-36 n.s.	1

EQ5D = european quality of life 5 dimensions, HADS = Hospital Anxiety and Depression Scale; HRQL = health related quality of life, ICUAW = ICU-acquired weakness, MRC = medical research council, n.s. = not significant, PICS = postintensive care syndrome, pts = patients, SF-36 = short form 36, SMD = standard mean difference

#### Early rehabilitation increases muscle strength but does not influence cognitive and mental outcomes.

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Reference, Study Type	Cases and (Participant #, o Tot	characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
285 Rebel 2019 (PMID: 29703636 DOI: 10.1016/j.aucc.20 18.03.004) <b>Specification of</b> <b>study:</b> Retrospective study	<ul> <li>patients with therapy at one during their ad</li> </ul>	119 pts. ria: ient vasoactive or more points mission in od ria:	none	Mobilization with Vasoactive therapy	Patients acted as their own controls	No sample size calculation (retrospective study) <b>Primary Endpoint:</b> - frequency and intensity of mobilization in patients receiving vasoactive therapy <b>Secondary Endpoints:</b> - occurrence of adverse events during mobilization	Primary Endpoint: - Frequency: Low (76.8%) and moderate (13.7%) dose vasoactive therapies associated with a higher probability of mobilization relative to high (9.4%) dose therapy (OR = 5.50, 95% CI = 2.23-13.59 and OR = 2.50, 95% CI= 0.95-6.59, respectively) -intensity: on vasoactive therapy (n = 72), maximum mobilization intensity was low (IMS = 1-2) in 31%, moderate (IMS = 3-5) in 51%, and high (IMS = 6-10) in 18% of vasoactive days Secondary Endpoints: - no SAE - AE: reversible hypotension requiring transient escalation of vasoactive therapy (7.3%), associated with lower mean arterial pressure (p = 0.001)	

pts. = patients; ICU=Intensive Care Unit; CI= confidence interval; OR= odds ratio; SAE=serious adverse event; AE= adverse event; IMS=ICU Mobility Scale

It appears that the level of vasoactive support may not be an absolute indicator of safety to mobilize.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
286 Medrinal 2018 (PMID: 29703223 DOI: 10.1186/s1305 4-018-2030-0) <b>Specification</b> of study: Randomised cross-over trial	20 pts admitted to ICU were included Inclusion criteria: - ≥18 years - intubated for at least 24h - ventilated with "pressure support" - Ramsay score ≥4 - sedated Exclusion criteria: - pacemaker - other contraindications for electrical stimulation - ventilated under "assist control ventilation" - were conscious Per Branch 19	1 patient excluded from the analysis (missing data)	PROM, passive cycle- ergometry, quadriceps electrical stimulation and FES cycling consecutive 10-min sessions with a 30-min rest period		Primary endpoint: - cardiac output during the exercises Secondary outcomes: - TAPSE - PASP - MAP - expiratory tidal volume - respiratory rate all were measured at baseline and every 3 min during the exercises relative change in: THb in the vastus lateralis muscle, oxyhaemoglobin and oxymyoglobin (HbO2) and deoxyhaemoglobin and deoxymyoglobin (HbD2) and deoxyhaemoglobin and deoxymyoglobin (HHb) were continuously recorded Power calculation: 19 subjects should be included to detect a difference between groups in mean CO of 1.1 L, and to reject the null hypothesis with power of 90% and associated type I probability error of 0.05.	<ul> <li>Primary results: <ul> <li>cardiac output increased significantly (+ 1 L/min) after 9</li> <li>min of FES cycling (7.7 L/min (6.7–8.7))</li> <li>no change in cardiac output over time during PROM,</li> <li>passive cycle ergometry or quadriceps electrical stimulation</li> <li>no differences between the increase in cardiac output</li> <li>during FES cycling in pts with or without cardiorespiratory comorbidities</li> </ul> </li> <li>Secondary outcomes: <ul> <li>significant increase in heart rate (97b/min (90–104)),</li> <li>TAPSE (2cm (1.8–2.2)) and MAP (91mmHg (85–97)) during FES cycling</li> <li>MAP increased during passive cycle ergometry (89mmHg (83–95))</li> <li>PASP was significantly higher during FES cycling than</li> <li>PROM and quadriceps electrical stimulation (51 (95% CI 36–67) mmHg vs. 45 (95% CI 32–59) mmHg (p = 0.007) vs. 46 (95% CI 35–57) mmHg (p &lt; 0.001))</li> <li>respiratory rate was significantly higher during FES cycling than during PROM and quadriceps electrical stimulation (respectively, 24 (95% CI 19–30) c/min vs.20 (95% CI 16–24) c/min (p &lt; 0.001) vs. 21 (95% CI 16–26) c/min (p= 0.005))</li> <li>at the end of PROM, level of THb decreased significantly by 23% (95% CI – 41.5 to – 4.9) (p = 0.046), significant reduction in HHb level (– 27% (95% CI – 50 to – 4), HbO2 did not change</li> <li>end of the passive cycle-ergometry, there was a nonsignificant increase in THb and nonsignificant increase in HbO2</li> <li>non-significant increase in THb, HHb and HbO2 at the end of the quadriceps electrical stimulation</li> <li>non-significant increase in THb during FES cycling, but significant increase in Hb of 24% (95% CI 1.1–46.7), HbO2 decreased significantly by 13% (95% CI – 31.8 to –4.7)</li> </ul> </li> </ul>	2

FES = functional electrical stimulation, ICU = intensive care unit, MAP = mean arterial pressure, PASP = pulmonary arterial systolic pressure, PROM = passive range of movements, TAPSE = tricuspid annular plane systolic excursion, THb = total haemoglobin

FES cycling was the only exercise that increased cardiac output and produced sufficient intensity of muscle work. No muscle or systemic effects were induced by the passive techniques.

Reference, Study Type	(Partic Charact	d Controls ipant #, ceristics) ital	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
289 Sarfati 2018 (PMID: 29660670 DOI: 10.1016/j.jcrc. 2018.03.031) <b>Specification</b> of study: Randomized controlled trial	n=145 Inclusion crite - MV for > 3 da - 18 years or o - no expectation on the day of s Exclusion crite - transfer to arra after a stay > 5 - central nervor injury - spine, pelvis, limb injuries Per B	ays Ider on of weaning screening eria: nother ICU 5 days ous system	n= 48 Intervention: n=7 did not receive treatment (5 died, 2 transferred to another ICU) n=9 missing data for primary endpoint Control: n=13 did not receive treatment (12 died, 1 transferred to another ICU) n=19 missing data for primary endpoint	TILT-Group daily: standard care + tilting for at least 1h/d (1 session/d): verticalized on an electrical tilt- table, secured to the table by Velcro straps at the torso and knees and gradually tilted from 30° to 60° in 10° steps	Standard care: daily: ≥ 1 TCI: PROM in- bed exercises and/or active ROM in-bed exercises. No TCI: sitting in armchair at least 2h/d (1 session/d)	<ul> <li>Primary endpoint: <ul> <li>MRC at ICU discharge</li> </ul> </li> <li>Secondary outcomes: <ul> <li>muscle recovery (median change in MRC from baseline to ICU discharge)</li> <li>AE</li> <li>time to ability to stand alone</li> <li>ICU-LOS</li> <li>hospital LOS</li> <li>MV duration</li> <li>use of sedatives and NMB</li> <li>hospital mortality</li> <li>infections</li> <li>severe ICU complications</li> </ul> </li> <li>Power: <ul> <li>MRC estimated to be 47 (control) vs. 50 (intervention) with SD 8</li> <li>85% power, 0.05 alpha, optimal n=50 evaluable pts in each group. With 30% attrition (e.g., mortality) = 150 pts</li> </ul> </li> </ul>	Primary endpoint: - MRC: 50 [45-56] vs. 48 [45-56], p = 0.56 Secondary outcomes: - muscular recovery: DMRC 14 [10-24] vs. 10 [5-15], p = 0.004 - hospital mortality 0 (0) vs. 6 (10), p = 0.010 - AE: n.s. - time to ability to stand alone: n.s. - time to ability to stand alone: n.s. - ICU-LOS: n.s. - hospital LOS: n.s. - hospital LOS: n.s. - use of sedatives and NMB: n.s. - infections: n.s. - severe ICU complications: n.s.	2 → 3

d = day, MRC = medical research council scale for muscle strength, PROM = passive range of motion, pts = patients, TCI = temporary contraindication for out-of-bed mobilization

# 1 h passive tilting per day added to standard care did not improve muscle strength at ICU discharge in surgical patients, however, increase of MRC over time until ICU discharge was significant.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
292 Babouth 2018 (PMID: 29580936 DOI: 10.1016/j.ap mr.2018.01.0 34) Specification of study: pragmatic, quasi- experimental , consecutive group comparison study	57 pts Inclusion criter - admitted to a ICU - with primary I - older than 18 Exclusion criter - secondary ICH n = 28	neurological ICH years r <b>ia:</b>		Pre- intervention	Post- intervention	Primary endpoints: - time of admission to first mobilisation out of bed (without lift, min. 5 sitting or standing). - number of mobilisations No sample size calculation: partially retrospective analysis, pre vs. post comparison	<ul> <li>Significant differences between groups in: <ul> <li>mobilisation on day 7 in pre-algorithm group 8 (29%) vs. post group 16 (55%), p = 0.04</li> <li>higher probability of the post-algorithm group to be mobilized on day 7, OR 8.7, 95% Cl 2.1 - 36.6; p= 0.003.</li> <li>mobilisations during NCCU: pre-group 9 (32%) vs. post-group 17 (59%) p = 0.045</li> </ul> </li> <li>No significant differences between groups in: <ul> <li>mobilisation on day 1, 3 and 5</li> <li>time to first mobilization, MW 2.6 days in both groups.</li> </ul> </li> </ul>	4

ICH = intracranial hematoma/hemorrhage, ICU = intensive care unit, NCCU = neuroscience critical care unit, pts = patients

Implementation of a progressive mobility algorithm was feasible, did not increase the number of adverse events, and was associated with a higher likelihood of mobilisation in the first week after spontaneous ICH for patients admitted to the ICU.

Reference,		d Controls Characteristics)	Drop- out	Intervention	Control	Optimal Population	Primary Results	Evidence
Study Type	T	otal	Rate				-	Grade
						Primary outcomes:		
	764 consecutive adr and 88 pts included Exclusion criteria:					- rate of walking and number of days needed to achieve walking (minimum of 45m)	Primary results: - walking independence,	
205 Wataraha		nical ventilation <24 h					n(%): non-ICU-AW 35 (87.5), ICU-AW 33 (67.4); p = 0.078	
295 Watanabe 2018	hospitalization					Secondary outcomes:	Secondary results:	
(PMID:	<ul> <li>death during hospitalization</li> <li>diagnosis of dementia before</li> <li>hospitalization</li> </ul>		Rehabilitation activity in the ICU based on		- MV days	- MV duration in days: non- ICU-AW 2, ICU-AW 3; p =		
32789228 DOI: 10.2490/prm.2	- unavailability of co	ming exercise due to		an EM Protocol and retrospective analysis of patients diagnosed		- rate of ICU-AD, discharge home, FSS-ICU	0.385 - ICU-AD, n(%): non-ICU-AW 3 (7.5), ICU-AW 19 (38.8); p	4
0180003)				with ICU-AW and those not diagnosed		- Bl score	= <0.0001 - discharge home, n(%): non-	
Specification of study:	Per I	Branch		with ICU-AW at hospital discharge			ICU-AW 28 (70.0), ICU-AW 27 (55.1); p = 0.031	
Retrospective cohort	ICU-AW n = 48	non-ICU-AW n = 40				Sample size calculation: estimated on the basis of a threshold walking independence of 35% and an expected walking independence of 50%, with	<ul> <li>FSS-ICU at ICU discharge: non-ICU-AW 22, ICU-AW 10; p = &lt;0.0001</li> <li>BI at Hospital discharge: non-ICU-AW 77.5, ICU-AW</li> <li>60; p = &lt;0.0001</li> </ul>	
					an 80% power level and a one-sided alpha value of 0.05, using the binomial test.			

BI score = Barthel index, EM = early mobilization, FSS-ICU = functional status score ICU, ICU-AD = intensive care unit acquired delirium, ICU-AW = intensive care unit acquired weakness, MV = mechanical ventilation, pts = patients

The amount of daily activity time significantly influenced to walking independence.

Reference, Study Type	(Participant #,	d Controls Characteristics) ttal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
296 Sawada 2018 (PMID: 29496765 DOI: 10.4037/ajcc 2018911) Specification of study: retrospective study	admission Per B	onia admitted to : ed pneumonia		<b>Early</b> <b>rehabilitation</b> (within 2 days of admission)	No early rehabilitation	Primary endpoint: - in-hospital mortality Secondary Outcomes: - length of ICU stay - length of hospital stay - total costs of hospitalization	Significant difference between groups in : - in-hospital mortality was lower in the early rehabilitation group (17.9% vs 21.9%, respectively; risk difference, 4.0%; 95% Cl, 0.5%-7.6%; number needed to treat, 25; p = 0.03) No significant differences between groups in: - length of ICU stay (p = 0.51) - length of hospital stay (p = 0.70) - total costs of hospitalization (p = 0.79)	4

CAP = community-acquired pneumonia, ICU = intensive care unit, pts = patients

Early rehabilitation within 2 days of admission was associated with a reduction in the in-hospital mortality of patients with CAP admitted to the ICU.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
295 Liu 2018 (PMID: 29484188 DOI: 10.1186/s40560- 018-0281-0) <b>Specification of</b> study: single-center prospective observational study	Total         232 patients         Inclusion criteria:         - 18 years of age or older         - unplanned admission to the ICU         Exclusion criteria:         - planned post-operative         - acute cardiovascular         - acute cerebrovascular disease         - progressive neuromuscular         disease         - post cardiopulmonary arrest         syndrome         - a condition limiting mobilization         such as an unstable pelvic fracture	Rate	Maebashi EM protocol	No control	Primary outcome: - incidence rate of adverse events in all rehabilitation sessions Secondary outcomes: - number of days to first rehabilitation and the number of days to progress to higher rehabilitation levels - percentage of patients who got out of bed, standing, or ambulating	<ul> <li>total of 587 rehabilitation sessions were conducted for 232 patients</li> <li>Primary results: <ul> <li>incidence rate of adverse events among all rehabilitation sessions was 2.2% (95% confidence interval [CI] 1.2–3.8%)</li> <li>no significant difference between the incidence rate in active rehabilitation, (levels 3 to 5, 387 sessions, 11 adverse events, 2.8%; 95% confidence interval [CI] 1.4–5.0%) and the incidence rate for non-active rehabilitation, (levels 1 and 2, 200 sessions, 2 adverse events, 1.0%; 95% confidence interval [CI] 1.0–3.6%), (<i>P</i> = 0.15)</li> </ul> </li> <li>Secondary results: <ul> <li>median number of days to the first protocolized rehabilitation session was 0.7 (IQR 0.0–0.9)</li> <li>C20( effective (n. 142) and effective for a first protocolized rehabilitation for a first protocolized first</li></ul></li></ul>	3
	Per Branch					- 62% of patients ( <i>n</i> = 143) got out of bed during their ICU stay, and the median time to first getting out of bed was 1.2 (IQR 0.1– 2.0) days	

CI = confidence interval, EM = early mobilization, ICU = intensive care unit

Protocolized EM led by ICU physicians can be initiated in the acute phase of critical illness without serious adverse events requiring additional treatment.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervent ion	Control	Optimal Population	Primary Results	Evidence Grade
300 Murat Türk, 2018 (PMID: 29404183 DOI: 10.5152/TurkTh oracJ.2017.170 36) Specification of study: Randomized Controlled Study	respiratory failure - SpO2 ≤ 90% and F - NIV therapy Exclusion criteria: - anatomical proble - terminal stage of t - experienced loss of clinical unstabilisati during follow-up (sh vasopressor suppor endotracheal intuba - couldn't remain in recumbent or latera	m for NIV their disease of consciousness or on at any time hock, need for t, GCS < 10, required ation) the semi-	19 pts (changed to another ventilatio n mode or intubated)	Pressure support (BiPAP-S mode)	Average volume targeted pressure support (AVAPS-S mode)	<ul> <li>Primary endpoints:</li> <li>ICU LOS</li> <li>course of PaCO2</li> <li>Secondary endpoints:</li> <li>obesity and course of PaCO2</li> <li>body positioning effects on the ventilation variables</li> </ul>	Primary outcome:           (BiPAP-S vs AVAPS-S)           -         ICU LOS 7.4±2.6 days vs 8.4±3.2 (p=0.17)           -         PaCO2 62.5±5.8 vs 65.1±7.2 (p=0.12)           Secondary outcomes:         no significant changes in course of PaCO2 (pts           BMI<30 vs pts BMI>30):         F=3.245, p=0.053 for BiPAP-S           F=2.931, p=0.097 for AVAPS-S         body position endpoints:           BiPAP-S         no significant changes for (semi-recumbent vs lateral):           -         peak inspiratory pressure (PIP) 17.4±3.5 vs 17.8±3.9 (p=0.87)           -         mean ventilation 10.3±1.8 vs 10.2±3.3 (p=0.18)           -         leak 26.9±5.1 vs 29.1±5.8 (p=0.11)           -         respiratory rate 23.4±4.6 vs 22.1±3.1 (p=0.07)           AVAPS-S         no significant changes for (semi-recumbent vs lateral):           -         peak inspiratory pressure (PIP) 22.1±4.9 vs 21.1±5.1 (p=0.42)           -         mean ventilation 10.2±2.9 vs 10.5±2.6 (p=0.9)           -         leak 24.8±3.8 vs 26.1±7.4 (p=0.96)           -         respiratory rate 22.6±4.9 vs 21.8±4.2 (p=0.57)	2 → 3 (downgraded as evaluation of body composition was not primary aim)
	33	29					·····	

AVAPS-S = average volume targeted pressure support, BiPAP-S = pressure support, GCS = Glasgow coma scale, LOS = length of stay, NIV = non-invasive ventilation, PIP = peak inspiratory pressure, pts = patients

No significant effect of semi-recumbent vs. lateral position in NIV patients.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
301 Klein 2018 (PMID: 29396165 DOI: 10.1016/j.iccn. 2018.01.005) Specification of study: prospective, longitudinal, non- equivalent, three-group comparative study	- deceased prior to t health assessment	ey, and hostility ish speaking, m, combativeness nd inability to cionnaire due to Ty to being approached		Nurse-driven EPM program: - immediate post intervention (group two) - late post intervention sustainability data (group three)	- pre- intervention (group one), not specified	Primary outcome: - sustainability of EPM programme over a 22- month period Secondary outcomes: - difference in clinical outcomes (LOS, 30- day mortality, discharge disposition and quality metrics that included DVT, VAP, BSI, and HAPI) and psychological health (depression, anxiety and hostility)	Primary outcomes: - in 260 pre-intervention, 377 post-implementation, and 480 12-month post- implementation pts (N = 1.117) walking increased post-implementation and was sustained at the 8- month (p < .001) Secondary outcomes: -ICU and hospital LOS and psychological distress were reduced compared to the pre-early mobility programs (all p < .001) - no differences in discharge disposition mortality or quality metrics	4

BSI = blood stream infection, DVT = deep vein thrombosis, EPM = early progressive mobility, HAPI = hospital acquired pressure injury, LOS = length of stay, n.s. = not significant, pts = patients, SD = standard deviation, VAP = ventilator associated pneumonia

A nurse-driven EPM program seems to have a benefit in relation to hospital and ICU length of stay.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
302 Woo 2018 (PMID: 31723855 DOI: 10.4266/acc. 2017.00542) <b>Specification</b> of study: Case Series – intraindividu al design	command		In-bed cycling: -20 min + FES: -only left thigh -20 min	In-bed cycling: -20 min	Outcomes - circumferences M. rectus femoris pre- and post- intervention via ultrasound - cross-sectional area rectus femoris pre- and post- intervention via ultrasound - MRC score	Significant differences between groups in: circumference (cm) right side- pre mean $\pm$ SD: 47.43 $\pm$ 5.79- post mean $\pm$ SD: 47.43 $\pm$ 5.79- post mean $\pm$ SD: 48.24 $\pm$ 5.56, p = 0.006 left side- pre mean $\pm$ SD: 47.83 $\pm$ 5.79- post mean $\pm$ SD: 48.75 $\pm$ 4.73, p = 0.027 cross-sectional area (cm <sup>2</sup> ) right side- pre mean $\pm$ SD: 5.28 $\pm$ 1.89- post mean $\pm$ SD: 6.59 $\pm$ 2.23, p = 0.003 left side- pre mean $\pm$ SD: 6.59 $\pm$ 2.23, p = 0.008No significant differences between groups in: MRC score right side- pre median (IQR): 4 (3.75 - 4.25)- post median (IQR): 4 (3.75 - 4.25)- post median (IQR): 4 (4 - 4), p = 0.368 No difference between the legs regarding all outcomes	3

FES = functional electrical stimulation, pts = patients

In-bed cycling increased surrogate parameters of muscle mass in a before-after design while not affecting muscle strength. No additional effect of NMES could be observed.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
305 Conceicao 2017 (PMID: 29340541 DOI: 10.5935/0103- 507X.20170076) <b>Specification of</b> <b>study:</b> systematic review	<ul> <li>37 publications (6.641 pts )</li> <li>(6x RCT, 1x prospective study, 9x retrospective study, 13x case series, 2x independent group design, 2x RCT protocol, 4x care delivery protocol)</li> <li>Inclusion criteria: <ul> <li>RCTs</li> <li>prospective and retrospective studies</li> <li>case series with at least 10 consecutive pts</li> <li>with independent or parallel group design</li> <li>RCT protocols and care delivery protocols</li> <li>&gt;18 years old</li> <li>admitted to the ICU</li> <li>MV for &gt; 24 hours.</li> <li>in Portuguese, English, Spanish and French</li> </ul> </li> <li>Exclusion criteria: <ul> <li>safety criteria to start EM not described</li> <li>review studies, monographs/</li> <li>dissertations/theses, annals, chapters from books</li> <li>experts' points of view or opinions</li> </ul> </li> </ul>		<b>Mobilization:</b> - under adequate monitoring and with due safety		<b>Endpoint</b> - most widely used safety criteria to start EM for pts under MV and admitted to the ICU	L rechiratory criteria the varianies	1 → 3 (not only RCTs, no metanalysis)

EM = early mobilization, ICU = intensive care unit, MV = mechanical ventilation, pts = patients

The parameters and variables located in the present systematic review can be used as orientation for safety criteria to start EM.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
307 Boyd 2018 (PMID: 29246774 DOI: 10.1016/j.hrtIn g.2017.11.006) <b>Specification</b> of study: Prospective, single-center, cohort study	91 pts - pts>18y - MV in the ICU for cardiothoracic surgery <b>Exclusion criteria:</b> - pts<18y - no MV - expected death Per Branch		<b>Mobilization:</b> - on the basis of a traffic light system for risk stratification and for deciding on the type of possible mobilisation		Outcomes: -AEs	<ul> <li>- 10 (0.0182%) AEs on 549 in- or out-of-bed mobilization units, all minor</li> <li>In-bed cycling: <ul> <li>despite red traffic light parameters, mobilization in bed in</li> <li>2/101 units (1.98%), but no AE</li> <li>despite yellow traffic light parameters in 72/101 units</li> <li>(71.28%), here 1 AE (1.38%, not considered significant as only bladder catheter disconnect).</li> <li>no AE with in-bed mobilisation under vaso-pressive or inotropic medication, 1 AE (0.87%) with tilt table use despite yellow/red parameters in patients under vaso-active support</li> <li>higher probability of AE in pts without inotropic support</li> </ul> </li> <li>Out-of-bed mobilization despite yellow parameters in 189/448 units (42.18%), here 1 AE (0.52%),</li> <li>despite red traffic light parameters in 43/448 (9.59%) units, here 4 AE (9.30%)</li> <li>AE significantly higher with red parameters and out-of-bed mobilisation (p &lt; 0.01)</li> </ul>	4

AE = adverse event, ICU = intensive care unit, MV = mechanical ventilation

The consensus recommendations are a useful tool in guiding safe exercise rehabilitation of mechanically ventilated patients. No detailed assessment was carried out further because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
DOI: 10.1038/s41598- 017-17624-3)	- ≥18 years of age		<b>Physical therapy</b> : - evaluation treatment based on consultation from the primary physician service line		Outcomes: - days of physical therapy treatment during hospitalization - days requiring mechanical ventilation - time to first physical therapy evaluation - comorbidity score - age during hospitalization - CT ICU LOS - hospital LOS	<ul> <li>Outcomes:</li> <li>days of physical therapy treatment during hospitalization: post CABG and Valve surgery had fewer mean days (CABG 3.6 ± 2.6/ Valve surgery 4.1 ± 3.2, no p-value)</li> <li>days requiring mechanical ventilation: no distinguishable difference was found (no p-value stated)</li> <li>time to first physical therapy evaluation: with respiratory failure more days than all the other subgroups (no p-value stated)</li> <li>comorbidity score, post CABG and Valve surgery showed the lowest CCI respiratory failure had a much larger CCI (CABG 4.0 ± 2.8, Valve surgery 3.9 ± 2.7, respiratory failure 5.9 ± 3.2, no p- value stated)</li> <li>age during hospitalization not stated</li> <li>post CABG or post Valve surgery have shorter CT ICU LOS (CABG 4.0 ± 2.6, Valve 4.1 ± 2.9) and hospital LOS (statistically significant differences in between: CABG 10.4 ± 6.9, Valve 17.2 ± 16.9, no p-value stated)</li> <li>with respiratory failure significantly different in hospital LOS (44.9 ± 43.9) and CT ICU LOS (17.6 ± 22.9) (no p-value stated)</li> </ul>	

CCI = Charlson comorbidity score, CT = cardiothoracic, ICU = intensive care unit, LOS = length of stay

Timing and amount of physical therapy in patients with cardiac and respiratory illness differs more based on procedure required during hospitalization than on patient comorbidity and is associated with hospital and CT ICU LOS in this patient population.

					Primary Results	Grade
<ul> <li>310 Guerin 2017</li> <li>ARI</li> <li>Berli</li> <li>29218379</li> <li>Intu</li> <li>DOI:</li> <li>10.1007/s00134-</li> <li>017-4996-5)</li> <li>Specification of study:</li> <li>international 1-</li> <li>duu provalance</li> </ul>	usion criteria: DS criteria according to the in definition e ≥ 18 years. ubated or tracheotomized and hanically ventilated usion criteria: t intubated on the day of the y ARDS on the day of the study n if ARDS criteria had been led between ICU admission the study day Per Branch	РР	Νο ΡΡ	Primary outcome: - prevalence of use of PP in ARDS patients Secondary outcome: - physiological effects of PP, and the reasons for not using it	Primary outcome: - rate of PP use was 5.9% (11/187), 10.3% (41/399) and 32.9% (49/149) in mild, moderate and severe ARDS, respectively (P = 0.0001) Secondary outcome: - before and at the end of the first PP session: PaO2/FIO2 increased from 101 (76–136) to 171 (118–220) mmHg (P = 0.0001); driving pressure decreased from 14 [11–17] to 13 [10–16] cmH2O (P = 0.001); Pplat decreased from 26 [23–29] to 25 [23–28] cmH2O (P = 0.04)	3 → 4

ARDS = acute respiratory distress syndrom, ICU = intensive care unit, PP = prone position, pts = patients

PP was associated with low complication rates, significant increase in oxygenation and a significant decrease in driving pressure.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
312 Martinez 2017 (PMID: 29196586 DOI: 10.4037/ccn 2017531) Specification of study: A before-and- after study	<ul> <li>refused to</li> <li>participate</li> </ul>		Diagnostic phase: preintervention providing baseline Intervention period: (Multicomponent strategy): - physiotherapy and early mobilization - daily reorientation - drug reorientation - prevention of sensory deprivation -drug reviews - pain control, - sleep hygiene, - environmental stimulation, - monitoring of urinary and rectal function, - avoidance of restraints, - family participation in care		<b>Endpoints:</b> - delirium rates - overall mortality - duration of MV - total ICU LOS	Delirium was strongly associated with removal of feeding tubes (RR, 12.9; 95% CI, 1.72-96; p < 0.001) Significant differences between groups in: -interventional period, delirium developed in 55 pts (24%; 95% CI, 19.0%-30.7%), a significant reduction when compared with the diagnostic phase (RR, 0.64; 95% CI, 0.43-0.95; p = 0.03) -reduction in self-withdrawals of implements in the interventional phase, RR 0.42 (95% CI, 0.19-0.92; p = 0.04) No significant differences between groups in: -mortality: p = 0.32, pts with delirium had a no significant increase in risk of death (RR, 1.28; 95% CI, 0.65-2.5; P = 0.54) -duration of MV: median [IQR], 2 [1-5] days vs 1 [0-3] days; p = 0.29 -total ICU LOS: median [IQR], 3 [2-5] days vs 3 [2-6] days; p = 0.066)	4

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients

#### Multicomponent interventions are effective in preventing delirium among the critically ill.

No detailed assessment was carried out further because higher-quality evidence is available on this topic.

Reference, Study Type	(Partio Charac	nd Controls cipant #, cteristics) otal	Drop-out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
313 Li-Bassi 2017 (PMID: 29149418 DOI: 10.1007/s0 0134-017- 4858-1) <b>Specificatio</b> <b>n of study:</b> multicenter RCT	≥ 48 h - within 12 endotrache intubation	from 18 to be on MV hours from	5 pts: 1 excluded by clinician, 3 risk conditions, 1 withdrew consent, 1 randomized twice	LTP: - with the head of the bed tilted 5–10° down	<b>SRP:</b> - with the head of the bed elevated at least 30°	Primary endpoint: - incidence of microbiologically confirmed VAP Secondary outcomes: - ICU mortality - duration of mechanical ventilation - ICU LOS	Primary endpoint: - microbiologically confirmed VAP 0.5% vs. 4.0%, RR 0.13 (95%Cl 0.02-1.03, risk difference -3.5% (95%Cl -6.4 to -0.6), p = 0.04 Secondary outcomes: - ICU mortality: SRP = 48 (23.9%), LTP = 59 (30.4%), (95%Cl, risk difference) 1.27 (0.92-1.76); p = 0.17, no difference in hospital or 28-d mortality (p > 0.05) - duration MV: SRP = 4 (2–9), LTP = 5 (2–-), (95%Cl, risk difference) 0.00 (-1.00 to 1.00); p = 0.73 - ICU LOS (days): SRP = 16 (9–30), LTP = 15 (8–28), 95%Cl, risk difference -2.00 (-5.00 to 1.00), p = 0.24	2 → 3 (premature study stop due to low VAP incidence)

AE = adverse events, CI = confidence interval, ICU = intensive care unit, LOS = length of stay, LTP = lateral Trendelenburg position, MV= mechanical ventilation, pts = patients, SRP = semi recumbent position, VAP = ventilator-associated pneumonia

# LTP seems to decrease the incidence of microbiologically confirmed VAP, but implementation seems difficult and safety concerns exist. Study was stopped prematurely due to low VAP incidence.

Reference, Study Type	(Partic Charac	d Controls tipant #, teristics) otal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
315 Munshi 2017 (PMID: 29068269 DOI: 10.1513/Ann alsATS.2017 04-343OT) Specification of study: Systematic Review and Meta- Analysis	prone positio in the supine adults with Al reported mor - pts with Ber ARDS	eria: Impared MV in n to ventilation position in RDS and		<b>Prone position</b> : -12 hours or longer per day	Supine or prone position: - less than 12 h	Primary outcome: -28-day mortality Secondary outcomes: - 90-day mortality - 6-month Mortality -absolute PaO2/FIO2 ratio on Day 4 - adverse events (unplanned central catheter removal, unplanned extubation, endotracheal tube obstruction, ventilator associated pneumonia, and pressure sores)	Primary outcome: - no difference in mortality (RR, 0.84; 95% Cl, 0.68–1.04) - subgroup analyses found lower mortality with 12h or greater duration prone (5 trials; RR, 0.74; 95% Cl, 0.56–0.99) and for patients with moderate to severe ARDS (5 trials; RR, 0.74; 95%Cl, 0.56–0.99) Secondary outcome - PaO2 /FIO2 ratio on Day 4: higher for n=1093 (MD, 23.5; 95% Cl, 12.4–34.5, I <sup>2</sup> , 24%) - prone positioning associated with higher risks of endotracheal tube obstruction (RR, 1.76; 95% Cl, 1.24– 2.50; I <sup>2</sup> , 26%; three studies [5, 20, 21]) and pressure sores (RR, 1.22; 95% Cl, 1.06–1.41; I <sup>2</sup> , 0%)	1

AE = adverse event, ARDS = acute respiratory distress syndrome, CI = confidence interval, FiO2 = inspiratory oxygen concentration, MV = mechanical ventilation, paO2 = partial oxygen pressure, pts = patients, RR = risk ratio

Prone positioning was associated with a reduction in mortality in patients with moderate to severe ARDS (PaO2/FIO2 < 200) if applied for a longer duration (>12 h), but also with an increase in endotracheal tube obstruction and pressure sores.

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Reference, Study Type	(Partici Charact	d Controls ipant #, eristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
317 Bartolo 2017 (PMID: 28980699 DOI: 10.2340/1650 1977-2269) Specification of study: Secondary analysis of prospective observational study	103 pts Inclusion crite - admitted at with sABI Exclusion crite - premorbid C disability - neurological - neoplastic d metastatic inv the CNS Per B Mobilized (MOB) 68 pts	ICU/NICU eria: CNS-related diseases isease with	6 pts (missing data)	Early passive- active- assisted mobilization including: - sitting over the edge of the bed - sitting on a chair - use of a tilt bed/table to ≥40°	Not well defined, no mobilizati on	Primary outcomes: - clinical and functional status measured with GCS, DRS, LCF (at each visit), ERBI (at admission and discharge), GOS, FIM (at discharge only), - in-hospital death	Primary outcomes: Significant difference between groups in: - LOS, MOB group (26.2 (SD) 13.7 days) and NoMOB group (19.5 (SD) 14.2 days), p=0.01. - ERBI, MOB -225 [-250, -125], NoMOB mean (95% Cl): -250 [-325, -175], p=0.005 - GOS, MOB (3 (95% Cl 3; 3)) vs NoMOB (2 (95% Cl 2; 3)), p = 0.009 - FIM cognitive, MOB 7 (95% Cl 5; 14) vs NoMOB 5 (95% Cl 5; 8.75) ( <i>p</i> = 0.04) <b>No significant difference at discharge between groups in:</b> - GCS, MOB 10.3 (9.2–11.6), NoMOB mean (95% Cl): 7.3 (6.1– 8.7), p=0.480 - DRS, MOB 20.4 (19.1–21.8), NoMOB mean (95% Cl): 24.2 (22.1–26.4), p=0.291 - LCF, MOB 3.5 (3.0–4.1), NoMOB mean (95% Cl): 2.3 (1.9–2.9), p=0.707 - FIM total score, MOB 21 (95% Cl 18; 27) vs NoMOB 18 (95% Cl 18; 21.75) - in-hospital death p=0.375	4

CI = confidence interval, CNS = central nervous system, DRS = disability rating scale, ERBI = early rehabilitation Barthel index, FIM = functional independence measure, GCS = Glasgow Coma Scale, ICU = intensive care unit, LCF = levels of cognitive functioning, LOS = length of stay, NICU = neurological intensive care unit, pts = patient, sABI = severe acquired brain injury

Data from this study show that early mobilization seems to benefit clinical and functional recovery in ICU patients with sABI.

Reference, Study Type	Cases and Con (Participant #, Char Total		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
323 Wright 2016 (PMID: 28780504 DOI: 10.1136/thor axjnl-2016- 209858) <b>Specification</b> of study: multicenter, parallel- group, randomized controlled trial	308 pts Inclusion criteria: - pts 18 years or old admitted at ICU - received 48+ hours invasive or non-inva mechanical ventilati Exclusion criteria: - end-of-life care - acute brain or spin injury - multiple burns - rapidly progressive neuromuscular dise - enrolled in anothe trial without a co-er agreement in place - previously enrolled trial Per Branc 150	rs of asive tion nal cord e ease er clinical nrolment ed in this	total 98: - intervention: 43 (29%) died, 11 (7%) withdrawn, 34 (23%) lost to follow-up - control: 56 (35%) died, 5 (3%) withdrawn, 43 (27%) lost to follow-up	Physical rehabilitation: - functional training and individually tailored exercise programs + respiratory physiotherapy - goal of 90 minutes per day (Monday to Friday) split in at least 2 sessions	Physical rehabilitation: - functional training and individually tailored exercise programs + respiratory physiotherapy - goal of 30 minutes per day (Monday to Friday)	Primary endpoint: - PCS at 6 moths follow up to assess quality of life Secondary outcomes: - MCS - physical ability at ICU discharge - LOS (hospital and ICU) - exercise capacity (6-minute walk test) - FIM - hand grip strength - survival status and place of residence at 3 and 6 months after randomization Power analysis 80% power and a significance level of 0.05 required 77 pts to contribute primary outcome data at 6 months	Primary endpoints: - PCS, mean (SD): 37 (12.2) in the intervention group and 37 (11.3) control with an adjusted difference in means –1.1 (95% CI –7.1 to 5.0) Secondary outcomes: - ICU LOS, days, median (IQR): 6 (4–9) intervention vs 5 (4–8) control. - only 1 FIM at 3months was significantly different between groups - other outcomes n.s	2 → 4 (downgraded as intervention goal not reached)

FIM = functional independence measure, ICU = intensive care unit, IQR = interquartile range, LOS = length of stay, MCS = mental health component summary, n.s = not significant, PCS = physical component summary, pts = patients, SD = standard deviation

In this context, ICU-based physical rehabilitation did not appear to improve physical outcomes at 6 months compared with standard physical rehabilitation.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Recommendations	Evidence Grade
324 Hashimoto 2017 (PMID: 28770093 DOI: 10.1186/s40560-017- 0222-3) <b>Specification of study:</b> Guideline	Systematic review of RCTs regarding PP in adult pts with ARDS. 8 RCTs included	<ol> <li>PP reduces mortality (RR 0.77; 95% CI 0.62-0.96)</li> <li>Mortality was also reduced in moderate/severe ARDS (RR 0.71; 95% CI 0.52-0.97)</li> <li>No reduction in mortlity in prolonged PP (&gt;8h): RR 0.77; 95% CI 0.58-1.02</li> <li>No increase in adverse events (endotracheal complications): (RR 1.29; 95% CI 0.87-1.91 but sig. increase in incidence of decubitus ulcers (RR 1.36; 95% CI 1.06-1.75)</li> </ol>	1

ARDS = acute respiratory distress syndrome, PP = prone positioning, pts = patients, RCT = randomized controlled trial

#### Prone positioning is suggested in adult patients with ARDS (especially in patients with moderate to severe respiratory dysfunction).

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From February 2016 to September 2015: 32 included mechanical ventilated pts. at ICU of the AMC       Results:         331       Inclusion criteria:       - 12 (no - mechanical ventilation >48h       No sample size calculation specified       - 4 480         (PMID: 28549273 DOI: 10.1016/j.jcrc.       - mechanical ventilation >48h       - 12 (no consent or ICU discharge       - 14 of 54 sessions: participants would not have been able to walk (FAC O)       - 40 of 54 sessions: participants would not have been able to walk (FAC O)       - 40 of 54 sessions: participants would be able to walk fm with BWSTT - with BWSTT participant waiked >10m valked >10m valient or ICU PT       - patients antifaction: median 5 (I	Reference, Study Type	(Participant #,	d Controls characteristics) otal	Drop-out - Rate	Intervent ion	Control	Optimal Population	Primary Results	Evidence Grade
20 none	Sommers 2017 (PMID: 28549273 DOI: 10.1016/j.jcrc. 2017.05.010) Specification of study: proof of concept prospective	2016: 32 included r ventilated pts. at IC Inclusion criteria: - ICU patients > 18 v - mechanical ventila Exclusion criteria: - imminent to death - one or more ampu extremities - language barrier (r - S5Q <5 - MRC score 0-1 for muscle strength - contraindications exercise according Statement for ICU F	nechanical CU of the AMC years ation >48h h utated lower dutch language) M. quadriceps for physical to Evidence PT Stranch	consent or ICU	BWSTT	none	specified <b>Outcomes:</b> - eligibility - recruitment rates - number of staff needed - adverse events - successful number of BWSTT - number of patients that could not have walked without BWSTT - patient satisfaction (1 = very unhappy – 5 =very happy) - patient anxiety (0 = no anxiety – 10 = severe anxiety) - MRC score	<ul> <li>- 54 sessions BWSTT with median of 2 (IQR of 1-3) for each participant</li> <li>- median MRC-Score 40 (IQR 32.5- 47.5) with 75% having ICU-AW (MRC &lt;48)</li> <li>- median duration 25 minutes (IQR 20-30)</li> <li>- number of staff needed: 2 (IQR 2-3)</li> <li>- no adverse events occurred</li> <li>- walking distance: median 31 (3-95) steps</li> <li>- 40 of 54 sessions: participants would not have been able to walk (FAC 0)</li> <li>-14 of 54 sessions: participants would be able to walk 5m with BWSTT -&gt; with BWSTT participant walked &gt;10m</li> <li>- patient satisfaction: median 5 (IQR 3-5)</li> </ul>	4

Pts. = patients, AMC = Academic Medical Center, ICU = Intensive Care Unit, BWSTT = Body Weight-Supported Treadmill Training, S5Q = Short 5 item Questionnaire, MRC = Medical Research Council, PT = physiotherapy, FAC = functional ambulation Categories, IQR = interquartile range, ICU-AW = intensive care unit acquired weakness

#### BWTT in critically ill patients is feasible, safe, and potentially effective.

#### No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
332 Schieren 2017 (PMID: 28538631 DOI: 10.1097/TA.0 0000000000 1572) <b>Specification</b> of study: Systematic review and meta-analysis	8 publications from 1988 - 2012 (7 randomized, 1 non- randomized, n = 422 pts) <sup>1-8</sup> Inclusion criteria: -prospective controlled trials -comparing CLRT to conventional manual positioning in trauma pts Per Branch		<b>CLRT</b> (prophylactic in 4 studies (n=243), therapeutic in 4 studies (n = 179))	Standard of care: - manual turning in regular intervals	No primary endpoint defined Extracted endpoints: - rates of pneumonia - ICU LOS - hospital mortality	Significant differences between groups: - pCLRT decreased HAP (OR: 0.33 [95% CI: 0.17, 0.65], p = 0.001, I2 = 0%; NNT = 4) No significant differences between groups in: hospital mortality -pCLRT OR 1.39 [95% CI: 0.69, 2.43], p = 0.42, I <sup>2</sup> = 0% -tCLRT OR 0.54 [95%CI 0.22, 1.33], p = 0.18, I <sup>2</sup> = 0% duration of MV -pCLRT: -1.88 d [95%CI -4.72, 0.97], p = 0.20, I <sup>2</sup> = 0% -tCLRT: -2.97 d [95%CI -7.44, 1.50], p = 0.19, I <sup>2</sup> = 41% ICU LOS -pCLRT: 0.91 d [95%CI -2.79, 4.60], p = 0.63, I <sup>2</sup> = 58% -tCLRT: -1.43 d [95%CI -5.60, 2.74], p = 0.50, I <sup>2</sup> = 0% HAP frequency (tCLRT): OR 1.00 [95%CI 0.15, 6.53], p = 1.00	1 → 2 (downgraded for indirectness)

CLRT = continuous lateral rotation therapy, HAP = hospital acquired pneumonia, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pCLRT = prophylactic CLRT, pts = patients, tCLRT = therapeutic CLRT

Prophylactic CRLT seems to decrease the rate of HAP in trauma patients.

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Reference, Study Type	Cases and Con (Participant #, Chara Total		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
333 Semler 2017 (PMID: 28487139 DOI: 10.1016/j.ch est.2017.03. 061) Specificatio n of study: RCT	260 pts undergoing endotract ICU Inclusion criteria - ≥ 18 years Exclusion criteria: - intubation was required too perform randomization - treating clinicians felt a spec patient position was required performance of the procedur Per Branch	o emergently to cific d for the safe re		Ramped position	Sniffing position	<ul> <li>Primary outcome <ul> <li>lowest arterial</li> <li>oxygen saturation</li> <li>between induction</li> <li>and 2 minutes after</li> <li>intubation</li> </ul> </li> <li>Secondary outcomes: <ul> <li>Cormack-Lehane</li> <li>grade of glottic view</li> <li>difficulty of</li> <li>intubation</li> <li>number of</li> <li>laryngoscopy</li> <li>attempts</li> </ul> </li> </ul>	Primary outcome (ramped vs sniffing) - p3% [84%-99%] vs 92% [79%- 98%] (p=0.27) Secondary outcomes: ramped position increased: - incidence of grade III or IV view (25.4% vs 11.5%) (p=0.01) - incidence of difficult intubation (12.3% vs 4.6%) (p=0.04) Ramped position decreased: - rate of intubation on the first attempt (76.2% vs 85.4%) (p=0.02)	2

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial

#### A ramped position in relation to a sniffing position for intubation seems to have no clinical benefit.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
334 Fan 2017 (PMID: 28459336 DOI: 10.1164/rcc m.201703- 0548ST) <b>Specification</b> of study: Guideline	2.129 pts (8 RCTs) <sup>1-8</sup> Inclusion criteria: - patients with ARDS - mechanical ventilation in adult patients Exclusion criteria: - cointerventions (e.g., higher PEEP) - did not mandate LTV in the control group Per Branch		<b>PP</b> in pts with ARDS	<b>SP</b> in pts with ARDS	Outcomes: - mortality - endotracheal tube obstruction - pressure sores - barotrauma	Significant differences between groups in: - mortality reduced, in trials with prone duration > 12h/d (5 RCTs; 1002 pts; RR 0.74; [95% CI 0.56-0.99]; high confidence) - PP associated with higher rates of endotracheal tube obstruction (3 studies, 1594 pts; RR 1.76 [95% CI 1.24- 2.50]; moderate confidence) - PP associated with higher rates of pressure sores obstruction (3 studies, 1109 pts; RR 1.22 [95% CI 1.06- 1.41]; high confidence) No significant difference between groups in: - mortality: prone vs. supine groups (8 RCTs; 2129 pts; RR 0.84; [95% CI 0.68–1.04]; moderate confidence) - barotrauma: (4 studies, 988 pts; RR 0.77 [95% CI 0.48- 1.24]; moderate confidence)	1

ARDS = acute respiratory distress syndrome, CI = confidence interval, RR = risk ratio

Prone positioning with a duration > 12h/d seems to reduce mortality but increases the rate of endotracheal tube obstruction and pressure sores in ARDS patients.

Reference, Study Type	Cases and C (Participant #, Cha Total	aracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
339 Hester 2017 (PMID: 28328648 DOI: 10.1097/CCM .000000000 002305) <b>Specification</b> of study: retrospective study	2.645 pts. Inclusion criteria: - Neuro-ICU LOS ≥ 2 - ≥18 years old Per Bran 731 Post Period 796 Sustained Period			Post period: immediately after implementati on of the PUMP Plus program + mobility program <u>Sustained</u> <u>period:</u> 2 years after implementati on of the PUMP Plus program + mobility program	before implementation of the PUMP Plus program	Primary outcome: - economic impact of the progressive mobility program (total cost per case) Secondary outcomes: - Neuro-ICU and hospital LOS - ventilator days - percentage requiring mechanical ventilation - discharge disposition - mortality - 30-day readmissions - falls/falls with injury rates - HAI rates - central line—associated bloodstream infection - catheter-associated urinary tract infection (CAUTI) - protocol utilization compliance	Significant differences between groups in: - Mean total cost per case comparison with preintervention: post and sustained period (p < 0.05) -Neuro-ICU LOS [days] shorter in the post period (5.2±6.9) vs preintervention period (6.5±9.1) (p = 0.031) - hospital LOS shorter in post (8.6±8.8) and sustained periods (8.8±9.3) vs LOS in the preintervention period (11.3±14.1) (p < 0.001) - discharge disposition home (p=0.008) and long-term Care (p=0.003) No significant differences between groups in: - ventilator days n.s. - percentage requiring mechanical ventilation (p=0.076) -30-day-readmissions (p=0.335) - falls/falls with injury rate (P= 1.0) -HAI (p=0.607) - CAUTI (p=0.583) - protocol utilization compliance not stated	4

CAUTI = catheter-associated urinary tract infection, HAI = hospital acquired infections, ICU = intensive care unit, LOS = length of stay, Neuro-ICU = neuro-ICU, n.s. = not significant, PUMP = Progressive Upright Mobility Protocol

The implementation of the 'Progressive Upright Mobility Protocol' with a mobility program seems to have a benefit in relation to Neuro-ICU and hospital LOS.

No detailed assessment was carried out further because higher-quality evidence is available on this topic.

Reference, Study Type	(Participant #,	l Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
340 Maffei 2017 (PMID: 28279659 DOI: 10.1016/j.ap mr.2017.01. 028) Specification of study:	40 pts Inclusion criteria - aged >18 - registered on th waiting list - consent - absence of moto major neuromyo score <36) before Exclusion criteria - important hemo instability or seve	: e liver transplant or paralysis and pathy (MRC e LT : odynamic		Intensive and early mobilization protocol: - started by physiotherapist assessment - applied 2x day for 5 days/week	Usual care: - rehabilitation as prescribed by the physician -applied 1x day for 5 days/week	Primary endpoints: - tolerance measured by number of adverse effects defined as: HR <35 or >130 bpm, MAP <60mmHg, RR >35 breaths per minute, SpO2 <88%, NPS >5 (out of 10) - feasibility Secondary outcomes: - LOS in ICU	Significant differences between groups in: - AE: 38/3584 vs 21/1376, p>0.05 - feasibility: first sitting on the edge of bed (3±2 vs. 10±13 d, p=0.018), first transit (4±2 vs. 6±3 d, p= 0.015) No significant differences between groups in:	2 →3 (downgraded for lack of blinding and power analysis)
pilot, prospective, randomized, single-center study	<b>Рег В</b> 20	ranch 20				<ul> <li>LOS in a department of abdominal surgery</li> <li>duration of ventilation</li> <li>No power analysis</li> </ul>	<ul> <li>first sitting on chair n.s.</li> <li>first walking n.s.</li> <li>MV duration n.s.</li> <li>ICU LOS n.s.</li> <li>Hospital LOS</li> </ul>	

bpm = beats per minute, HR = heart rate, ICU = intensive care unit, LOS = length of stay, LT = lung transplantation, MAP = mean arterial pressure, MRC = medical research council, MV= mechanical ventilation, NPS = numerical pain scale, pts = patients, RR = respiratory rate, SPO2 = peripheral oxygen saturation

# An ongoing progressive mobility program in the neurological critical care population has clinical and financial benefits associated with its implementation and should be considered.

Reference, Study Type	Cases and Co (Participa Characteris Total	int #, istics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
342 Gaudry 2017 (PMID: 28236174 DOI: 10.1186/s136 13-017-0235- z) Specification of study: Retrospective multicenter cohort study	98 pts Inclusion criter - ARDS (PaO2/I <300 mmHg w or CPAP ≥5 cm a context of re (less than 7 da' abdominal sur Exclusion crite - laparoscopy - pts who died next 48h follow surgery Per Bran 36	/FiO2 vith PEEP hH2O) in ecent ays) rgery eria: l in the wing		PP	SP	Primary endpoint: - number of pts who had at least one surgical complication induced or worsened by PP Secondary outcomes: - number of revision surgeries due to complication induced or worsened by PP - effects of PP on oxygenation - duration of MV - mortality - LOS no sample size calculation	Primary outcome: -no significant difference in rate of surgical complications induced or worsened by PP [respectively, 14 (39%) vs 27 (44%); p = 0.65] Secondary outcomes: Significant differences between groups in: - PaO2/FiO2 ratio, the first PP significantly increased from 95 ± 47 to 189 ± 92 mmHg, p < 0.0001 No significant differences between groups in: - revision surgery (p = 0.10) - duration of MV (p = 0.72) - ICU LOS (p= 0.77) - ICU mortality (p= 0.43)	4

ICU = intensive care unit, LOS = length of stay, PP = prone position, pts = patients, SP = supine position

### Prone position of ARDS patients after abdominal surgery was not associated with an increased rate of surgical complication.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
343 Nydahl 2017 (PMID: 28231030 DOI: 10.1513/Ann alsATS.20161 1-843SR) <b>Specification</b> of study: Systematic review and meta-analysis	48 publication (6 RCTs, 2 non- RTCs, 5 before/after studies, 22 prospective cohort studies, 2 1-day point prevalence studies, 7546 total pts) <sup>1-48</sup> <b>Inclusion criteria:</b> - pts received mobilisation- related interventions in ICU - studies reported on safety events <b>Exclusion criteria:</b> - the majority (>50%) of pts were under 18 years old - data on the incidence of potential safety events could not be calculated - interventions did not involve pts mobilisation - sample size was less than 10 pts <b>Per Branch</b>		Mobilisation/ Rehabilitation in the ICU	No mobilisa tion while ICU stay	Primary endpoint: -safety incidents defined as: 1) hemodynamic changes (high HR > 125–140 beats/min, low MAP < 55–70 mm Hg, low systolic BP < 80–90 mm Hg, high MAP > 100–140 mm Hg, and high systolic BP > 180–200 mm Hg) 2) desaturation (using the categories, < 80, <85, <88, and <90%)	<ul> <li>Primary endpoint: <ul> <li>safety: total 22351 mobilisation/rehabilitation sessions with 583 reported potential safety events, for a cumulative incidence of 2.6%.</li> <li>most frequently reported types of event: oxygen desaturation and hemodynamic changes, each reported in 33 studies (69% of studies), and removal or dysfunction of intravascular catheter in 31 studies (65% of eligible studies)</li> </ul> </li> <li>Meta-analysis: <ul> <li>high HR, 6 publications, 319 pts and 1,784 mobilisation/rehabilitation sessions, pooled incidence of 1.9 episodes (95% CI = 0.3–15) per 1,000 mobilisation/rehabilitation sessions (I2 = 0%).</li> <li>low BP, 11 publications, 2,793 pts and 8,757 mobilisation/ rehabilitation sessions, pooled incidence of 4.3 episodes (95% CI = 1.6–12.1) per 1,000 mobilisation/rehabilitation sessions (I2 = 67%)</li> <li>low systolic BP, 9 publications, 329 pts and 2,808 mobilisation/ rehabilitation sessions (I2 = 0%).</li> <li>high BP, 1,931 pts and 6,517 mobilisation/ rehabilitation sessions, pooled incidence of 1.8 episodes (95% CI = 0.8–3.9) per 1,000 mobilisation/ rehabilitation sessions (I2 = 0%).</li> <li>high BP, 1,931 pts and 6,517 mobilisation/ rehabilitation sessions, pooled incidence of 3.9 episodes (95% CI = 1.0–14.8) per 1,000 mobilisation/ rehabilitation sessions (I2 = 31%)</li> <li>high systolic BP, 6 studies, 317 pts and 2,896 mobilisation/rehabilitation sessions, pooled incidence of 0.3 episodes (95% CI = 0.1–1.2) per 1,000 mobilisation/rehabilitation sessions, total pooled incidence of 1.9 episodes (95% CI = 0.9–4.3) per 1,000 mobilisation/rehabilitation sessions (I2 = 6%)</li> <li>Oxygen desaturation, 24 publications, 3,051 pts and 12,798 mobilisation/ rehabilitation sessions (I2 = 6%)</li> <li>oxygen desaturation, 24 publications, 3,051 pts and 12,798 mobilisation/ rehabilitation sessions (I2 = 6%)</li> <li>no significant difference in subgroup analysis results comparing prospective and retrospective studies (P = 0.719), nor in comparing intervention and control groups</li></ul></li></ul>	1

BP = blood pressure, CI = confidence interval, HR = heart rate, ICU = intensive care unit, MAP = mean arterial pressure, pts = patients, RCT = randomized controlled trial

Patient mobilisation and physical rehabilitation in the ICU appears safe, with a low incidence of potential safety events, and only rare events having any consequences for patient management.

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Reference, Study Type		and Controls t #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
344 Moyer 2017 (PMID: 28230563 DOI: 10.1097/JNN.00 000000000025 8) Specification of study: prospective cohort study with historical control group	Exclusion crite - intolerance to clamping - sustained into hypertension - fluctuating ro- examination co mobilization	co 30min of drain cracranial (ICP > 20		Early mobilization algorithm	historical control group of patients with SAH	Primary endpoints: - time to first mobilization - ICU and hospital LOS Secondary outcomes: - ventilator days	Significant differences between groups in: - decreased the mean length of time to the first mobilization from 18.7 to 6.5 days (p<0.0001) No significant differences between groups in: - ICU and hospital LOS n.s. - ventilator days n.s.	4

EVD = external ventricular drain, ICU = intensive care unit, LOS = length of stay, n.s. = not significant, pts = patients, SAH = subarachnoid hemorrhage

## Implementation of an early mobilization algorithm for patients with EVD seems to decrease the mean length of time to first mobilization.

Reference, Study Type	(Participant #	nd Controls #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
345 Yamashita 2017 (PMID: 28210060 DOI: 10.1589/jpts. 29.138) Specification of study: retrospective study	of daily wake- - usual care PT introduction w mobilization Per	ore introduction up attempts as well as after	-	<b>Early mobilization:</b> - 7d/week in cooperation with PT/nursing -activity according to tolerance	Deep sedation and usual care PT: - activity level of the pts according to the doctor's instructions and trained only by therapists	Primary outcome A-time to first mobilization -duration of sedation - analgesia, -intubation - MV - LOS no sample size calculation (retrospective study)	Significant differences between groups in: - duration of sedation (7 (5-8) vs. 5 (4-7)) days, $p < 0.05$ -analgesia (5 (4-6.5) vs. 4 (3-6) days) - duration of ventilation (7 (6-9) vs. 5 (5- 7) days), $p < 0.05$ -duration of intubation (7 (6-9) vs. 5 (4- 7) days), $p < 0.05$ - time to first mobilization out of bed (10 (8-15) vs. 7 (6-11) days), -time to stand (11 (8.5-18.5) vs. 9 (7-13) days), $p < 0.05$ - walking (13 (9.5-20.5) vs. 11 (7-16) days), $p < 0.05$ -LOS (11 (8.5-18.5) vs. 9 (7-13) days)	4 → 5

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, PT = physical therapy, pts = patients

These results suggest that the new sedation and cooperative rehabilitation methods for critically ill patients were effective in the early stage of treatment and shortened the duration of stay in the ward.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
347 Dall'Acqua 2017 (PMID: 28101565 DOI: 10.2340/16501 977-2168) Specification of study: RCT	38 pts         Inclusion criteria:         - both sexes         - ≥ 18 years         - hospitalized for no longer than 15 days         - received ≥ 24 h of IMV         Exclusion criteria:         - neuromuscular diseases associated with motor deficits.         - extubated within 48 h after inclusion         - complications during the protocol         - prolonged weaning (failed 3 spontaneous breathing trials)         - BMI > 35 kg/m²         - pacemaker         - haemodynamic instability         (noradrenaline > 0.5 µg/kg/min for a mean arterial pressure > 60 mmHg)         - history of epilepsy         - postoperatively with abdominal or chest incision         neuromuscular blockers for 2 or more consecutive days         Per Branch         19       19	13 (34,2%) Intervention: n=8 (clinical decompensatio n (n=3), surgical wound abdominal (n=1), comfort measures (n=1), extubated (n = 1)) Control: n=5 (clinical decompensatio n (n=3); EVA (n=1); death (n=1))	NMES: - chest and abdominal muscles - for 30 minutes up to day 7 or extubation Convention al physical therapy: - twice daily for 30 minutes until day 7 or extubation	Sham NMES: - chest and abdominal muscles - for 30 minutes up to day 7 or extubation Conventional physical therapy: - twice daily for 30 minutes until day 7 or extubation	Primary endpoint: - difference in M. rectus abdominis and chest muscle thickness via ultrasound between day 1 and 7 or extubation Secondary outcomes: - diaphragm muscle thickness - diaphragm motion during inhalation and exhalation - ICU LOS - duration of invasive MV - successful extubation - mortality	Primary endpoint: - muscle thickness M. rectus abdominis MD (95%Cl): -0.07 (-0.100.04), $p > 0.001$ - muscle thickness chest, MD (95%Cl): -0.06 (- 0.100.02), $p > 0.001$ Secondary outcomes: - diaphragm muscle thickness: MD (95%Cl): - 0.02 (-0.05 - 0.03), $p = 1.000$ - inspiratory diaphragmatic motion, MD (95%Cl): 0.05 (-0.23 - 0.33), $p = 1.000$ - expiratory diaphragmatic motion, MD (95%Cl): -0.04 (-0.28 - 0.20), $p = 1.000$ - LOS ICU (days), mean (SD): control 16 (9) vs intervention 10 (4), $p = 0.045$ - duration of IMV (days), mean (SD): control 8 (3) vs intervention 7 (2), $p = 0.607$ - reintubation rate, $n$ (%): control 5 (38) vs intervention 3 (25), $p = 1.000$	2 → 4 (bias risk and pilot size)

BMI = body mass index, EVA = encephalic vascular accident, IMV = invasive mechanical ventilation, LOS = length of stay, MD = mean difference, NMES = neuromuscular electrical stimulation, pts = patients

#### Neuromuscular electrical stimulation reduced loss of chest and abdominal wall muscle thickness.

Reference, Study Type		es and Controls ant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
348 van Willigen 2016 (PMID: 28090326 DOI: 10.1136/b mjquality. u211734. w4726) Specificati on of study: Quality improvem ent study	Inclusion criteria: - ventilated < 72 hou - expected to remain - cognitively intact and prior to admission Exclusion criteria: - age < 18 - rapidly deterioration - raised intracranial p - post cardiac arrest - BMI > 35	n ventilated for ≥ 24 hours nd functionally independent ng neuromuscular disease,		Quality improvement project to deliver early mobilization: - twice-daily 30-minute sessions of rehabilitation therapy - addition to standard physiotherapy sessions for ≥ 5days per week - mobility therapy was started within 72 hours of the pts being intubated and ventilated, and was continued until discharge from ICU	Pre-QI time	Derived outcomes - first out of bed mobilization - ICU and hospital LOS	<ul> <li>Derived outcomes</li> <li>pts mobilized out of bed</li> <li>8.3 days earlier</li> <li>reduction in mean ICU LOS</li> <li>by 6.6 days after QI</li> <li>implementation</li> <li>mean number of therapy</li> <li>sessions received by ICU</li> <li>survivors doubled</li> <li>hospital LOS decreased, by</li> <li>11.9 days following</li> <li>improvement cycle 1 and by</li> <li>a further 3.9 days following</li> <li>improvement cycle 2</li> </ul>	4

BMI = body-mass index, ICU = intensive care unit, LOS = length of stay, pts = patients, QI = quality improvement

# An implementation of a quality improvement (QI) project to deliver early mobilization seems to have a benefit in relation to ICU and hospital LOS and patients are mobilized out of bed earlier.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
349 Wollersheim 2017 (PMID: 28065165 DOI: 10.1186/s13054 -016-1576-y) Specification of study: Pilot interventional study	19 pts. from mixed ICU and a neurosurgical ICU at university hospital Inclusion criteria: - critically ill patients with mechanical ventilation >48hours - ICU stay at least 7 days Exclusion criteria: - lack of informed consent - age <18 - preexisting neuromuscular disease - implanted pacemaker or defibrillator - pregnancy - acute venous thrombosis - unhealed fractures or recently attached implants in body region to be stimulated - recent eye surgery - acute herniated discs or recently history of herniated disc - participant in another study - terminal cases	none	Passive PT followed by a single session of WBV in supine position (Promedi, Vibrosphere/Galil eo, 26 Hz, 9 times for 1 minute or home-ICU, 24 Hz, 3 times for 3 minutes)	none	Outcomes: - safety and tolerability of WBV - heart rate and blood pressure - hemodynamic parameters via PiCCO <sub>2</sub> (CO, SV, SV range, CPO) - indirect calorimetry - BGA (pO <sub>2</sub> , pCO <sub>2</sub> , pH, sodium, potassium, blood glucose)	Results: - diastolic BP elevated during PT compared with baseline (p=0.014) - HR, MAP, systolic BP and SpO <sub>2</sub> did not differ from baseline, PT, WBV, and resting periods - CPO: significant decrease (p=0.047) during WBV, no changes in CO or BP - SV range: variability increased during PT in comparison with baseline (p < 0.001) - increased EE (p=0.0007) during WBV compared with baseline: oxygen uptake levels increased (p=0.012), carbon dioxide production enhanced (p<0.001) - PT increased elimination of carbon dioxide (p=0.041) - PT (p<0.01) and WBV (p<0.001) increased respiratory rate - RQ increased during PT (p=0.003) - BGA: WBV was associated with increase of potassium compared with baseline (p=0.048)	3 → 4

Pts. = Patients, ICU = intensive care unit, WBV = whole-body vibration, PT = physiotherapy, PiCCO = Pulse Contour Cardiac Output, BGA = blood gas analyses, ICP = intracranial pressure, CO = cardiac output, SV = stroke volume, CPO = cardiac power output, IGF-1 = insulin-like growth factor 1, pH = potential hydrogen, BP = blood pressure, HR = heart rate, MAP = mean arterial pressure, SpO<sub>2</sub> = peripheral capillary oxygen saturation, EE = energy expenditure, RQ = respiratory quotient

Whole-body vibration is safely applicable even to critically ill patients in severe condition.

Reference, Study Type		s and Controls It #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
351 Lai 2016 (PMID: 27979608 DOI: 10.1016/j.ap mr.2016.11.0 07) Specification of study: quality improvement study	153 adults pts w 90 phase 2 (intervention period), Phase 3 (maintenance period)	vith MV Per Branch 63 phase 1 (preintervention phase)		<b>Early mobilization</b> <b>program:</b> - within 72 hours of MV - twice daily, 5d/wk during the 30-minute family visiting time, and, if possible, cooperating with family	preintervention phase	<b>Clinical outcomes:</b> - MV duration (d) - ICU and hospital LOS (d)	Significant differences between groups in: - MV duration (d) 4.7+-2.3; 7.5+-7.0; p<0.001 - ICU LOS 6.9+-3.5; 9.9+- 7.6; p=0.001 No significant differences between groups in: - hospital LOS n.s.	4 (downgra ded due to historic control)

d = days, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, n.s. = not significant, pts = patients, wk = week

### An early mobilization program seems to have a benefit in relation to a shorter MV duration and ICU LOS.

447 pts. January through August 2012         Inclusion criteria:         - ICU pts. 18 years or older         352         Smith 2016         - ICU pts who were delirium-positive on admission	Reference, Study Type	Cases and (Participant #, C Tot	haracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Image: Primite 27963224       - were transferred to a lower level of care or laterally transferred from the intervention group to the control group       - consisting of:       1. Sedation       - consisting of:       1. Sedation       - incidence of delirium       - increases in age, length of stay in the ICU, and use of mechanical         Specification of study:       - mere transferred form the intervention a controlled interventional cohort study       - mere transferred form the intervention group       - consisting of:       1. Sedation       - incidence of delirium       - increases in age, length of stay in the ICU, and use of mechanical         Note:       - mere transferred to a lower level of care or laterally transferred from the intervention group       - consisting of:       1. Sedation       - incidence of delirium       - increases in age, length of stay in the ICU, and use of mechanical         Specification of study:       - mere transferred to a lower level of care or laterally transferred from the intervention and control group       - secondary outcomes:       - increases in age, length of stay in the ICU, and use of mechanical         Note:       - mere transferred form the intervention and control group       - mere transferred form the intervention and control group       - secondary outcomes:       - increases in age, length of stay in the ICU, and use of mechanical         Note:       - mere transferred form the intervention and control group       - mere transferred form the intervention and control group       - mere transferred form the intervention and control group	Smith 2016 (PMID: 27965224 DOI: 10.4037/ajcc2017 374) Specification of study: a controlled interventional	447 pts. January throug Inclusion criteria: - ICU pts. 18 years or ol Exclusion criteria: - ICU pts who were deli admission - ICU stay for 4 months - were transferred to a laterally transferred fro group to the control gro Per Br	gh August 2012 der rium-positive on or longer lower level of care or om the intervention oup <b>anch</b> n = 298 (control		-implemented by nurses - consisting of: 1. Sedation cessation 2. Pain control 3. Sensory stimulation 4. Early mobility 5. Sleep		<ul> <li>incidence of delirium</li> <li>Secondary outcomes:</li> <li>risk factors associated</li> </ul>	<ul> <li>significant reductions (78%) in the relative risk for delirium in intervention group (odds ratio, 0.22; 95% CI, 0.08-0.56; <i>P</i> = .001)</li> <li>Secondary outcomes: <ul> <li>increases in age, length of stay in the ICU, and use of mechanical ventilation and restraints were associated with significant increases in the relative risk of delirium (all p &lt;.001)</li> <li>-pts' race, number of comorbid conditions, and sex were not</li> </ul> </li> </ul>	4

CI = confidence interval, DPB = delirium prevention bundle, ICU = intensive care unit, pts = patients

### The delirium prevention bundle was effective in reducing the incidence of delirium in critically ill medical-surgical patients

Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
355 Munshi 2017 (PMID: 27898220 DOI: 10.1513/Ann alsATS.20160 6-484OC) Specification of study:	107 pts with E0 ICU-ECMO coh 2010 - 2015 -> ARDS Inclusion criter - veno-venous Exclusion crite - ECMO as a br transplant - post-transpla - ECMO for isol failure	ort between 61 (57%) with ria: ECMO ria idge to lung nt ECMO		PT/Mobilisation	Bed rest	No sample size calculation (retrospective study) <b>Primary outcome</b> - association between ICU PT and ICU mortality <b>Secondary outcome</b> : - factors associated with a higher IMS	Primary outcome:         - ICU- and in-hospital mortality: 22% who         underwent ICU PT compared with 64% who did not         (p = 0.006)         Significant differences in ICU-mortality for:         - ICU-physiotherapy (OR, 0.19; 95% CI, 0.04-0.98)         - APACHE II score (OR, 1.13; 95% CI, 1.01-1.26)         - sex (OR, 9.4;95% CI, 1.71 -41.7)         No significant differences between groups in:         - APACHE II score (p = 0.63)         - pre ECMO PF ratio (p = 0.30)	4
retrospective study	Per Branch					- $PaO_2$ on Day 1 post-ECMO (p = 0.65)		
	50	11						

ARDS = acute respiratory distress syndrome, APACHE II = acute physiology and chronic health evaluation II, ECMO = extracorporal membranous oxygenation, ICU= intensive care unit, IMS = ICU mobility scale, PF = PaO<sub>2</sub>/FiO<sub>2</sub> ratio, PT = physical therapy, pts = patients

ICU physiotherapy while on ECMO was significantly associated with reduced ICU mortality.

Reference, Study Type	(Partic Charact	d Controls ipant #, :eristics) ıtal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidenc e Grade
358 Tipping 2017 (PMID: 27864615 DOI:10.100 7/s00134- 016-4612- 0) <b>Specificati</b> of study: systematic review and meta- analysis	14 publicatio pilot RCT, 2 c observationa included 175 Inclusion crit - adult patier years) admitt ICU for great Per B	control Il study) 3 pts t <b>eria</b> hts (>16 ted to the		Active early mobilisation	Usual care	Primary endpoint: - hospital mortality Secondary outcomes: - 6 and 12-month mortality - days alive and out of hospital at 180 days - functional status - mobility - muscle strength - quality of life and mood state at ICU/hospital discharge and 6- 12 months follow-up - LOS ICU - duration of ventilation - discharge destination	Significant differences between groups in: - muscle strength at discharge from ICU (mean 8.62 points in MRC Sum Score, 95% Cl 1.39-15.86, p = 0.02) - likelihood of walking unassisted at discharge from hospital (odds ratio 2.13, 95% Cl 1.19-3.83, p = 0.01 - more days alive and days out of hospital at day 180 (MD 9.69, 95% Cl 1.7-17.66) No consistent effects regarding: functionality, quality of life, length of stay in ICU without hospital or mechanical ventilation.	1

CI = confidence interval, ICU = intensive care unit, LOS = length of stay, MD = mean difference, MRC = medical research council scale, pts= patients, RCT = randomized controlled trial

Active early mobilization has no impact on mortality, but may have an impact on muscle strength. A subgroup of early (within 72 hours) mobilized patients spent more days alive and out of hospital at 180 days.

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Reference, Study Type	(Participant #,	d Controls Characteristics) Ital	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
359 Bounds 2016 (PMID: 27802955 DOI: 10.4037/ajcc2 016209) <b>Specification</b> of study: Retrospective pre and after case control study	in death	or older nan 24 hours ssure increased rom first ICU bitalization without use of res only as he medical al orders for life-	2 pts (incomplete documentation)	Delirium prevention bundle: - 6 components - of which one was EM	historical control (usual care)	Primary outcomes: - prevalence and duration of delirium - ICU and hospital LOS - days of mechanical ventilation no sample size calculation	Primary outcome: Significant differences between groups in: -days of delirium decreased (mean, SD): $3.8\pm2.9$ vs. $1.72\pm0.8$ (p<0.001) -number of pts with delirium-free stays increased (from 62% to 77%; p=0.01) - decreases in delirium prevalence (from 69% to 31%; p< .001) and duration (from 2.96 to 0.56 days, p< .001) in ICU pts with mechanical ventilation -pts with mechanical ventilation who had delirium-free stays increased (from 31% to 69%; p < .001) No significant differences between groups in: - ICU LOS (p =0.47) or hospital LOS (p=0.15) - total days of mechanical (p=0.78)	4

EM = early mobilization, GCS = Glasgow coma scale, LOS = length of stay, pts = patients

The implementation of an ABCDE bundle was associated with a decrease in prevalence and duration of delirium. *No detailed assessment was carried out further because higher-quality evidence is available on this topic.* 

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total						
(PMID: 27762595 DOI: 10 1164/rccm 20	3 systematic reviews <sup>1-3</sup> Inclusion criteria: - acutely hospitalized adults mechanically ventilated for more than 24 hours Per Branch		Early mobilisation	SOC without early mobilisation	Outcomes: - mortality - ICU Length of stay - ability to walk at ICU and hospital discharge - 6-minute-walk distance at hospital discharge - duration of mechanical ventilation - ventilator-free days - serious adverse events - arrhythmias	No Significance stated: -mortality (mean difference 3; 95% CI, -58 – 103) - ICU Length of stay (mean difference –0.56; 95% CI, -2.76 – 1.63) -more likely to be able to walk at hospital discharge (64.0 vs. 41.4%; RR, 1.56; 95% CI, 1.15–2.10) - 6-minute-walk distance at hospital discharge (Mean difference 53; 95% CI, -16.96 to 122.96) -shorter duration of mechanical ventilation (mean difference 2.7 fewer days; 95% CI, 1.19–4.21) - ventilator-free days (mean difference 2.4; 95% CI, -3.59 to 8.39) - serious adverse events (6.5 events per 1,000 PT treatment sessions) - arrhythmias (1.9 events per 1,000 PT treatment	1

ICU = intensive care unit, PT = physio therapy, SOC = standard of care

## For acutely hospitalized adults who have been mechanically ventilated for more than 24 hours, protocolized rehabilitation directed toward early mobilization is suggested.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Primary Results	Evidence Grade
361 Cho 2016 (PMID: 27790273 DOI: 10.4046/trd.2016.79.4.214)	Patients with acute respiratory distress syndrome No data available	<ul> <li>Recommendations regarding mobilization: <ul> <li>Prone position can be applied to patients with moderate or above ARDS to reduce mortality if it is not contraindicated (grade 1B).</li> <li>Prone position should be applied when there is no improvement of oxygenation at early stage of mechanical ventilation.</li> <li>Prone position is recommended at least for 10 hours.</li> <li>Lung protective strategy should also be applied during prone positioning.</li> </ul> </li> </ul>	1
Specification of study: Clinical Practice Guideline	Definition of EM	Grading of quality level of evidence following GRADE recommendations (1 = high recommendation, 2 = weak recommendation; A to D = Quality level of evidence)	

ARDS = acute respiratory distress syndrome, FiO2 = fraction of inspired oxygen, GRADE = grading of recommendations, assessment, development and evaluations, HFOV = high frequency oscillatory ventilation, ICU = intensive care unit, iNO = inhaled nitric oxide, PaO2 = partial pressure of oxygen, PEEP = positive post-endexpiratory pressure, pts = patients

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
363 Corcoran 2017 (PMID: 27346093 DOI: 10.1016/j.pm rj.2016.06.01 5) Specification of study: cohort study, historical control	283 ICU pts         Inclusion criteria:         - admitted to the hospital on or after March 10, 2014         - discharged from the hospital on or before June 30, 2014         - admitted to the ICU within 3 days of hospital admission         - 18 years or older         - received PT or OT orders within 3 days of ICU admission         Exclusion criteria:         - transferred from outside facility         - independent at hospital admission in both mobility and activities of daily living         - non-ambulatory preadmission         - receiving end-of-life care         - transferred         out of the ICU         - refusing rehabilitation         therapy for more than 3 days         - requiring subsequent surgery within 1 week of initial surgery         secondary to complications         - progressive neurological, muscular, orthopedic or medical disorders         precluding mobility         - moderate-to-severe Alzheimer disease         - awaiting organ transplant         - complications of         pregnancy         - moderate-to-severe stroke postoperative         - post-left ventricular         assist device surgery         - extracorporeal membrane         oxygenation		Initiation of "Performance Improvement Project": -including physiotherapy -1-2/day -occupational therapy 1/d	historical control, not specified	Primary outcomes: - ICU and hospital LOS - intensity of service - medications - pain - discharge disposition - functional mobility - average cost per day	Primary outcomes: - rehabilitation therapy services increased from 2012 to 2014 by approximately 60mins/patient - average ICU LOS decreased by almost 20% from 4.6 days (pre- PIP) to 3.7 days (PIP) (P = 0.05) - increased percentage of PIP patients, (40.5%) discharged home without services compared with (18.2%) the pre-PIP phase (P <0.01) - average cost per day in the ICU and floor bed decreased in the PIP group, resulting in an annualized net cost savings of \$1.5 million	4
	160 123						

LOS = length of stay, OT = occupational therapy, PIP = performance improvement project, PT = physical therapy, pts = patients

Benefits of this performance improvement program included reduced hospitalization LOS, decreased health care costs, and decreased need for post-acute care services.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
364 McWilliams 2017 (PMID: 27745753 DOI: 10.1016/j.aucc .2016.09.001) <b>Specification</b> of study: single center prospective before and after study	80 ICU pts         Inclusion criteria:         - ventilated for ≥ 5 days         - > 18 years         Exclusion criteria:         - contraindications to         mobilization         - severe neurological injury         or neuromuscular disease         or motor neuron disease         - MV >48h         - poor preadmission level of         mobility         - over 6ft 5in tall         - weight over 440lbs         40       40	control n=9 -7 died -2 transferred to another hospital intervention n=8 -7 died -1 transferred to another hospital	Training and use of "Sara Combilizer®"	Standard care without "Sara Combilizer®"	<ul> <li>Primary endpoint: <ul> <li>Time to 1<sup>st</sup> mobilization (MMS)</li> </ul> </li> <li>Secondary endpoints: <ul> <li>SOFA score at 1<sup>st</sup> mobilization</li> <li>ICU LOS</li> <li>Duration of ventilation</li> <li>MRC at ICU discharge</li> <li>MRC at hospital discharge</li> <li>Readmission to ICU</li> </ul> </li> </ul>	Primary outcome: (control vs intervention)Significant differences between groups in: - time to 1st mobilization (MMS of≥2): 13.6 (11.7–15.8) 10.6 (9.1–12.4) days (p=0.028)Secondary outcomes: (control vs intervention)Significant differences between groups: - SOFA 2.9 (0.5) vs 5.1 (2.4) (p=0.005) - ICU LOSNo significant differences between groups in: - ventilation duration 11 (6, 15) vs 8 (6, 12) (p=0.104) - ICU LOS 17.1 (14.3–20.5) vs 15.3 (13.3– 17.5) (p=0.331) - MRC at ICU discharge 51 (41, 54) [n = 16] vs 47 (34, 56) [n = 22] (p=0.579) - MRC at hospital discharge 58 (48, 60) [n = 19] vs 54 (50, 60) [n = 27] (p=0.855) - readmission to ICU 3 (10%) vs 1 (3%) (p=0.355)	4

ICU = intensive care unit, LOS = length of stay, MMS = Manchester mobility score, MV = mechanical ventilation

## The Sara Combilizer<sup>®</sup> may be a useful adjunct to an early mobility protocol within the ICU. *No detailed assessment was carried out further because higher-quality evidence is available on this topic.*

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
365 Silva 2017 (PMID: 27732921 DOI: 10.1016/j.jcrc.20 16.09.012) <b>Specification of</b> <b>study:</b> prospective observational study	11 pts admitted at ICU (from February to July 2013 in a tertiary public hospital in Teresina, Brazil) Inclusion criteria: ≥ 18 years - APACHE II > 13 - MV from 24 to 48h - prediction to stay in MV for ≥ 3 days Exclusion criteria: - MAP < 65 or > 110 mmHg - lesions on the skin that prevent the realization of protocol - fractures in lower limbs, vertebral fractures - brain death N=11		NMES: - for 15 min (90 contractions) daily for 3 days - pulse width equal to chronaxie, pulse frequency of 100 Hz, ON time 5 seconds, OFF time of 5 seconds, no rise time, and decay - on tibialis anterior and hamstrings, quadriceps femoris	No control group	<b>Outcome</b> (not exactly defined) - creatine kinase - lactate - central venous oxygen saturation - burn injuries - chronaxie assessments	No significant differences: - creatine Kinase (UI/L): - baseline – mean (SD): 470 (270) - 24 hours – mean (SD): 350 (245) - 48 hours – mean (SD): 430 (245) - 72 hours – mean (SD): 430 (280), p-value <0.99 - lactate on days 1, 2, and 3 pre to post stimulation - central venous oxygen saturation on days 1, 2, and 3 - central venous oxygen saturation and serum lactate: same pattern with no significant variations (P = .23 and P = .8, respectively) - no burn injuries on the skin - comparisons of intermuscular groups over day 2 and day 3 did not demonstrate any significant difference Significant difference - day 1: gluteus maximus=550 (±150) ms vs. quadriceps=300 (±90) ms; quadriceps= 300 (±90) ms vs. tibialis anterior= 540 (±160) ms (P = .005 and P = .005)	4

APACHE II = acute physiology and chronic health evaluation, ICU= intensive care unit, MAP = mean arterial pressure, ms = microseconds, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, pts = patients, SD = standard deviation

## No differences in laboratory parameters as surrogates for muscle damage could be observed after neuromuscular electrical stimulation. *No detailed assessment was carried out further because higher-quality evidence is available on this topic.*

Reference, Study Type		l Controls Characteristics)	Drop- out	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	То	tal	Rate					
369 Booth 2016 (PMID: 27618376 DOI: 10.1097/JTN.00 00000000002 34) Specification of study: Observational study, retrospective		NTICU achieved		Mobilisation	Bed rest	Outcomes: - venous thromboembolism (VTE) - ICU and hospital LOS - duration of ventilation - falls - resp. failures - pneumonia No sample size calculation (pre- intervention cohort analyzed retrospectively)	Significant differences between groups in: - incidence/VTE pre-intervention group (21%) and post-intervention group (7.5%) (p = 0.0004). No significant differences between groups in: - hospital and ICU LOS - average duration of ventilation - mortality - falls, - respiratory failure - pneumonia no adverse events (extubation, hypoxia, falls)	4

ICU = intensive care unit, LOS = length of stay, MOVE = myocardial stability/oxygenation adequate/vasopressor(s) minimal/elevated intracranial pressure, NTICU = neurotrauma intensive care unit, RASS = Richmond agitation sedation score, VTE = venous thromboembolism

Progressive mobility protocols reduced the incidence of VTEW in the at-risk intensive care trauma patient population. *No detailed assessment was carried out further because higher-quality evidence is available on this topic.* 

Reference, Study Type	Cases and Contro (Participant #, Charact Total	teristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
370 Deng 2016 (PMID: 27595451 DOI: 10.1016/j.bur ns.2016.07.02 9) <b>Specification</b> of study: cohort study, historical control	73 ICU pts (survivors) Inclusion criteria: - admitted to the BICU f January 2011 to Decem 2013 - within 7 days of severa - 16–65 years old - TBSA burns equal to o than 50% - length of BICU stay was same as the length of histay - received rehabilitation BICU - survived Per Branch	nber re burns or more as not nospital		Active PT	Passive PT only	Outcomes: -ICU and hospital LOS - ROM - ADL (assessed with BI and FIM) No sample size calculation	Significant differences between groups in: - ICU LOS 65 ± 38 h vs. 39 ± 16 h, p=0.002 - hospital LOS 184 ± 141 vs. 101 ± 42, p=0.010 - ROM: mobility training group better performance in shoulder abduction (p=0.013), wrist extension (p=0.001), hip flexion (p=0.003) hip abduction (p=0.001), knee flexion (p=0.001), ankle dorsiflexion (p<0.001) and plantar flexion (p=0.012) - cognitive subscale of the FIM in the mobility training cohort lower (p<0.001) Not significant differences between groups in: - total Score of FIM (p=0.627) - BI total score (p=0.552)	4

ADL = activities of daily living, BI = Barthel index, BICU = burn intensive care unit, FIM = functional independence measure, ICU = intensive care unit, LOS = length of stay, PT = physio therapy, pts = patients, ROM = range of motion, TBSA = total body surface area

# Mobility training in the BICU was shown to be feasible and effective in achieving better outcomes than passive training for severe burn patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total						
372 Hickman 2016 (PMID: 27553652 DOI: 10.1186/s1361 3-016-0184-y) <b>Specification</b> of study: cohort study	171 ICU pts, 731 patient days Inclusion criteria: - pts either already hospitalized in or newly admitted to ICU between December 1, 2014, and January 31, 2015 Exclusion criteria for EM (3% of patient days): - active bleeding (n = 7), - increased intracranial pressure with major instability (n = 3) - unstable pelvic fractures (n = 2) - therapy withdrawal (n = 10) Per Branch	22 patient days (3%) fulfilled their local exclusion criteria for EM	Protocolized early mobilization		<ul> <li>Primary outcome: <ul> <li>feasibility of:</li> <li>mobilisation (passive, active-assisted, active, active-resisted)</li> <li>passive/active transfer in chair</li> <li>cycle ergometer in bed/chair (legs/arms)</li> <li>verticalization / standing / leg press / assisted walk</li> </ul> </li> <li>Secondary outcomes: <ul> <li>safety of early mobilisation</li> <li>early mobilization rate in MV according to hypoxemia severity - pts' perception</li> </ul> </li> <li>No sample size calculated</li> </ul>	<ul> <li>Primary outcomes: <ul> <li>intervention on 86 % of pts days,</li> <li>bed-to-chair transfer 74 %, at least.</li> <li>1 PT session 59 %.</li> <li>time to 1st PT 19 h (IQR = 15–23)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>(mild) adverse events 0.8%</li> <li>(reversible hypotension or arrhythmia)</li> <li>in MV pts bed-to-chair transfer was achieved on 68 % of patient-days and at least one early mobilisation activity on 80 %</li> <li>pts were comfortable with intervention</li> </ul> </li> </ul>	3

EM = early mobilisation, ICU= intensive care unit, MV = mechanical ventilation, PT = physical therapy, pts = patient

### Early mobilisation was feasible and safe.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
374 Floyd 2016 (DOI: 10.1097/DCC.00 000000000019 7) Specification of study: Retrospective matched paired study	Preintervention: 517 cardiac surgery pts and         65 thoracic surgery pts. From June 2014 –         November 2014         Postintervention: 392 cardiac surgery pts and         59 thoracic surgery pts. from December 1,         2014 to June 30, 2015         Inclusion criteria:         - ICU patients age >16 or <99	none	PMP: Level 1: active/passive ROM in Bed Level2: sitting on edge of bed Level 3: Stand up & lateral side steps along bed Level 4: OOB to chair via stand pivot transfer Level 5: Ambulation <50 ft. Level 6: Ambulation 100 ft Level 7: Ambulation >100ft	Standard care	No sample size calculation <b>Outcomes:</b> - ICU readmission within 30 days - ICU LOS - hospital LOS - pressure ulcer prevalence - DVT or PE	Results: - mean Hospital LOS: cardiac group: preintervention 8.6 days, postintervention group: 6.5 days (p=0.502) thoracic group: preintervention 12.6 days, postintervention group: 9.8 days (p=0.779) - mean ICU LOS cardiac group: 2.6 days for pre- and postintervention group thoracic group: preintervention: 6.3 days, postintervention: 4.6 days - DVT: 2 preintervention group (cardiac + thoracic), 0 postintervention group (p=0.492) - PE: 0 preintervention group, 1 postintervention group (cardiac+ thoracic) (p=1.0) - ICU readmission: preintervention group: 3, postintervention: 1, (p=0.301) - Pressure ulcers: preintervention group: 1, postintervention group: 0, (p=0.313)	4→5

Pts = Patients; ICU = intensive care Unit; ECMO = extracorporeal membrane oxygenation; VAD = ventricular assist device; PMP = progressive Mobility control; ROM = range of motion; OOB = out of bed; ft = feet; LOS = length of stay; DVT = deep vein thrombosis; PE = pulmonary embolism

Progressive mobility control had no significant influence on patient outcomes.

Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
375 Frazzitta 2016 (PMID: 27447483 DOI: 10.1371/jour nal.pone.015 8030) <b>Specification</b> of study: RCT	<ul> <li>40 pts with DOC</li> <li>within 24 hours fr</li> <li>Inclusion criteria:</li> <li>≥18 years</li> <li>GCS ≤8 for ≥24h</li> <li>diagnosis of VS of the CRSr on the the</li> <li>injury</li> <li>adequate pulmodexchanging functities</li> <li>stable hemodyne</li> <li>Exclusion criteria</li> <li>sedation</li> <li>unstable ICP</li> <li>CPP &lt;60mmHg</li> <li>fractures or skin</li> <li>deep vein throwne</li> <li>body weight&gt;136</li> <li>height&gt;210 cm</li> </ul>	admitted to ICU om a severe ABI from the Event or MCS according to hird day after the nary gas on amics : lesions bosis	9 pts died (intervention 5, control 4)	early stepping verticalization (Erigo. Hocoma AG, Switzerland) - 30 min sessions - 5x week for 3 consecutive weeks - plus 30 min conventional physiotherapy	<b>conventional</b> <b>physiotherapy</b> - 60 min sessions	Primary outcomes: - GCS - DRS - CRSr - LCF - [all measured at TO (3d day after injury), T1 (ICU discharge), T2 (neurorehabilitation discharge)] Secondary outcomes: - ICU LOS - Hospital LOS - Adverse Events Power analysis - none	Significant differences between groups in: - ICU LOS ( $38.8 \pm 15.7 \text{ vs } 25.1 \pm 11.2 \text{ days}, p = 0.01$ ) - $\Delta$ DRS (T2-T0) (-20.0 (-22.0,-4.5); -6.0 (-12.7,-2.0); p=0.04) - $\Delta$ CRSr (T2-T0) (17.0 (5.1,18.8); 5.0 (2.3,11.0); p=0.033) No significant differences between groups in: - $\Delta$ GCS (T2-T0) (n.s.) - $\Delta$ LCF (T2-T0) (n.s.) - hospital LOS (n.s.) - no adverse events	3 (risk of bias, pilot size)

ABI = acquired brain injury, CRSr = coma recovery scale revised, CPP = cerebral perfusion pressure, DOC = disorders of consciousness, DRS = disability rating scale, GCS = Glasgow coma scale, ICP = intracranial pressure, ICU = intensive care unit, LCF = levels of cognitive functioning, LOS = length of stay, MCS = minimally conscious State, n.s. = not significant, pts = patients, VS = vegetative state,  $\Delta$  = delta

#### An early stepping verticalization seems to have a benefit on DRS and CRSr but may result in a longer length of stay in the ICU.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
380 Fields 2015 (PMID: 27347435 DOI: 10.1097/JAT.00 00000000000 12) <b>Specification</b> of study: Retrospective descriptive study	L botwoon lung 2010 and		Data was extracted on all documented mobility activity (nursing, by PT or by OT)		<b>Primary outcome:</b> - PAC complications	Primary outcome: - physician notes reported 15 occurrences of PAC complications in 15 different pts - PAC complications included: bleeding from PAC site (n = 3), PAC dislodgement or accidental removal (n = 5), or PAC induced arrhythmia (n = 7) - no PAC complications during any physical therapy or occupational therapy session - no PAC complications were associated with nursing reported mobility activities	4

OT = occupational therapist, PAC = pulmonary artery catheter, PT = physical therapist, pts = patients

The data suggest that participation in mobility activities does not place patients with an indwelling PAC at increased risk of PAC-related complications.

Reference, Study Type	(Participant #	nd Controls , Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
383 Wutzler 2016 DOI: 10.1007/s00068- 016-0692-3) <b>Specification of</b> <b>study:</b> Prospective cohort study (observational)	Total         264 pts (76 pts with CLRT of 1         trauma center from 2011-2013; 188         pts from the German         TraumaRegister®)         Inclusion criteria:         -       ISS ≥16 (blunt and			CLRT	No CLRT/ Standard of Care	<b>Derived endpoints:</b> - time on MV - ICU/ hospital LOS - rates of pneumonia - rates of sepsis - rates of ARDS - hospital mortality - rates of re-intubation	<ul> <li>Outcomes: CLRT vs. no CLRT</li> <li>Significant differences between groups in: <ul> <li>time on MV: (7.8 vs. 11.1 days)</li> <li>p=0.002</li> <li>intensive care unit LOS (11.9 vs. 15.8 days) p&lt;0.001</li> </ul> </li> <li>No significant differences between groups in: <ul> <li>ARDS (5.3 vs 9) p=0.438</li> <li>Sepsis (18.9 vs 14.3) p=0.524</li> <li>hospital mortality (6.6 vs 11.2)</li> <li>p=0.365</li> </ul> </li> <li>Total patients: <ul> <li>re-intubation rate 9.2%</li> <li>rates of pneumonia 25%</li> </ul> </li> </ul>	4

CLRT = continuous lateral rotational therapy, ISS = injury severity score, AIS=abbreviated injury score; ICU=Intensive Care Unit; ARDS=acute respiratory distress syndrome; LOS = length of stay, MV = mechanical ventilation

### CLRT remains a therapeutic option to reduce pulmonary complications after severe chest trauma.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
384 McGarrigle 2016 (PMID: 27256069 DOI: 10.2522/ptj.2 0150644) Specification of study: Retrospective Case-Series	10 pts. Inclusion criteria: - pts who received VAD support - pts awake and able to consent to rehabilitation - consent for data use - sternum surgically wired closed, cannulae surgically secured with confirmation from the surgeon Exclusion criteria: - inability to actively participate - cardiovascular instability: ongoing ECMO support, multi-organ failure unresponsive to medical therapy - ongoing sedation Per Branch		Early mobilisation with VAD		Primary outcomes: - feasibility - safety - rehabilitation strategy Secondary outcome: - physical function (CPAx)	Primary outcomes: - all 10 pts were at least partially mobilized (arm and leg movements) - 330 sessions in total (X=33, SD=18.1, range=16–72) and progressed to ambulation on 71 occasions (X=7.1, SD=7.7, range=1–27) - distance ambulated ranged from 7 to 1,200 m (X=157.7, SD=367.3) - 8 minor adverse events - no major adverse events Secondary outcome: - CPAx score for 7 pts improved from a median of 0 (interquartile range=0–1) on day 1 to a median peak score of 39 (interquartile range=37– 42)	4

CPAx = Chelsea critical care physical assessment tool, ECMO = extracorporeal membrane oxygenation, pts = patients, VAD = ventricular assist device

Early rehabilitation and ambulation of recipients of short-term VAD support was safe and feasible.

Reference, Study Type	Cases and Controls (Participant #, Characteristics Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
385 Sigler 2016 (PMID: 27255089 DOI 10.14423/SMJ.0000 00000000472)	32 pts Inclusion criteria: - ventilated ICU pts in a MICU		Early mobilisation according to new protocol		<b>Extracted outcomes:</b> - feasibility - safety - ICU LOS	Outcomes: - ambulation of 32 ventilated pts "feasible ", ambulation distance was 102 ± 152 f. and usually required three ICU staff members with 5 to 10 minutes of preparation before ambulation	4
Specification of study: Retrospective Case-Series	Per Branch					<ul> <li>no adverse events</li> <li>decrease in ICU LOS (from 4.8 to 4.1 days)</li> </ul>	

ICU= intensive care unit, LOS = length of stay, MICU= medical intensive care unit, pts = patients

Early mobilisation is safe and effective in ventilated ICU patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
386 Connolly 2016 (PMID: 27220357 DOI: 10.1136/thora xjnl-2015- 208273) Specification of study: Systematic Review	SR based on 5 SR from 2013 to 2015 Inclusion criteria: - SR reporting on RCTs - any physical rehabilitation (exercise and mobility programs, cycle ergometers or NMS) - critically ill patients Per Branch		Early mobilisation or mobilisation via PT during ITS stay or NMS	Usual care or Placebo or Bed rest	Outcomes: - impairment (peripheral and respiratory muscle strength, CIP/CIM) - activity limitation (physical function, QoL) - Healthcare utilisation (VFD, ICU-LOS, hospital LOS, mortality, duration of MV)	No meta-analysis Outcomes from SR: a) Early mob/mob. via PT - impairment: peripheral muscle strength <sup>1</sup> (n = 244), Hedge's g=0.27 (0.02 to 0.52), p=0.03 - respiratory muscle strength <sup>1</sup> (n = 105), Hedge's g=0.51 (0.12 to 0.89), p=0.01 - CIP/CIM (Hermans et al, n=104), RR 0.62 (0.39 to 0.96) p=0.03 - activity limitation: physical functionality <sup>1</sup> (n=143), Hedge's g=0.46 (0.13 to 0.78), p=0.01 - participation restriction: quality of life <sup>1</sup> (n = 154), Hedge's g=0.46 (0.08 to 0.71), p=0.01 - health care utilisation: VFD <sup>1</sup> (n = 334), Hedge's g=0.38 (0.16 to 0.59), p<0.001, - ICU LOS <sup>1</sup> (n = 597), Hedge's g=-0.34 (-0.51 to -0.18), p<0.001 - LOS <sup>1,2</sup> (n= 441) Hedge's g=-0.34 (-0.53 to -0.15), p<0.001 - mortality <sup>1,2</sup> (n=274), OR 1.0. (0.54 to 1.85) p=1.0, - duration of MV <sup>2</sup> (n=not reported), median (IQA) 3.4 d (2.3 to 7.3) vs 6.1 d b) NMS - impairment: muscle strength <sup>3</sup> (n= 66), SMD 0.77, (0.13 to 1.40), p=0.02 - CIP/CIM <sup>2</sup> (n= 52), RR 0.32 (0.10 to 1.01), p=0.05	1 → 5 (indirectness)

CIM = critical illness myopathy, CIP = critical illness polyneuropathy, LOS = length of stay, MV = mechanical ventilation, NMS = neuromuscular stimulation, RCT = randomized controlled trial, SR = systematic review, VFD = ventilator-free days

# Early mobilisation improves muscle strength, physical function and quality of life and reduces time on ventilation, length of stay but not mortality. Neuromuscular stimulation improves muscle strength.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

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Reference, Study Type	· · · · · · · · · · · · · · · · · · ·	d Controls characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
387 Thelandersson 2016 DOI: 10.1007/s12028- 016-0278-2 <b>Specification of</b> <b>study:</b> Prospective study	the risk of vasosp -fractures of the s extremities -severe infections -severe obesity -non-Swedish-spe	4 014 to February arction, or rebellar uiring intensive ed a: emorrhage due to pasm spine or lower s	/	20-min leg exercise using a bedside cycle ergometer (SP, backrest of the bed slightly elevated)	own controls	-Safety and feasibility with regards to ICP and	Significant differences between groups: -20-min bedside cycle exercise increased MAP (p = 0.029) and SV (p = 0.003) -After exercise CPP, MAP, CO, and SV decreased significantly versus during exercise (p < 0.01) No significant differences between groups in: -20-min bedside cycle exercise increase in CO (p = 0.066) and CPP (p = 0.057) -changes in ICP, HR, SVV, or SpO2 during the procedure (n.s.) -no differences between data obtained before versus after exercise in any of the recorded variables	3

Pts.=patients; NICU=neurointensive care unit; TBI= traumatic brain injury; ICP=intracranial pressure; SP=supine position; CPP=cerebral perfusion pressure; MAP= mean arterial blood pressure; HR= heart rate; CO=cardiac output; SV=stroke volume; SVV=stroke volume variation; SpO2=peripheral oxygen saturation

Early passive exercise with a bedside cycle ergometer for patients with severe brain injuries or stroke is considered a safe procedure as it does not increase ICP and, if anything, increases CPP.

Reference, Study Type	Cases and (Participant #, To	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade	
388 Lee 2016 (PMID: 27189339 DOI: 10.1159/000446175 ) <b>Specification of</b> <b>study:</b> Review	29 pts Inclusion criteria: - pts in medical ICU 2014 and August 20 - CRRT - received PT PROM group (n= 15) (3 pts underwent both PROM and active mobilization)			Active mobilisation	PROM	Primary outcomes: - occurrence of safety events - vital signs changes	Primary outcomes: - no safety events during 33 sessions with PROM, 2 events during 48 active mobilisation sessions (4.1%) (both events: ECMO + CRRT delivered) - systolic BP, diastolic BP, mean arterial pressure, heart rate, respiratory rate, or peripheral oxygen saturation before and after both PROM and active mobilisation PT sessions: n.s	5

BP = blood pressure, CRRT = continuous renal replacement therapy, ECMO = extracorporeal membrane oxygenation, n.s. = not significant, PROM = passive range of motion, PT = physical therapy, pts = patients

Active mobilisation can be performed safely in patients who are being treated with CRRT without significant hemodynamic changes, but patients with ECMO should be monitored carefully.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
389 Hewitt 2016 (PMID: 27169365 DOI: 10.1002/14651 858.CD007205. pub2) Specification of study: Systematic review (Cochrane Review)	24 publications (24 RCTs ) <sup>1-24</sup> Inclusion criteria: - lateral positioning - manual/automated turns - duration of body position > 10 minutes - randomized and quasi randomized trials with - at least 1 comparator - single therapy/repetitive therapy		Single/repeated use of lateral positioning	Other body positions	Primary endpoints: - in-hospital mortality - incidence of morbidity - clinical adverse effects during or after repositioning Secondary endpoints: - pulmonary physiology or hypoxia score - vital signs - duration of assisted ventilation - LOS in critical care area - LOS in hospital - differences in participant comfort or satisfaction	Significant differences between groups: - meta-analysis: favoured good lung down in participants with unilateral lung disease (MD - 85.33 points, 95% CI -107.14 to -63.53; P value < 0.00001) - heart rate: 30 minutes after turning for supine position versus allograft lung down (MD -7.64, 95% CI -13.00 to -2.29; P value = 0.005) and five minutes after turning for supine position versus native lung down (MD 3.36, 95% CI 0.29 to 6.42; P value = 0.03) - temperature: 17.60 fewer hours with fever for repetitive lateral positioning versus supine positioning at 72 hours (MD -17.60, 95% CI - 26.12 to -9.08; P value < 0.00001) - ICU LOS: repetitive lateral positioning over supine immobilization (MD -18.60, 95% CI - 33.07 to -4.13; P value = 0.01) No significant differences between groups: - No study reported to reveal adverse events - no study reported mortality as outcome of interest - data were unavailable for Morbidity. - no analyses of pulmonary physiology possible.	1 → 3 (due to lack of sufficiently consistent data for meta- analyses)

RCTs = randomized controlled trials

Insufficient data and reporting, therefore no conclusive recommendation is possible. Good lung down seems better for oxygenation than bad lung down.

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Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidenc e Grade
391 Azuh 2016 (PMID: 27107920 DOI: 10.1016/j.amjmed.2 016.03.032) <b>Specification of</b> <b>study:</b> cohort before-after study, historical control	3233 MICU pts Inclusion criter - admission to I - Braden Scale s Per I 3233	<b>ia:</b> MICU		<b>(Early) mobilisation protocol:</b> - time to implementation not defined	Standard care	Primary endpoint: - occurence of pressure ulcers Secondary endpoints: - rate of VAP - hospital LOS - ICU LOS - hospital readmission rate No sample size calculation	<ul> <li>Primary outcome:</li> <li>pressure ulcer incidence of 6.1% (vs. 9.2% before intervention), p = 0.0405</li> <li>Secondary outcomes:</li> <li>VAP: n.s.</li> <li>hospital readmission rate 11.50% vs 17.10%, p=0.001</li> <li>ICU LOS 11.7 vs. 10.7 days, p=0.17</li> <li>hospital LOS: not reported</li> </ul>	4

LOS = length of Stay, MICU = medical intensive care unit, VAP = ventilator-associated pneumonia

The implementation of a mobilization protocol reduced the incidence of pressure ulcers and hospital readmissions as well as shortening the length of stay in the ICU.

106 adult ICU pts Inclusion criteria: - underwent CABG - disease in the left anterior descending artery, circumflex artery or right coronary anglography or NNHA IV) - invasive coronary anglography showed severe luminal stenosis > 75%, - prolonged mechanical ventilation (>72h) - stable oxygen saturation, fraction of inspired oxygen 55%, and positive end expiratory pressure ≤ 8 cm H2O       Significant differences between groups in: - duration of mechanical ventilation (days) 8.1 ± 3.3 vs 13.9 ± 4.1 (p=0.01) - dopamine at a dose of < 10 µg/kg/minute and epinephrine at a dose of < 0.10 µg/kg/minute and epinephrine at a dose of < 0.10 µg/kg/minute and therapy lish - a doser of choric mental illness - had normal cognitive function Evelusion criteria: - increased intracranial pressure - wree admitted to ICU after cardiopulmonary resuscitation - received radiotherapy or chemotherapy within the previous 5 months - acute myocarditis, peripheral vascular thrombosis/embolism, cerebrovascular actioned - received radiotherapy or chemotherapy within the previous 5 months - acute myocarditis, peripheral vascular thrombosis/embolism, cerebrovascular thrombosis/embolism, cerebrovascular thrombosis/emboli	Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Dong 2016 (PMID: 26973269 DOI: 10.1536/ihj.1 5-316) Specification of study: Randomized controlled	Inclusion criteria:         - underwent CABG         - disease in the left anterior descending artery, circumflex artery or right coronary artery (angiography or NYHA IV)         - invasive coronary angiography showed severe luminal stenosis > 75%         - prolonged mechanical ventilation (>72h)         - stable oxygen saturation, fraction of inspired oxygen         ≤ 55%, and positive end expiratory pressure ≤ 8 cm         H2O         - dopamine at a dose of < 10 µg/kg/ minute and epinephrine at a dose of < 0.4 µg/kg/minute		<b>therapy</b> - Mobilisation before ICU	<b>care:</b> -mobilisation after ICU	<ul> <li>duration of MV</li> <li>hospital and</li> <li>ICU LOS</li> <li>Hospital</li> <li>mortality</li> <li>Time of death</li> <li>No sample size</li> </ul>	<ul> <li>- duration of mechanical ventilation (days) 8.1 ± 3.3 vs 13.9 ± 4.1 (p=0.01)</li> <li>- ICU LOS (days) 11.7 ± 3.2 vs 18.3 ± 4.2 (P=0.01)</li> <li>- hospital LOS (days) 22.0 ± 3.8 vs 29.1 ± 4.6 (p=0.01)</li> <li>Not significant differences between groups in:</li> <li>- hospital mortality 2 (4%) vs. 3 (6%) (p=0.65)</li> </ul>	(downgraded for indirectness and lack of power

CABG = coronary artery bypass surgery, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilated, NYHA = New York heart association, pts = patients

The results provide evidence for supporting the application of early rehabilitation therapy in patients requiring prolonged mechanical ventilation after CABG.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
401 Wahab 2016 (PMID: 28979452 DOI: 10.1177/175 11437156051 18)	before and afte implementatio mobilization p	n of an early rotocol xclusion criteria		Implementation of an early mobilisation protocol	Usual care	Primary outcomes: -ICU and hospital LOS No sample size	Primary outcomes: - ICU LOS: 5.8 ± 7.6 vs 5.4 ± 7.0 days, p < 0.001 - hospital LOS: 14.7 ± 16.7 vs 13.9 ± 15.6	4
Specification of study: retrospective cohort study with historical control						calculation	days, p < 0.001 - no PT: 21% vs 69%, p < 0.001	

ICU = intensive care unit, LOS = length of stay, PT = physio therapy, pts = patients

A multi-ICU, coordinated implementation of an early rehabilitation program markedly increased rehabilitation treatments in the ICU and was associated with reduced ICU and hospital LOS as well as increased ICU admissions.

Reference, Study Type		s and Controls nt #, Characteristics) Total	Drop-out Rate	Interven -tion	Control	Optimal Population	Primary Results	Evidence Grade
402 Fischer 2016 (PMID: 26825278 DOI: 10.1186/s130 54-016-1199- 3) <b>Specification</b> of study: RCT	surgery - anticipate ≥ 48h <b>Exclusion d</b> - < 18 year: BMI >40 kg - metal imp - skin lesion area - neuromu: - implanted device or in pump	nt cardiothoracic ed to stay in the ICU criteria: s g/m <sup>2</sup>	Interventi on group: 14 (6 lost to follow- up at ICU discharge, 8 lost to follow-up at hospital discharge) Control group: 19 (7 lost to follow-up at ICU discharge, 12 lost to follow-up at hospital discharge,	NMES: - 2x daily for 30 min - until ICU discharg e or day 14	Sham NMES	Primary endpoints: - muscle layer thickness M. quadriceps femoris - muscle strength via the MRC Secondary outcomes: - hand grip strength - FIM-Score - TUG-Score - TUG-Score - SF-12 - average mobility level - satisfaction - ICU LOS - mortality	Primary endpoints: muscle layer thickness (cm) - postoperative day - effect in a linear mixed model (95%CI: -0.08 (-0.110.06); p < 0.001) - NMES - effect in a linear mixed model (95%CI: -0.18 (-0.59 - 0.23); p = 0.38) - postoperative day x NMES - effect in a linear mixed model (95%CI: 0.02 (-0.01 - 0.06); p = 0.21) - MRC postoperative day - effect in a linear mixed model (95%CI): 0.02 (-0.02 - 0.05); p = 0.40 - NMES - effect in a linear mixed model (95%CI: - 0.45 (-0.880.03); p = 0.04) - postoperative day x NMES - effect in a linear mixed model (95%CI: 0.09 (0.03 - 0.14); p = 0.002) Secondary outcomes: patient satisfaction - comfortable Sensation, n (%): intervention 12 (44.4) vs control 5 (18.5), p = 0.03 - discomfort, n (%): intervention 5 (18.5) vs control 0 (0%)), p = 0.048 ICU LOS, median (IQR): intervention (3 - 23) vs control 7 (3 - 213), p-value n.s - Hand Grip Strength/ FIM-Score/ TUG-Score/ SF-12 (PCS-12 + MCS-12)/Average Mobility Level: No difference between groups stated ICU Mortality, n (%): intervention 1 (3.7) vs control 3 (11.1) p-value: n.s	2
					l			

ICU = intensive care unit, NMES = neuromuscular electric stimulation, n.s. = not significant, pts = patients

No effect of neuromuscular electrical stimulation on muscle thickness could be observed but regaining muscle strength in the ICU stay was quicker.

Reference, Study Type	(Partici	l Controls pant #, eristics) tal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
403 Toonstra 2016 PMID: 26788890 DOI: 10.1097/MAT.0000 00000000239	1.313 pts from July 1 <sup>st</sup> , 2013, to July 31 <sup>st</sup> , 2014 <b>Inclusion criteria:</b> - pts on the MICU		408 pts did not receive physiotherapy 848 pts. Received PT	Physiotherapy during CRRT	MICU	Primary endpoint: - feasibility and safety PT	Primary Results: - No CRRT-specific safety events occurred (0%; 95% upper confidence interval, 6.3%). - 6 non-CRRT–related potential safety events (2.2% of all physical therapy sessions; 95% confidence interval, 0.6– 8.2%), all transient changes in blood	3
Specification of	Per B	Per Branch					pressure	
study: prospective observational study	57 1256							

CRRT = continuous renal replacement therapy, MICU = medical intensive care unit, pts = patients; PT=physical therapy

Provision of bedside physical therapy while patients underwent CRRT is feasible and appears safe.

Reference, Study Type	(Partici charact	d Controls ipant #, eristics) tal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
404 Karadas 2016 DOI: 10.1016/j.ge rinurse.2015 .12.003 RCT	94 ICU pts Inclusion crit -min. 24h on -65y and old - no previous Per B	MV er		Early ROM Exercises (10 repetitions, lying down, 30 min.)	Routine clinical measures	<b>Primary Outcomes:</b> - delirium incidence - delirium duration	Primary Outcomes: -delirium (incidence 8.5% in intervention vs. 21.3% in control group p > 0.05, X2 = 3.02) -delirium duration 15 h (3-144 h) in intervention vs 38 h (9-120 h) in control ( p > 0.05; Z =0.997).	2 → 3 (high risk of bias)

ICU = Intensive care unit; pts = patients; ROM = Range of motion

No significant difference in delirium occurrence and duration.

Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop- out Rate	Interven- tion	Control	Optimal Population	Primary Results	Evidence Grade
409 Ayzac 2016 (PMID: 26699917 DOI: 10.1007/s00134- 015-4167-5) <b>Specification of</b> <b>study:</b> Secondary Analysis of RCT	466 pts Inclusion criteria: - adults (18 years or - endotracheally intu - ongoing for the pre - severity criteria (Pa inspired oxygen (FiO under FiO2 C 0.6 pos expiratory pressure and tidal volume (VT predicted body weig 12–24 h stabilizatior - gave consent to pa Per Bi 237	ubated for ARDS evious 36 h iO2/fraction of 2)\150 mmHg sitive end- (PEEP) C5 cmH2O c) = 6 ml/kg (ht) fulfilled after a in period rticipate		РР	SP	Primary endpoint: - incidence of the first episode of VAP - mortality Secondary endpoints: - fatality rate during the ICU stay up to 90 days after randomization - number of days free from ventilator support - duration of the ICU stay - duration of organ failure - appropriateness of the antibiotic therapy	Primary endpoint: - incidence rate for VAP: 1.18 (0.86–1.60) vs 1.54 (1.15–2.02) per 100 days of invasive mechanical ventilation (p = 0.10), - VAP was associated with an increase in the mortality rate during the ICU stay [HR 1.65 (1.05–2.61), p = 0.03] Secondary endpoint: - cumulative probability of VAP at 90 days estimated at 46.5 % (27–66) in PP and at 33.5 % (23–44) in SP - difference between the two cumulative probability curves was not statistically significant (p = 0.11)	3

ARDS = acute respiratory distress syndrome, PP = prone position, pts = patients, SP = supine position, VAP = ventilator associated pneumonia, VT = tidal volume

In severe ARDS patients prone positioning did not reduce the incidence of VAP and VAP was associated with higher mortality.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Eviden ce Grade
411 Fraser 2015 (PMID: 26600359 DOI: 10.1097/01.NAJ .0000475292.2 7985.fc) <b>Specification of</b> study: Retrospective cohort with historical controls	132 ICU pts, retrospectively "randomly" chosen Inclusion criteria:         - at least 18 years of age         - admitted directly to an ICU         - intensivist as attending or consulting physician         Exclusion criteria:         - inability to walk without assistance before ICU admission         - neuromuscular disease that would prevent weaning from mechanical ventilation         - acute stroke, body mass index greater than 45 kg/m admission by the trauma service, acute lower extremi fracture, unstable cervical spine or pathologic fracture hospitalization 30 days prior to admission, hospice cat immediate plans to transfer to an outside hospital,         - score greater than 60 on the initial Barthel         Per Branch         66       66	y ,	Implementation of an early mobilization protocol	Usual care	Primary outcomes: - readmission rate - quality outcomes (falls, ventilator- associated events, pressure ulcers, urinary tract infections) - costs - LOS No sample size calculation	Significant differences between groups in: - readmission: 10.6 vs 22.7% (p<0.001) - quality outcomes 25.7 vs 1.5% (p<0.001) No significant differences between groups in: - LOS: n.s - costs: savings of \$111,566 (\$1,690 per patient) for the mobility group (\$125,309 versus \$127,000; t130 = -0.42; P = 0.68)	4

ICU = intensive care unit, LOS = length of stay, n.s. = not significant, pts = patients

It is feasible for a community hospital to create and implement a dedicated ICU mobility team. Early mobilisation of ICU patients contributed to fewer delirium days and improved patient outcomes, sedation levels, and functional status.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out - Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#412 Bloomfield 2015 PMID: 26561745 DOI: 10.1002/14651 858.CD008095. pub2 Specification of study: Systematic Review and MA	<ul> <li>9 RCTs with 2165 pts<sup>1-9</sup></li> <li>Inclusion criteria: <ul> <li>RCTs that examined the effects of PP vs supine/semi recumbent position</li> <li>during conventional MV</li> <li>in adult pts with acute</li> </ul> </li> </ul>		PP	Supine/ semi recumbent position	Endpoints: - risk ratio for mortality - risk ratio or mean difference for secondary outcomes	Significant differences between groups in: - pressure ulcers (4trials; 823 pts) with an RR of 1.25 (95% Cl 1.06 to 1.48), p-value = 0.02) - tracheal tube obstruction increased with PP (RR of 1.78 (95% Cl 1.22 to 2.60), p-value = 0.003) - reduced arrhythmia with PP (RR of 0.64 (95% Cl 0.47 to 0.87), p-value = 0.005) No significant differences between groups in: - short- and longer-term mortality (6 trials): RR of 0.84 to 0.86 in favor of the PP Primary analysis: - short term mortality RR of 0.84 (95% confidence interval (Cl) 0.69 to 1.02) - longer-term mortality RR of 0.86 (95% Cl 0.72 to 1.03)	1

MV = mechanical ventilated, PP = prone position, RCT = randomized controlled trials, RR = risk ratio

There is no convincing evidence of benefit nor harm from universal application of PP in adults with hypoxaemia and mechanical ventilation in intensive care units (ICUs).

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Reference, Study Type	(Participant #	nd Controls <sup>e</sup> , characteristics) <sup>-</sup> otal	Drop- out Rate	Interve ntion	Control	Optimal Population	Primary Results	Evidence Grade
413 Kimmoun 2015 DOI: 10.1186/s1361 3-015-0078-4 Specification of study: Retrospective study	January 2012 and J Inclusion criteria: - PP during VV-ECM - severe ARDS defir consensus - one unsuccessful - refractory hypoxe - persistent high pla Exclusion criteria: - no PP during vaso - recent open chest	10 ned by BERLIN ECMO weaning mia ateau pressure pressor treatment	none	PP > 24 hours	none	Outcomes: - safety data - oxygenation - respiratory system compliance	<b>Results:</b> - total of 27 sessions - PaO <sub>2</sub> /FiO <sub>2</sub> ratio increased from 111 (IQR 84-128) to 173 (IQR 120-203) mmHg after 24 hours of PP - RS compliance increased from 18 (IQR 12-36) to 32 (IQR 15-36) ml/cmH <sub>2</sub> O - tidal volume: increased from 3.0 (IQR 2.2 - 4.0) to 3.7 (IQR 2.8 - 5.0) ml/kg - PaO <sub>2</sub> /FiO <sub>2</sub> increased over 20% in 14/14 sessions for late sessions (>7 days), and in 7/13 sessions for early sessions (<7 days) - 1 oxygenator thrombus, 1 fluid resuscitation	4
	n = 17							

VV = venovenous, ECMO = extracorporeal membrane oxygenation, ARDS = acute respiratory distress syndrome, PP = prone positioning, RS = respiratory system, IQR = interquartile range

PP improved oxygenation during VV-ECMO and was not associated with side effects.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, c Tot	characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
414 Bartolo 2016 <u>PMID:</u> 26530213 <b>Specification</b> of study: Prospective multicenter observational study	102 consecutive se pts. admitted to IC Inclusion criteria: - CNS damage due nontraumatic caus - GCS ≤8 Exclusion criteria: - previous sABI pts consciousness diso - neoplastic disease involvement of the Per Br 102	to traumatic or tes with persistent order e with metastatic e CNS	15 (1 missing, 14 died)	Early rehabilitation	Without early rehabilitation	No sample size was calculated. <b>Outcomes:</b> - which early rehabilitation treatment is carried out in Italian ICU/NICUs - which kind of treatment is performed - which care pathways are indicated for sABI pts. at discharge	Results: Rehabilitation treatments: - postural changes were performed in 65 (63.7%) pts. - passive/active assited multijoint mobilization was prescribed in 52 (51%) pts. - mobilization was executed in all pts. by phyiotherapists - rehabilitation interventions (respiratory rehabilitation and/or bronchial drainage, speech therapy, multisensory stimulation Discharge destinations: - 38 pts. severe acquired brain injury unit - 18 pts. extensive rehabilitation clinic - 18 pts. neurosurgery - 13 pts. other destination (e.g. other ICU/NICU, other acute ward)	3

DRS = disability rating scale, ERBI = Early rehabilitation Barthel Index, FIM = Functional Independence Measure, GCS = Glasgow coma scale, GOS = Glasgow Outcome Scale, LCF = levels of cognitive functioning, pts = patients; CNS = central nervous system; ICU = intensive care unit; NICU = neurological intensive care unit; sAIB = severe acute brain injury

More than half of all sABI patients received multijoint mobilization and postural changes at ICU/NICU.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
415 Culbreth 2016 https://doi.org/10.4 187/respcare.03882 Specification of study: Systematic review	. ,	n/a	PP and ECMO simultaneous ly	No control group due to study design	No primary endpoint defined Extracted endpoints: - ECMO Cannula Complications - Central Venous and Arterial Catheter Complications - Chest Tube Complications - Airway Dislodgment and Obstruction - Hemodynamic Instability During Positioning - Miscellaneous Non-Life- Threatening Complications - PP Maneuver Type: Mechanical Versus Manual - ECMO Equipment and Cannula Site - Outcomes: Oxygenation and Survival	Extracted endpoints: - No occurrence of ECMO cannula dislodgment; CSB was common among these studies, CSB is a frequent occurrence of subjects receiving ECMO due to anticoagulation therapy. - Only 1 study reported catheter complications - None of the adult studies reported chest tube dislodgment in this review. - No episodes of tracheal or endotracheal tube dislodgment was found. - 2 studies reported episodes of hemodynamic instability. (e.g., Bradycardia, decrease in systolic blood pressure). - None of the studies in this review reported cutaneous pressure sores. - Only 1 study reported the use of automated, rotating beds to perform PP of subjects. - The type of ECMO equipment used, all studies reported using either a centrifugal pump system or an occlusive pump system. - 3 studies found a significant difference between the PaO2/FIO2 ratio before and after PP.	1 → 4 (not only RCTs, no metaanalysis)

ECMO= Extracorporeal membrane oxygenation; PP=prone position; RF=respiratory failure; CSB= cannula site bleeding;

#### More studies are needed to assess the clinical efficacy of the addition of PP therapy to ECMO for patients in severe RF.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out Rate	Intervention	Cont rol	Optimal Population	Primary Results	Evidence Grade
	Total	nate					
419 Pandullo 2015 (PMID: 26346813 DOI: 10.1016/j.jcrc .2015.08.007)	Per Branch		Retrospective analysis of patient mobility achievements (JH-HLM) 3 groups depending on highest ICU JH- HLM: bed (n = 51), chair (n =		Primary outcomes: - hours between ICU admission and bed - hours between ICU admission and chair, - hours between ICU admission and ambulation - hours to regain/exceed mobility level after transfer - ambulation on day of discharge from hospital - ambulation at any	Primary outcomes: - hours between ICU admission and bed, median (IQR): bed:1.8 (0.3, 4.0), chair:1.8 (0.5-4.8), ambulation 1.4 (0.5- 4.0); p =0.27 - hours between ICU admission and chair, median (IQR): bed: 118 (75-238), chair: 59 (29-94), ambulation: 39 (19- 65); p <0.001 - hours between ICU admission and ambulation, median (IQR): bed: 177 (111-355), chair: 135 (89-200), ambulation: 60 (37-96); p<0.001 - hours to regain/exceed mobility level after transfer, median (IQR): bed: 2.5 (0.5-5.9), chair: 16 (4-26), ambulation: 7 (3-19); p<0.001 - ambulation: 37 (59.7); p>0.001 - ambulation at any time during hospitalization, n (%):	4
Specification of study: Retrospective cohort study	Bed group: n=51 Chair group n=69 Ambulation group n=62		69), ambulation (n = 62)		time during hospitalization Secondary outcomes: -ICU-LOS -post-ICU LOS -hospital LOS	bed: 25 (49.0), chair: 51 (73.9), ambulation: 62 (100) <b>Secondary outcomes:</b> -ICU LOS(h), median (IQR): bed: 80 (57, 161), chair: 97 (71-131) ambulation: 88 (62-138); p=0 .96 - post-ICU LOS (h), median (IQR): bed: 237 (96-436), chair: 186 (108-297), ambulation: 84 (51-131); p<0.001 - hospital LOS (h), median (IQR): bed: 382 (216-724), chair: 355 (230-550), ambulation: 230 (140-358); p<0.001	

IQR = interquartile range, JH-HLM = John Hopkins highest level of mobility, LOS = length of stay, pts = patients

Study findings show the need for improvement in maintaining early ICU mobilization achievement during the crucial phase between ICU stay and hospital discharge.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
424 Yusuke 2016 (PMID: 26311924 DOI: 10.1589/jpts. 27.2053)	86 pts Inclusion criteri - admitted to IC Exclusion criter - <64 years - bedridden bef pneumonia - with serious co such as severe h - discharged du	ia: ore the onset of omplications neart failure	15 pts: 11 control (died), 4 Intervention	<b>Early physical</b> <b>therapy:</b> - 40 min per day - begin the day after admission	Standard intervention	Primary endpoints: - ICU LOS - FIM score	Primary endpoints: Significant differences between groups in: - ICU admission period shorter in early intervention (12.03 ± 4.14 days) vs control (15.45 ± 3.76 days, p < 0.01) - rate of change in the FIM smaller in early intervention (14.3 ± 5.7) than in standard	4
Specification	Per B	Franch	(died)				intervention (20.3 ± 7.6, p < 0.01)	
of study: Single Centre Cohort Study Before After	38	33						

FIM = functional independence measure, ICU = intensive care unit, LOS = length of stay, pts = patients

Physiotherapy should be recognized as an effective treatment method that prevents complications and improves the prognosis associated with activities of daily living, and not solely as a method to prevent disuse syndrome.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
425 Polastri M 2015 (PMID: 26274362 DOI: 10.1002/pri.1 644) Specification of study: Systematic Review Case series	<ul> <li>9 publications<sup>1-9</sup>( 54 pts, 3 cohort studies, 6 case reports/case studies)</li> <li>Inclusion criteria: <ul> <li>pts in ICU</li> <li>describe the physiotherapeutic activities of subjects on awake VV ECMO</li> <li>publication date January 2010 to November 2014</li> <li>in English, French or Italian</li> </ul> </li> <li>Exclusion criteria: <ul> <li>editorials, opinion pieces, conference proceedings and citations that did not describe physiotherapeutic interventions in subjects on awake VV ECMO</li> </ul> </li> </ul>		Awake ECMO Combination active and passive physiotherapy (commenced within 2-5 days)		<b>Primary endpoint:</b> - assess advantages and safety of physiotherapeutic interventions	Primary endpoints: - physiotherapy was commenced as soon as possible (within 2–5days) in almost all patients, and this was clear in all studies - mobilization (passive and active movements and postural changes), in-bed positioning (either sitting or upright) and ambulation were the most commonly used physiotherapeutic interventions	3

ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit, pts = patients, VV = veno-venous

# Patients on awake ECMO usually received a combination of passive and active physiotherapy, and most achieved an acceptable degree of autonomy after treatment.

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Reference, Study Type		and Controls t #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
434 Castro-Avila 2015 (PMID: 26132803 DOI: 10.1371/journal.po ne.0130722) <b>Specification of</b> <b>study</b> : Systematic Review Meta Analysis	Inclusion criteria: - randomised or control - comparing rehabilitat patients - adult pts admitted to - followed for outcome Exclusion criteria: compared passive to u - started rehabilitation - evaluated interventio - enrolled more than 2 - had pts admitted to a conditions or trauma t	ion to usual care in ICU/HDU ICU/HDU for at least 48 hours s until ICU discharge		Early rehabilitation / mobilisation	Usual Care	Primary endpoint: - functional Status at ICU discharge Secondary outcomes: - walking ability - muscle strength - quality of life - duration of MV - hospital and ICU LOS - time in rehabilitation after hospital discharge	Significant differences between groups in: - (n=4) improved walking without assistance at discharge (pooled risk ratio 1.42, Cl 1.17-1.72), p =0.02 No significant differences between groups in: - functional status at ICU discharge (no meta- analysis) - all other outcomes are non-significant: muscle strength, QoL, MV duration, ICU LOS, hospital LOS, time in rehabilitation	2

CI = confidence interval, ER = early rehabilitation, HDU = high-dependency unit, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, QoL = quality of life, RCT = randomized controlled trial

# Early rehabilitation did not improve functional status at ICU discharge, muscle strength, quality of life, or healthcare utilization. However, early mobilisation improved walking ability without assistance at hospital discharge.

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Reference <i>,</i> Study Type	(Partic charact	d Controls ipant #, teristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#437 Daniel 2015 PMID: 25995558 DOI: 10.1589/jpts.27.1067 <b>Specification of study:</b> retrospective cross- sectional study	and July 2013 Inclusion crite - ≥ 18 years of - admission to - mechanically Exclusion crite - incomplete r - length of ICU hours - > 30 days of I Per B	age the ICU ventilated eria: ecords	not applic able	female	male	Primary endpoint: - time interval needed to be able to perform active exercises (e.g., to sit) out of bed (days) Secondary Outcomes: - time to sitting out of bed (days) - time to the withdrawal of sedation (days) - duration of MV - duration of weaning from MV - ICU length of stay (days)	Primary endpoint: - time interval needed to be able to perform active exercises (e.g., to sit) out of bed (days): Female $3.7 \pm 4.0$ vs Male $5.7 \pm 5.9$ (p = significant) Secondary Outcomes: - time to sitting out of bed (days): Female $3.1 \pm 4.1$ vs. $5.0 \pm 6.8$ (p = n.s.) - time to the withdrawal of sedation (days): Female $2.0 \pm 2.1$ vs Male $3.6 \pm 2.3$ (p = significant) - duration of MV (days): Female $4.8 \pm 4.4$ vs Male $6.7 \pm 5.5$ (p = significant) - duration of weaning from MV (days): Female $1.6 \pm 3.6$ vs $2.2 \pm 3.9$ (p = n.s.) - ICU length of stay (days): Female $6.7 \pm 5.0$ vs $8.2 \pm 5.9$ (p = n.s.)	4

ICU = Intensive Care Unit, LOS = length of stay, MV = mechanical ventilation, n.s. = non significant; pts.=patients

Women generally have a better functional response when admitted to the ICU, as they spend less time in the unit and are able to perform active exercises earlier.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

99 patients, admitted to the medical intensive care unit of a single hospital in Korea between May 1 and December 31, 2013, retrospectivel evaluated       Inclusion criteria:       Inclusion criteria:	Reference, Study Type	(Participant #,	d Controls characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	2015 PMID: 25957499 https://doi.org/10.1 016/j.jcrc.2015.04.0 12 <b>Specification of</b> <b>study:</b> Retrospective	intensive care unit of a Korea between May 1 2013, retrospectively Inclusion criteria: - No deep vein thro - RASS -2 to +2 - PEEP <10 cmH2O - FiO2 <0.6 - SpO2 >90% - Respriratory rate Exclusion criteria: - Systolic blood pre >200 mmHg - Mean arterial pre <65 mmHg - Arrhythmia - Increment of dos	a single hospital in and December 31, evaluated ombosis or bleeding <35/min essure <90 mmHg or essure >110 mmHg or e of vasopressors		factors for safety events (adverse events) during mobility physical	acted as their own	calculation (retrospective study) Endpoints: - safety events - variables associated with potential safety	26 SE of 520 mobilization sessions (5,0% CI 3,4-7,3%) in 17 of 99 patients (17,2% CI 10,6-26,4%) After multivariate logistic regression analysis for safety events revealed: ECMO was associated with SE during physical mobility therapy (OR 5,8 CI 2,2-	4

RASS = Richmond agitation sedation scale; PEEP = positive endexpiratory pressure; FiO2 = oxygen fraction of the air; SpO2 = oxygen saturation of the blood; SE = safety events; CI = confidence interval; ECMO = extracorporeal membrane oxygenation; OR = odds ratio

Early mobility physical therapy performed by a newly established group was feasible, but ECMO was associated with SE during physical mobility therapy.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, C Tota	haracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
439 Ota H 2015 (PMID: 25931747 DOI: 10.1589/jpts.27. 859) Specification of study: Retrospective Cohort Descriptive	111 pts Inclusion criteria: - age ≥ 18 years ad - performance stat - independent livin prior to hospitaliza - duration of MV f - survival after MV Exclusion criteria: - cervical spine inju neuromuscular dis burns Per Bra 48	tus score of 0–2 ng at their home ation for > 48h ury, teases, or major	18(12/15 in EM group and 3/15 in control died, 3/18 missing medical records)	<b>EM program:</b> - passive and active limb exercise - relaxation of the muscles - deep breathing exercises - chest physiotherapy - elevation of the head up to 30–90 degrees - changing pts position from supine to up to a 135-degree lateral position	Bed rest	<b>Derived endpoints:</b> - delirium after weaning from MV - tracheostomy - duration of MV - hospital LOS after initiating MV - discharge disposition	Significant difference between groups in: - duration of MV, median 13 (IQR 7–22) in EM and 8 (IQR 6– 12) in control, p < 0.05 - tracheostomy, 29/48 pts(60%) in EM and 23/60(38%) in control, p<0.05 - discharge disposition to home, 28/48 pts EM vs 18/60 pts control, p<0.05 No significant difference between groups in: - delirium incidents, 13(27%) EM vs 17(28%) control - hospital LOS, median 56days(IQR 38-85) EM vs 58 days(IQR 36-78) control group	4

EM = early mobilisation, ICU = intensive care unit, IQR = interquartile range, LOS = length of stay, MV = mechanical ventilation, pts = patients

#### Early mobilisation program resulted in an improved rate of discharge to home among survivors after mechanical ventilation.

Reference, Study Type	(Participant #,	d Controls , characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
440 Ko Y 2015 DOI: 10.1097/MAT.000 00000000239 <b>Specification of</b> <b>study:</b> Retrospective Case Series Descriptive	<ul> <li>stable vital sig Hg, respiratory beats/minute, a saturation high</li> <li>stable cannula</li> <li>Exclusion criter</li> <li>coagulopathy</li> <li>bleeding from</li> <li>use of vasopre</li> <li>open surgical</li> <li>unstable ECM</li> </ul>	ia: perative patient perative patient (MAP > 60mm rate less than 30 arterial oxygen er than 95%) ation site ria: cannulation site essor wound	Not specified	Mobilization during ECMO: Daily assessment for early mobilization on ECMO by multi- disciplinary team	NA	No sample size calculation through study design <b>Outcomes:</b> -safety events during PT -PT interruptions due to unstable vital signs	<b>Results:</b> - no clinically significant adverse event in patients - Three sessions (5%) were stopped due to tachycardia (n = 1) and tachypnea (n = 2).	4

Pts.=patients; MAP=mean arterial pressure; ECMO=extracorporeal membrane oxygenation; PT=physiotherapy

It is feasible and safe to perform PT and mobilization for patients on ECMO in an experienced ECMO center.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Con (Participant #, Chara Total		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
443 Kayambu 2015 (PMID: 25851383 DOI: 10.1007/s0013 4-015-3763-8) <b>Specification</b> of study: RCT; Single center	50 pts Inclusion criteria: - ≥ 18 years admitted - MV ≥48 h - diagnosed with sep sepsis, or septic shoce Exclusion criteria: - head injuries - burns - spinal injuries - multiple fractured I limbs, - with septic shock b unresponsive to max treatment - moribund or had ar mortality within 48 h Per Brance	epsis, severe ock lower out iximal an expected h	8 at discharge (4 died, 4 had delirium) for primary endpoint ACIF + 20 (16 death, 3 non- contactable, 1 readmitted) for SF-36	Early targeted physical rehabilitation: -electrical stimulation, active and passive range of motion, sitting, transfer, ambulation - 30 min, 1 or 2 times daily until discharge - within 48h of diagnosis	Standard of care: physical therapy strategies	Primary endpoint: - physical function via ACIF - QOL via SF-36 at 6 months post discharge Secondary outcomes: - PFIT - muscle strength via MRC muscle score - anxiety on discharge - duration of MV - ventilator-free days - ICU and hospital LOS - ICU readmission - ICU and 90-day mortality and resuscitation status Power analysis: A sample size of 35 per group (total 70) was calculated with an effect size of 0.7 and 90 % power with a type 1 error rate of 0.05 and 0.025 with Bonferroni adjustment	Primary endpoints: - physical function, ACIF final scores ( $61.1 \pm 33.1 vs. 55.0 \pm 24.4$ , p = 0.45) and mobility scores ( $39.8 \pm 38.2 vs.$ $34.5 \pm 27.1$ , p = 0.67) - exercise group QOL improvement in the domains of physical function ( $81.8 \pm 22.2 vs. 60.0 \pm 29.4$ in control, p = 0.04) and physical role ( $61.4 \pm 43.8 vs. 17.1 \pm 34.4$ in control, p = 0.005) Secondary outcomes: - duration of MV (p=0.22), - ventilator-free days (p=0.71), - ICU and hospital LOS (p=0.43 and p = 0.80), - ICU readmission (p=0.13), - ICU and 90-day mortality (p=0.34 and p=0.08 respectively), - resuscitation status (p=0.15), - MRC scores (p=0.24), - PFIT scores (p=0.61)	2 → 3 small pilot RCT

ACIF = acute care index of function, h = hours, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, PFIT = physical functional ICU test, pts = patients, QOL = quality of life, RCT = randomized controlled trial

Early ICU exercise can moderate the detrimental effects of sepsis.

Reference,	Cases and Controls	Drop-					Evidence
Study Type			Intervention	Control	Optimal Population	Primary Results	Grade
	(Participant #, characteristics) Total 192 pts. Between August 2012 and March 2013 Inclusion criteria: -independently able to mobilize prior to the current hospital admission. -in the ICU <72 hours -receiving invasive ventilation for >24 hour, expected to stay invasively ventilated for at least the next 48 hours. Exclusion criteria: -age <18 years -proven or suspected neurological Impairment -inability to communicate in English	out Rate	Early mobilization	Control	Optimal Population Extracted endpoints: -mobilization during invasive ventilation -Sedation RASS -Duration of MV -Co-interventions	Primary Results Results: -Mortality at day 90 was 26.6% (51/192) -no mobilization occurred in 1,079 (84%) -maximum levels of mobilization were exercises in bed (N = 94, 7%), standing at the bed side (N = 11, 0.9%) or walking (N = 26, 2%) -at ICU discharge and 48 (52%) had ICU-acquired weakness	Grade
Specification of study: Prospective Multi-centre Cohort study	-inability to communicate in English -cognitive impairment prior to the ICU admission - unstable fractures or any other injury that would require specific medical bed rest orders -ICU admission for palliative care or proven or suspected primary myopathic or neurological process associated with prolonged weakness or ICU readmission Per Branch	-			-ICU acquired weakness -Mortality 90 days 6 month -functional recovery	-MRC-SS score was higher in those patients who mobilized while mechanically ventilated ( $50.0 \pm 11.2$ versus 42.0 ± 10.8, P = 0.003) -survived to ICU discharge but who had died by day 90 had a mean MRC score of 28.9 ± 13.2 compared with 44.9 ± 11.4 for day-90 survivors (P <0.0001)	
	192	1					
	132						

Pts. = patients; ICU=intensive care unit; RASS=Richmond Agitation and Sedation Scale; MV=mechanical Ventilation

More than 50% of patients discharged from the ICU had developed ICU-acquired weakness, which was associated with death between ICU discharge and day-90.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total						
448 Miyamoto 2014	ICU patients of a tertiary care hospital with respiratory failure						
PMID: 25705410	→ 15 pts.					Results:	
https://doi.org/1 0.1186/s40560- 014-0052-5	<ul> <li>Inclusion criteria:</li> <li>PP &gt; 40 hours</li> <li>Pts. With respiratory failure</li> </ul>		Extended duration PP (> 40 hours)		<b>Extracted Endpoint:</b> -PaO2/FiO2 ratio	<ul> <li>- PP improved the PaO2/FiO2 ratio (mean ± SD):</li> <li>a. baseline vs. 8h: 193.8 ± 70.1 vs. 274.7 ± 70.7 mmHg (p = 0.02)</li> <li>b. baseline vs. 16 h: 193.8 ± 70.1 vs. 294.1 ± 78.0 mmHg</li> </ul>	4
Specification of study:	Exclusion criteria: - PP < 40 hours					(p = 0.23)	
Retrospective	Per Branch						
monocenter study	15						

Pts = patients, ICU = intensive care unit, PP = prone positioning, PaO2 = partial pressure of oxygen, FiO2 = fraction of inspired oxygen

# Extended duration-prone positioning resulted in a progressive improvement of oxygenation during the first 8 hours of treatment exclusively.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	-	trols characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
449 Rand 2015 PMID: 25701637 https://doi.org/10.1 016/j.apmr.2015.02. 008 <b>Specification of</b> <b>study:</b> single center before- after cohort study	pts Inclusion criter - ≥ 18 years - pts from a pri with hemorrha to Internationa Diseases, Ninth Modification d	mary stroke center gic stroke according Il Classification of Revision, Clinical		Daily mobility intervention based on patient's LOF	standard of Care	<b>Endpoints:</b> - LOF before and after introduction of a mobility intervention in NICU - variables associated with higher functional outcomes - similarities among pts achieving a LOF of 5 at discharge No power analysis	<ul> <li>Primary Endpoints: <ul> <li>LOF before and after introduction of a mobility intervention in NICU: Pts with hemorrhagic stroke had a 2.3-fold increase in LOF &gt; 5 at discharge</li> <li>variables associated with higher functional outcome (according to a MLRM including NICU LOS as a covariate [OR; 95% CI]): <ul> <li>a. the intervention (5.28; 2.52-11.06)</li> <li>b. LOF of 5 at admission (6.02; 1.45 – 24.96)</li> <li>c. SAH stroke type (3.78; 1.83 – 7.80)</li> <li>d. third (vs. lowest) quartile of NICU LOS (2.94; 1.16 – 7.47)</li> <li>e. absence of aphasia and/or hemiplegia (17.77; 6.59 – 47.92)</li> </ul> </li> </ul></li></ul>	4

Pts = patients, LOF = level of function, NICU = Neurointensive care unit, ICH = intra-cerebral hemorrhage, MLRM = multivariable logistic regression model; CI = confidence interval, SAH = subarachnoid hemorrhage, OR = odds ratio, LOS = length of stay

Evidence-based mobility intervention can improve outcomes for patients with hemorrhagic stroke and is feasible in any intensive care setting. *No detailed assessment was carried out because higher-quality evidence is available on this topic.* 

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Recommendations	Evidence Grade
450 Sommers 2015 PMID: 25681407 DOI: 10.1177/02692 15514567156 <b>Specification</b> of study: National Guideline	Definition of early mobilization		1 → 5 (outdated)

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervent ion	Control	Optimal Population	Primary Results	Evidence Grade
456 Mora- Arteaga 2015 (PMID: 25599942 DOI: 10.1016/j.med in.2014.11.003 ) Specification of Study: Systematic Review			РР	SP	Outcomes: - mortality after maximum follow-up - stay in intensive care (days) - days on mechanical ventilation - adverse effects and complications - severity of ARDS (Berlin classification) - daily duration of pronation - start of pronation and duration of ARDS - tidal volume used	<b>Significant differences between groups in:</b> - subgroup mortality in pts. ventilated with low tidal volume (OR: 0.58; 95%CI: 0.38-0.87 p = 0.009, I2 33%), - prolonged pronation (OR: 0.6; 95%CI: 0.43-0.83; p = 0.002, I2 27%), - start within the first 48 h of disease evolution (OR 0.49; 95%CI 0.35-0.68; p = 0.0001, I2 0%) - severe hypoxemia (OR: 0.51: 95%CI: 0.36-1.25; p = 0.0001, I2 0%). <b>No significant differences between groups in:</b> - overall mortality: (OR: 0.76; 95%CI:0.54-1.06; <i>p</i> = 0.11, <i>I</i> 2 63%)	2

ARDS = acute respiratory distress syndrome, APRV = airway pressure release ventilation, HFOV = high-frequency oscillation ventilation, PP = prone position, pts = Patients, SP = supine position

Prone position ventilation is a safe strategy and reduces mortality in patients with severely impaired oxygenation. It should be started early, for prolonged periods, and should be associated with a protective ventilation strategy.

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Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop-out - Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
458 Schallom 2015 (PMID: 25554555 DOI: 10.4037/ajcc2 015781) Specification of study: Cross-over RCT	<ul> <li>15 ICU pts</li> <li>Inclusion criteria:</li> <li>confirmed gastric feeding tube</li> <li>ventilated per en</li> <li>at least 18 years of approval to rando</li> <li>45º</li> <li>anticipated MV and tube feeding of hours</li> </ul>	dotracheal tube old omize pts to duration of 48	4 pts (extubated early and had partial data included in the analysis)	HOB -elevated at 30º for 12h on day 1 -at 45º for 12h on day 2	HOB - elevated at 45° on day 1 -elevated at 30° on day 2	Primary outcomes: - reflux - aspiration - pressure ulcers	<ul> <li>Primary outcomes</li> <li>overall mean HOB angle and the % of pepsin-positive oral secretions for each HOB assignment demonstrated a significant negative correlation (t = -0.536, p = 0.008 at 30° and t = -0.433, p = 0.03 at 45°)</li> <li>no significant difference in aspiration/pepsin positive tracheal secretion (p = 0.37)</li> <li>no pts developed a pressure ulcer</li> </ul>	4

HOB = head of bed elevation, ICU = intensive care unit, pts = patients, RCT = randomized controlled trial

HOB angle seems to have a benefit in relation to aspirations.

15171)- Intubation within the preceding 2 weeks - weight ≥ 159 kgbefore start of interventi on- acclimation mode: gradual increase in the degree of rotation over several hours from 25° to the maximum lateral angle)right) at least 45° head elevation ≥ 30°- ICU LOS 11.1 [IQR 5.4- 23.4] vs. 8.2 [IQR 3.6-14.9] days - ICU mortality 25% vs. 29%Specification of study: Pilot RCT- Day 7 or - death or - transfer from study unit or - consent revoked Follow up until ICU discharge- Mode: gradual interventi on- ICU LOS 11.1 [IQR 5.4- 23.4] vs. 8.2 [IQR 3.6-14.9] days - ICU mortality 25% vs. 29%Per Branch- Day 7 or - death or - consent revoked Follow up until ICU discharge- ICU dischargePer Branch- Day 7 or - consent revoked- ICU mortalityPer Branch- Per Branch- Hot daysParticle Allow of 0.05- ICU LOS 11.1 [IQR 5.4- - UL OS 11.1 [IQR 5.4- - ICU Mortality 25% vs. - ICU mortality	Reference, Study Type		es and Controls nt #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Hannemann 2015 (PMID: 25554551 DOI: 10.4037/ajcc20 15171) Specification of study:	<ul> <li>medical, 1 medical-</li> <li>Inclusion criteria: <ul> <li>≥ 18 y</li> <li>MV ≤ 8 h</li> </ul> </li> <li>Exclusion criteria: <ul> <li>pulmonary mass hemothorax, ple potential source</li> <li>systolic bp &lt; 90 r support</li> <li>injuries requiring</li> <li>head injury requ monitoring</li> <li>Intubation within</li> <li>weight ≥ 159 kg</li> </ul> </li> <li>Study duration till <ul> <li>Day 7 or</li> <li>discontinuation of</li> <li>death or</li> <li>transfer from stu</li> <li>consent revoked</li> </ul> </li> </ul>	surgical ICU) , pneumothorax, ural effusion, or other of compression atelectasis mmHg with vasopressor g immobilization iring intracranial pressure n the preceding 2 weeks of MV or udy unit or <b>I discharge</b>	ion group): death before start of interventi	Triadyne Proventa bed - rotation angle 45° in the lateral positions Head elevation ≥ 30° (At beginning of protocol) - acclimation mode: gradual increase in the degree of rotation over several hours from 25° to the maximum lateral	care: - manual turning every 2 hours (back to left to back to right) at least 45° head	calculation: - None for pilot study. Primary endpoint: - incidence and progression or resolution of PPCs by serial chest Xrays Secondary outcomes: - turning-related AEs - duration of MV - ICU LOS	no significant difference (p = 0.16, no effect size) Secondary endpoints: - AEs (n.s.) - found no statistically significant differences between groups in turning-related adverse events, duration of MV, ICU LOS or ICU mortality - MV duration 6.0 ± 5.0 vs. 5.2 ± 4.3 days - ICU LOS 11.1 [IQR 5.4- 23.4] vs. 8.2 [IQR 3.6-14.9] days - ICU mortality 25% vs. 29% Posthoc power analysis: a sample size of 54 patients (27 per group) necessary to detect an effect on PPCs with 80%	

AEs = adverse events, bp = blood pressure, CLRT = continuous lateral rotation therapy, ICU = intensive care unit, IQR = interquartile range, LOS = length of stay, MV = mechanical ventilation, PPCs = preventable pulmonary complications (e.g., atelectasis or pneumonia)

#### CLRT showed no benefit compared to standard of care. 54 pts would be necessary to detect an effect on PPC with 80% power.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
460 Klein 2015 (PMID: 25517476 DOI: 10.1097/CCM .000000000 000787) <b>Specification</b> of study: prospective cohort study	<ul> <li>- confusion, combativeness,</li> <li>- chronic psychiatric condition</li> <li>- expiration or discharge from the</li> </ul>		Early progressive mobilisation - 16 mobility levels - initiated on day of admission	Standard of Care - no early mobilization (Pre-EM)	<ul> <li>Primary endpoint: <ul> <li>daily mobility levels</li> </ul> </li> <li>Secondary outcomes: <ul> <li>hospital and NICU LOS</li> <li>30-day mortality</li> <li>discharge disposition</li> <li>VAP</li> <li>blood stream infection</li> <li>DVT</li> <li>HAPUS</li> <li>anxiety</li> <li>depression/hostility</li> </ul> </li> <li>Power analysis: <ul> <li>300 pts (150 per study phase)</li> <li>would provide 80% power to</li> <li>detect a decrease in mean LOS</li> <li>of at least 30% (assuming LOS</li> <li>was distributed log-normally</li> <li>with a coefficient of variation</li> <li>of 1.25 and that a significance</li> <li>level of 0.05)</li> </ul></li></ul>	Significant differences between groups in: - higher mobility levels in intervention (p < 0.001) - LOS of hospital and NICU stay for pts in the EM group were reduced by 33% and 45% respectively (both $p < 0.001$ ) - prevalence of blood stream infection was reduced by 3% ( $p = 0.015$ ) -prevalence of HAPU was reduced by 2.7% ( $p = 0.026$ ) - EM pts had lower anxiety scores ( $p = 0.029$ ) No significant differences between groups in: - 30-day mortality ( $p = 0.12$ ) - VAP ( $p=0.11$ ) - DVT ( $p=0.12$ ) - depression ( $p=0.055$ ) - hostility ( $p=0.18$ )	3

DVT = deep vein thrombosis, EM = early mobilization, HAPU = hospital-acquired pressure ulcer, ICU = intensive care unit, LOS = length of stay, NICU = neurologic ICU, pts = patients, VAP = ventilator-associated pneumonia

# An early progressive mobility protocol increased patients' highest level of mobility and decreased hospital and NICU LOS, but did not affect psychological profile.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total
461	Number of publications not stated
Hodgson 2014	Inclusion criteria: - adults
PMID: 25475522	-mechanically ventilated, intensive care unit patients
DOI: 10.1186/s1305	Definition of categories
4-014-0658-y	Safety parameters for
Specification of study: National Guideline	mobilization categories: 1.respiratory 2.cardiovascular 3.neurological 4.other

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total						
465 Burke 2016 (PMID: 25353646 DOI: 10.1111/crj.1223 4) Specification of study: Systematic Review + Meta- Analysis	12 publications (11 RCT, 1 case control) <sup>1-12</sup> Inclusion criteria: - adult ICU pts - ≥ 18 years of age Exclusion criteria: - cadaveric studies - cardiac pacing - spinal cord stimulation - phrenic nerve stimulation - stable pts. not requiring ICU admission - incomplete data Per Branch		Percutaneous neuromuscular electrical stimulation	Usual care	<b>Outcomes:</b> - muscle bulk - muscle strength with MRC - cardiovascular fitness - independence from MV - activity limitations	Significant differences between groups in: - MRC, MD: 95%CI): 0.93 (0.51 – 1.35) P-value: < 0.0001 - three RCTs supported NMES to preserve muscle strength using a fixed- effects model [n = 146; standardised mean difference 0.93 (0.51, 1.35) P = 0.0002]	2

ICU = intensive care unit, MRC = medical research council, MV = mechanical ventilation, RCT = randomized controlled trial

Neuromuscular electrical stimulation increased muscle strength in a meta-analysis including 3 out of 12 studies.

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Reference, Study Type	Cases and Co (Participant #, Cha Total		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
295 McWilliams, 2015 (PMID: 25316527 DOI: 10.1016/j.jcrc.20 14.09.018)	582 pts Inclusion criteria: - invasively ventilated for Exclusion criteria: - significant neurologic i - orthopedic injury with to mobilize - significant burn - poor preadmission mo yards) reported by the p admission	njury contraindication bility levels (<10		New supportive rehabilitation team was created, with a focus on promoting early and enhanced rehabilitation for patients at high risk for prolonged	Previous 12 month without new care	<b>Primary endpoints:</b> - mobility level at ICU discharge (MMS) - mean ICU LOS - post-ICU LOS - ventilator days	Significant differences between groups in: - significant increase in mobility at ICU discharge - ICU LOS (16.9 vs 14.4 days, P=0.007) - ventilator days (11.7 vs 9.3 days, p <0.05) - total hospital LOS (35.3 vs 30.1	4
Specification of	Per Branch			ICU and hospital LOS	team	- in-hospital mortality	days, p < 0.001)	
<b>study:</b> quality improvement project	N=292	N=290					- in-hospital mortality (39% vs 28%, p<0.05)	

ICU= intensive care unit, LOS = length of stay

The implementation of a new rehabilitation team with focus on early and enhanced rehabilitation was associated with significant reduction of mortality, ICU and hospital LOS and increase of mobility at discharge.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Interven tion	Control	Optimal Population	Primary Results	Evidence Grade
468 Kho 2015 (PMID: 25307979 DOI: 10.1016/j.jcrc.20 14.09.014) <b>Specification of</b> <b>study:</b> RCT	<ul> <li>36 pts</li> <li>Inclusion criteria: <ul> <li>≥ 18 years of age</li> <li>MV for ≥ 1 day</li> <li>expected to remain in the ICU ≥ 2 days</li> </ul> </li> <li>Exclusion criteria: <ul> <li>BMI ≥ 35 kg/m2</li> <li>moribund status</li> <li>ICU LOS &gt; 7 days before enrolment</li> <li>&gt; 4 days of continuous MV before enrolment</li> <li>known intracranial process</li> <li>primary systemic neuromuscular disease</li> <li>unable to speak English</li> <li>baseline cognitive impairment before ICU admission</li> <li>conditions preventing NMES or primary outcome evaluation</li> <li>unable to transfer independently from bed to chair before ICU admission</li> <li>implanted cardiac pacemaker or defibrillator</li> <li>Ilimitation in core other than no cardiopulmonary resuscitation</li> <li>pregnancy</li> <li>suspected malignancy in the legs</li> </ul> </li> </ul>	n = 2 interventiona l pts (due to new information regarding presence of an exclusion criteria)	NMES: 60 minutes per day	Sham stimulation	Primary endpoint: lower extremity muscle strength via MRC Secondary outcomes: - muscle strength via MRC - dynamometry of the M. quadriceps, tibialis anterior und gastrocnemius - HGS - MIP - FSS for ICU - MWD - duration of MV - ICU LOS - hospital LOS - ICU randomisation - hospital mortality - total hospital charges - survivors' hospital discharge disposition - iADLs	<ul> <li>Primary endpoints:</li> <li>lower extremity MRC, [mean (SD)] at hospital discharge: intervention 28 (2) vs control 27 (3), p = 0.072</li> <li>Secondary outcomes: <ul> <li>lower extremity MRC, [mean (SD)] at</li> <li>first awakening: intervention 23 (6) vs. control 25 (5), p = 0.271</li> <li>UC discharge, [mean (SD)]: intervention 27 (23) vs. control 25 (4), p = 0.139</li> <li>increase in first awakening to ICU discharge [mean (SD)]: litervention 5.3 (5.9) vs. control 0.8 (3.8);</li> <li>p-value: 0.047</li> <li>increase in first awakening to hospital discharge [mean (SD)]: intervention 5.7 (5.1) vs. control 1.8 (2.7), p-value: 0.019</li> <li>overall MRC at</li> <li>first awakening: intervention [mean (SD)]: 42 (10) vs. control 45 (11), p-value: 0.374</li> <li>ICU discharge [mean (SD)]: intervention 49 (6) vs. control 48 (8), p-value: 0.374</li> <li>ICU discharge [mean (SD)]: intervention 53 (4) vs. control 50 (7), p-value: 0.141</li> <li>dynamometry M. tibialis anterior (kg) at</li> <li>first awakening [mean (SD)]: intervention 18 (11) vs. control 16 (9), p-value: 0.874</li> <li>ICU discharge [mean (SD)]: intervention 21 (10) vs. control 19 (9), p-value: 0.874</li> <li>ICU discharge [mean (SD)]: intervention 21 (10) vs. control 19 (16), p-value: 0.874</li> <li>ICU discharge [mean (SD)]: intervention 25 (16) vs. control 32 (12), p-value: 0.309</li> <li>ICU discharge [mean (SD)]: intervention 31 (17) vs. control 32 (12), p-value: 0.473</li> <li>dynamometry M. guadriceps femoris (kg) at</li> <li>first awakening [mean (SD)]: intervention 23 (11) vs. control 23 (12), p-value: 0.473</li> <li>dynamometry M. quadriceps femoris (kg) at</li> <li>first awakening [mean (SD)]: intervention 23 (11) vs. control 33 (14), p-value: 0.458</li> <li>hospital discharge [mean (SD)]: intervention 28 (14) vs. control 33 (14), p-value: 0.458</li> <li>hospital discharge [mean (SD)]: intervention 28 (7.5 (28/7.5) vs. control 39/10.5 (43/10.0), p-value: 0.472/421</li> <li>ICU discharge [mean (SD)]: intervention -34/9.4 (26/7.2) vs.</li></ul></li></ul>	3

Р	Per Branch			<ul> <li>hospital discharge [mean (SD)]: intervention 61 (16) vs. control 51 (37), p-value: 0.68</li> <li>FSS-ICU at:</li> </ul>
Contr n = 1	01	tervention n = 16		<ul> <li>first awakening [mean (SD)]: intervention 12 (8) vs. control mean 13 (6), p-value: 0.503</li> <li>ICU discharge [mean (SD)]: intervention 20 (10) vs. control 19 (6), p-value: 0.897</li> <li>hospital discharge [mean (SD)]: intervention 30 (7) vs. control -26 (8), p-value: 0.140</li> <li>increase first awakening to ICU discharge [mean (SD)]: intervention 11.4 (6.2) vs. control 4.3 (5.6), p-value: 0.019</li> <li>MWD (feet) at: <ul> <li>first awakening [mean (SD)]: intervention 64 (123) vs. control 29 (97), p-value: 0.458</li> <li>ICU discharge [mean (SD)]: intervention -216 (343) vs. control 29 (97), p-value: 0.458</li> <li>ICU discharge [mean (SD)]: intervention 514 (398) vs. control 251 (210), p-value: 0.250</li> <li>hospital discharge [mean (SD)]: intervention 514 (398) vs. control - [mean (SD)]: 26 (8), p-value: 0.050</li> </ul> </li> <li>number of iADL at: <ul> <li>first awakening [mean (SD)]: intervention 0 (0) vs. control 0.1 (0.5), p-value: 0.410</li> <li>ICU discharge [mean (SD)]: intervention 1.2 (1.8) vs. control 0.9 (1.7) p-value: 0.728</li> <li>hospital discharge intervention 4.0 (2.3) vs. control 2.4 (2.6), p-value: 0.101</li> </ul> </li> <li>ICU LOS [mean (SD)]: intervention 26.8 (20.9) vs. control 27.7 (18.1), p-value: 0.905</li> <li>hospital LOS [mean (SD)]: intervention 3 (17) vs. control 3 (19), p-value: 1.000</li> <li>ICU mortality [n (%)]: intervention 1 (5) vs. control 3 (19), p-value: 0.323</li> <li>duration of mechanical ventilation (days) [mean (SD)]: intervention 16 (15) vs. control 20 (18), p-value: 0.492</li> </ul>

BMI = body mass index, FSS = functional status score, HGS = hand grip strength, iADL = independent activities of daily living, ICU = intensive care unit, LOS = length of stay, MIP = maximum inspiratory pressure, MRC = medical research council, MV = mechanical ventilation, MWD = maximum walking distance, NMES = neuromuscular electrical stimulation, pts = patients

Neuromuscular electrical stimulation did not improve leg strength at ICU discharge.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
469 Dirks 2015 (PMID: 25296344 DOI: 10.1042/CS2014044 7) <b>Specification of</b> <b>study:</b> RCT – intraindividual design	9 pts Inclusion criteria: -ICU pts Exclusion criteria: - <18 or >80 years of age - not expected to undergo complete sedation - suffering from spinal cord injury - recent arterial surgery on the legs - local wounds that prohibit the application of NMES - chronic use of corticosteroids - intake of certain anti-thrombotic drugs - presence of an implantable cardioverter- defibrillator (ICD) and/or pacemaker - expected sedation time estimated by the responsible physician was <3 days Per Branch	3 pts (33,3%) because of early awakening (after <3 study days) and death	NMES	Usual care	Primary endpoint: - MFCSA difference between first and second measurement)	<b>Primary endpoint:</b> MFCSA- Type I (μm <sup>2</sup> ), mean (SD): - control pre/post: 4560 ± 261 / 3879 ± 484, p < 0.05 - intervention pre/post: 4414 ± 441 / 4512 ± 550, p-value: n.s MFCSA- Type II (μm <sup>2</sup> ), mean (SD): - control pre/post: 3412 ± 530 / 2647 ± 51, p < 0.05 - intervention pre/post: 3168 ± 607 / 3246 ± 590, p-value n.s	4

ICD = implantable cardioverter-defibrillator, ICU = intensive care unit, MFCSA = muscle fiber cross sectional area, NMES = neuromuscular electrical stimulation, n.s = not significant, pts = patients, SD = standard deviation

#### Neuromuscular electrical stimulation did not increase MFCSA.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
474 Dong 2014 (PMID: 25215147 DOI: 10.5847/wje m.j.issn.1920 - 8642.2014.0 1.008) Specification of study: RCT	60 pts admitted to the ICU Inclusion criteria: - ventilated for 48-72h - >18y, expected MV ≥1 week - clear consciousness - cardiovascular stability - respiratory stability - no unstable fracture Exclusion criteria: - inability to do activities independ - rapid development of neuromused disorders, -an estimated 6-month mortality > - increased intracranial pressure - absent limbs - preadmission glucocorticoids >20 - ICU admission after cardiopulmo - tumor radiotherapy and chemoth - acute myocardial infarction or ur 80	cular disease, and irreversible > 50% D days (prednisone >20 mg/d) nary resuscitation herapy within 6 months		Early rehabilitation: - until hospital discharge - heading up actively, transferring from SP to sitting position at the edge of the bed or sitting in chair, and from sitting to standing, and walking bedside - 2x daily - intensity was adjusted according to the condition of the pts	Standard of care	Primary endpoint: - not defined (feasibility study) Derived endpoints: - duration of MV in days - ICU LOS in days - APACHE II Score - hospital mortality No power analysis (feasibility study)	Significant difference between groups in: - duration of MV, $5.6\pm2.1$ intervention vs $7.3\pm2.8$ control, p = 0.005 - ICU LOS, $12.7\pm4.1$ intervention vs $15.2\pm4.5$ control, p = 0.01 No significant difference between groups in: - APACHE II Score ( $10.0\pm3.1$ interventions vs $10.0\pm3.2$ control, p = 0.50) - hospital mortality (2 pts ( $6.7\%$ ) intervention vs 3 pts ( $10\%$ ) control, p = $1.0$ )	2

APACHE II = acute physiology and chronic health evaluation, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patient

Early rehabilitation therapy reduces the duration of mechanical ventilation and the length of stay in the ICU.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
478 Wang 2014 PMID: 25069952 https://doi.org/10. 1186/cc14001 <b>Specifiation of</b> <b>study:</b> Prospective cohort study	Pts. requiring CVVH, 35 pts. included (40 planned)         Exclusion control (passive mobilization):         - RASS +3 or +4         - HR >160 or <40 beats/min or new arrhythmia	1 (permanent dialysis access)	Mobilization group: 1. Low-level 2. High-level	<b>Baseline Pts.:</b> -passive mobilization	No sample size calculation à Convenience sample of 40 Pts. <b>Primary</b> endpoints: -AE Secondary endpoints: -Filter life (duration, subgroup) -Intervention feasibility (measured by filter alarm rates, pressures (access, return, transmembrane), blood flow recorded each minute from the digital output screen)	Primary results: -No AEs occurred Secondary results: -Intervention filters lasted longer than nonintervention filters (regression coefficient = 13.8, robust 95% confidence interval (CI) = 5.0 to 22.6, P = 0.003). -femoral filter subgroup (regression coefficient = 15.7, robust 95% CI = 4.6 to 26.7, P = 0.008), but not in the nonfemoral access filter subgroup (regression coefficient = 9.2, robust 95% CI = −6.0 to 24.4, P = 0.20) (Figure 2). -Feasibility: ○ 61% of the time no filter alarm ○ No differences in pressures in the first and final phases of the interventions	3

Pts. = patients; CVVH = continuous veno-venous hemofiltration; AE = adverse events; CI = confidence interval; RASS= Richmond Agitation–Sedation Scale; HR=heart rate; MAD= Mean arterial blood pressure

# Mobilization during renal replacement therapy via a vascular catheter in patients who are critically ill is safe and may increase filter life. *No detailed assessment was carried out because higher-quality evidence is available on this topic.*

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Interventi on	Control	Optimal Population	Primary Results	Evidence Grade
479 Wageck 2014 (PMID: 25060511 DOI: 10.1016/j.med n.2013.12.003 Specification of study: Systematic review with metaanalysis	9 randomized and quasi- randomized controlled trials, 274 pts <sup>1-9</sup> , 2 trials included in meta-analysis Inclusion criteria: - randomized and quasi- randomized controlled - non-invasive NMES applied to lower and/or upper limbs - critical pts in ICU Exclusion criteria: - < 18 years of age - NMES < 48h Per Branch Intervention group (n=135) Control			Not specifie d	Primary outcomes: - muscle strength - muscle structure Secondary outcomes: - ICU LOS - duration of mechanical ventilation - complications from immobilization and bed rest	<b>Primary outcomes:</b> - meta-analysis on the effects of NMES on quadriceps femoris strength showed effect of NMES in MRC Scale (standardized mean difference 0.77 points; $p = 0.02$ ; 95% CI: 0.13-1.40) <b>Mixed results for muscle structure</b> -3 studies: no difference; - Gerovasili et al: smaller decrease in diameter for the NMES group for all muscles, except left rectus femoris ( $-0.13 \pm 0.10$ cm vs $-0.19 \pm 0.16$ cm, respectively; $p = 0.07$ ) - Bouletreau et al: smaller elimination during NMES application only for creatinine (79.2 $\pm 25 \mu$ mol/kg/day vs 92.4 $\pm 6.8 \mu$ mol/kg/day, respectively; $p < 0.01$ ) and 3-methyl histidine ( $3.15 \pm 0.32 \mu$ mol/kg/day $3.78 \pm 0.37 \mu$ mol/kg/day, respectively; $p < 0.01$ ) <b>Secondary outcomes:</b> -ICU LOS and ventilation: Rousti et al: no difference between groups for average time in ICU and average time in MV - Rousti et al.: better performance for the weaning period in NMES group when (median 1 day, range 0-10 vs 3 days, range 0-44, respectively; $p = 0.003$ ) - Rousti et al: shorter period between extubation until ICU discharge (days off MV) for the NMES group (median 4 days, range 0-16 vs 6 days, range 0-41, respectively; $p =$ 0.003) <b>Complications:</b> Velmhos et al.: higher venous flow velocity for NMES group in superficial femoral left vein (21 ± 6 cm/min vs 16 ± 5 cm/min, respectively; $p = 0.02$ ) and in the left popliteal vein (22 ± 10 cm/min vs 15 ± 9 cm/min, respectively; $p = 0.03$ ; - Rousti et al.: development of critical illness polyneuropathy between groups and found an odds ratio = 0.22 (95% CI = 0.05-0.92; $p = 0.04$ ) in favor of the NMES	1 → 2 (downgraded as

LOS = length of stay, MRC = medical research council, NMES= neuromuscular electrical stimulation, pts = patients

NMES has good results when used for the maintenance of muscle mass and strength.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evide nce Grade
480 Roth 2014 (PMID: 24985500 DOI: 10.1007/s12028- 014-0004-x) <b>Specification of</b> <b>study:</b> A retrospective analysis	29 pts Inclusion: - severe intracranial pathologies - documented kinetic therapy due to respiratory failure Exclusion criteria: - < 18 years - MV in pressure-controlled mode Per Branch		PP	SP	Endpoints: -ICP -CPP -PEEP -pCO2 -P/F ratio -MAP No sample size calculation	Significant differences between groups: - mean ICP baseline in SP 9.5 $\pm$ 5.9 mmHg (range 0–40 mmHg), increased during PP to 15.4 $\pm$ 6.2 (range 0–40 mmHg) (p < 0.0001) - MAP decreased from 72.6 $\pm$ 17.5 mmHg in SP to 64.7 $\pm$ 17.5 mmHg in PP (p < 0.001) - pCO2 increased In PP (during and after PP) - PaO2/FiO2 ratio increased In PP (during and after PP) - ICP values >20 mmHg occur more often in PP (17.9 %, n = 145/831) compared to SP (4 %, n = 28/703, p < 0.0001) - more often episodes of decreased CPP in PP (24.4 %, n = 203/831) vs SP (17.9 %, n = 126/703, p = 0.0022) No significant difference between the groups: - CPP in SP (82 $\pm$ 14.5 mmHg, range 37–137 mmHg) or PP (80.1 $\pm$ 14.1 mmHg, range 37–118 mmHg) (p = 0.0591) - PEEP not significant	4

CPP = cerebral perfusion pressure, ICP = intracranical pressure, MAP = mean arterial pressure, MV = mechanical ventilated, PEEP = positive end expiratory pressure, PP = prone position, pts = patients, SP = supine position

A significant elevation of ICP during prone positioning is shown and an achieved benefit for oxygenation by far exceeded the changes in ICP.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Eviden ce Grade
485 Parry 2014 (PMID: 24768534 DOI: 10.1016/j.jcrc. 2014.03.017) <b>Specification</b> of study: interventional observational study	<pre>16 pts Inclusion criteria: - 18 years or older - diagnosis of sepsis or severe sepsis - predicted to MV &lt; 48 hours -expected to remain in IC ≥ 4 days Exclusion criteria: - presence of an external fixator, pacemaker or defibrillator - open wound or skin abrasions - obesity, BMI &gt; 40 - physician deemed the p to be approaching imminent death</pre>		Usual care + FES-cycling - within 96h of admission - daily until ICU discharge - min 20 min - max 60 min/d - 5x/week	Usual care - early mobility activities: sitting on the edge of bed, sitting out of bed, standing, marching in place and walking to a maximum of 15min/d	Primary endpoints: Feasibility of FES cycling defined as: - time from ICU admission to 1 <sup>st</sup> training session - total number of sessions - % of total potential sessions completed and reasons not completed - number of sessions with muscle contractions Safety, defined as: - recording variability in cardiovascular + respiratory bedside parameters - behavioral pain score / VAS Secondary outcomes: - PFIT-s scored on awakening - time to reach functional milestones - incidence and duration of delirium	Primary endpoints: - time from recruitment to 1 <sup>st</sup> intervention session: 15.3 (12.0-31.5) h - cycling sessions conducted 8.6 (SD 2.5) - 69 sessions out of 95 (73%) - one minor adverse event - greatest difference between min and max values recorded observed with HR with variation of 20-40 bpm - RR/HR: values at start (5 min prior to exercise) and 30 min post similar - FES-cycling session time 35.8± 10.7 min, quadriceps intensity of 67.0±29.6 mA - visible quadriceps muscle contraction 49/69 sessions (71%); palpable (not visible) contraction 6/69(9%) Secondary outcome: - fewer required rehabilitation in intervention group (43%) compared to control group (86%) p=0.5 - duration of delirium significantly shorter in intervention group (p=0.042)	3

BMI = body mass index, bpm = beats per minute, FES = functional electrical stimulation, HR = heart rate, ICU = intensive care unit, MV = mechanical ventilated, PFIT = physical function in intensive care test-scored on awakening, pts = patients, SD = standard deviation, VAS = visibal analoge scala

# FES-Cycling seems to be safe and feasible, but the sample size is too small regarding functional outcomes and frequency and duration of delirium

Reference, Study Type	Cases and (Particip character Tota	ant #, ristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
490 Kim 2014 PMID: 24567696 https://doi. org/10.158 9/jpts.26.1 49 <b>Specificatio</b> n of study: A prospective multicenter study	NSICU pts of a t hospital with <u>ac</u> → 37 pts Inclusion criter -below G3 in a strength test -no existing cor would disrupt treatment -no Amputatior -no disfigureme -no external wo -no other defor with regard to extremities Per Bra 25 experimental	ia: muscle nditions that medical ns ents ounds rmations upper		Early bilateral passive ROM exercise - Twice a day - Five days per week - Four weeks	Standard of care (participan ce in bilateral passive ROM exercise two weeks after diagnosis)	No primary endpoint defined Extracted endpoints: - Function of upper extremities - ADLs	<ul> <li>Hesults:</li> <li><u>function of upper extremities:</u> <ul> <li>a. edema (baseline, two weeks, four weeks; mean ± 5D; mm)</li> </ul> </li> <li>affected finger: <ul> <li>a. intervention (73.3 ± 6.9, 69.2 ± 6.8, 65.9 ± 6.7) vs. control (73.7 ± 6.3, 77.6 ± 6.6, 77.9 ± 7.0), p = 0.001</li> <li>b. difference in change between groups at four weeks significant, p = 0.002</li> </ul> </li> <li>affected wrist: <ul> <li>a. intervention (171.6 ± 12.6, 167.4 ± 12.4, 163.7 ± 11.6) vs. control (173.8 ± 15.2, 180.5 ± 13.4, 180.5 ± 12.7), p = 0.022</li> <li>b. difference in change between groups at four weeks significant, p = 0.016</li> </ul> </li> <li>affected elbow: <ul> <li>a. intervention (250.7 ± 23.2, 242.5 ± 22.0, 235.7 ± 19.8) vs. control (256.1 ± 29.4, 262.2 ± 26.5, 263.1 ± 28.0), p = 0.001</li> <li>b. difference in change between groups at four weeks significant, p = 0.037</li> <li>unaffected finger: intervention (68.8 ± 7.7, 66.5 ± 7.0, 64.0 ± 7.0) vs. control (71.7 ± 5.8, 70.3 ± 4.9, 67.8 ± 5.1), p = 0.001</li> </ul> </li> <li>5. unaffected virst: intervention (167.2 ± 12.9, 164.2 ± 12.7, 161.2 ± 12.4) vs. control (253.3 ± 21.4, 169.0 ± 10.2, 165.6 ± 9.4), p = 0.001</li> <li>anaffected elbow: intervention (245.3 ± 21.0, 239.1 ± 21.3, 233.8 ± 19.5) vs. control (253.3 ± 27.4, 249.5 ± 25.6, 244.9 ± 24.8), p = 0.001</li> <li>b. ROM of affected shoulder (baseline, two weeks, four weeks; mean ± 5D, ")</li> <li>I. Flexion: <ul> <li>a. intervention (n = 19; 11.4 ± 13.0, 116.7 ± 12.8, 119.0 ± 12.6) vs. control (n = 18; 109.1 ± 20.2, 109.8 ± 20.7, 111.1 ± 21.1); non-significant differences</li> <li>b. difference in change between groups at four weeks significant, p = 0.001</li> </ul> </li> <li>Extension: <ul> <li>a. intervention (n = 19; 25.2 ± 5.2, 27.1 ± 4.9, 29.5 ± 5.3) vs. control (n = 18; 31.2 ± 4.7, 31.3 ± 4.7, 31.9 ± 4.8), p = 0.007</li> <li>b. difference in change between groups at four weeks significant, p = 0.001</li> </ul> </li> <li>Extension: <ul> <li>a. intervention (n = 19; 91.3 ± 19.8, 53.8 ± 19.5, 55.6 ±</li></ul></li></ul>	3 → 4 261

a. intervention (n = 19; 46.4 ± 28.2, 48.5 ± 28.7, 50.2 ± 28.5) vs. control (n = 18; 49.0 ± 18.9, 49.5 ± 19.1,
$49.8 \pm 19.0$ )
b. difference in change between groups at four weeks significant, p = 0.001
3. Pronation:
a. intervention (n = 19; 53.7 ± 16.1, 56.0 ± 16.0, 57.3 ± 15.7) vs. control (n = 18; 64.6 ± 11.7, 65.1 ± 11.7, 65.7 ± 11.7)
b. difference in change between groups at four weeks significant, p = 0.001
d. ROM of affected wrist (baseline, two weeks, four weeks; mean ± SD, °)
1. Flexion:
a. intervention (n = 19; 40.3 ± 7.4, 42.0 ± 7.3, 42.9 ± 7.0) vs. control (n = 18; 46.0 ± 3.6, 46.6 ± 3.6, 47.1 ± 3.7); non-significant differences
b. difference in change between groups at four weeks significant, p = 0.016
<ol> <li>Extension: intervention (n = 19; 36.7 ± 7.3, 38.6 ± 6.6, 40.1 ± 6.6) vs. control (n = 18; 37.0 ± 7.2, 37.5 ± 7.1, 38.0 ± 7.3), p = 0.007</li> </ol>
3. Ulnar deviation:
a. intervention (n = 19; 20.7 ± 5.0, 22.8 ± 4.5, 24.1 ± 4.2) vs. control (n = 18; 23.1 ± 2.3, 23.5 ± 2.1, 24.0 ± 2.5); non-significant differences
b. difference in change between groups at four weeks significant, p = 0.001
4. Radial deviation:
a. intervention (n = 19; 15.4 ± 5.8, 17.0 ± 5.3, 17.7 ± 5.2) vs. control (n = 18; 15.5 ± 3.8, 15.8 ± 3.7, 16.1 ± 3.8); non-significant differences
b. difference in change between groups at four weeks significant, p = 0.001
- ADLs (two weeks to four weeks; points): Intervention (16.84 to 18.21) vs. control (12.50 to 12.67), p = 0.001

NSICU= neurosciences intensive care unit, Pts = patients, ICU = intensive care unit, ROM = range of motion, ADLs = activities of daily living

#### Early passive range of motion exercise improves function of upper extremities and activities of daily living in patients with acute stroke.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
491 Sricharoenchai 2014 PMID: 24508202 https://doi.org/1 0.1016/j.jcrc.201 3.12.012 Specification of study: Monocenter, prospective observational study	ICU patients from a tertiary hospital during July 2009 and December 2011 → 1787 pts Inclusion criteria: - ICU admission for at least 24 hours - Receiving physical therapy intervention Per Branch		Physical therapy		<ul> <li>No sample size calculation stated</li> <li>Endpoints: <ul> <li>Number of physical therapy sessions</li> </ul> </li> <li>Incidence of abnormal events: <ul> <li>a. cardiac arrhythmia, hypertension (mean arterial pressure greater than 140 mm Hg)</li> <li>b. hypotension (mean arterial pressure less than 55 mm Hg)</li> <li>c. desaturation (oxygen saturation less than 85% for more than 3 minutes)</li> <li>d. fall</li> <li>e. removal of medical device</li> <li>f. cardiorespiratory arrest</li> </ul> </li> <li>Number of events with consequences for the prevalence of additional treatments, cost, length of stay</li> </ul>	<ul> <li>Number of physical therapy sessions (n [%]): 1110 pts (62%) participated in 5267 physical therapy sessions</li> <li>Incidence of abnormal events (n [%]): 34 (0.6%) a. arrythmia: 10 (0.2%) b. hypertension: 8 (0.2%) c. hypotension: 5 (0.1%) d. no data for other abnormal events</li> <li>Number of events with consequences (n [%]): 4 (0.1%)</li> </ul>	3

Pts = patients, ICU = Intensive Care Unit

Physical therapy in critically ill patients seems safe.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and C (Participa character Tota	ant #, istics)	Drop-out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
494 Balas 2014 PMID: 24394627 https://doi.or g/10.1097/cc m.00000000 0000129 <b>Specification</b> of study: before-after cohort study	surgical ICU Exclusion crite -no legal repre available withi hours post adr	e-down natology nit eria: with ernal or eria: esentative in 48 mission	4 (control/ ,pre' group) withdrew from study	Fixed protocol for early complex treatment: ABCDE- bundle	Standard of care	No sample size calculation <b>Primary Endpoint:</b> -days without MV within 28 days <b>Secondary Endpoints:</b> -prevalence, duration and % of ICU pts with delirium or coma -mobilization rate -Mortality -number of discharges not home -adverse events	Significant differences between groups in: -days without MV, control median 21d [IQA 0 - 25] vs intervention median 24 d [IQA 7 - 26]; p = 0.04 -delirious pts: control 62.3% vs intervention 48.7%; p = 0.02 -delirium duration/d: - 17% (control 50% [IQA 30 - 64.3] vs intervention 33.3% [IQA 18.8 to 50]; p = 0.003), significance retained when adjusting for sex, co-morbidity APACHE II, age and MV -mobilization rate out of bed: control 48% vs intervention 66% within IICU time, p = 0.002 -pts mobilized according to fixed ABCDE-bundle protocol with significantly higher probability of mobilization for at least 1 unit out of bed 95% CI, 1.30-3.45, p = 0.003 -unadjusted mortality/illness in intervention (p = 0.04) No significant differences between groups in: -unadjusted mortality/ICU, p = 0.07 -mortality rate control 19.9% vs intervention 11.3% (OR 0.56, 95% CI 0.28-1.10; p = 0.09) -discharge rates -no adverse events	4

Pts. = patients; ICU = Intensive Care Unit, MV = Mechanical Ventilation, APACHE II = Acute Physiology and Chronic Health Evaluation II

The ABCDE Bundle seems to reduce the duration of mechanical ventilation, delirium and mortality while also increasing the rate of mobilization out of bed.

Reference, Study Type		and Controls : #, Characteristics)	Drop -out	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	Total		Rate					
496 Lee 2014 (PMID: 24368348 DOI: 10.1097/CC M.0000000 0000122) Specification of study: Meta- Analysis	(PaO2/FIO2 ≤ 30) acute lung injurt - mechanical ver - randomly assig or more groups, supine positioni - all-cause mort regardless of the collection Exclusion criter - pediatric patie - randomized cri assigned patient supine groups	pts ) <sup>1-11</sup> <b>a:</b> nic respiratory failure D0 mm Hg), including y (ALI) and ARDS ntilatory support gned patients to two , including prone or ing, during ventilation ality was reported e timing of data <b>ia:</b>		PP	SP	Primary outcome: - overall mortality at the longest available follow-up Secondary outcome: - mortality stratified to: 1. the duration of prone position 2. lung protective ventilation - adverse events	Primary outcome:         - overall mortality: Prone position group (OR, 0.77; 95% Cl, 0.59–0.99; p = 0.039, I = 33.7%)         Secondary outcome:         - duration of prone position: effect on mortality was not significant (p=0,130)         - duration of prone ventilation more than 10 hr/session showed a significant reduction in overall mortality (p < 0.001)	1
	1142 PP	1104 SP						

ARDS = acute respiratory distress syndrome, pts = patients, PP = prone position, SP = supine position

Ventilation in the prone position significantly reduced overall mortality in patients with severe acute respiratory distress syndrome.

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Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
499 Yosef- Brauner 2015 PMID: 24345055 DOI: 10.1111/crj.1 2091 Specification of study: a prospective, single- blinded study	1 center from June 2011 to Februar         2012 → 18 pts.         Inclusion criteria:         - over the age of 18         -independent before the current         hospitalization         -fully conscious and able to perform         simple commands         - MRC physical strength examinatio         score lower than 48 points         Exclusion criteria:         -unconsciousness         -central or peripheral neurological         damage         -hemodynamic instability (i.e., bloo         pressure >200 or <80 mmHg, heart	n/a	Group I/ Routine Care group: PT according to daily custom protocol	treatment group: same protocol,	No sample size calculation stated No primary endpoint defined <b>Extracted</b> <b>Endpoints:</b> -MRC physical strength examination -MIP -hg dynamometer -SB -ICU LOS -ventilation time Performed at: T1(at baseline), T2(48-72h after), T3(ICU discharge)	<b>Significant differences between groups:</b> -improvement for MIP and MRC in the intensive treatment group II in Mean diff(SE) T2 – T1 (MIP: (–)6.5 (0.613) p=0.018; MRC: 8.333 (3.454) p=0.029) -decrease in the number of intensive care hospitalization days in favor of the intensive treatment group: LOS was 18.11 ± 3.1 days in group I vs 13 ± 4.6 days in group II (P = 0.043) -strong positive relationship between the MRC index and the SB (r = 0.673); between the MRC index and the right hg dynamometer test (r = 0.619) at T1 -strong negative correlation between the average changes in MRC in relation to average changes in MIP (r = -0.623) between T1 and T2 <b>No significant differences between groups in:</b> -no difference at baseline between groups in any endpoint -ventilation time in group II (9 ± 5 days) compared with group I (16.22 ± 2 days; P = 0.076) -no difference in percentage of pts who were able to walk during hospitalization in the ICU (P = 0.343)	(pilot RCT)

pts. = patients; MRC=Medical Research Council; PT=physical therapy; MIP= maximal inspiratory pressure; SB= sitting balance; LOS=Length of stay; hg=hand grip

#### It is possible that an intensive therapy protocol may facilitate the initial recovery process in patients who suffer from ICUAW.

55 pts. From December 2009 to December 2012 in two academic medical centers505 Winkelman 2018Inclusion criteria: - Pts. not enrolled in another study - received MV for 36 hr and expected to require 24 hr more of MVPMID: 29902939- ICU LOS of 14 or more days prior to eligibility to enroll, - weight >350 lbhttps://doi.org /10.1177/1099 800418780492- a history or acute diagnosis of neurological or orthopedic injury that precluded the ability to participate in volitional and progressive EM - new myocardial infarction - open fascia from abdominal or lower extremity surgery - end-stage or end-of-life or intensivist opinion						
that the individual was moribund <ul> <li>patients without a surrogate or with a surrogate</li> <li>who could not be contacted over a 2-day period.</li> </ul> Per Branch 29 26	1 from the twice daily branch	EM Group: 1. Protocol based EM twice daily 2. Protocol based EM once daily	Pts. acted as their own control in a before after design	<ul> <li>Sample Size calculation: it was estimated that a sample size of 50 would have .80 power to detect a .30 effect size with an alpha of .10</li> <li>Primary Endpoint: <ul> <li>Change scores of Interleukins 6, 10, 8, 15, and TNF-α collected from serum before and after EM</li> </ul> </li> <li>Secondary outcomes: <ul> <li>Manual muscle and handgrip strength</li> <li>delirium onset</li> <li>duration of MV</li> <li>ICU LOS</li> </ul> </li> </ul>	<b>Primary Endpoint:</b> TNF-α level was significantly and negatively associated with frequency, however the CI includes 0 (-0.35 to 0.01) <b>Secondary endpoints:</b> -Only ICU LOS was "significantly" different between the groups (Once daily:18.76 + 14.47; Twice daily:13.40 + 7.97; P=0.06 (they choose 0.10 as significance level) -no difference in the other secondary endpoints	2

Pts = patients; MV = mechanical ventilation; hr = hour; ICU = intensive care unit; LOS = Length of stay; EM = early mobilization; CI = confidence interval; TNF= Tumor necrosis factor

Twice daily mobility interventions did not alter serum inflammatory markers.

of study: multi- center, pilot- RCTinde writter rest in bed orders due to documented injury or process that precluded mobilization such as suspected or proven instability of spine or pelvis - severe acute brain injury - unsafe to commence mobility therapy - cardiovascular or respiratory instabilityto follow up, 2 declined)to follow up, 2 declined)inde works down to maximize activity- ICU-acquired weakness at <48h after ICU discharge - follow up at 6 months: independent activities, return to work, health-related quality of life, healthcare utilization, hospital anxiety and depressiongroup 3.0 d [2.4–4.5 d]; p = 0.88; time to walk: median [IQR], intervention 6.0 d [3.0–12.0 d] vs control group 6.0 d [3.0– 8.0 d]; p = 0.97) - duration of MV: p=0.18 - ICU LOS: p=0.28 - hospital LOS: p=0.33 - total LOS: p=0.37 - ventilator-free days: p=0.4 - no differences in all outcomes at 6 months follow up	Reference, Study Type		l Controls Characteristics) tal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Hodgson 2016 PMID: 26968024 DOI: 10.1097/CC M.0000000 00001643 Specification of study: multi- center, pilot-	Inclusion criteria: - invasively ventilate tomorrow, - >18 years old Exclusion criteria: - second or subseque during a single hospi - unable to follow sir commands in English - inevitable/imminer - unable to walk with to the ICU admission - diagnosed with der current acute illness - had written rest in documented injury of precluded mobilizati suspected or proven or pelvis - severe acute brain - unsafe to commend - cardiovascular or re	ent ICU admission ital admission mple verbal n it death nout assistance prior mentia prior to bed orders due to or process that ion such as i instability of spine injury ce mobility therapy espiratory instability	8/29 (2 died in ICU, 4 lost to follow up, 2 declined at 6 months) and 5/21 (1 died in ICU, 2 lost to follow up, 2	concept): - active functional activities - start at the highest level of activity pts can sustain and works down to maximize		<ul> <li>feasibility of intervention delivery (higher maximal level of activity measured via IMS, increased duration of activity measured with min/day)</li> <li>Secondary outcomes: <ul> <li>time from admission to</li> <li>randomization and from admission to mobilisation</li> <li>duration of MV, ICU and hospital LOS, and total inpatient stay</li> <li>serious AEs</li> <li>ventilator-free days and ICU-free days on day 28</li> <li>physical function</li> <li>ICU-acquired weakness at &lt;48h after ICU discharge</li> <li>follow up at 6 months: independent activities, return to work, health-related quality of life, healthcare utilization, hospital anxiety and depression</li> </ul> </li> </ul>	<ul> <li>higher IMS in intervention vs control (mean IMS (95% Cl) 7.3 (6.3–8.3) vs 5.9 (4.9–6.9), unadjusted p = 0.05 at ICU discharge, and after adjustment mean IMS (95% Cl) for intervention 7.5 (6.5– 8.5) vs control 5.6 (4.6–6.6), p = 0.01</li> <li>duration of activity was &gt; in intervention, median 20min/d [IQR, 0– 40] for EGDM vs 7min/d [IQR, 0–15] for control; p = 0.002</li> <li>Secondary outcomes:</li> <li>time from admission to randomization (3[2-6] intervention vs 3[2-4] control, p=0.5)</li> <li>time from admission to mobilisation (time to stand: median [IQR], intervention 3.0 d [2.0–6.0 d] vs control group 3.0 d [2.4–4.5 d]; p = 0.88; time to walk: median [IQR], intervention 6.0 d [3.0–12.0 d] vs control group 6.0 d [3.0– 8.0 d]; p = 0.97)</li> <li>duration of MV: p=0.18</li> <li>ICU LOS: p=0.28</li> <li>hospital LOS: p=0.37</li> <li>ventilator-free days: p=0.4</li> <li>no differences in all outcomes at 6</li> </ul>	Pilot RCT

AE = adverse effects, CI = confidence interval, EGDM = early goal-directed mobilization, ICU = intensive care unit, IMS = ICU mobility scale, IQR = interquartile range, LOS = length of stay, min = minute, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial

# EGDM was feasible, safe and resulted in increased duration of active exercises and an increase in the mobility milestones achieved during ICU stay.

Reference, Study Type		and Controls #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#507 Machado 2017 PMID: 28538781 DOI: 10.1590/S18 06- 3756201600 0000170 Specificatio n of study: RCT	Exclusion cri - palliative ca - amputees - leg fracture - neuromuso disease - ICU-AW - joint/muso disorder	teria: of sedation mically stable iteria: are es cular/neurological	11 pts died: (4 Intervention, 7 control	Passive cycling + conventional PT 5 days a week (20 minutes, fixed 20 cycles/minute)	<b>Conventional PT:</b> - 2x a day for 30 minutes - 7 days a week	<b>Outcomes:</b> - peripheral muscle strength (MRC Score) - cardiovascular parameters (SpO2, HR, mean arterial pressure) - duration of sedation - time to first treatment - time to first muscle strength assessment	<b>Outcomes:</b> - peripheral muscle strength: intervention 38.73 ± 11.11 vs. 47.18 ± 8.75; control: 40.81 ± 7.68 vs. 45.00 ± 6.89, p < 0.001) - MRC score pre- and post- implementation periods: IG 8.45 ± 5.20 vs. GG 4.18 ± 2.63; p = 0.005) - MV, Hospital LOS, ICU LOS n.s.	2

CG = control group, ICU = intensive care unit, IG = intervention group, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, n.s = not significant, PT =physio therapy, pts = patients

The results suggest that the performance of continuous passive mobilization on a cyclical basis helps to recover peripheral muscle strength in ICU patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#508 Schaller 2016 PMID: 27707496 DOI: 10.1016/S0140- 6736(16)31637-3 Specification of study: multicenter RCT	200 pts         Inclusion criteria:         - SICU pts 18 years or older         - MV<48h	7 / 104: (3 ineligible, 4 withdrew consent) Loss of follow up at 3 months: 57/104 and 52/96	Early goal directed mobilization (SOMS concept)	Standard of care	<ul> <li>Primary endpoints: hierarchically tested</li> <li>mean mobilization score (SOMS level)</li> <li>SICU LOS</li> <li>function: mmFIM at hospital discharge</li> <li>Secondary outcomes:</li> <li>global muscle strength via MRC sum score</li> <li>QoL at 3 months after hospital discharge</li> <li>Tertiary outcomes: daily high serum glucose concentrations, functional status at discharge, hospital LOS, in-hospital mortality, 3-month mortality, discharge disposition, ICU delirium- free days, ventilator-free days, ICU sedation-free days, neuromuscular blocking agent-free days, vasopressor- free days, mean daily morphine equivalent dose (mg), number of days receiving corticosteroids, and daily high serum sodium concentration (mmol/L)</li> <li>Power analysis: With the assumption of an 11% mortality rate, and an 11% attrition rate, it is estimated that enrolling 100 pts in each treatment group would result in a &gt; 80% power to identify an inter-group difference with a two-sided α error of 0-05</li> </ul>	Primary endpoints: - SOMS higher in intervention vs control (2.2 (1.0), 1.5 (0.8), p<0.0001) - ICU LOS shorter in intervention (7 (5-12) vs 10 (5-15), p=0.0054) - functionally independent at hospital discharge: 44 (51) intervention vs 25 (28) control, p = 0.0030. Secondary outcomes: - no significant difference between groups in QoL (p=0.69) and muscle weakness (0.95) Tertiary outcomes: Significant difference between groups in: - functional status at ICU discharge (p=0.009) - hospital LOS (p=0.011) - discharge disposition (p=0.0007) - ICU delirium-free days (p=0.016) No significant difference between groups in: - in-hospital mortality (p=0.09) - 3-months mortality (p=0.35) - daily high serum glucose (p=0.83) - ICU sedation-free days (p=0.38) - neuromuscular blocking drug-free days (p=0.38) - vasopressor-free days (p=0.12) - ventilator-free days (p=0.31) - mean daily morphine equivalent dose (p=0.62) - corticosteroid days (p=0.42) - daily high serum sodium (p=0.32)	2

GCS = Glasgow coma scale, ICP = intracranial pressure, LOS = length of stay, MI = myocardial infarction, MRC = medical research council, MV = mechanical ventilation, RCT = randomized controlled trial, SICU = surgical intensive care unit, SOMS = SICU optimal mobilization score

Early, goal-directed mobilization improved patient mobilization throughout SICU admission, shortened patient length of stay in the SICU, and improved patients' functional mobility at hospital discharge.

#509       S0 pts Inclusion criteria: - 18-80 years - MV > 48h - ambulate independently before acute illness available       Daily Intensive upright nobilization: - MV duration       Primary endpoints: - MV duration       Primary endpoints: - MV duration       - MV duration (median [IQR]), 8.8 days (6.4–19.3) in intervention vs 7.8 days (8.4–10.6) in intervention vs 1.0 days (8.4–10.6) in intervention vs (8.4–10.6) in control, p= 0.86 - hospital JOS (median [IQR]), 3.6.9 days (21.5–55.7) in intervention vs (downgrade; under- powered)         https://doi.org/ 169.2019.1615       Daily initiated after absolitization: instability, severe head injuries or substantial unstable fractures)       Daily initiated after absolitication: instability, severe head injuries or substantial unstable fractures)       Daily initiated after absolitication: based on Burtin et al. 36 pts necessary and α 0.05. Planned to include 120       Primary endpoints: - MV       Primary endpoints: - MV         29       21	Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
pts. $-$ employment n.s., $p = 0.65$	Amundadottir 2019 PMID: not available <u>https://doi.org/</u> 10.1080/21679 169.2019.1645 <u>880</u> Specification of study:	Inclusion criteria: - 18-80 years - MV > 48h - ambulate independently before acute illness Exclusion criteria: - poor survival prognosis - admitted to the hospital >2 weeks prior to admission to the ICU - progressive upright mobilization contraindicated (prolonged hemodynamic instability, severe head injuries or substantial unstable fractures)		Intensive upright mobilization: - IMS ≥ 3 - twice a day - initiated after 48h after start	<b>mobilization:</b> - 1x daily - commenced after 96h of	<ul> <li>- MV duration</li> <li>- Hospital/ICU LOS</li> <li>Secondary outcomes: <ul> <li>health-related QoL via SF-36v2, at baseline, 3/6/12 months after ICU discharge.</li> <li>physical function via 6MW, MRC-SS, and MBI (at baseline, ICU discharge, hospital discharge, 3/6/12 months after ICU discharge</li> </ul> </li> <li>Additional endpoints: <ul> <li>hospital mortality</li> <li>employment 12 months after ICU discharge</li> </ul> </li> <li>Sample size calculation: <ul> <li>based on Burtin et al. 36 pts necessary for 50 m in 6MWT with 80% power and α 0.05. Planned to include 120</li> </ul> </li> </ul>	<ul> <li>MV duration (median [IQR]), 8.8 days (6.4–19.3) in intervention vs 7.8 days (5.4–17.7) in control, p =0.89</li> <li>ICU LOS (median [IQR]), 12.4 days (8.4–19.6) in intervention vs 11.0 days (7.3–22.8) in control, p=0.86</li> <li>hospital LOS (median [IQR]), 36.9 days (21.5–55.7) in intervention vs 24.6 days (15.5–56.6) in control, p = 0.29</li> <li>Secondary outcomes: <ul> <li>health-related QoL across time points n.s. (12 months SF36 PCS: p =1.0, 12 months SF36 MCS: p = 0.99)</li> <li>functionality across time points n.s (6MWT 3 monts, 6months and 12 months: p = 1.0, MRC hospital discharge p = 0.9, MRC 12 months p = 1.0)</li> </ul> </li> </ul>	2 → 3 (downgrade; under-

ICU = intensive care unit, LOS = length of stay, MBI = modified Barthel Index, MRC-SS = the medical research council sum-score, MSC = mental component score, MV = mechanical ventilation, PSC = physical component score, pts = patients, QoL = quality of life, RCT = randomized controlled trial, SF-36v2 = short-form 36 health survey version 2; 6MWT = six-minute walking test

#### There was no difference in short-term or long-term outcomes in the intensive twice-daily mobilization group.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#515 Higgins 2019	9 publications (3 retrospective cohort, 2 prospective cohort, 2 prospective observational, 1 bidirectional case-control, 1retrospective control, 15 to 1132 pts) <sup>1-9</sup> <b>Inclusion criteria:</b>					Significant differences between groups in: - MV duration, shorter in intervention: mean difference -	
PMID: 31526602	<ul> <li>adult trauma ICU pts</li> <li>compared EM vs no/SOC</li> <li>≥ 1 relevant outcome (mortality, hospital</li> </ul>		EM:		Derived	1.18 days, 95% Cl, -2.17 – -0.19, p =0.02, l <sup>2</sup> = 0%	1→3
DOI: 10.1016/j.inj ury.2019.09. 007	LOS, ICU LOS, duration of MV) Exclusion criteria:		- any mobilization in the ICU delivered earlier than intervention	No mobilization or SOC	endpoints: - in-hospital mortality - hospital LOS	No significant differences between groups in: - hospital mortality	(downgrade, heterogenity and small effect)
Specification	<ul> <li>- case series or reports</li> <li>- &lt;18 years</li> <li>- EM delivered as part of a bundle intervention</li> </ul>		in standard care		- ICU LOS - MV duration	<ul> <li>ICU LOS</li> <li>hospital LOS</li> <li>Quality of studies and risk of bias:</li> </ul>	
of Study:	Per Branch					Only 1 study was judged as good	
Systematic						quality with low risk of bias across	
review and meta-						the 3 domains of selection,	
analyses						comparability, and outcome.	

CI = confidence interval, EM = early mobilization, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, SOC = standard of care

# The results of the meta-analysis showed a reduction in the duration of mechanical ventilation among patients who received EM, but no difference in mortality or LOS.

1. Gillick BT, Marshall WJ, Rheault W, Stoecker J. Mobility criteria for upright sitting with patients in the neuro/trauma intensive care unit: an analysis of length of stay and functional outcomes. Neurohospitalist 2011;1:172–7.

2. Clark DE, Lowman JD, Griffin RL, Matthews HM, Reiff DA. Effectiveness of an early mobilization protocol in a trauma and burns intensive care unit: a retrospective cohort study. Phys Ther 2013;93:186–96.

3. Taylor S, Pelham L, Dickinson S. Can the utilization of an early mobility protocol improve outcomes in the burn patient? J Burn Care Res 2013;34:S97.

4. Booth K, Rivet J, Flici R, Harvey E, Hamill M, Hundley D, et al. Progressive mobility protocol reduces venous thromboembolism rate in trauma intensive care patients: a quality improvement project. J Trauma Nurs 2016;23:284–9.

5. Teichman A, Scantling D, McCracken B, Eakins J. Early mobilization of patients with non-operative liver and spleen injuries is safe and cost effective. Eur

J Trauma Emerg Surg 2018;44:883–7.

6. Wang E, Inaba K, Byerly S, Mendelsberg R, Sava J, Benjamin E, et al. Safety of early ambulation following blunt abdominal solid organ injury: a prospective observational study. Am J Surg 2017;214:402–6.

7. Deng H, Chen J, Li F, Li-Tsang CW, Liu Q, Ma X, et al. Effects of mobility training on severe burn patients in the BICU: a retrospective cohort study. Burns 2016;42:1404–12.

8. Andelic N, Bautz-Holter E, Ronning P, Olafsen K, Sigurdardottir S, Schanke AK, et al. Does an early onset and continuous chain of rehabilitation improve the long-term functional outcome of patients with severe traumatic brain injury? J Neurotrauma 2012;29:66–74.

9. Bartolo M, Bargellesi S, Castioni CA, Intiso D, Fontana A, Copetti M, et al. Mobilization in early rehabilitation in intensive care unit patients with severe acquired brain injury: an observational study. J Rehabil Med 2017;49:715–22.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#516 Akar 2017 PMID: 26597394 DOI: 10.1111/crj.12 411 Specification of study: RCT	30 pts Inclusion criteria: - intubated COPD pts (COPD stage C or D) - monitored ≥ 24 h on MV - no DVT - no comorbidities e.g. renal failure, congestive heart failure, cerebrovascular diseases, neuromuscular diseases, diabetes mellitus, malignancy Exclusion criteria: - monitored on MV < 24 h - discharged ≤ 48 h from the ICU - infection during the study - unconscious pts - DVT or pulmonary embolism - hemodynamically unstable pts Per Branch NMES + exercise: 10 pts Exercise: 10 pts		3 Groups NMES + exercise: - NMES 5 days a week for a total of 20 sessions -active exercise training NMES: - NMES 5 days a week for a total of 20 sessions Exercise: - active exercise training		Outcomes: - MRC score - ICU LOS - MV duration - time to sit up assisted in bed - time to sit up unassisted in bed - time to sit up unassisted at bedside - time to st up unassisted at bedside - time to stand assisted - time to stand unassisted - time to move from bed to chair - ICU discharge	<b>Outcomes:</b> MRC score: - NMES + exercise (lower extremities, median [min -max]): before 3 [3-5], after 5 [4-5], p = 0.014 - NMES + exercise (upper extremities, median [min-max]): before 4 [3-5], after 5 [4-5], p = 0.038 - NMES (lower extremities, median [min-max]): before 4 [3-5], after 5 [3-5], p = 0.046 - NMES (lower extremities, median [min-max]): before 4 [3-5], after 5 [3-5], p = 0.046 - exercise (lower extremities, median [min-max]): before 4 [3-5], after 5 [3-5], p = 0.046 - exercise (lower extremities, median [min-max]): before 4 [3-5], after 5 [3-5], p = 0.034 - exercise (upper extremities, median [min-max]): before 4 [4-5], after 5 [4-5], p = 0.034 - ICU length of stay (days, median [min-max]): before 4 [4-5], after 5 [4-5], p = 0.034 - ICU length of stay (days, median [min-max]): NMES + exercise 2 [1-3], NMES 2 [2-9], exercise 4 [2-17], p = 0.781 - time to sit up assisted in bed (mean ±SD): NMES + exercise 1.25 ± 0.5, NMES 3.33 ± 4.04, exercise 4.40 ± 3.91, p = 0.712 - time to sit up assisted in bed (mean ± SD): NMES + exercise 1.5 ± 1.0, NMES 3.66 ± 4.61, exercise 6.80 ± 3.96, p = 0.500 - time to sit up anassisted at bedside (mean ± SD): NMES + exercise 3.75 ± 2.50, NMES 4.00 ± 5.19, exercise 7.60 ± 4.90, p = 0.402 - time to sit up unassisted at bedside (mean ± SD), NMES + exercise 3.75 ± 2.50, NMES 6.00 ± 3.35, exercise 7.60 ± 4.50, p = 0.304 - time to stand assisted (mean ± SD): NMES + exercise 3.75 ± 2.50, NMES 6.00 ± 3.24, p = 0.671 - time to stand anssisted (mean ± SD): NMES + exercise 5.25 ± 2.62, NMES 8.00 ± 4.35, exercise 12.00 ± 5.61, p = 0.123 - time to move from bed to chair (mean ± SD): NMES + exercise 5.25 ± 2.62, NMES 8.33 $\pm 4.04$ , exercise 12.60 $\pm 6.30$ , p = 0.102 - ICU discharge (n (%): NMES + exercise 8 (80), NMES 8 (80), exercise 5 (50), p = 0.240	2 → 3 (methodo logical flaws)

COPD = chronic obstructive pulmonary disease, DVT = deep venous thrombosis, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, MV= mechanical ventilation, NMES = neuromuscular electrical stimulation, pts = patients

#### Neuromuscular electrical stimulation could not show an effect on muscle strength or functional milestones.

60-019-0417- x       injury       for controls       week       Secondary         y       pregnancy       -skin lesions in       extubation,         specification of study:       the region to be       intervention - n (%): 0 (0), RR (95%CI): 16 (2.9 - 88.9), p = 0.0001; evoked peak force         rectus femoris: between group comparison day 14: control - n (%): 4 (13),       intervention - n (%): 0 (0), RR (95%CI): 16 (2.9 - 88.9), p = 0.0001; evoked peak force         specification of study:       intervention the vertebral column and lower limbs       intervention - mean difference (95%CI): 2.34 (1.89 - 2.79), p < 0.0001; between group difference         Per Branch       Per Branch       intervention - median [IQR]: 14.0 [8.0 - 18.0], p = 0.65         Hospital LOS:       intervention - median [IQR]: 12.5 [2.0 - 27.3] vs. intervention - median [IQR]: 34.0 [10.0 - 26.0], p = 0.58         Hospital LOS:       Hospital LOS:       intervention - median [IQR]: 34.0 [10.5, -24.2], p = 0.06	Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Silva 2019 PMID: 31890221 DOI: 10.1186/s405 60-019-0417- x Specification of study:	Inclusion criteria: - 18-60y of age - MV ≤ 24h - traumatic brain injury Exclusion criteria: - history of alcoholism - HIV - chronic kidney failure - spinal cord injury - pregnancy - skin lesions in the region to be treated - unstable fractures in the vertebral column and lower limbs	10 interventio ns (death, extubation) 10 controls (death, extubation,	Usual care:	<b>care:</b> - with PT 2x	endpoints: -muscle architecture -neuromuscular electrophysiologic al disorders -evoked peak force Secondary outcomes: -ICU LOS -hospital LOS -duration of MV	muscle thickness difference day 1 until day 14 M. tibialis anterior (mm) -interaction time x group: effective size = 0.35, p < 0.0001; control-mean (95%Cl): - 0.33 (-0.390.26), p < 0.0001 vs intervention – mean (95%Cl): 0.01 (-0.069 – 0.08), p = 0.78 M. rectus femoris (mm): interaction time x group: effective size = 0.34; control – mean (95%Cl): -0.49 (-0.580.4), p < 0.0001; intervention – mean (95%Cl): -0.04 (-0.11 – 0.02), p = 0.15 Echogenicity difference day 7 until day 14 M. tibialis anterior: interaction time x group: effective size = 0.23, p < 0.0001 M. rectus femoris: interaction time x group: effective size = 0.24, p < 0.0001 chronaxie difference day 1 until day 14 M. tibialis anterior: interaction time x group: effective size = 0.22, p < 0.0001 M. rectus femoris: interaction time x group: effective size = 0.22, p < 0.0001 Incidence of neuromuscular electrophysiological disorders M. tibialis anterior: control: day 1 – n (%): 3 (10%), Day 14 – n(%): 14 (47%), p = 0.003; intervention: day 1 – n (%): 5 (17%), Day 14 – n(%): 0 (0%), p = 0.06; between group comparison day 14: RR (95%Cl): 16 (2.9 – 88.9), p = 0.0001 M. rectus femoris: between group comparison day 14: control – n (%): 4 (13), intervention – n (%): 0 (0), RR (95%Cl): 1.56 (-2.0 – 3.8.9), p = 0.0001; woked peak force (kg/F) difference day 1 until day 14; -interaction time x group: np2 = 0.55, p < 0.0001; control – mean difference (95%Cl): 2.34 (1.89 – 2.79), p < 0.0001; between group difference day 7: p < 0.0001 <b>Secondary Outcomes:</b> - duration of MV (days): control – median [IQR]: 15.5 [8.8 – 19.9] vs intervention – median [IQR]: 14.0 [8.0 – 18.0], p = 0.65 - ICU LOS: control – median [IQR]: 19.5 [12.0 – 27.3] vs. intervention – median [IQR]: 19.0 [10.0 – 26.0], p = 0.58 - Hospital LOS: control – median [IQR]: 42.0 [20.0 – 56.0] vs -intervention – median	2 → 3 (risk of

ICU = intensive care unit, IHT = inter-hospital transfers, LOS = length of stay, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, PT = physiotherapy

Reference, Study Type	(Partic Charact	d Controls ipant #, teristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#523 Moss 2016 PMID: 26651376 DOI: 10.1164/rcc m.201505- 1039OC Specification of study: RCT	120 ICU pts Inclusion crite - at least 4d or - older than 18 Exclusion crite - physical impa - cognitive imp - cardiopulmor - lived >45 mile hospital - unlikely to su months - patient/docto Per Branch	n MV Sy eria: hirment hary risk es from rvive after 6		Mobilisation: - intensified PT until d28 Inpatient: - 7d/week - 30 min in ICU - up to 60 min. on normal ward Outpatient/ home: - 3d/week 5 components of intensive PT: - techniques for proper breathing during exercise - progressive ROM - therapeutic exercises focusing on muscle strengthening - exercises to improve core mobility and strength - functional mobility retraining, including bed mobility, transfers, gait, balance.	SOC: -until d28 Inpatients: -3d/week Outpatients: -information only ROM exercises, positioning and functional movement training. As soon as possible, assistance with ADL (transfers to bed or chair and walking)	Primary endpoint:         - CS-PFP-10 after 1 month         Secondary Outcomes:         - CU- and hospital-free days         on d28         - discharge home         - morbidity on d28         - days without         institutionalization on d90         and 180 (def. as living, not in         hospital, AHB, long-term         care or similar)         Power analysis: enrollment         of 120 pts could detect a         difference of 12.3 points         between the group mean         CS-PFP-10 score at 1 month         with a significance level (α)         of 0.05 and a power of 80%         using a two-sided	Primary endpoint: - CS-PFP-10 scores at 1, 3 and 6 months: $p = 0.73$ , $p = 0.29$ , $p = 0.43$ - total CS-PFP-10 score trajectory: $p = 0.71$ Secondary outcome: - mortality: 17%, 10/ 59 intensive PT vs. 10%, 6/61 SOC, $p = 0.25$ - d without ITS on day 28: p = 0.69 - d without hospital on d28: $p = 0.97$ - discharge home: $p = 0.84$	2 → 3 (high risk of bias)

CS-PFP-10 = continuous scale physical, functional performance test short form, d = day, ICU = intensive care unit, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial, ROM = range of motion, SOC = standard of care

#### Intensified physical therapy does not improve the functional outcome measured by the CS-PFP-10.

Reference, Study Type	Cases and Controls (Participant #, characteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total 8 publications until February 2019 (8 RCTs, n = 3941 pts)					Significant differences between groups:         - Cumulative incidence of PI:         a. 3-hourly vs. 4-hourly repositioning frequency:         reduction of incidence might be associated with 3-hourly repositioning (RR 0.20,	
524 Gillespie 2020	<ul> <li><sup>1-8</sup></li> <li>Inclusion criteria:</li> <li>- RCTs or cluster RCTs</li> </ul>				Primary outcome:	<ul> <li>95% Cl 0.04 – 0.92), low certainty of evidence; (n = 1 RCT with 407 pts<sup>1</sup>)</li> <li>b. 4-hourly vs. 6-hourly repositioning frequency: 27% reduction of incidence associated with 4-hourly repositioning (RR 0.73, 95% Cl 0.53 – 1.02 %), very low certainty of evidence; (n = 1 RCT with 129 pts<sup>2</sup>)</li> <li>c. 2-hourly repositioning frequency using a 20° tilt vs. standard of care: reduction of incidence associated with 2-hourly repositioning (RR 0.28, 95% Cl 0.10 – 0.75), very low certainty of evidence; (n = 1 RCT with 1312 pts<sup>6</sup>)</li> </ul>	
PMID: 32484259 https://doi.org/1 0.1002/1465185 8.CD009958.pub 3 Specification of	<ul> <li>Adults without existing PI in any healthcare or long-term care setting</li> <li>Assessment of effects of repositioning regimes</li> <li>Measurement of PI incidence</li> </ul>		Repositioning regimes	Standard of care	<ul> <li>Cumulative incidence of Pl</li> <li>Secondary outcome:         <ul> <li>health- related quality of life</li> <li>procedural</li> </ul> </li> </ul>	<ul> <li>Non-significant differences between groups: <ul> <li>Cumulative incidence of PI:</li> <li>2-hourly vs. 3-hourly repositioning frequency: due to high heterogeneity (I<sup>2</sup> = 77%) <i>data was not pooled</i>; no clear differences were found (n = 2 RCTs with 1229 pts)<sup>1,2</sup></li> <li>2-hourly vs. 4-hourly repositioning frequency: fixed-effect-model; I<sup>2</sup> = 45%, pooled RR 1.06, 95% CI 0.80 – 1.41, no clear difference in incidence of PI, very low certainty of evidence (n = 3 RCTs with 1074 pts)<sup>1,2,4</sup></li> <li>30° vs. 90° tilt: random-effect-model; I<sup>2</sup> = 69%, pooled RR 0.62, 95% CI 0.10 – 3.97, very low certainty of evidence, no clear difference in the incidence of stage 1 or 2 PI; (n = 2 RCTs with 259 pts)<sup>5,7</sup></li> <li>30° HOB elevation vs. 45° HOB elevation vs. standard of care: no PI occurred, low certainty of evidence; (n = 1 RCT with 120 pts<sup>3</sup>)</li> </ul> </li> </ul>	1 → 3 (high uncertainty
study: Systematic review and meta-analysis	Per Branch				<ul> <li>procedural pain</li> <li>patient satisfaction</li> <li>costs</li> </ul>	<ul> <li>h. prone positioning vs. supine positioning: increase of incidence of PI stage 1 associated with prone positioning, low certainty of evidence; (n = 1 RCT with 116 pts<sup>8</sup>)</li> <li>health-related quality of life, procedural pain, patient satisfaction not reported in the publications</li> <li>costs: <ul> <li>a. Comparing 2-hourly repositioning regimen with 3-/4-hourly regimens a cost reduction of 11.05, 16.74 CAD per resident per day resulted, respectively (n = 1 RCT<sup>1</sup>)</li> <li>b. Comparing 30° tilt 3-hourly repositioning regimen with 90° tilt 6-hourly repositioning regimen for 588 individuals, who were completely immobile or had very limited mobility an annual cost difference of 512800€, equivalent to 21462 hours of nursing time resulted; mean nurse time cost per patient 206.6 € vs. "53.1 €, incremental difference -46.5€, 95% Cl -1.25 to -74.6€; (n = 1 RCT<sup>5</sup>)</li> </ul> </li> </ul>	

Pts = patients, RCTs = randomized controlled trials, PI = pressure injury, RR = risk ratio, CI = confidence interval, CAD = Canadian Dollar, HOB = head of bed

#### The effectiveness of repositioning frequency and positioning for PI prevention remains unclear due to low certainty levels of evidence.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#526 Hermans 2014 PMID: 24477672 DOI: 10.1002/14651	1 publication <sup>1</sup> Inclusion criteria: - RCTs in humans - ≥ 18 years of age - any treatment used to prevent or reduce the incidence of CIP or CIM as a primary or secondary outcome Exclusion criteria: - not stated Per Branch		NMES	Usual care	Primary endpoint: incidence of CIP or CIM Secondary outcomes: duration of MV ICU LOS death on 30- and 180- days	Primary endpoint: incidence of CIP/CIM - 0.81 RR (95%CI) 0.94 (0.78 – 1.15), p = 0.56 Secondary outcomes: no significant differences between groups in: - duration of MV - ICU LOS - death on 30- and 180-days	1 → 2 (only 1 study included)

CIM = critical illness myopathy, CIP = critical illness polyneuropathy, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, RCT = randomized controlled trial

NMES does not significantly reduce the incidence of CIP/CIM compared to usual care.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#527 Herling 2018 PMID: 30484283 DOI: 10.1002/14651858 .CD009783.pub2 Specification of study: Systematic review with meta analysis	12 RCTs, 3.885 pts only 1 study with physical therapy as intervention (n=65) <sup>1</sup> Inclusion criteria: - RCTs - adult patients in internal medicine or surgical ICU - any intervention to prevent delirium/ICU - control via standard of care, placebo or both - search period: 1980-2018 No exclusion criteria defined Per Branch		Prevention of immobilization	Not defined	Primary outcomes: - event rate of delirium in ICU (CAM-ICU positive) - in-hospital mortality Secondary outcomes: - number of delirium- and coma-free days - ventilator-free days - ICU-LOS - MMSE - AEs of interventions	Primary outcome: - event rate of delirium: not reported - In-hospital mortality: RR 0.94, 95% Cl 0.40 to 2.20; p = 0.88, n = 65 Secondary outcomes: - number of delirium- and coma- free days: MD -2.77, 95% Cl -10.09 to 4.55; p = 0.46, n = 65 - ventilator-free days: median days 25.3 versus 27.4; p = 0.81, n = 65 - ICU-LOS: MD 1.23, 95% Cl -0.68 to 3.14; p = 0.21, n = 65 - MMSE: MD 0.97, 95% Cl-0.19 to 2.13; p = 0.10, n = 30 - AEs: no calculations	1 → 4 (only 1 study with PT)

AE = adverse event, ICU = intensive care unit, LOS = length of stay, MMSE = mini mental state examination, PT = physical therapy, RCT = randomized controlled trial

#### PT does not seem to reduce in-hospital mortality

#### References

1 Brummel NE, Girard TD, Ely EW, Pandhariphande PP, Morandi A, Hughes CG, et al. Feasibility and safety of early combined cognitive and physical therapy for critically ill medical and surgical patients: the Activity and cognitive Therapy in ICU (ACT-ICU) trial. Intensive Care Medicine 2014;40(3):370-9. [DOI: 10.1007/s00134-013-3136-0

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1001 Abroug 2008 (PMID: 18350271 DOI: 10.1007/s00134- 008-1062-3) <b>Specification of study:</b> Meta-Analysis	6 RCTs to November 2007 Inclusion criteria: - adults with ARDS or ALI Exclusion criteria: - non-controlled studies - studies that only examined the physiological effects of prone positioning Per Branch		Ventilation in prone position whatever its duration, on a 24-h basis, and during the ICU stay	Conventional ventilation in supine position	Primary endpoint: - mortality in the ICU or at 28 days Secondary outcomes: - effect on PaPO <sub>2</sub> /FiO <sub>2</sub> ratio - rate of VAP - procedure-related major airway complication - ICU LOS	Significant differences between groups in: - PaPO <sub>2</sub> /FiO <sub>2</sub> by 25mmHg; 95% Cl 15–35, p for effect <0.00001, p for heterogeneity = 0.06, l2= 56% No significant differences between groups in: - mortality [249 of 713 pts (34.9%) in the prone ventilation group versus 234 of 659 pts (35.5%) in the supine position]: OR 0.97, 95% Cl 0.77–1.22, p for effect = 0.79, p for heterogeneity = 0.35; l2= 9.3% - rate of VAP: n.s. - complications: n.s. - ICU LOS: n.s.	1 → 2 (downgrade)

ALI = acute lung injury, ARDS = acute respiratory distress syndrome, ICU LOS = intensive care unit length of stay, pts = patients, RCT = randomized controlled trial, VAP = ventilator-associated pneumonia

#### Prone positioning has no significant effect on the mortality of critical ill patients but seems to improve the PaPO<sub>2</sub>/FiO<sub>2</sub> ratio.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1002 Abroug 2011 (PMID: 21211010 DOI: 10.1186/cc940 3) Specification of study: Meta-Analysis	or ARDS Per Branch		<b>Prone positioning</b> (7-24h/day) while on mechanical ventilation		<b>Primary</b> endpoints: - ICU-mortality - adverse effects	Significant differences between groups in: - ICU- mortality in pts. with ARDS (n=540): (OR = 0.71; 95% CI = 0.5 to 0.99; P= 0.048; NNT= 11; $I_2$ = 0%) Non-significant differences between groups in: - ICU-mortality overall: non-significant 9% reduction (OR = 0.91, 95% CI= 0.75 to 1.1; P= 0.39; $I_2$ = 0%) - adverse effects: n.s. OR = 1.16; 95%CI = 0.75 to 1.78; P= 0.5	1

ALI = acute lung injury, ARDS = acute respiratory distress syndrome, ARI = acute respiratory failure, ICU = intensive care unit, NNT = number needed to treat, RCT = randomized controlled trial

# Prone positioning has no significant effect on the mortality of respiratory patients overall but significantly reduces mortality in ARDS patients.

#### References

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1004 Alsaghir 2008 (PMID: 18216609 DOI: 10.1097/01.CCM .0000299739.98 236.05) <b>Specification of</b> <b>study:</b> Meta-analysis	incidence of VAP		Prone positioning: sessions of ≥ 6h (n=4) or single sessions	Supine positioning (n=4) or SP in combination with high- frequency ventilation (n=1)	<ul> <li>mortality</li> <li>changes in PaO2/FiO2</li> <li>total ventilator days</li> <li>incidence of VAP</li> </ul>	<ul> <li>Significant differences between groups in: <ul> <li>post-hoc analysis: mortality for patients with SAPS II of &gt; 50</li> <li>mortality at 10 days: PP vs. SP 19.4% vs. 28.5% (RR, 0.4; 95% CI, 0.19-0.85)</li> </ul> </li> <li>changes in <ul> <li>PaO2/FiO2:</li> <li>early stage (12 hours to 2 days) (n=4): WMD of 51.5 (95% CI, 6.95–96.05)</li> <li>intermediate stage (day 4) (n=3):</li> <li>WMD of 43.87 (95% CI, 13.86 –73.88)</li> <li>late stage (day 7-10) (n=4):</li> <li>WMD of 24.89 (95% CI, 15.3–34.48)</li> </ul> </li> <li>Non-significant differences between groups in: <ul> <li>ICU-mortality (n=3): PP vs. SP (pooled OR, 0.79; 95% CI, 0.71–1.28</li> <li>90d-mortality (n=4): pooled OR, 0.99; 95% CI, 0.77–1.27</li> <li>total ventilator days (n=2)</li> <li>incidence of VAP (n=3)</li> </ul> </li> </ul>	1

MV = mechanical ventilation, PP = prone positioning, pts = patients, RCT = randomized controlled trial, SP = supine positioning, VAP = ventilator-associated pneumonia, WMD = weighted mean difference

PP has a significant positive effect on mortality and early as well as late-stage oxygenation but does not reduce the number of ventilator days or the rate of VAP.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1006 Niël-Weise 2011 PMID: 21481251 <u>https://doi.org/ 10.1186/cc101</u> <u>35</u> <b>Specification of</b> <b>study:</b> Systematic Review with meta-analysis	3 RCTs (337 pts) <sup>1-3</sup> Inclusion criteria: - RCTs and quasi randomized trials - published as full papers - stated outcomes - sufficient data to calculate the risks in both the treatment and the control group Per Branch		Semi-upright positioning 45° bed head elevation	25°, 10°, or 0° elevations	Primary endpoints: - clinically suspected and microbiologically confirmed VAP Secondary outcomes: - mortality - venous thromboembolism - hemodynamic instability - duration of mechanical ventilation - ICU LOS - decubitus - ulcers - patient comfort and safety	Primary outcomes: - it was uncertain whether a 45° bed head elevation was effective or harmful with regard to the occurrence of clinically suspected or microbiologically confirmed VAP (test of overall effect clinical: Z=1.62; p=0.10; microbiology: Z=0.71,p=0.48) Secondary outcomes: - it was unknown whether 45° elevation for 24h a day increased the risk for thromboembolism or hemodynamic instability - uncertain whether a 45° bed head elevation was effective or harmful with regard to the occurrence of decubitus and mortality (test for overall effect: Z=0.58,p=0.56) -not indicated: ICU LOS, duration of mechanical ventilation, ulcers, patient comfort, and safety	1 → 3 (not only RCTs, heterogenity, indirectness)

ICU = intensive care unit, LOS = length of stay, pts = patients, RCT = randomized controlled trial, VAP = ventilator associated pneumonia

#### Experts prefer elevated position in ventilated patients, even though this study could not show clinical benefits.

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Reference, Study Type	Cases and (Participant #, C Tot	haracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1013 Beitler 2014 (PMID: 24435203 DOI: 10.1007/s00134-013- 3194-3) <b>Specification of study:</b> Meta-Analysis	7 RCTs including 2 Inclusion criteria: - adults meeting t definition of ARDS Exclusion criteria: - review for non-coventilation in the - non-randomized Per Bra 1088	the Berlin S conventional control arm d design	-	nrone	Supine positioning	Endpoints: - risk ratio of death at 60 days - ICU mortality + other duration of MV	Significant differences between groups in: - decrease in mean baseline tidal volume of 1 ml/kg PBW was associated with a decrease in risk ratio of death at 60 days by 16.7 % (95 % CI 6.1–28.3; p = 0.001) - prone positioning: decrease in risk ratio of death using low tidal volumes (RR = 0.66; 95 % CI 0.50–0.86; p = 0.002)	1

ARDS = acute respiratory distress syndrome, ICU = intensive care unit, MV = mechanical ventilation, PBW = predicted body weight, PP = prone positioning, RCT = randomized controlled trial, SP = supine positioning, TV = tidal volume

#### Prone positioning reduces 60-day mortality in patients receiving low tidal volume but not in those receiving high tidal volumes.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidenc Grade
1016 Göcze 2013 (PMID: 23622019 DOI: 10.1186/cc12 694) Specification of study: prospective randomized multivariable analysis	202 pts Inclusion criteria: - hemodynamically stable - MV - 18 years or older - central venous catheter situated in the superior vena cava Exclusion criteria:	2 pts from 202 (severe hypotension requiring volume and inotropic resuscitation)	sequence of HBE positions (0°, 30°, and 45°) was adopted in random order	pts acted as their own controls	Primary endpoints: - effect of head of bed elevation (HBE) on hemodynamic status - factors that influence MAP and central venous oxygen saturation (ScvO2) when pts were positioned at 0°, 30°, and 45°	Primary endpoints: - changing HBE from supine to 45° caused significant reductions in MAP (from 83.8 mmHg to 71.1 mmHg, P < 0.001) and ScvO2 (76.1% to 74.3%, P < 0.001) - mode and duration of mechanical ventilation (p= <0.001), the norepinephrine dose (p=0.005), and HBE (p= <0.001) had statistically significant influences - PCV was the most influential risk factor for hypotension when HBE was 45° (odds ratio (OR) 2.33, 95% confidence interval (CI), 1.23 to 4.76, P = 0.017)	3

HBE = head of bed elevation, MAP = mean arterial pressure, MV = mechanical ventilation, PCV = pressure-controlled ventilation, pts = patients

HBE is associated with decrease in MAP and ScvO2 in mechanically ventilated patients.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1021 Chiumello 2012 PMID: 22187085 DOI: 10.1007/s00134- 011-2445-4 <b>Specification of</b> <b>study:</b> Observational prospective study	5 centers → 26 pts. Inclusion criteria: -pts with ARDS enrolled in a randomized multicenter trial (PSII study) Exclusion criteria: -not stated Per Branch 13 13	n/a	РР	SP	No sample size calculation No primary endpoint defined <b>Extracted</b> <b>Endpoints:</b> -long-term pulmonary function -quality of life (HRQL; SF-36)	<ul> <li>Results:</li> <li>-Pulmonary function in the normal range without any differences between the two groups</li> <li>Quantitative lung CT scan analysis (PP vs. SP): similar amounts for not aerated (8.1 ± 3.2% versus 7.3 ± 3.4%), poorly aerated (15.3 ± 3.6% versus 17.1 ± 4.9%), and well-aerated (64.0% ± 8.4 versus 70.2 ± 8.4%) lung regions overaerated lung region was slightly higher in the PP (12.5 ± 6.5% versus 5.3 ± 5.5%)</li> <li>-no difference in quality of life stated</li> </ul>	
	13 13						

pts. = patients; ARDS = acute respiratory distress syndrome; PP = prone position; SP = supine position; HRQL = health-related quality of life; SF-36 = short-form-36; CT = computer tomography

No differences in pulmonary function or quality of life were observed in this small group of ARDS survivor patients treated in PP vs. SP.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
1025 Keeley, 2007 (PMID: 17983363 DOI: 10.1111/j.147 8- 5153.2007.00 247.x) <b>Specification</b> of study: RCT	30 patients Inclusion criteria: - intubated within 12 h Exclusion criteria: - previous intubation within the last 30d - recent abdominal surgery with vacuum dressin that requires changes of pts position to gain a se or renew the dressing - severely obese pts unable to tolerate head elevation of 45° - haemodynamic instability (i.e. mean arterial pressure below 60 mmHg for more than 30 min refractory to colloid therapy or inotropic suppor - pts receiving renal replacement therapy whose body position results in insufficient flow to continue therapy - pregnancy - spinal surgery or trauma that necessitates nurse the patient flat - intubated for more than 12 h prior to admission	treatment group: 12 (developed VAP, Died) t control group: 14 (developed VAP, Died)	45° raised head of bed	25° raised head of bed	Primary endpoint: -incidence of VAP Secondary outcomes: - ventilator hours - tracheostomy - mortality	Primary endpoints: - 29% (5) in the treatment group and 54% (7) in the control group contracted VAP (p < 0.176) Secondary outcomes: - ventilator hours: 63.1 h in treatment group, 61.5h in control group - tracheostomy: 11 of 12 pts with VAP had tracheostomies - mortality: ICU mortality rate of those pts who developed VAP was 50%, with a hospital mortality rate of 58% - no p-values stated for ventilator hours, tracheostomy, mortality	2→3
	17 13						

pts = patients, RCT = randomized controlled trial, VAP = ventilator acquired pneumonia

There was no significant reduction of VAP in patients with 45° raised head of bed.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	(Participant #, characteristics)     Drop -out     Drop       Bate     Optimal Population		Optimal Population	Primary Results	Evidence Grade	
1027 Davis, 2007 PMID: 17495725 DOI: 10.1097/TA.0 b013e31804d 490b <b>Specification</b> of study: Retrospective study	61 pts Inclusion criteria: - ALI or ARDS Exclusion criteria: - placed on a kinetic therapy bed for prophylaxis against atelectasis or pneumonia - did not tolerate the bed surface Per Branch 17 pts prone position (including 4 cross-over patients)		Supine positioning in oscillating bed	Prone positioning in oscillating bed	Outcomes: - Mortality - Pulmonary associated mortality - PaO2/FiO2 ratio - FiO2 requirement - Ventilator days - Hospital LOS - GCS - Use of pressors - Use of Intracranial pressure monitors - Presence of pneumonia - Days on the kinetic bed - Dynamic compliance - Age - CVP - ISS - RTS - Base deficit - Head AIS - Chest AIS - Abdominal AIS - Probability of survival	Significant differences between groups (SP vs. PP):- Mortality (pts): 18 vs. 1, $p < 0.01$ - PaO2/FiO2 ratio day 5 in cross-over patients (n=4):146 ± 16 vs. 238 ± 6, $p < 0.001$ Significant results (Between groups analysis not stated):- FiO2 requirement decreased in both groups:o Supine group: 0.63 to 0.45 ( $p < 0.001$ )o Prone group: 0.58 to 0.4 ( $p < 0.001$ )Non-significant differences between groups (SP vs. PP):- Pulmonary-related mortality (pts): 7 vs. 0, $p = 0.051$ - PaO2/FiO2 ratios:o Baseline: 149 vs. 153, $p > 0.05$ o Day 5: 200 ± 14 vs. 243 ± 13, $p = 0.066$ - PaO2/FiO2 ratios by day 5:200 vs. 243, $p = 0.066$ )- Ventilator days: 24.2 vs. 13.6, $p = 0.12$ )- Hospital LOS (40 vs. 22 days, $p = 0.08$ )- GCS : 9.8 vs. 13, $p = 0.063$ - Use of pressors: 54% vs. 46%, $p > 0.05$ - Intracranial pressure monitors: 12 vs. 2 ( $p = 0.2$ )- Presence of pneumonia: 22 pts vs. 6 pts, $p = 0.8$ - Bed days: 6.2 ± 0.7 vs. 5.3 ± 0.5, $p > 0.05$ - Dynamic compliance: 29.8 vs. 32.8, $p = n.s.$ )- No difference between the groups in age, CVP, ISS, RTS, basedeficit, head AIS score, chest AIS score, abdominal AIS score, orprobability of survival	4 → 5

ISS = injury severity score; AIS = Abbreviated Injury Scale score; RTS = revised trauma score; GCS = Glasgow coma scale; CVP = central venous pressure; LOS = length of stay, ALI = acute lung injury, ARDS = adult respiratory distress syndrome, n.s. = not stated

Prone kinetic therapy was associated with a reduction in mortality, but not length of stay and decreased duration of ventilation. Due to methodological deficits, the results should be interpreted with caution.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1034 Fernandez 2008 (PMID: 18427774 DOI: 10.1007/s00134- 008-1119-3) <b>Specification of</b> <b>study:</b> RCT		d MV der urs ntilation a: ension needing (Cardiovascular in injury c or spinal res dition another trial	n = 2 (n = 1 in supine group, n = 1 prone group)	Prone position for about 20h/d	Supine position	<ul> <li>Primary endpoint: <ul> <li>mortality</li> </ul> </li> <li>Secondary outcomes: <ul> <li>ICU LOS (days)</li> <li>hospital LOS (days)</li> <li>MV duration (days)</li> <li>prevalence of pneumothorax</li> <li>prevalence of unplanned extubation</li> <li>prevalence of VAP</li> </ul> </li> <li>Sample size calculation: <ul> <li>based on an expected 60% mortality in severe ARDS, the estimated sample size required to confirm a 15% absolute reduction with an alpha error of 0.05 and a power of 80% was 250.</li> </ul> </li> </ul>	This study was stopped prematurely because of slow inclusion process and therefore was underpowered. <b>Primary endpoint</b> (SP vs. PP): - mortality: SP vs. PP 10 (53%) vs. 8 (38%), p = 0.3 <b>Secondary outcomes</b> (SP vs. PP): - ICU LOS: $17.5 \pm 16.1$ vs. $14.7 \pm 9.7$ , p = 0.5 - hospital LOS: $25.5 \pm 17.4$ vs. $31.3 \pm$ 26.4, p = 0.4 - MV duration: $15.7 \pm 16.9$ vs. $11.9 \pm 9.2$ , p = 0.5 - prevalence of pneumothorax: 1 (5%) vs. 0 (0%), p = 0.5 - prevalence of unplanned extubation: 1 (5%) vs. 1 (5%), p = 1.0 - prevalence of VAP: 1 (5%) vs 3 (14%), p = 0.6	2> 3 (down- graded)

ARDS = acute respiratory distress syndrome, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, SOFA = sequential organ failure Assessment, VAP = ventilator associated pneumonia

Prone position compared to supine position did not improve mortality, ICU LOS, hospital LOS or MV duration.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1037 Galiatsou 2006 (PMID: 16645177 DOI: 10.1164/rccm.200 506-899OC) <b>Specification of</b> <b>study:</b> Non-randomized, non-controlled interventional study	n = 22 pts Inclusion criteria: - ALI/ARDS - ability to be safely transported to the radiology department Exclusion criteria: - contraindications to the prone position - cardiogenic pulmonary edema - chronic lung disease - hemodynamic instability Per Branch	n = 1 (because of accidental extubation)	recruitment maneuver with subsequent prone position		Outcomes: - respiratory system compliance - pCO <sub>2</sub> - pO <sub>2</sub> /FiO <sub>2</sub>	<ul> <li>Respiratory system compliance (Mean ± SD): <ul> <li>lobar ARDS:</li> <li>baseline vs. post-RM: 32.75 ± 4.23 vs. 37.12 ± 6.31, p = 0.061; 95% CI of the difference: -9.01 - 0.27</li> <li>post-RM vs. prone position: 37.12 ± 6.31 vs. 43.12 ± 6.56, p = 0.019; 95% CI of the difference: -10.69 - 1.31</li> <li>diffuse ARDS: no significant differences</li> </ul> </li> <li>pCO<sub>2</sub>(Mean ± SD): <ul> <li>lobar ARDS:</li> <li>baseline vs. post-RM: 44 ± 6.18 vs. 42.7 ± 5.03, p = 0.095; 95% CI of the difference: -0.28 - 2.78</li> <li>post-RM vs. prone position: 42.7 ± 5.03 vs. 35.25 ± 3.41, p = 0.01; 95% CI of the difference: 3.56 - 9.4</li> <li>diffuse ARDS: no significant differences</li> </ul> </li> <li>pO<sub>2</sub>/FiO<sub>2</sub>(Mean ± SD): <ul> <li>lobar ARDS:</li> <li>baseline vs. post-RM: 106.25 ± 15.88 vs. 143 ± 12.27, p = 0.000 (<i>p</i>-value not further described); 95% CI of the difference: -43.4230.08</li> <li>post-RM vs. prone position: 143 ± 12.27 vs. 225.00 ± 37.82, p = 0.000 (<i>p</i>-value not further described); 95% CI of the difference: -112.86 - 1.14</li> <li>diffuse ARDS:</li> <li>baseline vs. post-RM: 117.8 ± 25.99 vs. 149.6 ± 20.38, p = 0.04; 95% CI of the difference: -60.323.28</li> <li>post-RM vs. prone position: 149.6 ± 20.38 vs. 180.4 ± 17.87, p = 0.0003; 95% CI of the difference: -38.11 - 23.49</li> </ul> </li> </ul>	3

ALI = acute lung injury, ARDS = acute respiratory distress syndrome, CI = confidence interval, pCO<sub>2</sub> = partial pressure of carbon dioxide, pO<sub>2</sub>/FiO<sub>2</sub> = ratio of partial pressure of oxygen and fraction of inspired oxygen, pts = patients, RM = recruitment maneuver, SD = standard deviation

#### Prone positioning seems to be superior to a recruitment maneuver in recruiting lung volume

Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1038 Gattinoni 2010 PMID: 20473258 DOI: not available Specification of study: Review with meta-analysis		573 pts) n: n of the effects ient outcome		РР	SP	Mortality	<ul> <li>No significant differences between groups.</li> <li>No significant differences between groups in: <ul> <li>mortality (PP vs. SP): absolute reduction at the last follow-up approximately 10% (ranging between 6-21%).</li> <li>Kaplan-Meier estimates of survival rates at the latest follow-up in severly-hypoxaemic pooled showed higher survival in PP vs. SP at each time-point, Log-rank = 0.03, p not stated.</li> </ul> </li> </ul>	1

PP = prone positioning, pts = patients, RCTs = randomized controlled trials, SP = supine positioning

#### Prone positioning may reduce the absolute mortality of severely hypoxemic ARDS patients.

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- 2. Guerin C, Gaillard S, Lemasson S, Ayzac L, Girard R, Beuret P et al. Effects of systematic prone positioning in hypoxemic acuterespiratory failure: a randomized controlled trial. JAMA 2004;292:2379-87
- 3. Mancebo J, Fernández R, Blanch L, Rialp G, Gordo F, Ferrer M, et al. A multicenter trial of prolonged prone ventilation in severe acute respiratory distress syndrome. Am J Respir Crit Care Med 2006;173:1233-9.
- 4. Taccone P, Pesenti A, Latini R, Polli F, Vagginelli F, Mietto C et al. Prone positioning in patients with moderate and severe acute respiratory distress syndrome: a randomized controlled trial. JAMA 2009;302:1977-84.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1042 Girard 2013 PMID: 24352484 <u>https://doi. org/10.100</u> 7/s00134- 013-3188-1 <b>Specificatio</b> n of study: Ancillary study of a RCT (PROSEVA Trial)	<ul> <li>466 pts.</li> <li>Inclusion criteria: Severe ARDS was defined by:         <ul> <li>PaO2/FIO2 (partial pressure oxygen in arterial blood/fraction of inspired oxygen) ratio of &lt;150 mmHg with a FIO2 of ≥0.6</li> <li>PEEP of ≥5 cm H2O</li> <li>tidal volume of 6 ml/kg predicted body weight</li> </ul> </li> <li>Per Branch</li> <li>PP group = 237</li> <li>SP group = 229</li> </ul>		PP fully horizontal prone position (180°) within 1 h after the randomization for sessions of ≥16 h until predetermined stopping criteria were met	SP	Sample size calculation was done in the parent trial. Primary endpoints: - Incidence of new pts with pressure ulcers at stage 2 or higher from randomization to ICU discharge Secondary endpoints: - incidence of new patients with pressure ulcers from day 1 to day 7 - incidence of new pressure ulcers from day 1 to day 7 and to ICU discharge - proportion of patients with pressure ulcers both overall and according to site at day 7 and ICU discharge and mean pressure ulcer score overall and by site	<ul> <li>Primary outcome: <ul> <li>incidence: 20.80 and 14.26 / 1,000 days of invasive mechanical ventilation (P = 0.061) and 13.92 and 7.72/1,000 of ICU days (P = 0.002) in both groups</li> </ul> </li> <li>Secondary outcomes: <ul> <li>incidence of new patients with pressure ulcers per 1,000 days of invasive ventilation from day 1 to ICU discharge was not significantly different between groups</li> <li>incidence of new patients with pressure ulcers at stages &gt;1 per 100 days of ICU stay was significantly higher in the PP</li> <li>incidence of new patients with pressure ulcers at stages &gt;1 per 100 days of ICU stay was significantly higher in the PP</li> <li>incidence of new patients with pressure ulcers from day 1 to day 7 was significantly higher in the PP group for both stage analyses and both denominators</li> <li>in both groups, the incidence of pressure ulcers was higher from day 1 to day 7 than during the stay as a whole</li> <li>at day 7, the rate of patients with pressure ulcers was significantly higher in the PP group (116/204 (57.1)) than in the SP group (79/186 (42.5)); P= 0.005; also significantly more often PU in the face (SP: 8/184 (4.3); PP: 58/197 (29.4); P= 0.0001) and anterior thorax (SP: 1/184 (0.5); PP: 35/195 (17.9); P = 0.0001)</li> <li>At the time of ICU discharge, the rate of patients with PUs was not different between groups SP group (85/225 (37.8)); PP group (103/232 (44.4)); P= 0.151, number of PUs involving the face (SP: 3/216 (1.4); PP: 41/223 (18.4) P = 0.0001) and the anterior part of the thorax (SP: 2/216 (0.9); PP: 14/219 (6.4): P= 0.0025) was still significantly higher in patients in the PP group</li> </ul> </li> </ul>	3

PP = prone position; SP = supine position; pts = patients; ARDS = acute respiratory distress syndrom; ICU = intensive care unit; PEEP = positive endexpiratory pressure; pts = patients

In patients with severe ARDS, prone positioning was associated with a higher frequency of pressure ulcers than the supine position, however, prone positioning was not a determining risk factor.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1045 Guerin, 2013 (PMID: 23688302 DOI: 10.1056/NEJ Moa1214103) <b>Specification</b> of study: RCT	466 pts with severe ARDS to undergo PP sessions of at least 16 hours or to be left in the SP <b>Inclusion criteria:</b> - ARDS (Pao2:Fio2 ratio of <150mmHG, FiO2 ≥ 0.6., PEEP ≥ 5cm H2O, Vt > 6ml/kgKG - endotracheal intubation and ventilation for <36h <b>Exclusion criteria:</b> - contraindication for prone positioning (e.g. Intracranial pressure > 30 mmHG, massive hemoptysis) - respiratory reason (e.g. NOi, ECMO) - clinical context (e.g. lung transplantation, severe burns) - others (e.g. end-of-life decision) Per Branch 237 229		Prone positioning (at least 16h), average number of sessions: 4±4 p. patient, mean duration per session: 17±3 h	Supine positioning (semi- recumbent position)	Primary endpoint: - mortality at day 28 Secondary outcomes: - mortality at day 90 - rate of successful extubation - time to successful extubation - ICU LOS - use of non-invasive ventilation - tracheotomy rate -ventilator settings - arterial blood gases - respiratory-system mechanics	Primary endpoint: - 28-day mortality n=237: 16%, n= 229: 32.8% (p<0.001) - hazard ratio for death with PP: 0.39 (95% confidence interval [CI], 0.25 to 0.63) Secondary outcomes: - 90-day mortality n=237: 23.6%, n=229: 41.0% (P<0.001), hazard ratio of 0.44 (95% CI, 0.29 to 0.67) - successful extubation was significantly higher in the prone group n=237: 80.5% [95% confidence interval [CI], 75.4–85.6], n=229: 65.0% [95% confidence interval [CI], 58.7–71.3] - ICU LOS n=229: 26 $\pm$ 27, n=237: 24 $\pm$ 22 (p=0.05) - non-invasive ventilation (at day 28) n=237: 1.8% [0.1–3.5], n=229: 4.7% [1.9–7.5] (p=0,11) - tracheotomy rate (at day 28) n= 237: 3.8% [1.4–6.0], n=229: 5.2% [2.3–8.1] (p= 0.37) - duration of invasive mechanical ventilation, length of stay in the ICU, incidence of pneumothorax, rate of use of noninvasive ventilation after extubation, and tracheotomy rate: n.s.	2

ARDS = acute respiratory distress syndrome, ECMO = extracorporeal membranous oxygenation, FiO2 = inspiratory oxygen concentration, LOS = length of stay, NOi = inhaled nitric oxide, n.s. = not significant, PEEP = positive end expiratory pressure, Vt = tidal volume

Prolonged prone-positioning sessions significantly decreased 28-day and 90-day mortality.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1051 Jozwiak 2013 (PMID: 24102072 DOI: 10.1164/rccm.201 303-0593OC) <b>Specification of</b> <b>study:</b> non-controlled interventional study	n = 18 pts Inclusion criteria: - ARDS with pulmonary artery catheter Exclusion criteria: - contraindication to transesophageal echocardiography - contraindication to PP - known chronic RV failure Per Branch		PLR test (to assess cardiac index) with following prone positioning		Outcomes: - respiratory variables - hemo- dynamic variables - tissue oxygenation variables - Echocardio- graphic variables - ICU mortality Outcomes not divided into primary or secondary	<ul> <li>Outcomes:</li> <li>pre-PP vs. post-PP (in n = 9 pts with significant change in cardiac index after PLR test previous to PP; median [IQR]):</li> <li>PaO2/FiO2 (mmHG): 137 (79-154) vs. 160 (134-202), p &lt; 0.05</li> <li>cardiac index (L/min/m2): 3.0 (2.3-3.5) vs. 3.6 (3.2-4.4), p &lt; 0.05</li> <li>stroke volume (ml/m2): 34 (29-47) vs. 42 (38-58)</li> <li>right atrial pressure (mmHg): 15 (13-18) vs. 17 (16-23)</li> <li>pulmonary artery occlusion pressure (mmHg): 19 (17-20) vs. 22 (19-26), p &lt; 0.05</li> <li>pulmonary artery mean-occlusion pressure gradient (mmHg): 16 (14-23) vs. 11 (9-21), p &lt; 0.05</li> <li>pulmonary vascular resistance (dyn*s/cm5/m2): 514 (333-885) vs. 234 (155-549), p &lt; 0.05</li> <li>pulmonary vascular resistance (dyn*s/cm5/m2): 514 (333-885) vs. 234 (155-549), p &lt; 0.05</li> <li>intra-abdominal pressure (mmHg): 16 (12-17) vs. 18 (17-20), p &lt; 0.05</li> <li>oxygen delivery (ml/min/m2): 355 (273-438) vs. 514 (424-590), p &lt; 0.05</li> <li>oxygen consumption (ml/min/m2): 65 (42-84) vs. 113 (101-126), p &lt; 0.05</li> <li>P(v-a)CO2/C(a-v)O2 (mmHg/m1): 1.4 (1.2-2.2) vs. 1.0 (0.8-1.3), p &lt; 0.05</li> <li>right/left ventricular end-diastolic area ratio (<i>no unit described</i>): 0.65 (0.55-0.80) vs. 0.60 (0.50-0.65), p &lt; 0.05</li> <li>left ventricular end-systolic area * systolic arterial pressure (cm2*mmHg): 603 (420-895) vs. 946 (765-1146), p &lt; 0.05</li> <li>pts with significant change in cardiac index after PLR test previous to PP (n=9) vs. pts without significant change in cardiac index after PLR test previous to PP (n=9); n [%]):</li> <li>left ventricular ejection fraction: Pre-PP 40 (35-56) and Post-PP 40 (36-49) vs. Pre-PP 57 (50-62) and Post-PP 60 (53-65), p &lt; 0.05</li> <li>pts with significant change in cardiac index after PLR test previous to PP (n=9); n [%]):</li> <li>ICU mortality: 5 (56%) vs. 4 (44%), non-significant</li> </ul>	3

ARDS = acute respiratory distress syndrome, PLR = passive leg raising, PP = prone positioning, pts = patients, RV = right ventricular

Prone Positioning seems to increase cardiac index in ARDS patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1053 Kopterides 2018 (PMID: 19272544 DOI: 10.1016/j.jcrc.200 7.12.014) <b>Specification of</b> <b>study:</b> Systematic Review and Meta-Analysis	4 publications (n = 4 RCTs, n = 1271 pts) <sup>1-4</sup> Inclusion criteria: - RCTs on prone positioning - providing data on mortality - population: adult patients with hypoxemic respiratory failure Exclusion criteria: - inappropriate study design - control group not standard of care		Prone positioning	Standard of care	<ul> <li>Primary outcomes:</li> <li>ICU mortality</li> <li>Secondary outcomes: <ul> <li>duration of prone positioning</li> <li>incidence of VAP</li> <li>ICU LOS</li> <li>duration of MV</li> <li>incidence of pneumothorax</li> <li>complications <ul> <li>new or worsening pressure sores</li> <li>complications related to ETT (accidental extubation, obstruction of ETT)</li> </ul> </li> </ul></li></ul>	Significant differences between groups in (PP vs. SP): ICU mortality [in a subset of the most severely ill pts (n = 195 pts)]: OR 0.34 (95% Cl: 0.18-0.66), p = 0.001; heterogeneity: p = 0.69, l <sup>2</sup> =0% Non-significant differences between groups in (PP vs. SP): ICU mortality (across all pts): OR 0.97 (265/662 pts) vs. 37.8% (230/609 pts) OR 0.97 (95% Cl: 0.77-1.22); heterogeneity: p = 0.22, l <sup>2</sup> = 32.0% duration of prone positioning: mean > 10 h/day in the 2 most recent published articles. ( <i>No further data available</i> ) incidence of VAP: OR 0.81 (95% Cl: 0.60-1.10); heterogeneity: p = 0.16, l <sup>2</sup> = 45.9% ICU LOS: 20.5 ± 18.2 vs. 19.1 ± 23.1 days, p = 0.7 duration of MV: Weighted mean difference: -1.14 days (95% Cl: -2.86-0.59) heterogeneity: p = 0.77, l <sup>2</sup> =% OR 0.8 (95% Cl: 0.47-1.34); heterogeneity: p = 0.33, l <sup>2</sup> = 0% Complications New or worsening pressure sores: 1135 pts, FEM OR 1.49 (95% Cl: 1.17-1.89) REM OR 1.50 (95% Cl: 1.12-2.00); heterogeneity: p = 0.32, l <sup>2</sup> = 13.1% Complications related to ETT 1271 pts, OR 1.30 (95% Cl: 0.94-1.80); heterogeneity: p = 0.35, l <sup>2</sup> = 8.4%	1→2

CI = confidence interval, ETT = endotracheal tube, FEM = fixed effect model, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, OR = odds ratio, PP = prone positioning, pts = patients, RCTs = randomized controlled trials, REM = random effect model, SP = supine positioning, VAP = ventilator-associated pneumonia

Except for most severely ill patients, PP seems not to influence mortality in patients with hypoxemic respiratory failure, although the incidence of VAP might decrease at the expense of more pressure sores and complications related to the endotracheal tube.

#### References

- 1. Gattinoni L, Tognoni G, Pesenti A, et al, Prone-Supine Study Group. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 2001;345:568-73.
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- 3. Voggenreiter G, Aufmkolk M, Stiletto RJ, et al. Prone positioning improves oxygenation in post-traumatic lung injury—a prospective randomized trial. J Trauma 2005;59:333-41 discussion 341-3.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1054 Lee, 2010 PMID: 20195404 DOI: 10.3904/kjim. 2010.25.1.58 <b>Specification</b> of study: retrospective search	96 patients Inclusion criteria: - ARDS (PaO2/ FiO2 ≤ 150 mmHg with a positive end- expiratory pressure (PEEP) of at least 8 cm H2O - bilateral chest radiography showing lung infiltrate without evidence of cardiac failure Exclusion criteria: - not stated Per Branch 96 divided in: PaO <sub>2</sub> responders (n=60) and PaO <sub>2</sub> non-responders (n=36)		PP for ≥ 12 hours and change from prone to supine due to improvement (then PaO <sub>2</sub> responder)	patients were divided in the intervention group by itself	Primary endpoint: - 28-day mortality Secondary outcomes: - gas exchange values after prone positioning - ventilatory parameters after prone positioning	<ul> <li>Primary endpoint: <ul> <li>28-day mortality: PaO<sub>2</sub> responders 28 (46.7) and PaO<sub>2</sub> non-responders 26 (72.2) (p=0.019)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>gas exchange values after prone positioning:</li> <li>PaO2 responders mean PaO2/FiO2 increase at 8 to 12 hours of PP 75.4 ± 47.2 mmHg (median, 64.3; range, 20 to 215) and for</li> <li>PaCO2 responders, mean PaCO2 change was - 10.6 ± 10.3 mmHg (median, - 7.4; range, - 42 to 1)</li> <li>ventilatory parameters after PP: no significant differences (p&gt;0.05)</li> </ul> </li> </ul>	4

ARDS = acute respiratory distress syndrome, PP = prone position; PEEP = positive endexspiratory pressure

The early oxygenation improvement after prone positioning might be associated with an improved 28-day outcome and may be an indicator to maintain prolonged prone positioning in patients with severe ARDS

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Chara To	ncteristics) Dtal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1056 Mancebo 2006 (PMID: 16556697 DOI: 10.1164/rccm.2005 03-353OC) <b>Specification of</b> <b>study:</b> Randomized Controlled Trial	136 pts Inclusion criteria: - intubation and MV - 18 years or older - ARDS - diffuse bilateral infi Exclusion criteria: - > 48 hours had elap criteria were met - participation in othe - pregnancy - systolic blood press despite vasopressors - pelvic/spine fractur - cranial trauma and/ intracranial pressure - moribund pts Per B 76	osed since inclusion er trials sure < 80 mmHg s res /or suspicion of high	Supine: n=2 (Case reports lost) Prone: n = 4 (1 lost, 2 Data lacking, 1 High PCWP)	Prone position for about 7h/d	Supine position	Primary outcome: - ICU mortality Secondary outcomes: - hospital mortality - complications - LOS	<ul> <li>Primary outcome: <ul> <li>ICU mortality was 58%</li> <li>(35/60) in supine group and</li> <li>43% (33/76) in prone group (p = 0.12)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>hospital mortality was higher in supine group (62% vs. 50%; p = 0.22)</li> <li>ICU LOS did not differ between groups</li> <li>total of 28 complications were reported, most were rapidly reversible</li> </ul> </li> </ul>	2
	76	60						

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, PCWP = pulmonary capillary wedge pressure, pts = patients

Prone positioning may reduce ICU and hospital mortality in patients with ARDS.

Reference, Study Type	(Participant #,	d Controls characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1062 Mounier 2009 PMID: 19741030 DOI: 10.1183/09031 936.00057509 <b>Specification</b> of study: prospective observational study	MV days - Bilateral lung - Absence of le hypertension Exclusion criteri -not stated	a: ≥ 2 days 48h after ICU 300 in the first 2 infiltrates eft atrial	-	<b>PP:</b> during the MV period, one PP session involving the pts remaining prone for > 6h/day	SRP	Sample Size calculation: Assuming a 50% VAP rate, at least 200 PP pts and 200 matched controls for a HR of 2 for VAP with > 90% power and 0,05 type I error risk Primary Endpoint: -Incidence of VAP Secondary outcome: -Mortality	Primary Endpoint: no significant difference in VAP incidence (p=0,14) Secondary endpoints: -No significant difference in mortality overall or with a single day of PP -Significant delay of mortality in the PP group (p=0,001) -Significantly lower mortality with ≥ 2 PP days (p=0.009) Posthoc power analysis: power of the study decreased by the lower than expected prevalence of VAP	3

MV = mechanical ventilation, VAP = ventilator associated pneumonia, ALI =acute lung injury, ARDS = acute respiratory distress syndrome, pts = patients; SRP: = Semi-recumbency position; HR=Hazard ratio; ICU=intensive care unit; PP=prone position

#### PP is not superior to SP to prevent VAP, but longer PP use may improve survival.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1064           Nekludov, 2006           (PMID: 16923086           DOI:           10.1111/j.1399-           6576.2006.01099.x)           https://pubmed.ncb           i.nlm.nih.gov/16923           086/           Specification of study:           prospective cohort	8 pts Inclusion criteria: - adults treated for TBI or SAH - GCS = 8<br - association with pulmonary pathology Exclusion criteria: - high or unstable ICP - circulatory unstable - high doses of inotropes - hemodialysis Per Branch		change between supine to prone positioning (same in all pts)		<b>Primary endpoints:</b> - hemodynamics - arterial oxygenation - respiratory mechanics - ICP and CPP	Significant differences between groups in: - significant improvement in PaO2 in the prone position, from 12.6 $\pm$ 1.4 kPa to 15.7 $\pm$ 3.2 kPa (p = 0.02) - intracranial pressure and mean arterial pressure increased in prone position, from 12 $\pm$ 6 to 15 $\pm$ 4 mmHg (p = 0.03) and from 78 $\pm$ 8 to 88 $\pm$ 8 mmHg (P = 0.005) - arterial pressure increased to a greater extent than ICP, resulting in improved CPP, from 66 $\pm$ 7 to 73 $\pm$ 8 mmHg (P 0.03) in the	3> 4 (downgraded for small sample size)
study						prone position	

CPP = cerebral perfusion pressure, GCS = Glasgow coma scale, ICP = intracranial pressure, pts = patients, SAH = subarachnoidal hemorrhage, TBI = traumatic brain injury

Oxygenation was improved during prone positioning as well as CPP, but it also may result in increased ICP.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1066 Papazian, 2005 (PMID: 16215365 DOI: 10.1097/01.cc m.0000181298 .05474.2b) <b>Specification</b> of study: Prospective, comparative randomized study	39 pts with ARDS Inclusion criteria: - PaO2/FIO2 ratio ≤ 150 mm Hg while on PEEP ≥ 5 cm H2O - bilateral radiographic pulmonary infiltrates - pulmonary artery occlusion pressure of ≤ 18 mm Hg Exclusion criteria: - younger than 18 years old - lack of informed consent - moribund status - severe chronic respiratory insufficiency requiring long-term oxygen therapy or long-term mechanical ventilation - head injury - unstable pelvic or vertebral fracture, extra-alveolar air in the chest radiograph - a chest tube in place with persistent air leak - patients who had participated in other investigational trials within 30 days Per Branch Prone CV: 13 Supine-HFOV: 13 Prone-HFOV: 13		12h period of: <u>Prone-CV:</u> conventional lung-protective mechanical ventilation in PP <u>Supine-HFOV:</u> HFOV in SP <u>Prone-HFOV:</u> HFOV in PP	only intervention groups	<b>Endpoints:</b> - oxygenation variables - respiratory variables - venous admixture, the other hemodynamic variables, and gas exchange - cytokines and cell differential counts	Endpoint: - oxygenation variables: prone-CV and prone-HFOV: improvement in PaO2/FIO2 (from 138 ± 58 mm Hg to 217 ± 110 mm Hg, p = .0001; and from 126 ± 40 mm Hg to 227 ± 64 mm Hg, p = .0001) - respiratory variables: mean airway pressure under HFOV was not different from the plateau pressure used during the periods that patients with CV (baseline supine-CV: 19 ± 4; supine-HFOV 25 ± 5; prone-CV 19 ± 5; prone-HFOV 25 ± 6; p = < .01) - venous admixture, the other hemodynamic variables, and gas exchange prone position (p < .0001) and HFOV (p < .001) reduced the venous admixture other hemodynamic variables (including cardiac index) remained unchanged (data not shown) modification of PaCO2 n.s. (no p-value) - cytokines and cell differential counts neutrophils counts were higher in the supine-HFOV group (median 475,000·mL <sup>-1</sup> , IQR 290,000– 875,000·mL <sup>-1</sup> ) than after prone-CV (median 110,000·mL <sup>-1</sup> , IQR 72,000– 310,000·mL <sup>-1</sup> ; p < 0.05) neutrophil count correlated with BAL IL-8 level at baseline and after all 12-hr periods (p < .001)	3

ARDS = acute respiratory distress syndrome, CV = conventional mechanical ventilation, HFOV = high-frequency oscillatory ventilation, PEEP = positive end-expiratory pressure, PP = prone position, pts = patients, SP = supine position

HFOV in the supine position does not improve oxygenation or lung inflammation, while the prone position improves both parameters in ARDS patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1075 Sud 2008 (PMID: 18427090 DOI: 10.1503/cma j.071802) <b>Specification</b> of study: Systematic review and meta- analysis	supine position - report of all-cause mortality,		mechanical ventilation in prone position		Primary endpoint: - all-cause mortality Secondary outcomes: - oxygenation on days 1-3 - VAP - number of days on MV - VFD - AEs	Significant differences between groups in: - VAP: PP reduces the risk of VAP (RR 0.81, 95% CI 0.66 to 0.99, p = 0.04) - AE: PP increased the risk of pressure ulcers (RR 1.36, 95% CI 1.07 to 1.71; p = 0.01, $l^2$ = 0%). - oxygenation on days 1-3: PP increases PaO <sub>2</sub> /FiO <sub>2</sub> ratio by 23%-34% on days 1-3 after randomization, PaO <sub>2</sub> /FiO <sub>2</sub> ratio remained 6-9% higher in pts in the PP group after they were returned to the SP after a prone maneuver - number of MV days (6 trials (n = 992)): shorter duration of MV in the prone group (weighted mean difference -0.9 days, 95% CI -1.9 to 0.1; p = 0.06, $l^2$ = 3% No significant differences between groups in: - mortality: (RR 0.96, 95% CI 0.84 to 1.09; p = 0.52), subgroup analysis: mortality between trials of short-term PP and prolonged PP does not differ. [RR 0.77, 95% CI 0.46 to 1.28 vs. RR 0.97, 95% CI 0.85 to 1.11; (p = 0.39 for comparison of RRs using z-score)] - VFD (4 trials (n = 148)): weighted mean difference 3.7 days, 95% CI -1.8 to 9.3; p = 0.19, $l^2$ = 67%	1 → 2 (downgraded for indirectness / applicability)

AE = adverse effects, AHRF = acute hypoxemic respiratory failure, CI = confidence interval, MV = mechanical ventilation, PP = prone position, Pts = patients, VAP = ventilator associated pneumonia, VFD = ventilator-free days

# Mechanical ventilation in the prone position does not reduce mortality or increase ventilator-free days despite improved oxygenation and a decreased risk of pneumonia.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1076 Sud 2010 (PMID: 20130832 DOI: 10.1007/s001 34-009-1748- 1) <b>Specification</b> of study: Systematic Review and Meta- Analysis	<ul> <li>1.867 pts in 10 publications (RCT)<sup>1-10</sup></li> <li>Inclusion criteria: <ul> <li>prone positioning used early</li> <li>(within 72 h after initiation of mechanical ventilation) and as late or rescue therapy (72 h after initiation of mechanical ventilation)</li> <li>prone ventilation was applied intermittently or continuously</li> </ul> </li> <li>Exclusion criteria: <ul> <li>patients received both treatment and control interventions in random order</li> <li>short-term trials in which the intervention was applied for ≤48 h</li> </ul> </li> </ul>		<b>Prone</b> <b>positioning</b> for ≥48H	Supine positioning	Primary endpoint: - hospital mortality (pts with PaO <sub>2</sub> /FiO <sub>2</sub> <100 mmHg vs. pts PaO <sub>2</sub> /FiO <sub>2</sub> >100 mmHg) Secondary outcomes: - hospital mortality (limited to pts. with ALI/ARDS) - rate of VAP - duration of MV - ventilator-free days on day 28 - adverse events	Significant differences between groups in: adverse events, PP increased risk of - pressure ulcers: RR1.29, 95% Cl 1.16–1.44, p <0.00001 - endotracheal tube obstruction: RR 1.58, 95% Cl 1.24–2.01, p=0.0002 - accidental chest tube removal: RR 3.14, 95% Cl 1.02–9.69, p=0.05 - PP reduced mortality in pts. with PaO <sub>2</sub> /FiO <sub>2</sub> <100 mmHg (RR 0.84, 95% Cl 0.74–0.96; p=0.01; N=555) NNT= 11 (95% Cl 6– 50) - mortality in pts. with ALI/ARDS: PaO <sub>2</sub> /FiO <sub>2</sub> <100 mmHg (RR 0.85,95% Cl 0.74–0.98, p=0.02) -VAP: RR 0.81, 95% Cl 0.67–1.00, p=0.05; n=1,066) No significant differences between groups in: - MV duration - ventilator-free days - mortality in pts with PaO <sub>2</sub> /FiO <sub>2</sub> >100 mmHg (RR 1.07, 95% Cl 0.93–1.22; p=0.36; N=1,169)	1> 2
	Per Branch						

AHRF = acute hypoxemic respiratory failure, ALI = acute lung injury, ARDS = acute respiratory distress syndrome, CI = confidence interval, MV = mechanical ventilation, PP = prone positioning, pts = patients, RCT= randomized controlled trial, VAP= ventilator-associated pneumonia

Prone positioning reduces mortality in patients with a PaO<sub>2</sub>/FiO<sub>2</sub> ration <100 mmHg but not in those with a higher ratio. It increases the risk of adverse events.

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Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1077 Taccone 2009 (PMID: 19903918 DOI: 10.1001/jam a.2009.1614 ) Specification of study: Randomized Controlled Trial	to moderate hyp hypoxia. Inclusion criteria -invasive MV and Exclusion criteria - < 16 years, - > 72h since ARD - history of organ - contraindication	: I ARDS diagnosis a: DS diagnosis I transplantation	2 drop-outs (1 in each group, both inclusion mistake)	<b>PP</b> - for ≥ 20h/day until resolution of ARDS or until day 28	SP	Primary endpoint: - death by any cause at day 28 Secondary outcomes: - death by any cause at ICU discharge and 6 months - SOFA-Score at day 28 - Ventilator-free days	Primary endpoint: - overall death by any cause at day 28, PP 52 vs SP 57 (RR=0.97 95% CI 0.84-1.13 p=0.72) - moderate hypoxia death: PP 24 vs SP 22 (RR=1.04 95% CI 0.89- 1.22 p=0.62) - severe hypoxia death: PP 28 vs SP 35 (RR=0.87 95% CI 0.66-1.14 p=0.31) Secondary outcomes: - mortality at ICU discharge: n.s. (p=0.47) - mortality at 6 months: n.s. (p=0.33) - SOFA-Score at day 28: n.s (p=0.87) - ventilator-free days n.s. (p=0.31)	2

ARDS = acute respiratory distress syndrome, ICU = intensive care unit, MV = mechanical ventilation, PP = prone positioning, pts = patients, RCT = randomized controlled trial, SOFA = sequential organ failure assessment, SP = supine positioning

#### Prone positioning does not have a significant effect on mortality in ARDS patients regardless of the severity of the disease.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1078 Theleandersson 2006 (PMID: 16923087 DOI: 10.1111/j.1399- 6576.2006.0103 7.x)( <u>https://pub</u> med.ncbi.nlm.ni <u>h.gov/16923087</u> <u>/</u> ) <b>Specification of</b> <b>study:</b> A prospective pilot study	12 pts all pts received PP; analysis focused of differences in SP to PP for each patient Inclusion criteria: - MV NICU pts with FiO2 of 0.4 - intraventricular catheter for ICP measurements Exclusion criteria: - unable PP (fracture) - MV in pressure-controlled mode Per Branch	n = 1 (ICP increase)	PP		Outcomes: - ICP - CPP - HR - PaCO2 - PaO2 - SaO2 - MABP - Respiratory system compliance (ml/cm H2O)	Significant differences after turning prone in:-PaO2 Baseline vs. $3h$ PP: $13.2 \pm 2.1$ vs. $19.1 \pm 6.1$ ; p < 0.05	3 → 4 Pilot / small sample size

CPP = cerebral perfusion pressure, HR = heart rate, ICP = intracranial pressure, MABP = mean arterial blood pressure, min = minutes, MV = mechanical ventilation, NICU = neuro intensive care unit, PaCO2 = partial pressure of arterial carbon dioxide, PaO2 = partial pressure of arterial oxygen, PP = prone position, pts = patients, SaO2 = saturation of arterial oxygen, SP = supine position

Prone positioning leads to improvement of oxygenation in NICU patients and did not influence CPP, ICP or MABP.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1079 Tiruvoipati 2008 (PMID: 18359427 DOI: 10.1016/j.jcr c.2007.09.00 3) <b>Specification</b> of study: Meta- analysis	Per Branch		ΡV	SV	Primary endpoint: - mortality Secondary outcomes: - changes in oxygenation - incidence of VAP - duration of MV - ICU LOS - hospital LOS - complications related to ET tube, intravascular catheters and pressure sores	Primary endpoint: - mortality: n.s. (OR: 0.98, 95% CI 0.7-1.3 p=0.91) Secondary endpoints: Significant differences between groups in: - changes in oxygenation: MD 21.2 mmHg (95% CI 12.4-30.0 p<0.001) - pressure sores: OR: 1.95, 95% CI 0.09-4.15, p=0.08 No significant differences between groups in: - incidence of VAP: n.s. - ICU LOS: n.s. - ET tube complications: n.s. - duration of MV: no meta-analysis - hospital LOS: no meta-analysis	1 → 2 (downgraded for indirectness / applicability)

ALI = acute lung injury, ARDS = acute respiratory distress syndrome, ARF = acute respiratory failure, ET = endotracheal, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, n.s. = not significant, pts = patients, PV = prone ventilation, RCT = randomized controlled trial, SV = supine ventilation, VAP = ventilator-associated pneumonia

#### Prone ventilation reduces the mortality compared to supine ventilation in ARDS and ALI patients.

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Reference, Study Type	(Participant #	nd Controls , Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1080 Vieillard-Baron 2007 (PMID: 17925425 DOI: 10.1378/chest.07- 1013) <b>Specification of</b> <b>study:</b> Retrospective study	were included bet and December 20 Inclusion criteria patients with: "severe" ARDS, Ia Pao2/fraction of ii (Fio2) ratio of 100 of respiratory sup stretch" respirato - treatment by PP week of respirato	eading to a nspired oxygen ) mm Hg after 48 h port with our "low- ry strategy during the first		Patients with acute cor pulmonale (defined by RV enlargement associated with septal dyskinesia) (transesophageal echocardiography before PP and 18 h after PP)	<b>Patients with</b> <b>normal RV</b> (transesophageal echocardiography before PP and 18 h after PP)	<b>Outcome</b> (not defined) - RV enlargement - septal dyskinesia - Respiratory compliance	Outcome - intervention group: significant decrease in mean (± SD) RV enlargement (from 0.91 ± 0.22 to 0.61 ± 0.21) after 18 h of PP (p =0.000) - intervention: significant reduction in mean septal dyskinesia (from 1.5 ± 0.2 to 1.1 ± 0.1) after 18 h of PP (p = 0.000) - significantly lower respiratory system compliance : intervention= 22 ± 7 vs control= 28 ±7 mL/cm H2O, respectively; p= 0.008	4

ARDS = acute respiratory distress syndrome, PP = prone position, RV = right ventricle

In the most severe forms of ARDS, PP was an efficient means of controlling RV dysfunction. No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1082 Voggenreiter 2005 (PMID: 16294072 DOI: 10.1097/01.t a.000017995 2.95921.49) <b>Specification</b> of study: PRT	40 multiple trauma pts of the ICUs of 2 university hospitals with ALI or ARDS Inclusion criteria: - multiple trauma pts in an ICU, 18–80 years - ISS ≥16 - MV (PEEP ≥5cm H2O, PaO2:FiO2 ≤ 200 mmHg for 8h or PaO2:FiO2 ≤ 300 mmHg for 24h) Exclusion criteria: - evidence of cardiogenic pulmonary edema, cerebral edema - intracranial hypertension - contraindicated the use of the PP (unstable spine fractures, hemodynamic instability) Per Branch 21 9		<b>PP:</b> 30 ± 17 days; first and third quartile, 18 to 39 days; kept prone for at least 8h and a max. of 23h/day	SP: 33 ± 23 days; first and third quartile, 17 to 45 days; were positioned according to standard care guidelines	Primary endpoint: - duration of mechanical ventilation Secondary endpoints: - days with ARDS/ ALI - days with lung injury score - course of PaO2:FiO2 ratio - Qs/Qt - total static lung compliance - PIP - PEEP - LIS - TISS-28 - SOFA - sepsis - prevalence of pneumonia - mortality -complications/adverse events - ARDS following ALI	Primary outcome: - duration of mechanical ventilation did not significantly differ (p=0.48) Secondary outcome: -number of days with ARDS: $2 \pm 2$ days in the prone group and $3 \pm 1$ days in the supine group (p = 0.07) -number of days with ALI: prone group $8 \pm 4$ days; supine group: $11 \pm 5$ days (p = 0.03) -PaO2:FiO2 ratio increased after 4 days: p = 0.03 in prone group -reduction of PEEP after 4 days of prone ventilation (p = 0.009) -ICU- mortality (p = 0,27): prone = 5%, supine = 16% -end of study period: spontaneous breathing by 19 patients (prone) and 15 pts(supine) -prone positioning: reduced the prevalence of pneumonia (p = 0.048) adverse effects: -pressure sores and skin lesions (p = 0.48) -persisting swelling and edema of the head and neck region (p = 0.26) -brady- or tachyarrhythmias (p = 0.31)	2 → 3

ALI = acute lung injury, ARDS = acute respiratory distress syndrome, ICU = intensive care unit, ISS = injury severity score, LIS = lung injury score, TISS-28, PEEP = positive end expiratory pressure, PIP = peak inspiratory pressure, PRT = prospective randomized trial, pts = patients

#### Prone positioning improves oxygenation and the duration of ARDS.

Reference, Study Type	(Partici Charact	l Controls pant #, eristics) tal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1087 Weig 2014 (PMID: 24666961 DOI: 10.1016/j.jcrc.2 014.02.010)	82 consecuti receiving PP	ive ARDS pts	12 pts died or were discharged within 7 days (unknown group)	PP was decided by staff (based on clinical and radiologic findings) 1 PP session =		<b>Endpoints:</b> - death - ICU discharge - renal failure - hepatic failure	<ul> <li>survival: 65.9% (in both groups)</li> <li>median ICU-LOS: 26d</li> <li>Significant differences between the groups:</li> <li>renal failure: obese pts. Showed higher rates of renal failure (p&lt;0.0001)</li> <li>mortality: obesity led to higher risk of mortality (p = 0.0004)</li> </ul>	4
Specification	Per B	ranch		12h			No significant difference between the	
of study: retrospective cohort study	SAD>26cm SAD<26cm : 41 : 41						<ul> <li>- hepatic failure</li> </ul>	

ARDS = acute respiratory distress syndrome, ICU = intensive care unit, PP = prone positioning, pts = patients, SAD = sagittal abdominal diameter

Prone positioning is associated with a higher risk for mortality and renal failure in obese patients.

No detailed assessment was carried out further because higher-quality evidence is available on this topic

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1088 Sud 2014 (PMID: 24863923 DOI: 10.1503/cma j.140081) Specification of study: systematic review and meta- analysis	<ul> <li>only trials with lung protective ventilation (&lt; 8 mL/kg)</li> </ul>		PP	SP	<ul> <li>Primary endpoint:         <ul> <li>all-cause mortality, at hospital discharge or the longest duration of follow-up</li> </ul> </li> <li>Secondary outcomes:         <ul> <li>change in oxygenation and AEs</li> <li>mortality with lung protective ventilation</li> <li>oxygenation</li> </ul> </li> </ul>	<ul> <li>Significant differences between groups in: <ul> <li>mortality:</li> <li>mortality (n = 6) was reduced with MLPV (RR 0.74, 95% CI 0.59–0.95; l<sup>2</sup> = 29%)</li> <li>prone positioning (&gt;16h daily) reduced all-cause mortality (RR 0.77, 95% CI 0.64–0.92: l<sup>2</sup> = 21%)</li> <li>prone positioning reduced all-cause mortality among patients with severe hypoxemia at baseline (RR 0.76, 95% CI 0.61–0.94: l<sup>2</sup> = 0%).</li> <li>oxygenation: PaO2/FiO2 ratios improvements were greater in PP group than SP group: 25%–36% during the first 3 days after randomization. (Day 1 l<sup>2</sup> = 49%, day 2 l<sup>2</sup> = 27%, day 3 l<sup>2</sup> = 0%).</li> </ul> </li> <li>AEs occurred: pressure Ulcers: RR 1.27 (1.16–1.40); obstruction of endotracheal tube: RR 1.60 (1.27–2.02); dislodgement of thoracostomy tube: RR 3.14 (1.02–9.69)</li> <li>Non-significant differences between groups in: <ul> <li>mortality with lung protective ventilation: no effect on mortality (n = 4) if higher tidal volumes were permitted than currently recommended (RR 0.98, 95% CI 0.86–1.12; l<sup>2</sup> = 0%), which differed when compared with trials using protective lung ventilation (interaction p = 0.05)</li> <li>subgroup-analysis of patients with mild and moderate hypoxemia: No mortality reduction</li> <li>AEs: There was no difference in other adverse events between the two groups.</li> </ul> </li> </ul>	1 → 2 (due to indirectness)

AEs = adverse events, ARDS = acute respiratory distress syndrome, CI = confidence interval, MV = mechanical ventilation, PP = prone position, pts = patients, RCTs = randomized controlled trials, RR = risk ratio, SP = supine position, MLPV= mandated lung protective ventilation

#### Prone positioning may reduce mortality and improve oxygenation in critically ill ventilated patients on ICU.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1104 Zeppos 2007 (PMID: 18047463 DOI: 10.1016/s0004- 9514(07)70009- 0) <u>https://doi.org/</u> 10.1016/s0004- 9514(07)70009-0 <b>Specification of</b> <b>study:</b> multi-centre prospective observational study	12.281 PT interventions all patients in 5 ICUs over 3 months Per Branch		PT intervention (including: directed positioning, mobilisation, transfer, active or passive exercise, manual hyperinflation, ventilator hyperinflation, recruitment maneuvers, application of oxygen, suction, insertion of airway, manual interventions)		Outcome: AEs	Outcomes: - 27 AEs in 12.281 sessions (0.2%) - 55% AEs related to blood pressure - 30% recovery after stop of intervention, 59% recovery after specific intervention, 11% unknown - pre-existing cardiac comorbidities in 96% - use of vasopressors in 86%	3

AEs = adverse events, ICU = intensive care unit, PT = physio therapy

AEs during PT interventions are rare and are self-limiting or treatable.

Grade
ained to ing) of 1 → 3 (downgraded for indirectness / applicability and not only RCTs) than the y by rge in tudies, nd
cli o s) iir ) s t an

AE = adverse event, MRC = medical research council, MV = mechanical ventilation, PF = physical function, pts = patients, SF-36 = short-form 36

#### Early physical therapy and ICU mobilization is feasible and safe, but effects on muscle strength and quality of life need to be studied further.

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Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1119 Bein 2011 PMID: 21939972 DOI: 10.1016/j.injur y.2011.08.034 Specification of study: prospective randomized study	27 pts Inclusion criteria: - posttraumatic ALI 200–300 mmHg aff and optimization o - absence of contra positioning therapy syndrome, instable spine, severe acute [Glasgow Coma Scale < 9] - age <18 years or 2 - absence of preexi chronic lung diseas obstructive lung disease) - absence of multip Per B	ter stabilization of ventilation aindications for y (acute shock e fractures of the e brain injury >80 years isting severe se (chronic		CLRT	Positioned conventionally	Primary endpoints: - levels of cytokines (Tumour Necrosis Factor, Interleukin 6, Interleukin 8 or Intercellular Adhesion Molecule-1) in BAL and blood Secondary outcomes: - haemodynamic, pulmonary, and laboratory values - ventilator-free days - organ-failure free days - ICU LOS - hospital LOS - mortality	<ul> <li>Primary endpoints: <ul> <li>d5: no significant differences were found in cytokine levels between groups, but a significant decrease in IL-8 (p &lt; 0.01) and TNF-a (p &lt; 0.05) serum levels and an increase in IL-8 BAL levels in the CLRT-group</li> <li>in general, cytokine BAL levels tended to be increased in both groups, but more pronounced during CLRT</li> </ul> </li> <li>Secondary outcomes <ul> <li>Significant differences:</li> <li>daily assessment of the severity of disease (SAPS-II, SOFA) significantly reduced in the study group on days 2–4 (p &lt; 0.05)</li> <li>d5: significant difference of pulmonary gas exchange between groups (p = 0.001); FIO2 at d5 was significantly different between groups (p = 0.035)</li> </ul> </li> <li>No significant differences: <ul> <li>haemodynamic values</li> <li>ventilator free days</li> <li>organ-failure free days</li> <li>ICU + hospital LOS</li> <li>mortality</li> </ul> </li> </ul>	2 → 3

BAL = broncho-alveolar lavage fluid, CLRT = continuous lateral rotational therapy, ICU = intensive care unit, LOS = length of stay, pts = patients

#### CLRT might reduce the inflammatory response to acute lung injury.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1123 Amidei 2012 PMID: 22390919 DOI: 10.1016/j.iccn. 2011.09.002 Specification of study: concept analysis	<ul> <li>17 publication unknown study type,</li> <li>12 analyzed<sup>1-12</sup></li> <li>Inclusion criteria: <ul> <li>published in English language</li> <li>incorporated mobilization as an</li> <li>intervention in a critically ill (acute or chronic) sample</li> <li>utilized at least one type of physiologic measure in data collection</li> </ul> </li> <li>Exclusion criteria: <ul> <li>reviews only</li> <li>addressed functional or other outcomes alone</li> <li>without discussion of physiologic measures</li> <li>addressed mobilization after resolution of the critical illness</li> <li>written in a language other than English</li> </ul> </li> </ul>		Mobilization	No Mobilization in critically ill	Outcomes: - physiologic outcome (Cardiopulmonary measures) - functional outcome (Borg Rating of Perceived Exertion, Medical Research Council Muscle Strength Grading Scale)	<b>Outcomes:</b> - physiologic outcomes: primarily used as indicators of safety; - cardiopulmonary measures comprised the majority of variables; - only the Borg rating of perceived exertion could be suitable for safety measurement; - medical research council muscle strength grading scale could be a physiologic outcome measure no statistically analysis stated and big variance in between the cited studies	1→2

Multiple physiologic variables should be measured when considering response to mobilization in critically ill patients.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1126 Andersen 2014 PMID: 24335413 DOI: 10.1097/EJA. 000000000 00028 Specification of study: prospective, controlled, single cohort study	52 pts in single group trial Inclusion criteria: - spinal surgery > 2h - 18 – 80y - ASA physical status 1-3 - free and painless movement of the neck Exclusion criteria: - history of cervical spine disease - central nervous system disorders - carotid vessel disease - BMI > 35 Per Branch	4 (1: no steady- state, 1: short surgey, 2: missing data)	<b>head rotated</b> <b>left and right</b> in prone position during surgery	head in neutral position in prone position during surgery	Outcome: - rScO <sub>2</sub> (measured by NIRS)	<ul> <li>rScO<sub>2</sub> was significantly different when the head was lifted vs when rested on a surface this is due to compression of sensors. Therefore, only lifted positions were compared.</li> <li>rScO<sub>2</sub> in lifted position: rotated left vs. neutral: n.s. (MD 1 [IQR -1 to 4.5]; p =0.37)</li> <li>rScO<sub>2</sub> in lifted position: rotated right vs. neutral: n.s. (MD - 0.5 [IQR -3.5 to 1]; p = 0.26)</li> </ul>	3

ASA = American Society of Anestesiologists, BMI = body mass index, NIRS = near-infrared spectroscopy, pts = patients, rScO<sub>2</sub> = regional cerebral oxygen saturation

#### Rotating the head in prone position during spinal surgery does not change the cerebral oxygen saturation compared to a neutral position.

Reference, Study Type	Cases and Controls (Participant #, Characteristics ) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1128 Bird 2010 PMID: 20479345 DOI: 10.1001/arch surg.2010.69 Specification of study: Secondary analysis of prospective observational study	45 pts Inclusion criteria: - ICU pts - MV Exclusion criteria not further described Per Branch		<ul> <li>VAP-prevention bundle:</li> <li>HOB elevation &gt; 30°</li> <li>Daily sedation break</li> <li>Daily assessment for extubation</li> <li>Peptic ulcer prophylaxis</li> <li>Deep vein thrombosis prophylaxis</li> </ul>		Primary Outcome: - Relationship between VAP bundle compliance and VAP incidence Secondary Outcome: - Cost savings resulting from the VAP bundle program	<ul> <li>Primary Outcome: <ul> <li>VAP compliance: Compliance increased in both participating ICUs in the course of the study.</li> <li>ICU A (Mean; (95% CI)): Baseline 63 (57-69); Post-interventional 81 (72-90)</li> <li>ICU B (Mean; (95% CI)): Baseline 53 (46-60); Post-interventional 91 (85-97)</li> </ul> </li> <li>Combined data concerning compliance not described <ul> <li>VAP incidence:</li> <li>baseline 10.2 VAP cases/1000 ventilator days</li> <li>during the study period of three years, the combined VAP rates significantly during the last two years. (No values states; p = 0.01 and p = 0.004, respectively)</li> </ul> </li> <li>Data concerning correlation between compliance/incidence not further described</li> <li>Secondary Outcome: <ul> <li>estimated costs of \$30.000(±20.000) per VAP case in combination with reduced VAP incidence resulted in \$1.080.000 (\$360.000-\$1.800.000) cost savings as a result of VAP prevention</li> </ul> </li> </ul>	4

HOB = head of bed, ICU = intensive care unit, MV = mechanical ventilation, pts = patients, VAP = ventilator-associated pneumonia

The VAP-prevention bundle seems to decrease VAP incidence and thereby save treatment costs by prevention.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1130 Fleegler 2009 PMID: 19855209 DOI: 10.1097/DCC.0b01 3e3181b3fff7 <b>Specification of</b> <b>study:</b> Observational study with historic control	46 patients Inclusion criteria: - the presence of mechanical ventilation - delivered percentage of inspired oxygen (FIO2) greater than 0.50 - PaO2/FIO2 (P/F) ratio less than 300 Exclusion criteria: -not defined Per Branch 23 intervention 23 control		Use of continuous lateral rotational therapy protocol	Retrospective identified control subjects	Primary Endpoints: - mortality - morbidity - mean ventilator days - ICU LOS - Hospital LOS Secondary Endpoints: - lag time to initiating therapy - effects of lag time on ventilator days, ICU LOS, Hospital LOS	Primary Outcomes: No significant differences between the groups in: (control vs CLRT) - observed mortality rate (0.39 vs 0.44) - mean acute physiology score (58.2 vs 65.8) p=0.203 - mean MV days (13.4 vs 11.6) p=0.403 - mean ICU LOS (15.4 vs 15.4) p=1 - mean hospital LOS (26.6 vs 23) p=0.425 Secondary Outcomes: (CLRT<5d n=20 vs CLRT≥5d n=14) Early initiation of continuous lateral rotational therapy resulted in significant decreases in: - ventilator days (11.5 vs 23.4) p=0.001 - ICU LOS (14.7 vs 27.9) p=0.002 No significant changes in: - Hospital LOS (22.5 vs 31.5) p=0.064	4 → 5 (downgraded for indirectness / applicability)

LOS = length of stay, ICU = intensive care unit, CLRT = continuous lateral rotational therapy, MV = mechanical ventilation

#### No benefit of CLRT.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1134 Bailey 2006 PMID: 17133183 DOI: 10.1097/01.CCM.000 0251130.69568.87 Specification of study: prospective cohort study	103 pts Inclusion criteria: - respiratory failure pts - >4 days of mechanical ventilation - pts admitted to respiratory ICU Exclusion criteria: - mechanical ventilation for ≤ 4 days Per Branch		Assessment of early activity as part of routine respiratory ICU care		<b>Primary outcomes:</b> - safety - feasibility	<ul> <li>Primary outcomes: <ul> <li>activity events included 233 (16%) sit on bed,</li> <li>454 (31%) sit in chair, and 762 (53%) ambulate</li> </ul> </li> <li>for pts with endotracheal tube, there were a total of 593 activity events (249 (42%) were ambulation)</li> <li>&lt;1% activity-related AEs (fall to the knees without injury, feeding tube removal, systolic blood pressure &gt;200 mm Hg, systolic blood pressure &lt;90 mm Hg, and desaturation &lt;80%)</li> <li>no patient was extubated during activity</li> </ul>	3

AE = adverse event, pts = patients

Early activity is safe and feasible in patients with respiratory failure.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1136 Bouadma 2010 PMID: 20068461 DOI: 10.1097/CC M.0b013e31 81ce21af Specification of study: Pre- and post- intervention observational study	1.649 ventilator-days Inclusion criteria: - mechanically ventilated pts Per Branch		<b>Educational session</b> about hand-hygiene, glove-and- gown use, backrest elevation, cuff-pressure maintenance, orogastric tube use, gastric overdistension avoidance, good oral hygiene and elimination of non- essential tracheal suction)	Before education	Outcomes: - compliance to each indicator - VAP	Outcomes: - compliance to each indicator (baseline vs 24-months after implementation): - hand-hygiene: n.s. - glove-and-gown use: n.s. - backrest elevation: 5% vs 58%; p < 0.001 - cuff-pressure maintenance: 40% vs 89%; p < 0.001 - orogastric tube use: 52% vs 96%; p < 0.001 - gastric overdistension avoidance: 20% vs 68%; p < 0.001 - good oral hygiene: 47% vs 90%; p < 0.001 - elimination of non-essential tracheal suction: 41% vs 92%; p < 0.001 - VAP: 26.7% vs 11.1%; p < 0.0001	3

VAP = ventilator associated pneumonia

Additional education improves the usage of preventive factors for VAP and reduces the rate of VAP.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
# 1138 Goldhill 2007	35 studies (20 RCTs, 15 nonrandomized, uncontrolled or retrospective studies) between 1987 and 2004					Outcomes:	
PMID: 17192526	only 15 RCTs were included in meta-analysis <sup>1-15</sup>		Rotational therapy using a programmable bed	Manual turning of patients by nurses every 2	Outcomes: - days of MV - days in ICU - mortality	<ul> <li>days of MV<sup>2, 7-9, 15</sup>: n.s.</li> <li>days in ICU<sup>2, 6,7,9,13,15</sup>: n.s.</li> <li>mortality<sup>1,2, 4-7, 10-15</sup>: n.s.</li> <li>incidence of pneumonia when used as</li> </ul>	1 → 3 (downgrade d for indirectness
DOI: not available	Inclusion criteria: - rotational therapy to prevent		that turns on its longitudinal axes	hours	- incidence of pneumonia	prophylaxis <sup>1-4, 7-11</sup> : OR: 0.40 (95% Cl 0.27, 0.58); l <sup>2</sup> = 0%	/ applicability and not only RCTs)
Specification of study:	or treat respiratory complications					- incidence of pneumonia when used as treatment <sup>15</sup> : OR 0.34 (95% CI 0.18, 0.67); $I^2 = 0\%$	KCTS)
Review and Meta-Analysis	Per Branch						

ICU = intensive care unit, MV = mechanical ventilation, OR = odds ratio, RCT = randomized controlled trial

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
# 1139 Bukhari 2012 PMID: 22426908 DOI: not available Specification of study: Prospective longitudinal study	n = 2747 pts Inclusion criteria: mechanically ventilated ICU pts Exclusion criteria: non-ventilated pts Per Branch		VAP prevention bundle: - elevation of the head of the bed (30-45°) - daily sedation weaning - daily readiness-to-wean from ventilator assessment - PUD prophylaxis - DVT prophylaxis		Primary outcome: - adherence to intervention Secondary outcomes: - rate of pneumonia - days on mechanical ventilation - ICU LOS	<ul> <li>Primary outcome: <ul> <li>adherence to intervention:</li> <li>78.9% compliance rate of VAP bundle overall</li> <li>correlation between the VAP rate and its bundle compliance (<i>r</i>-value not reported; p = 0.001)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>rate of pneumonia (Pre-interventional vs. post-interventional):</li> <li>2.5 infections per 1000 patient days vs. 1.98 infections per 1.000 patient's days (<i>no p</i>-value reported)</li> <li>reduction of VAP rate 1.41 per 1000 ventilator days (<i>no p</i>-value reported)</li> <li>days on mechanical ventilation: not reported</li> <li>ICU LOS: not reported</li> </ul> </li> </ul>	4

DVT = deep venous thrombosis, ICU = intensive care unit, MV = mechanical ventilation, pts = patients, PUD = peptic ulcer disease, VAP = ventilator-associated pneumonia

The VAP-prevention bundle is feasible and well tolerated by patients, relatives and staff.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1141 Hamlin 2013 PMID: 18510182 DOI: 10.1097/01.dcc .0000311593.8 7097.6a Specification of study: article	number of pts not stated Inclusion criteria: mechanical ventilated patients on the ICU Exclusion criteria: not stated Per Branch		Turning (Lateral Rotation)	Patients acted as their own control	<b>Endpoints:</b> hemodynamic effects of turning	Endpoint: - negative hemodynamic effects of PPV + lateral rotation: Increased pericardial pressure with constrained left ventricular filling/ reduced venous return/ reduced mean arterial pressure, stroke volume, cardiac output /change in the determinants of the venous pressure gradient / reduced SvO2 / inferior vena cava compression that creates a vascular waterfall condition no statistics or p-values mentioned	4

ICU = intensive care unit, PPV = positive pressure ventilation, pts= patients

There are several negative effects of PPV and Lateral Rotation. No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
# 1142 Balas 2013 PMID: 23758115 DOI: 10.3928/0098 9134- 20130530-06 Specification of study: Case study	no systematic inclusion of studies Per Branch		ABCDE-Bundle			<ul> <li>immobilization needs to be reduced</li> <li>ambulation protocols should be implemented</li> <li>contraindications need to be defined</li> <li>early mobilization improves DVT, LOS, functional status</li> </ul>	4

DVT = deep vein thrombosis; LOS = length of stay

No detailed assessment was carried out because there is higher-quality evidence available.

Reference, Study Type		and Controls t #, characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Eviden ce Grade
1155 Mauri 2010 PMID: 20196878 No DOI <b>Specification</b> of study: prospective pilot trial	<ul> <li>no pneumo</li> <li>Exclusion crit</li> <li>intubated </li> <li>hemodynam</li> <li>recent esop</li> <li>pulmonary re</li> <li>head or spin</li> </ul>	efore inclusion nia or ALI <b>teria:</b> 72h nic instability phageal, gastric or	1 withdrew consent (LHG)	Semi- recumbent group 30° for 64h	<b>Lateral-Horizontal</b> <b>group</b> Supine position with turning from side to side every 2- 4h 12-24h	<b>Outcomes:</b> - aspiration (measured as pepsin assay) - VFD - VAP	<b>Results:</b> - aspiration: n.s. - VFD: SRG 8 (0–21) vs LHG 24 (12–25); p = 0.04 - VAP: n.s.	3

MV = Mechanical Ventilation, ALI = Acute Lung Injury, SRG = Semi-recumbent Group, LHG = Lateral-Horizontal Group, VAP = Ventilator-associated pneumonia, VFD = Ventilator-free Days, pts.= patients

Lateral-horizontal positioning does not reduce the risk for aspiration or ventilator associated pneumonia but increases the number of ventilator-free days.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1156 Deye 2012 PMID: 23093247 DOI: 10.1007/s00134- 012-2727-5 Specification of study: prospective, crossover study	24 pts. Inclusion criteria: - at least 1 failure of SBT before the end of a 2h trial - and/or 1 unexplained extubation failure (need for reintubation within the 72 h after extubation not related to an untreated cardiac failure or an intercurrent infectious disease or to laryngeal dyspnea) Exclusion criteria: - hemodynamic instability - uncontrolled sepsis - patient refusal - age less than 18 years - current esophageal pathology Per Branch		three postures: seated position in bed (90°LD), the semi- seated (45°), and the supine (0°) positions (applied in random order)	patient acted as their own controls	Primary outcomes: - breathing pattern - occlusion pressure (P0.1) - PEEPi - inspiratory muscle effort	<b>Primary outcome:</b> - 45° position with lowest levels of effort ( $p \le 0.01$ ) and occlusion pressure ( $p < 0.05$ ) - Respiratory effort: lowest at 45° in 18/24 patients - PEEPi and PEEPi-related work higher in 0° ( $p \le 0.01$ ), - respiratory effort, heart rate, and P <sub>0.1</sub> values increased in 45° ( $p < 0.05$ ) - median Ccw highest in 0° ( $p = 0.03$ ), CcW lower in 45° ( $p < 0.05$ ) - correlation between PEEPi values and the PTP ( $p < 0.001$ ) - correlation PEEPi values and the WOB ( $p < 0.001$ ) - correlation PEEPi values and the P <sub>0.1</sub> ( $p < 0.001$ )	3

Ccw = chest wall compliance, iPEEP = intristic positive end expiratory pressure, LD = legs down, pts = patients, SBT = spontaneous breathing trial, WOB = work of breathing

A 45° position helps to unload the respiratory muscles, moderately reduces PEEP<sub>i</sub>, and is often considered comfortable and the semi-seated position may help the weaning process in ventilator-dependent patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Outcome	Primary Results	Evidence Grade
# 1158 Delaney 2006 PMID: 16684365 DOI: 10.1186/cc49 12 Specification of study: systematic review and meta-analysis	15 RCTs , 1169 pts <sup>1-15</sup> no trial met all the validity criteria. Inclusion criteria: - critically ill adults receiving MV - kinetic or rotating bed as intervention applied for > 24 hours - intermittent manual turns for the control group - prospective randomized or pseudo-randomized design - outcome measures included any of the incidence of nosocomial pneumonia, mortality, duration of mechanical ventilation, or ICU or hospital LOS		Kinetic or rotating bed applied for at least 24 hours in critically ill mechanically ventilated adult patients	Intermittent manual turns	Outcomes: - incidence of nosocomial pneumonia - the effect of the intervention on mortality, duration of mechanical ventilation, ICU length of stay and hospital length of stay - complications associated with the use of these beds	Significant differences between groups in: - reduction in the incidence of nosocomial pneumonia (pooled odds ratio (OR) 0.38, 95% confidence interval (CI) 0.28 to 0.53) No significant differences between groups in: - reduction in mortality (pooled OR 0.96, 95%CI 0.66 to1.14) - duration of MV (pooled standardized mean difference (SMD) -0.14 days, 95%CI, -0.29 to 0.02) - duration of ICU stay (pooled SMD - 0.064 days, 95% CI, -0.21 to 0.086) - duration of hospital stay (pooled SMD 0.05 days, 95% CI -0.18 to 0.27).	1→2

CI = confidence interval, ICU = intensive care unit, LOS = length of stay, OR = odds ratio, pts = patients, RCT = randomized controlled trial, SMD = standardized mean differences, VAP = ventilator associated pneumonia

Kinetic bed therapy is associated with a significant reduction in the odds of developing nosocomial pneumonia in mechanically ventilated patients. However, it is not associated with a significant reduction in the mortality, duration of mechanical ventilation, or ICU or hospital length of stay.

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Reference, Study Type	Cases and (Participant #, C Tota	haracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1162 Burtin 2009 PMID: 19623052 DOI: 10.1097/CCM .0b013e3181 a38937 Specification of study: RCT	90 critically ill pts Inclusion criteria - expected to have a p of at least 7 more day Exclusion criteria - conditions impairing movement - anticipated fatal out - body length <1.5 m - preexisting diagnosis neuromuscular weakr status epilepticus - coagulation disorder - intracranial pressure - psychiatric disorderss - cardiorespiratory ins Per Bra 45	the cycling come s causing ness, acute stroke, s >20 mmHg s or severe agitation stability	23 for ICU discharge assessment (14 interventio n, 9 control)	<b>Cycling exercise</b> - session 5 days a week, using a bedside cycle ergometer starting at D5 the earliest - standard of care	Standard of care: Respiratory + Physiotherapy and a standardized mobilization session of the upper and lower extremities on 5 days per week	Primary endpoint: - 6MWD at hospital discharge Secondary outcomes: - isometric quadriceps force and functional status - weaning time - ICU and hospital LOS - 1 year mortality Sample size - sample size of 36 pts was required in each group to demonstrate a difference of 50 m in 6MWD with a statistical power of 80% and an alpha level of 0.05	Primary outcome         - 6MWD (196 m [126–329         m] vs. 143 m [37–226 m];         29 [19–43] vs. 25 [8–36]         %pred., p < 0.05)	2

ICU = intensive care unit, LOS = length of stay, m = meter, n.s. = not significant, pts = patients, RCT = randomized controlled trial, 6MWD = 6 minute walking distance

Early exercise in critically ill patients led to improved functional exercise capacity and self-perceived functional status.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1164 Schellongowski 2007	12 pts					Significant differences between groups in:	
PMID: 17252227 DOI: 10.1007/s00134 -006-0513-y <b>Specification of</b> <b>study:</b> prospective observational study	<ul> <li>acute respiratory failure requiring MV</li> <li>diagnosis of ALI or ARDS made within 96h prior to inclusion</li> <li>decision to treat patients with CLRT taken within 48h prior to inclusion</li> <li>hemodynamically stable during rotation over the max. angle for at least 12h prior to inclusion</li> <li>18 – 85 years</li> </ul>	-	CLRT		<ul> <li>Primary endpoints:</li> <li>pulmonary gas exchange (blood gas analysis)</li> <li>respiratory mechanics (static lung compliance)</li> <li>hemodynamics (blood pressure, cardiac index, pulmonary shunt fraction)</li> </ul>	<ul> <li>lower static compliance was observed in lateral steep position than in supine position (p &lt; 0.001)</li> <li>PaCO2, lower in supine position than in left and right lateral steep position (p &lt; 0.01)</li> <li>No significant differences between groups in:</li> <li>no significant changes in PaO2/FiO2 ratio, mean arterial blood pressure, pulmonary shunt fraction, or cardiac index</li> </ul>	3

ALI = acute lung injury, ARDS = acute respiratory distress syndrome, CLRT = continuous lateral rotation therapy, MV = mechanical ventilation, pts = patients

Lateral steep position does not lead to benefits with respect to oxygenation or hemodynamics.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1167 Goldhill 2008 PMID: 18412649 DOI: 10.1111/j.1365- 2044.2007.0543 1.x Specification of study: Prospective observational study	n = 393 pts Inclusion criteria: - ICU pts Exclusion criteria: - incomplete data sheets Per Branch		Positioning of the patient		Outcomes: - time between turns - number of turns - type of positioning (Outcomes not divided into primary or secondary outcomes)	Outcomes:- time between turns: $\circ$ in total (h; mean [SD]; median [IQR]):4.85 [3.3]; 4.0 [3.0-5.5] $\circ$ per RASS (n [%] and hours between turns as median [IQR]):RASS = 1; 19 (5.0%); 3.6 [2.8-4.9]RASS = 2; 159 (41.5%); 4.0 [3.0-6.0]RASS = 3; 31 (8.1%); 4.5 [3.1-5.7]RASS = 4; 86 (22.5%); 3.7 [3.0-4.8]RASS = 5; 42 (11.0%); 4.0 [3.0-4.6]RASS = 6; 34 (8.9%); 4.2 [3.4-5.0] $\circ$ no significant association between average time between turns and age, weight, height, gender, respiratory diagnosis, intubated and ventilated, sedation score, day of week or nurse to patient ratio positions (% of time; mean [SD]): $\circ$ on back: 46.1 [24.1]turned to left: 28.4 [17.0]turned to right: 25.5 [16.1]turn to side < 30°: 46.3 [39.2]	3

ICU = intensive care unit, IQR = interquartile range, pts = patients, RASS = Ramsay agitation sedation score, SD = standard deviation

Time between turns seems not to be associated with age, weight, height, gender, respiratory diagnosis, intubated- or ventilated-status, sedation score, day of week or nurse to patient ratio.

Reference,	Cases and Controls (Participant #, Characteristics)	Drop- out	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	Total	Rate					
#1168 Zhiqiang 2013 PMID: 23127305 DOI: 10.1016/j.apmr.20 12.10.023 Specification of study: Systematic review	17 studies (7 RCT, 1 quasi-RCT, 7 case- series, 1 prospective cohort study, 1 historical controlled study), 1.614 pts <sup>1-17</sup> Inclusion criteria: - population consisted of adults, at least 60% with MV for 24 h or more - study design: RCT, quasi-RCT, or other comparative study with or without controls or case series with 10 or more cases - active mobilization in ICU or HDU setting - primary outcome: physical function - Secondary outcomes: hospital outcomes Exclusion criteria: - intervention started at home or was conducted both during hospital stay and hospital-discharge - studies which only assessed effects of passive mobilization		Active mobilisation	Standard of care / other form of mobilisation / no control	Primary outcomes: - physical function (muscle strength, physical activity, mobility and functional ability, and health-related QoL) Secondary outcomes: - hospital outcomes (weaning rate, duration of MV, ventilator- free days, LOS in the ICU/HDU and hospital, mortality, discharge destination, costs, adverse events)	no meta analysis was conducted	1 → 4 (different study types, no meta analysis, indirectness / applicability)

ADL = activities of daily living, AE = adverse event, BI = Barthel index, FIM = functional independence measure, HDU = high dependency unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, QoL = quality of life, 6MWD = six-minute walk distance

Active mobilisation therapy for patients who have undergone mechanical ventilation in ICU settings appears to have no severe adverse effects.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1169 Simonis 2011 PMID: 22729756 DOI: 10.1007/s0039 2-012-0484-7 Specification of study: RCT	89 patients Inclusion criteria: - cardiogenic shock (defined by a systolic blood pressure of<90 mmHg, or a cardiac index of <2.2 l/m2 and a pulmonary wedge pressure > 15 mmHg, or the need for inotropic or vasopressor support) - prolonged ventilator support, defined as modified oxygenation index (PaO2/ FiO2) <300 torr (40 kPa) after 24–30 h of ventilator therapy Exclusion criteria: - rhythmogenic instability requiring repeated resuscitation procedures - active bleeding precluding rotation - body weight above the upper weight limit for the KT device (i.e., more than 140 kg) Per Branch 45 KT 44 SC	n/a	Kinetic therapy = continuous lateral rotation - continuously turned through an arc of about 80° every 7 min - percussion was administered by the automated percussion mode of the beds at nine beats/s for 10 min every 2 h	Standard care	Primary outcomes: - occurrence of nosocomial pneumonia (defined as combined occurrence of fever, new radiological infiltrate occurring more than 48 h after admission, and growth of typical microorganism in tracheal aspirates) Secondary outcomes: - occurrence of pressure ulcer - all-cause mortality during the first year after hospital admission	Primary outcomes: - hospital-acquired pneumonia occurred in 10 patients in KT and 28 patients in SC (p<0.001) Secondary outcomes: - pressure ulcers were seen in 10 versus 2 patients (p<0.001) - hospital mortality tended to be lower in KT, and 1-year all- cause mortality was 41 % in KT and 66 % in SC (p = 0.028)	2 → 3

KT = kinetic therapy, SC = standard care

In this study the use of kinetic therapy reduced the rate of pneumonia and pressure ulcers and decreased mortality in patients with cardiogenic shock.

Reference, Study Type	(Participant #,	l Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1173 Staudinger 2010 PMID: 19789440 DOI: 10.1097/CCM .0b013e3181 bc8218 Specification of study: RCT		nonia, ALI, ARDS OS > 48h or rotation cured rib ht > 150kg, height //V		CLRT - rotation started with 60° angle and escalated to max. angle over 2-6 h - performed continuously, aiming for a rotation time of >18hrs/day	Standard of care	Primary endpoint: - 28-day prevalence of VAP Secondary outcomes: - hospital LOS - duration of MV - ventilator-free days during the first 28 days after intubation - ICU and Hospital Mortality - number and duration of atelectasis - prevalence of ALI/ARDS - changes in oxygenation and Lung injury score - complications (Pressure sores or Intolerance)	Primary endpoint: - prevalence of VAP was 11% in the rotation group and 23% in the control group (p = 0.048) Secondary outcomes: - hospital LOS shorter in CLRT group (p=0.01) - duration of ventilation (8 ± 5 vs. 14 ± 23 days, p = 0.02) - ventilator free days more in rotation group (p=0.04) - ICU und hospital Mortality (n.s.) - number and duration of atelectasis lower in rotation group (p=0.001) - prevalence of ALI/ARDS not stated - changes in oxygenation and lung injury score not stated - complications (pressure sores or	2
	75	75				sores or incolerance)	intolerance) not stated	

ALI = acute lung injury, ARDS = acute respiratory distress syndrome, LOS = length of stay, MV = mechanical ventilation, n.s. = not significant, pts = patients, VAP = ventilator associated pneumonia

# Application of CLRT led to a reduction of the prevalence of VAP, a shorter ventilation time and length of stay. The results were not statistically significant after adjusting for disease severity.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1177 Swadener- Culpepper 2008 PMID: 18574374 DOI: 10.1097/01.C NQ.00003250 51.91473.42 Specification of study: retrospective case control study			<b>CRLT</b> <u>1. Early:</u> begin within 48h <u>2.Late:</u> begin more than 48h	Without CLRT (comparison group)	Primary endpoints: - hospital LOS - number of ventilation days - overall treatment costs Secondary outcomes: - pts rates of readmission into ICU - rate of reintubation	Primary endpoints: - mean LOS in the ICU, early intervention group: 13.1 days, compared to late intervention group: 18.9 days (p=0.02) compared to comparison group: 18.4 days (p<0.05) - cost to treat for early intervention group was less than for late intervention group (p=0.01), compared with comparison group (p=0.056) - hospital LOS, ventilation days (n.s.) Secondary outcomes: - reintubation rate, readmission to ICU (n.s.)	4

CCU = critical care unit, CLRT = continuous lateral rotation therapy, LOS = length of stay, PEEP = positive end expiratory pressure, pts = patients; n.s.= not significant

#### CLRT reduced critical care LOS as well as treatment costs.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1178 Thomas 2007 PMID: 17444315 https://doi.org/1 0.1177/0310057 X0703500214 <b>Specification of</b> <b>study:</b> systematic review	12 publications between 1951 and 2007 (1 review and 11 empiric articles) <sup>1-12</sup> Inclusion criteria: - age > 16 years - RCTs - ICU MV pts - lateral positioning Exclusion criteria: - positioning during surgery or anaesthesia - pts with one-lung ventilation - pts with lung transplant or lung resection - several interventions - exclusively investigation of validity/repeatability of measurements from clinical monitoring after intervention		Lateral positioning in MV ICU patients	Standard of Care	Endpoints: - oxygenation - compliance - haemondynamics - incidence of pneumonia - mortality - long-term outcomes		1 → 4 (downgraded due to quality of evidence of included articles and indirectness/ applicability)

Pts = patients, ICU = intensive care unit, MV = mechanically ventilated

#### The effectiveness of lateral positioning on clinical outcomes in critically ill patients is unclear due to limited evidence. No detailed assessment was carried out because higher-quality evidence is available on this topic.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1182 Thomas 2006 PMID: 17628197 DOI: 10.1016/j.hrtIng.2 006.10.008 Specification of study: A prospective, within-subjects, randomized cross-over study	N=34 patients Inclusion criteria: presence on chest radiograph of: a) bilateral lung pathology consistent with ALI or ARDS criteria b) or unilateral lung pathology c) or no lung pathology intubated and mechanically ventilated hemodynamically stable with: a) heart rate 60–130 beats/min b) mean arterial blood pressure 70–120 mm Hg c) no compromising arrhythmias d) ICP<20 mm Hg (if measured) e) mean pulmonary arterial pressure<30 mm Hg, pulmonary capillary wedge pressure 8-17 mm Hg (if measured via pulmonary arterial (PA) catheter. - no, unilateral, or bilateral pulmonary infiltrates on chest radiograph Exclusion criteria: - age < 18 years - preexisting severe chronic respiratory disease (FEV1less than 40%) - burn injuries - chest wall abnormalities - pulmonary barotrauma (eg, pneumothorax) - paralysing medications - nitric oxide - contraindications to lateral positioning (eg, unstable spinal fractures). Per Branch		90 degree lateral position at the supine starting position (TO)	Same population but data at different time stamps - 30 min in lateral turn (T30) - 2 hours into lateral turn (T120) - 30 min post return to supine position (T150)	Primary endpoints: - arterial blood gas - respiratory mechanic - hemodynamic data Secondary endpoints: - AE	Primary outcomes: No significant differences between the groups in: - PaO2/FiO2 p=0.15 - RR p>0.05 - heart rate p>0.05 Significant differences between the groups in: - dynamic compliance (T0=56±18.6>(T30=49.9±18 ; T120=49.2±17) L/cmH20,P=0.01) - cardiac index increased at T30 (T0=3.7±1.2, T30=4.8±1.3 L/min/m2, P<0.01) Secondary outcomes: - 21% AEs but primarily minor and transient	2→3
	34 34						

AE = adverse event, ALI = acute lung injury, ARDS = acute respiratory distress syndrome, ICP = intracranial pressure

In this heterogeneous population, lateral positioning had no beneficial effect on gas exchange. However, in ventilated patients who were hemodynamically stable, it was well tolerated and not associated with significant serious adverse events.

Reference, Study Type	Cases and Co (Participant #, Cha Total	aracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1184 Clark 2012 PMID: 22879442 DOI: 10.2522/ptj.20 110417 Specification of study: Retrospective Cohort Study	2.176 pts Inclusion criteria: - patients admitted Exclusion criteria: - cardiovascular, pr and musculoskelet - vascular access re femoral or dorsal p line - nasotracheal intu to high extubation - use of pressor or medications to ma hemodynamic stat - conditions requiri continuous sedatic paralytic medicatic open abdominal w (fascia visible) Per Bran Group 1 n = 1044	ulmonary tal instability equiring pedis arterial ubation due trisk inotropic sintain bility ring on or ons, such as younds		Early mobilisation - group 1: Prior to implementation of EMP - group 2: After implementation of EMP EMP: - Level 1:		Primary outcome: - safety (related to nosocomial complication s and adverse events) Secondary outcome: - TBICU LOS - hospital LOS	Group differences (group 1 vs. group 2): - age [mean (SD]]: 44.1 (18.5) vs. 46.6 (19.6), p ≤ 0.01 - gender male (%): 75.1% vs. 70.5%, p ≤ 0.02 - ISS score [median (SD]]: 23.6 (12.8) vs. 22.2 (12.8), p = 0.01 - prevalence of arthrits (%): 5.5 vs. 9.7, p ≤ 0.001 - prevalence of cardiovascular disorder (%): 31.8 vs. 37, p = 0.01 - prevalence of neurologic disorder (%): 8.2 vs. 10.9, p = 0.03 - prevalence of obstructive sleep apnea (%): 1.6 vs. 3.0, p = 0.04 - prevalence of pulmonary disorder (%): 7.7 vs. 10.5, p = 0.03 Primary outcome (group 1 vs. group 2): - safety: ( <i>RRs adjusted for age and injury severity</i> ) ○ Nosocomial complications (%): - airway: 7.1 vs. 3.5, p < 0.001; Crude RR: 0.5 (95% CI: 0.34-0.73), p < 0.05; Adjusted RR: 0.52 (95% CI: 0.35-0.76), p < 0.05 - cardiovascular: 12.2 vs. 15.2, p = 0.04; Crude RR: 1.33 (95% CI: 1.06- 1.68), p < 0.05; Adjusted RR: 1.26 (95% CI: 0.99-1.59), p > 0.05 - psychiatric: 3.4 vs. 1.7, p = 0.02; Crude RR: 0.60 (95% CI: 0.35-1.04), p > 0.05; Adjusted RR: 0.60 (95% CI: 0.35-1.03), p > 0.05 - pulmonary (excluding pneumonia): 49.2 vs. 42.2, p ≤ 0.001; Crude RR: 0.81 (95% CI: 0.72-0.92), p < 0.05; Adjusted RR: 0.84 (95% CI: 0.74-0.95), p < 0.05 - renal/genitourinary: 18.3 vs. 15.0, p = 0.04; crude RR: 0.86 (95% CI: 0.74-0.95), p < 0.05 - vascular: 15.3 vs. 8.5, p ≤ 0.001; crude RR: 0.83 (95% CI: 0.67-1.02), p > 0.05 - vascular: 15.3 vs. 8.5, p ≤ 0.001; crude RR: 0.57 (95% CI: 0.40-0.73), p < 0.05; adjusted RR: 0.58 (95% CI: 0.45-0.75), p < 0.05 - vascular: 15.3 vs. 8.5, p ≤ 0.001; crude RR: 0.74 (95% CI: 0.48-0.85), p < 0.05; adjusted RR: 0.79 (95% CI: 0.50-0.90), p < 0.05 - pneumonia: 27.9 vs. 22.4, p ≤ 0.01; crude RR: 0.78 (95% CI: 0.66- 0.92), p < 0.05; adjusted RR: 0.79 (95% CI: 0.66-0.93), p < 0.05 - pneumonia: 27.9 vs. 22.4, p ≤ 0.01; crude RR: 0.78 (95% CI: 0.66- 0.92), p < 0.05; adjusted RR: 0.79 (95% CI: 0.66-0.93), p < 0.05 - Do.5 - TBICU LOS [mean (SD]]: 11.0 (16.2) vs. 10.4 (14.0), p = 0.33 - hospital LOS [mean (SD]]: 19.2 (28	4

EMP = early mobilisation protocol, LOS = length of stay, pts = patients, TBICU = trauma and burn intensive care unit

Implementation of an early mobilization program with daily screening and assistance in mobilization seems safe and feasible, as it reduces nosocomial complications (with exception of cardiovascular complications) and decreases hospital length of stay in critically ill patients admitted to trauma and burn ICU.

Iteration       Rate         18 patients (intervention and control group)       18 patients (intervention and control group)       Inclusion criteria: - ratio of partial pressure of arterial oxygen (FiO2) of or less than 200 while receiving positive end expiratory pressure (PEEP)of at least 5 cm of water - radiographic evidence of bilateral pulmonary infiltrates - absence of clinical evidence of left atrial hypertension or a pulmonary capillary wedge pressure of less than 18 mmHg       Lateral position       Supine position       Endpoints: comparing supine, right, left lateral positions (>60 degree) in: - PaO2 - arterial blood gas parameters - respiratory mechanics - hemodynamic parameters       Outcomes: no significant differences between the groups in: (supine vs decubitus) - mecan PaO2 (84.6 vs 03.9) p=0.23 - arterial blood gas parameters p=0.05 - respiratory mechanics - hemodynamic parameters       3 -         Specification of study: A pilot study       - othest X-ray showed pleural effusion, pneumothorax or atelectasis - contraindication to using the lateral position, such as fracture of the spine (within 2 weeks), thoracoabdominal surgery or severe hemodynamic instability       A       A	Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	# 1186 Tongyoo 2006 PMID: 17718246 DOI: not available Specification of study:	<pre>(intervention and control group) Inclusion criteria: - ratio of partial pressure of arterial oxygen (PaO2) to the fraction of inspired oxygen (FiO2) of or less than 200 while receiving positive end expiratory pressure (PEEP)of at least 5 cm of water - radiographic evidence of bilateral pulmonary infiltrates - absence of clinical evidence of left atrial hypertension or a pulmonary capillary wedge pressure of less than 18 mmHg Exclusion criteria: - aged &lt; 14 years - evidence of cerebral edema - chest X-ray showed pleural effusion, pneumothorax or atelectasis - contraindication to using the lateral position, such as fracture of the spine (within 2 weeks), thoracoabdominal surgery or severe hemodynamic instability Per Branch</pre>	Rate		•	comparing supine, right, left lateral positions (>60 degree) in: - PaO2 - arterial blood gas parameters - respiratory mechanics - hemodynamic	no significant differences between the groups in: (supine vs decubitus) - mean PaO2 (84.6 vs 90.3) p=0.23 - arterial blood gas parameters p>0.05 - respiratory mechanics p>0.05	3 → 4

The PaO2 increased while in the right lateral position in patients with predominant left pulmonary infiltration or bilateral infiltration. This effect may be due to the small sample size. A larger randomized controlled study is needed.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1198, Muscedere 2008 PMID: 18359430 DOI: 10.1016/j.jcrc. 2007.11.014 Specification of study: Practice guidelines	109 trials Inclusion criteria: database search from 1980 to October 1, 2006 for: - randomized controlled trials - systematic reviews - meta-analysis -> topic prevention of VAP Exclusion criteria: - RCTs of stress ulcer prophylaxis Per Branch		Depending on trial	Depending on trial	Endpoints: - physical strategies - positional strategies - pharmacologic strategy	Physical outcomes: recommendation to reduced VAP risk: - orotracheal intubation (1 level 2 trial, 4 level 2 trials) - new circuits for each patient (2 level 2 trials) - change airway humidifier every 5-7 days (2 level 2 trials) - closed endotracheal suctioning system (6 level 2 trials) - change of suctioning system for every patient (1 level 2 trial) - use of subglottic secretion drainage for patients MV > 72h no recommendation to reduce VAP risk: - Systematic search for maxillary sinusitis (1 level 2 trial) - Use of airway humidifier (12 level 2 trials - Use of bacterial filters (1 level 2 trial) Positional outcomes: positional strategies: recommendation to reduce VAP risk: - kinetic bed therapy (7 level 2 trials) - semi recumbent positioning (1 level 1 trial, 1 level 2 trial) no recommendation to reduce VAP risk: - prone positioning (2 level 2 trials)	$1 \rightarrow 3$ (outdated)

MV = mechanical ventilation, VAP = ventilator-associated pneumonia

There are a growing number of evidence-based strategies for VAP prevention, which, if applied in practice, may reduce the incidence of this serious nosocomial infection.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1214 Wang 2016 PMID: 26743945 DOI: 10.1002/146518 58.CD009946.pu b2 <b>Specification of</b> <b>study:</b> Systematic Review and Meta-Analysis	10 publications from 1999-2012 (10 RCTs, n = 878 pts) <sup>1-10</sup> Inclusion criteria: - RCTs - population: endotracheal intubated and mechanically ventilated adult pts - Studies comparing SRP vs. SP or different degrees of body positioning Exclusion criteria: - cluster randomisation (due to "herd effect") - cross-over design due to ("carry-over effect") - quasi-RCTs (due to potential problems with imbalanced prognosis and failure to conceal the treatment allocation) - >15% of pts. Ineligible for SRP Per Branch	24 pts (due to lost to follow- up in one trial)	SRP (30°-60°) or 45°	SP (0°-10°) or (25°-30°)	<ul> <li>Primary outcomes: <ul> <li>clinically suspected</li> <li>VAP (according to the definition of CDC 1997)</li> <li>microbiologically confirmed VAP,</li> <li>composite of clinically suspected and clinically confirmed VAP</li> <li>ICU mortality</li> <li>hospital mortality</li> </ul> </li> <li>Secondary outcomes: <ul> <li>ICU LOS</li> <li>hospital LOS</li> <li>duration of ventilation</li> <li>use of antibiotics</li> <li>adverse events (device-related, dysphagia, laryngospasm, aspiration, venous thromboembolism, pressure ulcers, haemodynamic instability)</li> </ul> </li> </ul>	<ul> <li>Significant differences between groups in:</li> <li>clinically suspected VAP [8 trials comparing SRP (30°-60°) vs. SP (0°-10°); n = 759 pts]</li> <li>14.3% vs. 40.2%, no p-value reported</li> <li>R R 0.36 (95% CI 0.25-0.5)</li> <li>heterogeneity: p= 0.2, l<sup>2</sup> = 29%</li> <li>R D 25.7% (95% CI 20.1%-30.1%)</li> <li>GRADE: moderate confidence in the estimate</li> </ul> <b>Non-significant differences between groups in:</b> <ul> <li>clinically suspected VAP [2 trials comparing SRP 45° vs. SRP 25° or 30°; n = 91 pts]</li> <li>22.2% vs. 26.1%, no p-value reported</li> <li>R R 0.74 (95% CI 0.35-1.56)</li> <li>GRADE: wery low confidence in estimates</li> </ul> microbiologically confirmed VAP <ul> <li>3 trials comparing SRP (30°-60°) vs. SP (0°-10°); n = 419 pts</li> <li>12.6% vs. 31.6%, no p-value reported</li> <li>R R 0.44 (95% CI 0.11-1.77),</li> <li>heterogeneity: p = 0.0006, l<sup>2</sup> = 87%</li> <li>GRADE: very low confidence in the estimate</li> <li>1 trial comparing SRP 45° vs. SP 25°; n = 30 pts</li> <li>23.5% vs. 38.5%, no p-value reported</li> <li>R 0.61 (95% CI 0.2-1.84)</li> <li>GRADE: very low confidence in estimates</li> </ul> composite of clinically suspected and clinically confirmed VAP: none of the included studies reported this outcome ICU mortality <ul> <li>2 trials comparing SRP (30°-60°) vs. SP (0°-10°); n = 307 pts</li> <li>29.8% vs. 34.3%, no p-value reported</li> <li>R R 0.57 (95% CI 0.59-1.27)</li> <li>heterogeneity: p = 0.43, l<sup>2</sup> = 0%</li> <li>GRADE: low confidence in the estimate</li> <li>1 trial comparing SRP (30°-60°) vs. SP (0°-10°); n = 346 pts</li> <li>23.5% vs. 30.8%</li> <li>R R 0.57 (95% CI 0.59-1.20)</li> <li>heterogeneity: p = 0.32, l<sup>2</sup> = 12%</li> <li>GRADE: low confidence in the estimates</li> </ul>	1

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			<ul> <li>RR 1.00 (95% CI 0.38 vs. 2.65)</li> </ul>
			<ul> <li>GRADE: very low confidence in estimates</li> </ul>
			- ICU LOS
			$\circ$ 3 trials comparing SRP (30°-60°) vs. SP (0°-10°);
			n = 346 pts
			<ul> <li>MD = -1.64 days (95% CI -4.41 to 1.14), no p-value reported</li> </ul>
			heterogeneity: p = 0.21, l <sup>2</sup> = 35%
			<ul> <li>GRADE: moderate confidence in the estimate</li> </ul>
			<ul> <li>1 trial comparing SRP 45° vs. SP 30°; n = 30 pts</li> </ul>
			<ul> <li>MD = -1.6 days (95% Cl -0.88 to 4.08), p = 0.21</li> </ul>
			<ul> <li>GRADE: very low confidence in the estimate</li> </ul>
			<ul> <li>hospital LOS [2 trials comparing SRP (30°-60°) vs. SP (0°-10°); n = 458 pts]:</li> </ul>
			<ul> <li>MD = -3.35 days (95% CI -7.8 to 1.09), no p-value reported</li> </ul>
			• heterogeneity: $p < 0.00001$ , $l^2 = 93\%$
			<ul> <li>GRADE: very low confidence in the estimate</li> </ul>
			- duration of ventilation
			<ul> <li>4 trials comparing SRP (30°-60°) vs. SP (0°-10°); n = 458 pts</li> </ul>
			<ul> <li>MD -3.35 days (95% CI -7.80 to 1.09), no p-value reported</li> </ul>
			<ul> <li>heterogeneity: p = &lt; 0.00001, l<sup>2</sup> = 93%</li> </ul>
			<ul> <li>1 trial comparing SRP 45° vs. SP 25°; n = not reported</li> </ul>
			<ul> <li>Pts without VAP: mean ventilated hours 61.5 vs. 63.1 (45° and 25° respectively); SD not reported</li> </ul>
			Pts with VAP: mean ventilated hours 160 vs. 172.5 hours (45° and
			25° respectively); SD not reported
			<ul> <li>use of antibiotics [3 trials comparing SRP (30°-60°) vs. SP (0°-10°); n = 284</li> </ul>
			pts]:
			<ul> <li>84.8% vs. 84.2%, no p-value reported</li> </ul>
			<ul> <li>RR 1.00 (95% Cl 0.97-1.03)</li> </ul>
			<ul> <li>adverse events [1 trial comparing SRP (30°-60°) vs. SP (0°-10°); n = 221</li> </ul>
			pts]:
			• pressure ulcers
			<ul> <li>28% vs. 30%, no p-value reported</li> </ul>
			<ul> <li>RR 0.91, 95% CI 0.6-1.38</li> </ul>
			<ul> <li>GRADE: low confidence in the estimate</li> </ul>
			<ul> <li>No other events across all studies reported</li> </ul>

CDC = Center for Disease Control and Prevention, CI = confidence interval, GRADE = quality of evidence according to study limitations, consistency of effect, imprecision, indirectness and publication bias, ICU = intensive care unit,  $I^2 = I^2$ -statistic testing for heterogeneity across studies, MD = mean difference, pts = patients, RCTs = randomized controlled trials, RD = risk difference, RR = risk ratio, SRP = semi-recumbent position, SP = supine position; VAP= ventilator associated pneumonia; LOS=Length of stay;

Semi-recumbent positioning (30°-60°) might reduce clinically suspected VAP compared to supine position (0°-10°), but there is high risk of bias and under-reporting of adverse events.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1226 McBeth, 2007 PMID: 17434374 DOI: 10.1016/j.am jsurg.2007.01 .013 Specification of study: prospective cohort study	37 non-consecutive patients with 300 observations Inclusion criteria: - a 3-way bladder catheter had been placed because of concerns regarding IAH or ACS Exclusion criteria: - could not be flexed at the waist because of concerns about spinal or hemodynamic stability Per Branch 37		HOB positions: 0° (supine) and at HOB increases of 10°, 20°, 30°, and 45°	patients acted as their own control	<b>Endpoints:</b> - IAP at each HOB angle -BMI, PEEP, temperature, diagnosis, Riker sedation score in correlation with IAP difference	Endpoint: - HOB increase associated with IAP, with stronger correlations at 30° and 45° (10° : p=0.04; 20°: p = 0.001, 30°: p < 0.001, 40°: p< 0.001) -BMI significant (p=0.01); PEEP (p=0.001), Temperature (p=0.02), Neurologic (non-trauma) diagnostic category (p <0.001) - Riker sedation score n.s. (no p-value)	3

ACS = abdominal compartment syndrome, BMI = body mass index, HOB = head-of-bed, IAP = intra-abdominal pressure, IAH = intra-abdominal hypertension, n.s. = not significant, PEEP = positive end-expiratory pressure, pts = patients

There is a significant, positive association between IAP and HOB positioning in critically ill patients.

Reference, Study Type	Cases and Controls (Participant #, characteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total	Nate					
1242 Gosselink 2008							
PMID: 18283429							1→5
https://doi.org/10.1007 /s00134-008-1026-7							(out of date)
<b>Specification of study:</b> ERS / ESICM guideline	Per Branch						

ERS = European Respiratory Society, ESICM = European Society of Intensive Care Medicine

Appropriately prescribed physiotherapy may improve clinical outcomes of critically ill patients and reduce risks and arising costs associated with intensive care.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	(Participant #	nd Controls , characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1251 Hanekom 2012 PMID: 23232109 DOI: 10.1186/cc118 94 Specification of study: Prospective study	Inclusion criteria: - not stated Exclusion criteria: - age <16 years	ICU in a tertiary rica → 193 patients <b>Branch</b>		Protocol Care: allocated Physiotherapist providing evidence- based/protocol care based on the ICU admission date	standard of care	Endpoints: - Ventilation - Mortality - LOS/ time to discharge - TISS-28 - BI	<ul> <li>Results: <ul> <li>pts admitted to ICU during protocol care were less likely to be intubated after admission (p = 0.005) or to fail an extubation (p = 0.04)</li> <li>protocol care pts were discharged from the hospital 4 days earlier than usual-care patients (p = 0.05), which did not reach statistical significance</li> <li>tendency noted for more pts to reach independence in transfers (p = 0.07) and mobility (p = 0.09) categories of the BI</li> <li>no difference in mortality (p = 0.52)</li> <li>mean difference in the cumulative daily unit TISS-28 score during the two intervention periods was 1.99 TISS-28 units (P = 0.04).</li> </ul> </li> </ul>	3
	96	97					(r - 0.04).	

ICU = intensive care unit, LOS = length of stay, pts = patients, BI = Barthel Index, TISS = Therapeutic Intervention Scoring System

A physiotherapy service approach that includes an exclusively allocated physiotherapist providing evidence-based/protocol care that addresses pulmonary dysfunction and promotes early mobility improves patient outcome.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1254, Vasquez, 2007 PMID: 17161433 DOI: 10.1016/j.jss.2 006.10.023 Specification of study: Prospective observational cohort study	n = 45 pts Inclusion criteria: - trauma patients aged 18 or older - admitted to the ICU with indwelling bladder catheter Exclusion criteria: - pregnancy - unstable pelvis fracture with pelvic hematoma - previous cystectomy - traumatic bladder ruptures - contraindications to supine - semi-recumbent, or tilt positioning - hemodynamic instability - massive infusion protocol - supra-pubic catheter Per Branch		bladder pressures measures in: (1) supine position, or 0° from horizontal; (2) 15° above horizontal; (3) 30° above horizontal; (4) semi-recumbent defined as 45° above horizontal; (5) 30° above horizontal with a 15° above- horizontal bed tilt	patients served as his/her own control	<ul> <li>Primary outcome:</li> <li>effect of HOB elevation on bladder pressure measurements</li> <li>effect of BMI Status on bladder pressure measurements</li> <li>BMI status as a covariate</li> </ul>	<ul> <li>Primary outcome: <ul> <li>effect of HOB elevation on bladder pressure measurements: HOB elevation (within-subjects effect) demonstrated statistically significant differences, F(4) = 114.478, P = 0.001; significant differences at the P = 0.001 level between all body positions</li> <li>effect of BMI status on bladder pressure measurements supine position, F(2) = 11.404, P = 0.001; between "normal" and "overweight" as well as and "obese,"</li> <li>15° HOB elevation, F (2) = 10.873, P = 0.001 between "normal" and "obese,"</li> <li>30° HOB elevation, F(2) = 6.473, P = 0.004 between "normal" and "obese"</li> <li>45° HOB position, F(2) = 7.112, P = 0.002 between "normal" and "obese"</li> <li>30° with 15° tilt HOB position, F(2) = 7.112, P = 0.001 between "normal" and "obese"</li> </ul> </li> </ul>	3

BMI = body mass index, HOB = head-of-bed, ICU = intensive care unit, pts = patients

Elevating HOB significantly increases bladder pressure measurement and bladder pressure measurements in non-supine positions may not provide valid interpretation for IAP, and more so in cases of increased body mass index.

Reference, Study Type	Cases and Con (Participant #, Chara Total	acteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1260, Yi, 2012 PMID: 22033056 DOI: 10.1016/j.jcrc.2011. 08.010 Specification of study: prospective cohort study	88 pts. Inclusion criteria: - 18 years or older - sedated - mechanical ventila - demonstrated at lef factor for IAH or ACS Exclusion criteria: - unable to tolerate body position (becars spinal precautions, intracranial hyperter hemodynamic instal - IAP measurements contraindicated (suc recent bladder surge or pregnancy) Per Brance	east 1 risk S changes in use of nsion, bility, etc) s were ch as ery, injury,		HOB elevation: supine, 10°, 20°, 30°, 45°	patients acted as their own control	Endpoints: - comparison of IAP, APP, and FG among body position (HOB angle elevated) - APACHE II - SOFA - IAH and ACS	Endpoints: - head of bed increase was found to be significantly associated with IAP, with stronger correlations at HOB increases of 30° and 45° (p < 0.05) - head of bed elevation was associated with clinically significant decreases in APP and FG (p< 0.05) - APACHE II: IAH group 17.36 ± 11.99, non-IAH: 13.12 ± 7.26 p = 0.05 - SOFA n.s. -prevalence of IAH and ACS were 28.4% and 2.3%	3
	88							

ACS = abdominal compartment syndrome, APACHE = acute physiology and chronic health evaluation, APP = abdominal perfusion pressure, FG = filtration gradient, HOB = head-of-bed, IAH = intraabdominal hypertension, IAP = intra-abdominal pressure, pts = patients, SOFA = sequential organ failure assessment

There is a significant and independent relationship between IAP and HOB positioning in critically ill patients, with the HOB of 30° and 45° showing significant difference.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1262, Kasotakis, 2012 PMID: 22067629 DOI: 10.1097/CCM .0b013e3182 376e6d Specification of study: Prospective single-center cohort study.	113 pts Inclusion criteria: - older than 18 years - expected to stay in the SICU for at least 24 hours - met criteria for baseline functional independence (defined as a Barthel Index score > 70 obtained from a proxy describing patient function 2 weeks before admission) Exclusion criteria: - enrolled in another clinical trial Per Branch	N=11 (Death)			Primary endpoint: - SOMS taken on the morning after SICU admission explains variance of SICU LOS. Secondary endpoint: - SOMS explains variance of hospital LOS and in-hospital mortality	<ul> <li>Primary endpoint:</li> <li>SOMS taken on the morning after SICU admission explains variance of SICU LOS.</li> <li>SOMS values of 0, 1, 2, 3, and 4 were associated with 8 (4–12), 7 (5–9), 6 (2.5–9), 3 (2–4), and 2 (1.5–3) days (means and confidence intervals [CI] in parentheses) of SICU LOS</li> <li>SOMS (coefficient,2651817; 95% CI –0.3508765 to –0.1794869; p = .0001) predicted SICU LOS</li> <li>Secondary endpoint:</li> <li>SOMS explains variance of hospital LOS and inhospital mortality:</li> <li>SOMS was the only variable that correlated with inhospital mortality (p = .001).</li> <li>SOMS (coefficient,1359776; CI –0.1747335 to – 0.0972217]; p = .0001) as independent predictor of overall hospital LOS</li> </ul>	3

LOS = length of stay, pts = patients, SICU = surgical intensive care unit, SOMS= SICU optimal mobility score

In surgical critically ill patients presenting without preexisting impairment of functional mobility, the surgical intensive care unit optimal mobility score is a reliable and valid tool to predict mortality and intensive care unit and hospital length of stay.

Reference,	(Participant #, Characteristics)		Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	Total	Rate			ropulation		Grade
#1263, Kayambu, 2013 PMID: 23528802 DOI: 10.1097/CCM.0b0 13e31827ca637 Specification of study: A systematic review and meta- analysis	<ul> <li>10 studies included in meta- analysis (10 RCTs, n=790 pts)<sup>1-10</sup></li> <li>Inclusion criteria: <ul> <li>RCTs, systematic reviews or meta-analyses from 1992 to 2012</li> <li>published in English, French, Chinese, and Tamil.</li> <li>investigating physical intervention in ICU patients (defined as activities such as positioning, stretching, EMS, ROM exercise, resistive exercise, ergometry, walking, splinting, mobilization activities and aerobic train)</li> </ul> </li> <li>Exclusion criteria: <ul> <li>unoriginal studies, such as case reports, reviews</li> <li>pre-post-designs, observational, retrospective designs</li> <li>only chest physical therapy</li> <li>non-randomized controlled trials</li> </ul> </li> </ul>		Physical intervention - passive or active limb mobilization - ambulation - electrical muscle stimulation - ergometry	standard of Care (no or minimal physical therapy)	<ul> <li>peripheral muscle strength <ul> <li>MRC score</li> <li>handgrip strength</li></ul> </li> <li>respiratory muscle strength</li><li>physical function</li><li>QoL</li><li>ventilator-free days</li><li>hospital LOS</li><li>ICU LOS</li><li>incidence of mortality</li></ul>	<ul> <li>Significant effect in pooled analysis:</li> <li>peripheral muscle strength (MRC): positive effect following physical intervention (pooled hedges g = 0.27; 95% CI: 0.02-0.52; n = 244 [127,117], p = 0.03)</li> <li>respiratory muscle strength: moderate effect following physical intervention (pooled hedges g = 0.51; 95% CI 0.12-0.89; n = 105 [53, 52], p = 0.01)</li> <li>physical function: small effect following physical intervention (pooled hedges g = 0.46; 95% CI 0.13, 0.78; n = 143 [74, 69], p = 0.01)</li> <li>QoL: Small effect following physical intervention (pooled hedges g = 0.40; 95% CI 0.08-0.71; n = 154 [78, 76], p = 0.01)</li> <li>ventilator-free days: small effect following physical intervention (pooled hedges g = 0.38; 95% CI 0.16-0.59; n = 334 [172, 162], p &lt; 0.01</li> <li>hospital LOS: small reduction following physical intervention (pooled hedges g = -0.34; 95% CI -0.53 - 0.15; n = 441), p &lt; 0.01)</li> <li>ICU LOS: small reduction following physical intervention (pooled hedges g = -0.34; 95% CI -0.53 - 0.15; n = 441), p &lt; 0.01)</li> <li>Non-significant effect in pooled analysis:</li> <li>peripheral muscle strength (handgrip strength): no effect following physical intervention (pooled hedges g = -0.34; 95% CI -0.51 - 0.18; n = 597 [285, 312], p &lt; 0.01)</li> <li>Non-significant effect in pooled analysis:</li> <li>peripheral muscle strength (handgrip strength): no effect following physical intervention: pooled hedges g = 0.07; 95% CI: -0.23-0.38; n = 194 [100,94], p = 0.03</li> <li>mortality: no effect following physical intervention (Odds ratio, 1.0; 95% CI 0.54, 1.85; n = 274 [120, 154], p = 1.0)</li> </ul>	$1 \rightarrow 3$ (downgraded as not only RCTs included and for indirectness / applicability)

EMS = electric muscle stimulation, ICU = intensive care unit, LOS = length of stay, pts = patients, QoL = quality of life, ROM = range of motion

Physical intervention in critically ill ICU patients improves peripheral and respiratory muscle strength, physical function, quality of life, increases ventilator-free days and shortens ICU as well as hospital length of stay.

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Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1272, Malkoc, 2009 PMID: 19011583 DOI: 10.1097/MRR.0b 013e3282fc0fce Specification of study: Retrospective and prospective study	568 patients who were in the ICU at Dokuz Eylu Inclusion criteria - MV - admitted to a six-bed, internal medicine ICU Exclusion criteria - ARDS - acute pulmonary eder - acute head injury, MA peak inspiratory airway H2O (as recorded from -acute bronchospasm, o patients had sustained developed any complication Per Br	na P less than 60 mmHg, pressure over 40 cm the ventilator) or whether the any injury or ation		<b>Chest physiotherapy</b> <b>program</b> (consisted of modifying postural drainage, percussion, vibration, coughing, and stimulation techniques, deep breathing exercises, suctioning, bed exercises, and mobilization)	Standard nursing care	outcome measurements - blood gas analysis - number of days when mechanical ventilation was provided - ventilation dependence - LOS ICU	Outcome (not subdivided in primary / secondary) - ventilation dependence (days) mean SD: intervention= 14.0 ± 5.9, control= 20.0 ± 6.1; p<0.05 - LOS ICU (days) mean SD: intervention= 15.8 ± 8.5, control= 25.5 ± 4.5; p<0.05 No statistical differences: - between the groups in the analysis of blood gas values - the length of time when mechanical ventilation was provided (mean 6.1 days physiotherapy group 5.2 days control group),	4
	N=277	N=233						

ARDS = acute respiratory distress syndrome, ICU = intensive care unit, LOS = length of stay, MAP = mean arterial pressure, MV = mechanical ventilation, SD = standard deviation

In conclusion, this study shows that the use of physiotherapy can result in reducing the period of treatment required in the ICU.

Reference, Study Type	Cases and Co (Participant #, Cha Total	aracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1274, Morris, 2008 PMID: 18596631 DOI: 10.1097/CCM.0b013e 318180b90e Specification of study: Prospective cohort study	330 ICU patients with acute requiring mechanical ventila inclusion criteria - age >18 years - mechanically ventilated via tube Exclusion criteria - inability to walk without as ICU illness - cognitive impairment befo (nonverbal) - preadmission immunocom (prednisone 20 mg/d for 2 w - neuromuscular disease tha weaning (myasthenia gravis, sclerosis, Guillian-Barre), acu - body mass index (BMI)>45 - hip fracture, unstable cerv fracture - mechanical ventilation 48 from an outside facility, curr transferring hospital stay 72 - CPR at admission, DNR at hospitalization within 30 day - cancer therapy within last - readmission to ICU within a hospitalization N= 165	ation a an endotracheal ssistance before acute re acute ICU illness upromised status veeks) at could impair , amyotrophic lateral ute stroke vical spine/ pathologic hrs before transfer rent hospitalization or hrs admission, ys before admission 6 months current		Mobility protocol ( daily mobility therapy)	Usual care	Primary outcome - proportion of patients receiving physical therapy in patients surviving to hospital discharge Secondary outcome - days until first out of bed - ventilator days - ICU LOS - hospital LOS	Primary outcome - in-hospital mortality control= 18.2%(: 30 of 165) vs. intervention=12.1%( 20 of 165 ); (p = 0.125); received physical therapy(with in- hospital death) : n=5 of (control, n=2; intervention, n=3) Secondary outcome - days to first out of bed: control= 13.7 (11.7–15.7) vs. intervention = 8.5 (6.6–10.5); p<0.0001 - ventilation days: control= 9.0 (7.5–10.4)vs. Intervention=7.9 (6.4–9.3); p=0.298 - ICU LOS: control= 8.1 (7.0–9.3) vs. Intervention=7.6 (6.3–8.8); p=0.084 - hospital LOS: control= 17.2 (14.2–20.2) vs. intervention= 14.9 (12.6– 17.1); p=0.048	3
	COT -N	COT-NI						

CPR = cardiopulmonary resuscitation, DNR = do not resuscitate, hrs = hours, ICU= intensive care unit

A mobility team using a mobility protocol initiated earlier physical therapy that was feasible, safe, did not increase costs, and was associated with decreased intensive care unit and hospital length of stay in survivors who received physical therapy during intensive care unit treatment compared with patients who received usual care.

	Total	-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1280 Olkwoski 2012 PMID: 22652987 https://doi.org /10.2522/ptj.2 0110334 Specification of study: Retrospective study	25 pts. In 1 American ICU from 01.2011 to 05.2011 Inclusion criteria: -ICU admission -Age > 18y -SAH-diagnosis through lumbar puncture or brain CT -Ability to open eyes to voice and move one extremity on command -Lindegaard ratio $\leq 3,0$ or MCA MFV $\leq 120$ cm/s -110 $\geq$ MAP $\geq 80$ mmHg -ICP $\leq 15$ mmHg -No AEs criterion present at inclusion Exclusion criteria: -Age < 18y -ICU-admission > 14 days -Withdraw of care -Trauma or AV-malformation as SAH cause -Seizure Per Branch 25	n/a	Early mobilization 30-60 min/day: positioning, education, functional training and exercise in supine, sitting, standing and walking position as long as the pt remained stable / no AEs happened		No sample size calculation due to study design <b>Primary Endpoint:</b> -Feasibility: number of sessions attempted, or failed due to unmet participation criteria, reasons why criteria were not met -Safety: 30-day mortality rate, quantity and types of AEs <b>Secondary outcome</b> : -Type of mobilization -Number of out-of-bed sessions and with walking ≥ 15,24m, -Time to out-of-bed and walking ≥ 15,24 m -Barthel at discharge -Post-discharge destination	Primary Endpoint:-Attempted sessions = 332-failed sessions = 46 (Lindegaard ratio ≥ 3.0 orMCA MFV ≤ 120 cm/s = 27, MAP ≤ 80 mm Hg = 6,ICP ≥ 15 = 6, unable to open eyes in response tovoice = 3, respiratory rate ≥ 40 = 2, MAP ≥ 110mm Hg = 1 and heart rate ≥ 40 = 1)-30-day mortality rate = 0%-AEs in 17/ 286 sessions (MAP < 70 mm Hg = 9,	4

Pts = patients, SAH = subarachnoid hemorrhage, ICU=intensive care unit; MAP = mean arterial pressure, ICP = intracranial pressure, HR = heart rate, RR = respiratory rate, MCA MFV = mean flow velocity in the middle cerebral artery, AEs = adverse events; BI = Barthel index; AV = arterio-venous; m=meters

An early mobilization program for patients with SAF is safe and feasible.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1288, Bezbaruah, 2022 PMID: not available DOI: http://dx.doi.org/10 .4103/2278- 344X.105081 Specification of study: RCT	15 patients who were May 25, 2011 and Oc the medical ICU, Fath College Hospital inclusion criteria patients : - on MV with respirat - in age group 30-60 y - out of sedation with Scale (GCS) of 14/15 - with stable vitals Exclusion criteria patients with: - any neurological im - unstable fractures, s and fractures of the I Per Br	e on MV between stober 30, 2011 at her Muller Medical tory pathology years n Glasgow Coma pairment spinal fractures, ower limb		EM	Usual care	Outcome (not more defined) - days first out of bed - days of weaning - LOS ICU	Outcome - first out of bed (mean days): intervention= 2.88 (min 2-max 4) (SD: 0.641) vs. control= 7.71 (min 7-max 9) (SD: 0.756), p=0.001 - mean days of weaning: intervention=5.38(min 5- max 6) (SD: 0.518) vs. control= 7.43 (min 7-max 9) (SD:0.787); p=0.001 - mean LOS ICU (days): intervention= 5.63(min 5 - max 6) (SD:0.518) vs. control= 8 (min 7 - max 9) (SD: 0.577); p=0.001	2 → 4 (downgraded for high risk of bias and pilot trial only)
	N=8	N=7						

EM = early mobilization, ICU = intensive care unit, LOS = length of stay, max = maximum, min = minimum, MV = mechanical ventilation, SD = standard deviation

Early mobilisation showed better outcome compared to routine physiotherapy in reducing the length of ICU stay in mechanically ventilated patients.

Reference, Study Type	(Participant #,	d Controls characteristics) ıtal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1290 Abrams 2014 PMID: 24571627 https://doi.org/10.1 186/cc13746 <b>Specification of the</b> <b>study:</b> Retrospective cohort study	BTR and BTT)	ry respiratory or		Active PT during ECMO	Without PT	No sample size calculation due to study design No primary endpoint defined Extracted Endpoints: - Intention for ECMO therapy - survival to transplant or discharge - discharge disposition among survivors - safety No power calculation.	<ul> <li>Results: <ul> <li>intention for ECMO therapy (n [%]):</li> <li>a. BTT: 26 pts (26%)</li> <li>b. BTR: 74 (74%)</li> </ul> </li> <li>survival to transplant or discharge: <ul> <li>a. survival to transplant of BTT pts (n [%]): 10 (53%)</li> <li>b. survival to discharge of BTR pts (n [%]): 14 (88%)</li> </ul> </li> <li>discharge disposition (n [%]): <ul> <li>a. home 13 (57%)</li> <li>b. acute rehabilitation 8 (35%)</li> <li>c. subacute rehabilitation 2 (9%)</li> </ul> </li> <li>safety: no patient-related or circuit-related complications as a result of physical therapy treatment sessions.</li> </ul>	4

Pts = patients, ICU = intensive care unit, ECMO = extracorporeal membrane oxygenation, BTR = bridge to recovery, BTT = bridge to transplant; PT=physical therapy

Active physiotherapy in patients treated with ECMO due to respiratory or cardiac failure seems safe. No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1292, Schweickert, 2009 PMID: 19446324 DOI: 10.1016/S0140- 6736(09)60658-9 Spezification of study: RCT	<ul> <li>104 pts</li> <li>Inclusion criteria</li> <li>≥18 years</li> <li>MV for less than 72 h</li> <li>expected to continue for at least 24 h</li> <li>baseline functional independence</li> <li>Exclusion criteria</li> <li>rapidly developing neuromuscular disease, cardiopulmonary arrest, irreversible disorders wit 6-month mortality estimated at &gt; 50%, raised intracranial pressure, absent limbs, o enrolment in another triated</li> <li>Per Branch</li> <li>49 55</li> </ul>	0	daily sedation interruption + exercise and mobilisation (physical and occupational therapy)	standard care with physical and occupation al therapy	Primary Outcome - number of patients returning to independent functional status at hospital discharge Secondary Outcomes - number of hospital days with delirium - MV free days within 28 days - ICU and hospital LOS - Barthel Index -number of functionally independent ADLs -distance walked without assistance -ICU-acquired paresis - hand-grip strength	Primary Outcome - return to independent functional status at hospital discharge 29 (59%) 19 (35%) p=0.02 Secondary Outcomes - ICU delirium (days) 2.0 (0.0–6.0) 4.0 (2.0–7.0) p=0.03 - time in ICU with delirium (%) 33% (0–58) 57% (33–69) p=0.02 - hospital delirium (days) 2.0 (0.0–6.0) 4.0 (2.0–8.0) p=0.02 - hospital days with delirium (%) 28% (26) 41% (27) p=0.01 - Barthel Index score at hospital discharge 75 (7,5–95) 55 (0–85) p=0.05 - ICU-acquired paresis at hospital discharge 15 (31%) 27 (49%) p=0.09 - ventilator-free days 23,5 (7,4–25,6) 21,1 (0,0–23,8) p=0.05 - duration of mechanical ventilation (days) 3.4 (2.3–7.3) 6.1 (4.0–9.6) p=0.02 - LOS in ICU (days) 5.9 (4.5–13.2) 7.9 (6.1–12.9) p=0.08 - greatest walking distance at hospital discharge (m) 33.4 (0–91.4) 0 (0–30.4) p = 0.004 - independent ADLs total at ICU and hospital discharge n.s. - MRC score n.s. - hand-grip strength n.s. - hospital LOS n.s. - mortality n.s.	2

ADL = activity of daily living, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, n.s. = not significant, pts = patients

The combination of daily interruption of sedation with physical and occupational therapy was safe and resulted in better functional outcomes at hospital discharge, a shorter duration of delirium and more ventilator-free days.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#1301, <b>Titsworth</b> <b>2012</b> PMID: 22462507 DOI: 10.3171/2012. 2.JNS111881 <b>Specification</b> <b>of study:</b> pre-post- study	all consecutive pa to NICU from Apr through July 31, 2 <b>Exclusion criteria</b> - < 18 years old - hemodynamicly - end of life care <b>Per B</b> 10 month preintervention	il 1, 2010, 2011 (n = 3291) ::	10.6% $\pm$ 4.7% of patients had to discontinue the PUMP plus program for clinical contraindications. Additionally, 2.2% $\pm$ 0.2% of patients per day refused to participate and only 1.4% $\pm$ 0.2% of patients had the protocol discontinued for inappropriate or indiscernible reasons	comprehensi ve mobility initiative utilizing the <b>Progressive</b> <b>Upright</b> <b>Mobility</b> <b>Protocol</b> <b>(PUMP) Plus</b>	Patients in the pre- intervention period	no sample size calculation Endpoints: - NCU LOS - hospital LOS - mobility level assessed with the I-MOVE tool - occurrence of pressure ulcers - AEs - hospital acquired infections - occurrence of VAP	<ul> <li>93.8% ± 4% of patients who had no contraindication to the protocol were participating</li> <li>Significant results: <ul> <li>overall mobility among neurointensive care patients increased by 300% (p&lt;0.0001)</li> <li>reduction in NCU LOS (p&lt;0.004), Hospital LOS (p&lt;0.001), hospital-acquired infections (p &lt; 0.05), and ventilator-associated pneumonias (p &lt; 0.001), and decreased the number of patient days in restraints (p &lt; 0.05)</li> </ul> </li> </ul>	3
	(8025 patient days)	(4455 patient days)					no increase in AEs was observed	

AE = adverse events, LOS = length of stay, NCU = neurointensive care unit, VAP = ventilator associated pneumonia

Among neurointensive care unit patients, increased mobility can be achieved quickly and safely with associated reductions in LOS and hospital-acquired infections using a structured mobilization program.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1303 Alexiou 2009 PMID: 19327314 https://doi.or g/10.1016/j.j crc.2008.09.0 03 <b>Specification</b> of study: systematic review with meta-analysis	7 publications until December 2007 (7 randomized with 1355 pts) <sup>1-7</sup> Inclusion criteria: - MV - treatment in ICU Exclusion criteria: - age < 18 years - examination of the effect of the position on oxygenation - intervention during surgical or radiographic procedure Per Branch		Prone- and semi- recumbent 45° positional strategies	Standard of Care	Endpoints: -incidence of VAP -all-cause mortality until ICU discharge -ICU LOS -duration of MV until death or extubation	<ul> <li>Significant differences between groups: <ul> <li>incidence of VAP: Comparison of 45° semirecumbent position vs. supine position on the development of <i>clinically</i> diagnosed VAP resulted in an effect favouring intervention (OR 0.47, 95% CI 0.27-0.82; n = 3 articles with 337 pts<sup>1-3</sup>)</li> </ul> </li> <li>Non-significant differences between groups: <ul> <li>incidence of VAP:</li> <li>a. comparison of prone position vs. supine position on the development of <i>clinically</i> diagnosed VAP resulted in a trend favouring intervention (OR 0.80, 95% CI 0.60-1.08; n = 4 articles with 1018 pts<sup>4-7</sup>)</li> <li>b. comparison of 45° semirecumbent position vs. supine position on the development of <i>microbiologically</i> diagnosed VAP resulted in a trend favouring intervention (OR 0.59, 95% CI 0.15-2.35; n = 3 articles with 337 pts<sup>1-3</sup>)</li> <li>all-cause mortality: inconsistent data <ul> <li>a. comparison of 45° semirecumbent position vs. supine position on the incidence of death resulted in a trend favouring intervention (OR 0.59, 95% CI 0.15-2.35; n = 3 articles with 337 pts<sup>1-3</sup>)</li> <li>comparison of 45° semirecumbent position vs. supine position on the incidence of death resulted in a trend favouring intervention (OR 0.86, 95% CI 0.54-1.37; n = 3 articles<sup>1-3</sup>)</li> <li>b. comparison of prone position vs. supine position on the incidence of death resulted in a trend favouring intervention (OR 0.92, 95% CI 0.72-1.18; n = 4 articles<sup>4-7</sup>)</li> <li>ICU LOS: No difference between prone and supine groups (WMDs: 1.54 days of ICU stay; 95% CI -1.54 to 4.62; n = 2 RCTs with 978 pts<sup>4.7</sup>)</li> <li>duration of MV: No difference between prone and supine groups (WMDs: -0.45 days of MV; 95% CI -1.58 to 0.68; n = 3 RCTs with 882 pts<sup>4.6,7</sup>)</li> </ul> </li> </ul></li></ul>	1 → 2 (indirect ness)

Pts = patients, ICU = intensive care unit, MV = mechanical ventilation, VAP = ventilator-associated pneumonia, LOS = length of stay, OR = odd's ratio, WMDs = weighted mean differences

45° semirecumbent positioning reduces the development of clinically diagnosed VAP in critically ill mechanically ventilated patients.

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Reference, Study Type	(Participant #,	d Controls , characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
1305 van Delft 2021 PMID: 23801900 DOI:10.1097/01823 246-201324020- 00003 <b>Specification of</b> <b>study:</b> Prospective Observational Study	Inclusion criteria: - 18 years of age of least one femoral of central venous cath catheters, and arter catheters for hemo monitoring) -met criteria for a l (awake, able to fol and hemodynamic Exclusion criteria: - pts. femoral shea	heters, dialysis erial odynamic PT intervention low most directions ally stable)		PT with femoral catheters		Extracted Endpoint:	<b>Results:</b> - no catheter related mechanical or thrombotic complications either during or immediately following a mobility session, which was usually 15 to 20 minutes after the activities	3

Pts. = patients; PT = Physical therapy; AE = Adverse events

Physical therapy sessions, including standing and walking were feasible and safe in cardiovascular ICU patients with femoral catheters.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2002 Alhazzani 2022 PMID: 35569448 DOI: 10.1001/jam a.2022.7993 Specification of study: Multicenter, non-blinded, randomized clinical trial	400 pts with COV Inclusion criteria: - adults - not intubated - requiring oxyger invasive ventilation Exclusion criteria - invasive MV - contraindication positioning - risk of complicat positioning - self-Prone Positi enrollment Per Bi 205	: (≥ 40%) or non- on : is to prone tions from prone foning prior to		Awake prone positioning (until relative improvement in FiO <sub>2</sub> requirement by 40% from the baseline value that was sustained for 24 hours; endotracheal intubation; discharge from ICU)	<b>Usual care</b> without prone positioning	Primary endpoint: endotracheal intubation within 30 days of randomization Secondary outcomes: - mortality at 60 days - days free from invasive MV or noninvasive ventilation at 30 days - days free from the ICU or hospital at 60 days - adverse events - serious adverse events	Awake prone positioning group: median duration of prone positioning 4 days after randomization 4.8 hours/day (IQR 1.8-8.0 hours/days) <b>Primary endpoint:</b> by day 30, 70 of 205 pts(34.1%) in the prone positioning group were intubated vs. 79 of 195 patients (40.5%) in the control group [hazard ratio: 0.81 (95% Cl, 0.59 to 1.12), p = 0.2; absolute difference: -6,37% (95% Cl, -15.83% to 3.1%)] <b>Secondary outcomes:</b> - mortality: Prone positioning did not significantly reduce mortality at 60 days [hazard ratio: 0.93 (95% Cl, 0.62 to 1.40), p = 0.54; absolute difference: -1.15% (95% Cl, -9.40% to 7.10%)] - days free from invasive MV or noninvasive ventilation at 30 days: n.s - days free from the ICU or hospital at 60 days: n.s - adverse events: 21 pts (10%) , most frequently reported musculoskeletal pain or discomfort from prone positioning [13 of 205 pts(6.34%)] and desaturation [2 of 205 pts(0.98%)] - serious adverse events: n>>one in either group	2

FiO<sub>2</sub> = inspired fraction of oxygen, ICU = intensive care unit, IQR = interquartile range, MV = mechanical ventilation, pts = patients

Awake prone positioning in patients with acute hypoxemic respiratory failure from COVID-19 does not significantly reduce endotracheal intubation within 30 days compared with usual care.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Inter- vention	Control	Optimal Population	Primary Results	Evidence Grade
#2003 Protti	15 patients Inclusion criteria: - a diagnosis of ARDS						
<b>2022</b> PMID:	<ul> <li>ongoing invasive mechanical ventilation with deep sedation and neuromuscular blockade</li> <li>prone positioning prescribed by the attending</li> </ul>				Endpoints: - lung morphological		
35526009 DOI:	physician within 3 days of endotracheal intubation Exclusion criteria:		РР	Patients acted as their own control	response - global inflation - regional inflation - lung functional response		4
10.1186/s1305 4-022-03996-0	<ul> <li>already undergone a lung CT after endotracheal intubation</li> <li>too unstable for transfer to the radiology unit</li> <li>body weight exceeded 100 kg</li> </ul>				- association between morphological and functional responses		
Specification of study: institutional	- none of the authors was available for collecting data, due to the exceptional clinical workload at that time						
review	Per Branch						

ARDS = acute respiratory distress syndrome, CT = computer tomography, PP = prone position

In fifteen patients with COVID-19, prone positioning decreased alveolar collapse, hyperinflation, and homogenized lung aeration. A similar response has been observed in other ARDS, where prone positioning improves outcome.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and (Participant #, Cl Tota	haracteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2008 Liu 2022 PMID: 35400079 DOI: 10.1155/2022 /4579030 Specification of the study: single center retrospective study	238 pts study duration: 3 consecutive days Inclusion criteria: - ARDS pts with PaO2/Fi mmHg - age 16-75 years Exclusion criteria: - non-invasive ventilation intubation - previous lung diseases - pelvic, cervical, or spin requiring a fixed positio - uncontrolled increase - multiple traumas with - pregnancy - severe hemodynamic i arterial blood pressure - < 60 mmHg or systolic mmHg) Per Bra	on before orotracheal nal fracture or n in ICP unstable fractures instability (mean blood pressure >200		РР	No PP	<b>Primary outcomes:</b> - P/F - compliance of respiratory system	Significant differences between groups in: - improvement of P/F and Crs in the PP group over 3 consecutive days (p < 0.05) - shorter total mechanical ventilation time ( $5.1 \pm 1.4$ vs. $9.3 \pm 3.1$ days, P < 0.05) - shorter invasive ventilation time ( $4.9 \pm 1.2$ vs. $8.7 \pm 2.7$ days, P < 0.05) - shorter ICU stay ( $7.4 \pm 1.8$ vs. $11.5 \pm 3.6$ days, P < 0.05) - higher extubation rate ( $95.6\%$ vs. 84.4%, P < 0.05) - less atelectasis ( $15$ vs. 74, P < 0.05) and pneumothorax ( $17$ vs. $24$ , P > 0.05) - more 28-day ventilator-free days ( $21.6 \pm 5.2$ vs. $16.2 \pm 7.2$ days, P < 0.05) - lower mortality ( $4.4\%$ vs. $13.3\%$ , P < 0.05).	4

ICP = intracranial pressure, PP = prone position, pts = patients

Among PC cases with moderate to severe ARDS, PP can correct hypoxemia more quickly, improve Crs, reduce atelectasis, increase the extubation rate, shorten mechanical ventilation time and length of ICU stay, and reduce mortality.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2010 Fralick 2022 PMID: 35321918 DOI: 10.1136/bmj- 2021-068585 Specification of study: Multicenter pragmatic randomized clinical trial	with verbal instr Exclusion criteri - ineligible or de - FiO2 >50% - unable to obtai - could not pror - > 48 hours afte - discharged befor- transferred to be consent - tracheostoma	suspected id-19 mental oxygen ion of inspired ndently lie prone uction <b>a:</b> clined in consent ne or admission ore consent	13 (n = 4 withdrawal of consent, n = 7 no consent, n = 2 determined as ineligible)	<b>Prone positioning:</b> median time spent in prone position up to the first 72 hours: 6h (1.5- 12.8)		Primary endpoint: - composite outcome of in-hospital death, mechanical ventilation, or worsening respiratory failure defined as needing at least 60% fraction of inspired oxygen for at least 24 hours Secondary endpoints: - time spent in prone position - change in the ratio of oxygen saturation to fraction of inspired oxygen - time to discharge from hospital - rate of serious events	Primary endpoint: - no differences between both groups (FiO <sub>2</sub> > 60%: Prone (18(14)) Control (17(14)) OR 0.92 (0.44 – 1.92)) Secondary outcome: - median (IQR) time spent in prone: 6 (1.5 -12.8) vs. 0 (0-2) - median (IQR) S/F ratio after 72 hours: 336 (216-438) vs. 336 (232-443) - median (IQR) change in S/F ratio in first 72 hours 14 (-52-94) vs. 49 (-32-102) - median (IQR) days to discharge 5 (3-9) vs. 4 (3 -8) - discharged 115 (91) vs. 118 (97) - serious adverse events 5 pts (4%) vs. 3 pts (2%)	2

ICU = intensive care unit, IQR = interquartile range, pts = patients, S/F = saturation of inspired oxygen/fraction of inspired oxygen

Awake prone positioning in patients with hypoxemia and laboratory confirmed or highly suspected of COVID-19 did not lead to significant differences in mortality, rate of mechanical ventilation or respiratory failure, compared with standard of care.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2011 Li 2022 PMID: 35305308 DOI: 10.1016/S2213- 2600(22)00043-1 Specification of study: Systematic review with meta analysis	with the supine position for non-intubated		Awake prone positioning for 1h to 16h	Supine positioning	<b>Primary endpoint</b> : - requirement of intubation <b>Secondary outcomes</b> : - all-cause mortality - escalated respiratory support - ICU-LOS - hospital-LOS - safety	Primary endpoint (for ICU pts only): - intubation: RR 0.83 (0.71- 0.97) Secondary outcomes (for ICU pts only): - mortality: n.s. - escalation of respiratory support: n.s - ICU-LOS: n.s. - hospital LOS: n.s. - safety: no calculations	1 → 2 (not only RCTs included)

COVID-19 = corona virus disease 2019, ICU = intensive care unit, LOS = length of stay, n.s. = not significant, pts = patients, RCT = randomised controlled trial, RR = risk ratio

Awake prone positioning reduces the risk of intubation in non-intubated ICU patients with COVID-19.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
2015 PozueloCarras cosa 2022 (PMID: 35193688 DOI: 10.1186/s405 60-022-00600- z) Specification of study: systematic review and network meta-analysis	<ul> <li>20 publications (RCTs)</li> <li>Inclusion criteria:         <ul> <li>RCTs comparing different body positions or alternative degrees of positioning of MV pts</li> <li>reported data on VAP incidence</li> <li>mechanical ventilation for at least 48 hours</li> </ul> </li> </ul>		Different body positions: supine, semi- recumbent, lateral, prone	Standard of care	Primary endpoint: - incidence of VAP Secondary outcomes: - ICU LOS - hospital LOS - duration of MV - mortality	<ul> <li>Primary endpoint: <ul> <li>protective effect of the semi-recumbent versus supine position (RR: 0.38, 95% CI: 0.25–0.52)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>mortality:</li> <li>prone position had a positive effect compared to the supine position (RR: 0.71, 95% CI: 0.50–0.91)</li> <li>ICU LOS:</li> <li>pts positioned in the lateral Trendelenburg position spent less time (1.25 days) in the ICU than pts positioned in the semi-recumbent position (MD: – 1.25, 95% CI: – 1.60 to – 0.90)</li> <li>hospital LOS:</li> <li>lateral–Trendelenburg position achieved a reduction in the hospital LOS compared to the semi-recumbent position (MD: – 1.25, 95% CI: – 1.92 to – 0.58)</li> <li>duration of MV:</li> <li>higher in pts positioned in the lateral Trendelenburg position than in those positioned in the semi-recumbent position (MD: 0.50, 95% CI: 0.27 to 0.73)</li> <li>lower duration of MV in pts positioning in the semi-recumbent position than in those in the supine position (raw MD: – 3.26, 95% CI: – 6.31 to – 0.20)</li> </ul> </li> </ul>	1

CI = confidence interval, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, RCT = randomized controlled trials, RR = risk ratio, VAP = ventilator acquired pneumonia

# The semi-recumbent positioning seems to have a protective effect in comparison to supine position in relation to the incidence of VAP (RR: 0.38).

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2018 Laghlam 2021 PMID: 35111786 DOI: 10.3389/fmed. 2021.810393 Specification of study: Prospective single cohort study	24 patients Included were all consecutive patients fulfilling the <b>Inclusion criteria</b> : - ARDS according to Berlin criteria - Vv-ECMO implantation - COV-19 positive by PCR <b>Exclusion criteria</b> : - <18 years old - pregnancy - patients under legal protection <b>Per Branch</b>		PP under vv- ECMO therapy in patients with severe ARDS	vv-ECMO patients	Endpoints: - number of PP sessions - ICU LOS - duration of ventilation - 28- and 60- day mortality - respiratory and hemodynamic parameters	<ul> <li>- a total of 38 PP sessions was performed in 10 patients (42%) with a mean duration of 17.4 ± 2.1 h</li> <li>- duration of VV-ECMO was significantly longer (20 (13–31) vs. 9 (4–17) days, p = 0.01) in patients on whom PP was performed</li> <li>- duration of mechanical ventilation, ICU length of stay, and Day-28 and Day-60 mortality rates were not different between the two groups of patients</li> <li>Respiratory mechanics:</li> <li>- under VV-ECMO, PP significantly increased the PaO2/FiO2 ratio by 14 ± 21% and compliance by 8 ± 15% and compliance by 8 ± 15%, and significantly decreased the oxygenation index by 13 ± 18% and driving pressure by 8 ± 12%</li> </ul>	3
	14 10						

ARDS = acute respiratory distress syndrome, COV-19 = Corona virus disease 2019, ICU = intensive care unit, LOS = length of stay, PCR = polymerase chain reaction, PP = prone positioning, vv-ECMO = venovenous extracorporeal membrane oxygenation

In patients with COVID-19 and severe ARDS, PP under vv-ECMO improved the respiratory mechanical and oxygenation parameters, and the effects of PP on respiratory mechanics persisted after supine repositioning.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2021 Schmid 2022 (PMID: 35054084 DOI: 10.3390/jcm11020 391) <b>Specification of</b> <b>study:</b> Systematic review and meta-analysis	5 RCTs, 2 RCTs with APP as intervention (n= 1196) <sup>1,2,</sup> 3 RCTs comparing NIV and HFNC Inclusion criteria: adult pts with severe respiratory failure due to COVID-19 receiving HFNC, NIV or invasive MV Exclusion criteria: - studies comparing HFNC or NIV to oxygen insufflation or invasive MV - studies comparing ventilator settings Per Branch		<b>Full APP</b> or 135° APP	Standard of care: 90° or supine positioning	Primary endpoints: - all-cause mortality (D28 and D60) - clinical status at D28, D60 an FU (deterioration/ death, discharged alive, QoL) - SAE - AE Secondary outcomes: - clinical status at D28, D60 and FU (intubation, weaning, liberation from supplemental oxygen, ventilator-free days, duration of MV and oxygen therapy) - admission to ICU at D28 - hospital LOS - skin lesions from prone positioning	Primary endpoints (only APP): - mortality D28 (n= 1196): RR 1.08, 95% CI 0.51- 2.31 - clinical deterioration/ death (n=1121): RR 0.86, 95% CI 0.75- 0.98 - SAE and AE not reported on Secondary outcomes (only APP): - weaning n.s. - hospital LOS: n.s. - ventilator-free days: n.s. - skin lesions: n.s.	1 → 2 (not only RCTs included)

AE = adverse event; APP = awake prone positioning, COVID-19 = corona virus disease 2019, D = day, FU = follow up, HFNC = high flow nasal cannula, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, NIV = non-invasive ventilation, n.s.= not significant, QoL = quality of life, RCT = randomised controlled trial, pts= patients, SAE = serious adverse event

# Prone positioning did not reduce the mortality on day 28 but reduced the combined risk of intubation or death within 28 days.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2022 Papazian 2022 PMID: 35037993 DOI: 10.1007/s001 34-021- 06604-x Specification of study: systematic review and meta analysis	13 publications from 2018-2021(12x observational, 1x RCT, 1836 pts) <sup>1-13</sup> Inclusion criteria: - cohort studies and rRCTs - adult ARDS pts receiving vvECMO - comparisons of pts under ECMO submitted to PP and ECMO pts not turned prone during ECMO Exclusion criteria: - vaECMO - extracorporeal O <sub>2</sub> -removal		РР	Standard care	Primary endpoint: -28 days survival Secondary outcomes: - survival: 60- days/90-days/6- months - ICU/hospital mortality - duration of MV	Significant differences between groups in: - 28-day survival (503 survivors among 681 pts in the PP group [74%; 95% CI 71–77] vs. 450 survivors among 770 pts in the control group [58%, 95% CI 55–62]; RR 1.31 [95% CI 1.21–1.41]; /2 22% [95% CI 0–62%]; p < 0.0001) - survival was also improved in terms of 60- day survival, 90-day survival, ICU survival, and hospital survival - duration of MV increased in vvECMO pts with PP (mean difference 11.4 days [95% CI 9.2–13.5]; 0.64 [95% CI 0.50–0.78]; /2 8%; p < 0.0001)	1 → 2 (not only RCTs included)

ICU = intensive care unit, MV = mechanical ventilation, PP = prone position, pts = patients, RCT = randomised controlled trial

According to this meta-analysis, survival was improved when prone positioning was used in ARDS patients receiving vvECMO. The impact of this combination on survival should be investigated in prospective randomized controlled trials.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2024 Giani 2022 PMID: 34986895 DOI: 10.1186/s13054- 021-03879-w Specification of study: A pooled individual patient data analysis	Five publications (monocentric prospective cohort studies); 889 pts <sup>1-5</sup> Inclusion criteria: - patients femoro-jugular approach (66%), followed by femoro-femoral (18%) and jugular dual-lumen (16%) ECMO-cannulation Per Branch 315 575	missing	<b>Prone</b> <b>position</b> during ECMO	Standard of care (supine position during ECMO)	Primary endpoint: ICU mortality Secondary outcomes: - hospital mortality - successful ECMO weaning - ICU length of stay	<ul> <li>median ECMO duration before prone position was 5 days</li> <li>Significant differences between groups in: <ul> <li>ECMO duration was significantly lower in the supine group (p&lt;0.001)</li> <li>higher successful ECMO weaning in prone group (p=0.003)</li> </ul> </li> <li>No significant differences between groups in: <ul> <li>association with reduced mortality between supine or prone position.</li> </ul> </li> <li>propensity score matching identified 227 patients in each group. ICU mortality of the matched samples was 48.0% and 39.6% for patients in the supine and prone group, respectively (p=0.072)</li> <li>ICU and hospital survival rates were 8.4% higher in the prone group (p=0.072 and 0.073)</li> </ul>	1 → 2 (data not only from RCTs)

ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit, pts = patients

# In a large population of ARDS patients receiving veno-venous extracorporeal support, the use of prone positioning during ECMO was not significantly associated with reduced ICU mortality. The impact of this procedure will have to be definitively assessed by prospective randomized controlled trials.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2025 Patton 2021 PMID: 34916149 DOI: 10.1016/j.aucc. 2021.10.003 Specification of study: Meta-Review	Total10 systematic reviews published from 2008 to 2017 including 15.979 pts1-10Inclusion criteria: - systematic reviews, published in English since 2005 - patients > 16 years - inpatient in an ICU, with no restrictions on the length of stay, diagnosis, comorbidities, or concurrent treatmentsExclusion criteria: - published systematic reviews focused on only pediatric ICU patients - coronary care units, step-down or high- dependency unitsPer Branch	Kate	Prone positioning	All other positions	Primary endpoints: - incidence of PI (cumulative and/or rate/ density) - prevalence (point and/or period) Secondary outcome: - PI stage - PI location - time to PI	Primary outcome:         the cumulative incidence of PIs in PP         ranged from 25.7% to 48.5%         Secondary outcomes:         PI stage (using AMSTAR-2):         -       three reviews high quality         -       six as moderate quality         -       one low quality         PI location (only one review): PIs were identified in 13 locations	1→2
	(included 5 reviews) Supine position n=2.140 (included 5 reviews)						

ICU = intensive care unit, PI = pressure injuries, pts = patients

This meta-analysis found 25% to almost 50% of adult ICU patients placed in the prone position developed a PI. The high incidence of PI in the prone position highlights the need for targeted preventative strategies.

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Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2026 Lucchini 2022 PMID: 34895799 10.1016/j.iccn. 2021.103158 Specification	1 center between February 2020 and January 2021 → 96 pts. Inclusion criteria: -diagnosis of COVID-19 pneumonia -under invasive MV and PP Exclusion criteria: -not stated Per Branch 59 37		standard (≤24 hours) PP	extended (>24 hours) PP	No sample size calculation (retrospective study) No primary endpoint defined <b>Extracted Endpoints:</b> - duration of PP, number of proning cycles -prevalence with pressure sore -MRC grade distribution and handgrip strength at 3 months follow up	<b>Results:</b> - extended PP had a median of 34 (30–41) hours vs. 16 (15–18) ( $p < 0.0001$ ) of patient receiving standard PP, a higher total time spent in PP [85 (43–136) vs. 33 (18–64) hours – $p < 0.0001$ ] during ICU stay, a higher number of proning cycles [3 (2–4) versus 2 (1–4) – $p =$ 0.017] -prevalence of patients with pressure sore was 51% ( $n = 19$ ) for patient with extended pronation and 32% ( $n = 19$ ) in patient with standard pronation ( $p =$ 0.032). -MRC grade distribution, between patients with and without extended pronation only for the right Elbow flexors test ( $p = 0.028$ ) at 3 months follow up -not observe any difference between standard and extended pronation groups in handgrip dynamometry results [33 (25.0–37) vs. 29 (20–39) kg- force - $p = 0.679$ ]	4

pts. = patients; COVID= coronavirus disease; MV=mechanical ventilation; PP= prone position; MRC= Medical Research Council; ICU=Intensive Care unit

Extended PP is feasible and might reduce the workload on healthcare workers without significant increase of major PP related complications.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop-out Rate	Intervention	Contro I	Optimal Population	Primary Results	Evidence Grade
2028 Nakano 2021 PMID: 34863251 https://doi. org/10.118 6/s13054- 021-03827- 8 <b>Specificatio</b> n of study: Single center historical control study	111 pts of which 61Intervention pts admitted toHitachi General Hospital ICUbetween 09.2020 and 12.202and 50 control pts admitted tothe same ICU between 11.2019and 02.2020Exclusion criteria:-Age < 20y	-5 control and 4 interventi on pts due to inappropr iate CT measure ments -1 more in the interventi on group, but the reason not stated	IGREEN Protocol: -20 min daily rehabilitation with intensity based on the IMS on the previous day, aiming at a higher IMS than the previous day, plus 20 min EMS when pts could not reach the standing position or if IMS on previous day < 3 -nutrition protocol: if EN not contraindicated, EN initial target at 20 kcal/kg/day if MUST < 4 and at 30 kcal/kg/day at day 4 if MUST ≥ 4. For all pts target at 30 kcal/kg/day after day 7. Protein target at 1,8 or 1 g/kg/day if protein restriction indicated. Correction of any shortage through PN.	SC	Primary Endpoint: -FVM loss on femoral CT in the first 10 days Secondary outcome: -achievement of IMS 3 or 4 -MRC scores, Grip strength, FSS-ICU at ICU discharge -BI at hospital discharge -mean calorie and protein delivery -Nitrogen balance -Number of EN failure -Mean values and change of N-tinin/Cre from days 1 to 7 -BUN, creatinine, Albumin, TLC and CRP at day 10 -Proportion of survival discharge -ICU length of stay -Hospital length of stay -Use of adjunctive therapy	Primary Endpoint: -FMV loss significantly lower in the IG (11,5 vs 14,5%, p=0,03) Secondary endpoints: -IG reached IMS 3 significantly earlier than SG (p = 0,03). -No significant difference for time to IMS 4, MRC, FSS-ICU, BI, survival discharge, length of hospital and ICU stay, adjunctive therapy -Mean calorie and protein delivery in the first 10 days higher in IG (20,1 vs 16,8 kcal/kg/day, p = 0,01 and 1,4 vs 0,8 g/kg/day, p < 0,01) -N-tinin/cre higher in the IG both as mean value and for decrease from days 1 to 7 (96,3 vs 46,2 pmol/mgCre and – 27,2 vs 4,5 pmol/mgCre, p < 0,01) -BUN on day 10 higher in the IG (36,6 vs 27,6 mg/dl, p = 0,02), -No significant difference for the other lab markers	4

IMS = ICU mobility score, EMS = Electrical Muscle Stimulation, EN = Enteral Nutrition, MUST = Malnutrition Universal Screening Tool, PN = parenteral nutrition, FVM = Femoral Muscle Volume, MRC = Medical Research Council, FSS-ICU = Functional Status Scores for the ICU, BI = Barthel Index, CRP = C reactive protein, TLC = Total Lymphocyte Count, IG = Intervention group, SC = standard of care, BUN = Bloor Urea Nitrogen

The IGREEN protocol reduced FMV loss in the first 10 days after ICU admission.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2033 Zhuo 2021 PMID: 34763512 DOI: 10.21037/apm- 21-2359 Specification of study: Systematic review and meta-analysis	7 RCTs including 740 adult critically ill mechanically ventilated pts. 1-7         Inclusion criteria:         - aged > 18 years and treated in the ICU with MV to support respiration         - intervention group of patients given MV in the 45° bed head elevation angle, with adjustments not greater than 5°, and a control group treated at the 30° bed head elevation angle         - the duration of bed head elevation must be identical for both the intervention group and the control group         - the outcome indicators included VAP incidence rate, gastric reflux incidence rate, pressure sores incidence rate, ventilation indicators, ventilation time, mortality, length of hospital stay, and other indicators.         Exclusion criteria:         - non-randomized studies, studies or observational studies, investigations, case analysis, reviews, guidelines, systematic review, etd         - literatures with repeated study contents with others; and (III) literatures with missing data, or data that could not be transformed and/or used         Per Branch         Intervention: 372		Mechanical ventilation in 45° bed head elevation	Mechanical ventilation in 30° bed head elevation	Derived outcomes: - incidence of VAP - incidence of gastric reflux - incidence of pressure sores - ventilation indicators - ventilation time - mortality - hospital- LOS	Significant differences between groups in: - incidence of VAP: (OR =0.48; 95% CI: 0.28 to 0.84; Z=2.59; P=0.009 - incidence of gastric reflux: OR =0.50; 95% CI: 0.27 to 0.96; Z=2.09; P=0.04 - incidence of pressure sores (OR =1.88; 95% CI: 1.05 to 3.36; Z=2.11; P=0.03) no meta-analysis for ventilation indicators, ventilation time, mortality, and hospital LOS.	1

CI = confidence interval, LOS = length of stay, pts = patients, RCT = randomised controlled trial, VAP = ventilator-associated pneumonia

### The 45° semi-recumbent position reduces the incidence of ventilator-associated pneumonia, gastric reflux and pressure sores.

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Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2034 Beran 2022 PMID: 34753813 DOI: 10.4187/respcar e.09362 Specification of study: Systematic review and meta-analysis	14 publications (5 RG retrospective cohort cohort; n = 3.324 pts Inclusion criteria: - published studies - RCTs and observati -compared APP vs c - in non-intubated CG - reported one of the outcomes: endotrac mortality, or hospita Exclusion criteria: - did not report endot intubation or mortal - single-arm studies, reviews, commentar peer reviewed), and Per Br	, 3 prospective) s) <sup>1-14</sup> onal studies ontrol group OVID-19 pts e following heal intubation, I LOS otracheal ity rates case reports, ies, preprints (not abstracts.		АРР	Standard of care	<b>Primary endpoint:</b> - need for endotracheal intubation - mortality <b>Secondary Outcomes</b> : - hospital LOS	No significant differences           between groups in:           - need for endotracheal intubation (27% vs. 29.8%; RR 0.85 [95% CI: 0.66-1.08]; p = 0.17)           - mortality (17.9 % vs 25.7%; RR 0.68 [95% CI 0.51-0.90]; p = 0.08; l <sup>2</sup> = 52%)           - hospital LOS (MD -3.09d [95% CI: -10.14-3.96]; p = 0.39, l <sup>2</sup> = 97%)           Significant differences between groups in:           - subgroup analysis of RCTs: need for endotracheal intubation: (RR 0.83 [95% CI: 0.72-0.97; p = 0.02; l <sup>2</sup> = 0%)	1 → 2 (downgrade since not all RCTs)

APP = awake prone positioning, CI = confidence interval, LOS = length of stay, RCT = randomized controlled trial, RR = risk ratio

APP reduced mortality in non-intubated COVID-19 subjects without a significant difference in the need for endotracheal intubation and length of hospital stay.

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- 13. Ehrmann S, Li J, Ibarra-Estrada M, Perez Y, Pavlov I, McNicholas B, et al. Awake prone positioning for COVID-19 acute hypoxemic respiratory failure: a randomized, controlled, multinational, open-label meta-trial. Lancet Respir Med 2021S2213-2600(2221)00356-00358.
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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2040 Zaaqoq 2019 PMID: 34582415 DOI: 10.1097/CCM.000000 0000005296 Specification of study: Observational study	232 pts with COVID-19 who were supported by venovenous extracorporeal membrane oxygenation         Inclusion criteria: $- \ge 18$ years         - confirmed COVID-19         - need for invasive mechanical ventilation and venovenous ECMO support         Prone position:         n= 67		Prone positioning: - pts were allowed to move between the prone and supine positions during their ECMO run	Standard care	Primary endpoints: - survival to hospital discharge - mortality through 90 days from ECMO initiation	<ul> <li>Significant differences between groups:</li> <li>PP associated with lower mortality in the cumulative outcome model: HR 0.31 (95% CI 0.14-0.68; p &lt; 0.05)</li> <li>PP associated with reduced discharge: HR 0.03 (95% CI 0.00 – 0.21; p &lt; 0.05)</li> <li>Non-significant differences between groups: <ul> <li>discharged from hospital alive</li> <li>a) all pts (n=232): 59 (25%)</li> <li>b) PP (n=67): 22 (33%)</li> <li>c) control (n=165): 37 (22%)</li> </ul> </li> <li>discharged to other facilities <ul> <li>a) all pts (n=232):: 40 (17%)</li> <li>b) PP (n=67): 12 (18%)</li> <li>c) control (n=165): 28 (17%)</li> </ul> </li> <li>remain in the hospital <ul> <li>a) all pts (n=232): 9 (4%)</li> <li>b) PP (n=67): 4 (6%)</li> <li>c) control (n=165): 5 (3%)</li> </ul> </li> <li>in-hospital death <ul> <li>a) all pts (n=232): 90 (39%)</li> <li>b) PP (n=67): 23 (34%)</li> <li>c) control (n=165): 67 (41%)</li> </ul> </li> <li>PP not associated with reduced mortality in Weibull survival model (HR 0,85; 95% credible interval 0.34-1.95)</li> <li>after inclusion of the interaction between cumulative prone and the day of ECMO run: <ul> <li>a) gradual decrease in the probability of death associated with the duration of PP (No data)</li> <li>b) PP continued to be associated with lower mortality: HR 0.95 (95% CI 0.92-0.98)</li> </ul> </li> </ul>	3

CI = confidence interval, ECMO = extracorporeal membrane oxygenation, HR = hazard ratio, ICU = intensive care unit, pts = patients

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and C (Participant #, ch Tota	haracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
ane.2021.07. 029 Specification of study: a retrospective	Exclusion criteria: - supported with noninvasive respiratory acidosis (pH <7.3 mmHg), PaO2/FiO2 ratio <15 a b b a d una pic in atchilite	the ICU for acute DVID-19 pneumonia gen therapy with a upon admission e or invasive MV due to 30 and PaCO2 >50 50, GCS score <12 points, from the moment of athologies (lung cancer, ad Kartagener's monia	N=24 in the APP group: PP less than 12 h a day due to noncomplian ce	APP group	Non APP group	No sample size calculation (retrospective study) No primary endpoint defined <b>Extracted Endpoints:</b> - PaCO2, PaO2, pH, SpO2 values and PaO2/FiO2 ratios at the beginning and 24th hour - intubation requirements - ventilator-free days - ICU LOS	Results: - At the 24th hour, the median SpO2 value of the APP group was 95%, the median PaO2 value was 82 mmHg, SpO2 value of the non-APP group 90% and the PaO2 value 66 mmHg. (p = 0.001, p = 0.002) - no difference between the groups in ICU LOS and ventilator-free days (n.s.) - short-term mortality and intubation requirements was lower in the APP group (p = 0.020, p = 0.001)	4
	23	25						

pts. = patients; COVID= coronavirus disease; ICU=intensive care unit; APP=awake prone position; MV=mechanical ventilation; GCS= Glasgow Coma Scale; PP=prone position; LOS= Length of stay

APP application in patients receiving non-rebreather mask oxygen therapy for respiratory failure due to COVID-19 pneumonia improves oxygenation and decreases the intubation requirements and mortality.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2045 Poon 2021 PMID: 34384475 DOI: 10.1186/s13054- 021-03723-1 Specification of study: systematic review and meta- analysis	12 studies, pts 640 (n = 6 single arm observational studies, n = 6 two-armed comparative studies) <sup>1-12</sup> Inclusion criteria: - keywords: "Extracorporeal Membrane Oxygenation" from 1 March 2021 - written in English - pts aged >18 years - undergoing ECMO for ARDS in which PP was explicitly described, - outcomes of PP therapy such as pts survival Exclusion criteria: - population < 10 pts - non-human studies - review articles and case reports - reviews of Extracorporeal Life Support Organization (ELSO) registry data - in studies taking place at the same institution across overlapping time periods the study with the larger number of pts was included, and all others were excluded		PP during ECMO	No PP during ECMO	Primary endpoint: - cumulative survival Secondary outcomes: - ICU length of stay - ECMO duration - changes in ABG values - ventilator mechanics - complication rates	Significant differences between groups: patients undergoing PP had longer ICU LOS (+ 14.5 days, 95% CI 3.4– 25.7, $p = 0.01$ ; 3 studies) patients undergoing PP had longer ECMO duration (+ 9.6 days, 95% CI 5.5–13.7, $p < 0.0001$ ; 6 studies). pre-PP-PaCO2 vs. Post-PP-PaCO2 44.7 [42.2-47.2] vs. 43.7 [41.2-46.2]; MD = -1.5 [-2.9 to -0.2]; $p = 0.03$ ) Pre-PP-aCO2/FiO2 vs. Post-PP- PaCO2/FiO2 112.2 [92.2-132.3] vs. 147.7 [131.4-164.0]; MD = +24.9 [+6.5 to + 43.2]; $p = 0.01$ ) pre-PP-driving pressure vs. Post-PP-driving pressure 11.5 [9.9-13.1] vs. 10.7 [9.2-12.1]; MD = -0.8 [-1.5 to -0.2]; $p = 0.01$ ) <b>Non-significant differences between groups:</b> cumulative survival in patients that underwent PP was 57% (95% CI 41.9–71.4, high certainty; 11 studies) cumulative survival PP vs. No PP: RR = 1.1.9 (95% CI 0.92-1.55, $p = 0.19$ ) pooled proportion of survival to hospital discharge in patients that underwent PP was 58% (95% CI 37.6-77.9; 7 studies) chance of survival to discharge (4 studies, RR = 1.18, 95% CI 0.96- 1.46, $p = 0.11$ ) pooled survival to 30-days post-discharge was 50% (95% CI 21.4 – 79.1; 3 studies) pooled survival to 60-days post-discharge was 72% (95% CI 63.6-80.5; 2 studies) survival to 90-days post-discharge was 64% vs. 42% (1 study) after sensitivity analysis (exclusion of studies with JBI score < 8] pooled cumulative survival for patients undergoing PP was 56% (95% CI 36.9-73.9; 8 studies) and chance for cumulative survival was 1.23 (95% CI 0.9-1.68, $p = 0.19$ ; 6 studies) pooled ICU LOS 42.5 days (95% CI 28.4-56.7; 7 studies) survival to ECMO weaning between groups: RR = 0.92 (95% CI 0.49- 1.71, $p = 0.78$ ; 3 studies) no major complications were reported.	1 → 3 (inclusion of mainly retrospective studies)

ABG = arterial blood gas, ECMO = extracorporeal membrane oxygenation, FiO2 = Fraction of inspired oxygen, ICU = intensive care unit, JBI = Johanna Briggs institute, MD = Mean Difference, PaCO2 = Partial pressure of carbon-dioxide, PaO2 = Partial pressure of oxygen, PP = prone positioning, pts = patients, RCT = randomized controlled trial, VV ECMO = veno-venous extracorporeal membrane oxygenation

PP during VV ECMO appears safe with a cumulative survival of 57% and may result in longer ECMO runs and ICU LOS. However, evidence from appropriately designed randomized trials is needed prior to widespread adoption of PP on VV ECMO.

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Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2047 Bahloul 2021 PMID: 34380290 https://doi.or g/10.4266/ac c.2021.00500 Specification of study: prospective	1 university hospital between September 1 and December 4, 2020→ 21 pts. included in PP group Inclusion criteria: -severe, critically ill adult COVID-19 patients, a confirmed SARS-CoV-2 infection, admitted into the ICU -spontaneous breathing, whose hypoxemia (oxygen saturation measured by pulse oximetry [SPO2] < 92%) did not resolve despite supplemental oxygen delivered via facial mask or HFNO cannula -accepted the PP Exclusion criteria: -admitted in cardiac arrest -required non-invasive and/or invasive MV on ICU admission -hemodynamic instability (shock) -neurological disorders (agitation and/or coma)		<b>PP group</b> (2-4h, followed by 2 h of SP during the day, to sleep in a PP at night)	PP-free group		(P<0.001) 1 hour later. -PP associated with reduction in respiratory rate from 31±10 to 21±4	3
	21 1/						

pts. = patients; COVID-19= coronavirus disease 2019; SARS-CoV-2= severe acute respiratory syndrome coronavirus 2; ICU=intensive care unit; HFNO= high-flow nasal oxygen; PP=prone position; MV=mechanical ventilation; RR=Riva Rocci

Early application of PP can improve hypoxemia and tachypnea in COVID-19 patients with spontaneous breathing. No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference,	Cases and Controls (Participant #, characteristics)		Intervention Contro		Optimal Population	Primary Results	Evidence
Study Type	Total	Rate					Grade
	2 University hospitals from February						
	2012 to September 2015 $\rightarrow$ 23 pts.						
			HUP			Significant differences between groups:	
	Inclusion criteria:		Intervention			-exp1, lowering the head from 30° to 15° and	
	- adults admitted to the ICU for acute		30° HUP			0° was associated with a gradual elevation in	
	brain injury, i.e., traumatic, vascular, or		10 Min		sample size calculation:	ICP, with a mean increase of 2.6 mm Hg (1.4–	
2052 Burnol	other injury		stabilization		20 pts. needed to detect a 25%	3.7; P<0.001) from 30° to 15° and of 7.4 mm	
2021	- ICP was monitored with an		Subsequently		posture-induced change from	Hg (6.3–8.6 mm Hg; P<0.001) from 30° to 0°	
	intraparenchymal ICP device		lowered to 15°		baseline in PbtO2 values with a	- PbtO2 and FVm improved from 30° to 0° by	
PMID:			and 0°		two-sided $lpha$ risk of 0.05 and a	1.2 mm Hg (0.2–2.3 mm Hg) and 4.1 cm/s	
34312789	Exclusion criteria:		positions	Pts.	power of 90%	(0.0–	
	- persistence of hemodynamic or			acted as		8.2 cm/s), respectively (both P<0.05)	
10.1007/s1202	respiratory instability despite	n/a	In 3	their	no primary endpoints defined	-PbtO2 and FVm were significantly higher	3
8-021-01240-1	Treatments		experiments:	own		during exp2 than exp1 (no p-value stated)	
	- severe brain hypoxia (defined as				Extracted Endpoints:		
Specification	PbtO2 less than 15 mm Hg)		during first 24h		<ul> <li>brain parameters (mean ICP,</li> </ul>	No significant differences between groups	
of study:	- refractory intracranial hypertension		after ICU		CPP, and PbtO2)	in:	
	(defined as ICP more than 30 mm Hg)		admission		<ul> <li>systemic variables (FVm,</li> </ul>	-CPP, arterial blood gases, hemoglobin content,	
Cohort Study	at baseline		Exp2			and body temperature remained unchanged	
	- development of cerebral vasospasm		repeated 24 h		content, and body temperature)		
	<ul> <li>no cerebral monitoring of ICP and</li> </ul>		later			<ul> <li>decompressive craniotomy nor the order in</li> </ul>	
	PbtO2		Exp3			which the head position was changed affected	
	Per Branch		96 h later			brain parameters	
	23						

pts. = patients; ICU=Intensive Care Unit; ICP= intracranial pressure; PbtO2= brain tissue oxygenation pressure; HUP= head-up posture; CPP= cerebral perfusion pressure; FVm= mean blood fow velocity;

Changing the positioning of stable patients with acute brain injury resulted in opposite changes of ICP versus brain oxygenation and circulation.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2054 Liu 2021 PMID: 34308257 DOI: 10.1007/s42399-021- 01008-w Specification of study: Systematic review with meta-analysis	465 pts (n = 6 retrospective studies) <sup>1-6</sup> Inclusion criteria:         - PP applied during VV-ECMO for respiratory failure in critical adult pts         Exclusion criteria:         - pts less than 18 years old         - received VA-ECMO or VAV-ECMO         ECMO         - reviews or case reports         212       253		VV-ECMO therapy and PP: between 8 and 24 hours (6 studies): 1: 8 hours, 1: 12 hours, 1: 15 hours, 1 24 hours and 2: time was not mentioned)	VV-ECMO and no PP	Derived outcomes: - Survival - ECMO duration - ICU LOS - complications	<ul> <li>Significant differences between groups in:</li> <li>ECMO duration (longer in intervention group): MD 5.37, 95% CI 4.19– 6.54, I2= 67%, p &lt; .00001</li> <li>ICU LOS (longer in intervention group): MD 7.29, 95% CI 4.06–10.52, I2= 64%, p &lt; .00001)</li> <li>survival (<i>Rillinger et al.</i><sup>2</sup>): Earlier PP (&lt; 17h) vs. Later or no PP: 82% vs. 33%, p &lt; 0.05</li> <li>Non-significant differences between groups in:</li> <li>improvement in PaO2/FiO2 ratio: higher in intervention group (higher with longer duration of PP)</li> <li>comparison of survival at discharge (<i>Giani et al.</i><sup>3</sup> and <i>Rilinger et al.</i><sup>2</sup>): OR 1.42, 95% CI 0.92-2.18; p = 0.11</li> <li>overall survival rate of all six studies: Intervention group= 61.8% vs. control group= 45.8%</li> <li>complications: <ul> <li>a) no dislodgement of ECMO cannules when applying PP</li> <li>b) no displacement of vascular lines, ECMO cannula, endotracheal tube, or chest tubes</li> <li>c) reversible complications (<i>Giani et al.</i><sup>3</sup>): desaturation (2.5%), bleeding (1.2%), decrease of blood flow (1.2%), hemodynamic instability (0.6%), increased PaCO2 (0.3%), thigh swelling (0.3%), face swelling (0.3%) and vomiting (0.3%).</li> <li>d) n = 1 membrane thrombosis, n = 1 drop in ECMO blood flow (<i>Kimmoun et al.</i><sup>1</sup>)</li> <li>e) n = Pneumothorax during PP (<i>Guervilly et al.</i><sup>6</sup>)</li> </ul> </li> </ul>	1 → 3 (retrospective studies and high risk of bias)

CI = confidence interval, FiO2 = fraction of inspired oxygen, ICU = intensive care unit, LOS = length of stay, MD = mean difference, OR = odds risk, PaCO2 = partial pressure of carbon-dioxide, PaO2 = partial pressure of oxygen, PP = prone positioning, pts = patients, VA-ECMO = veno-arterial extracorporeal membrane oxygenation, VAV-ECMO = veno-arterial-venous ECMO, VV-ECMO = veno-venous ECMO

Performance of PP during ECMO for refractory respiratory failure is safe, reduces ECMO duration, ICU LOS, might increase survival and improve PaO2/FiO2 ratio.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Total					
#2055 Gonzalez-Seguel 2021 PMID: 34301802 DOI: 10.4187/respcare.09 194 Specification of study: Scoping review	<ul> <li>41 publications <ul> <li>n = 15 retrospective</li> <li>observational study</li> <li>n = 8 case report</li> <li>n = 4 prospective</li> <li>observational study,</li> <li>n = 1 RCT</li> <li>n = 5 clinical practice</li> <li>guideline</li> <li>n = 3 national</li> <li>guideline</li> <li>n = 2 clinical</li> <li>commentary</li> <li>n = 2 care protocol</li> <li>n = 1 checklist</li> </ul> </li> <li>Inclusion criteria: <ul> <li>mechanically</li> <li>ventilated pts in prone</li> <li>position due to ARDS</li> </ul> </li> <li>Exclusion criteria: <ul> <li>reporting on awake</li> <li>prone positioning</li> <li>pediatric population</li> <li>animal or</li> <li>experimental studies.</li> </ul> </li> </ul>	Prone positioning	No control required Supine position in 3 studies	Primary Endpoint: AEs related to: - pressure sores/ skin injuries - invasive devices - respiratory system - cardiovascular system - musculoskeletal system - visual system - gastrointestinal system - nervous system	Outcomes (number of studies reporting on the AE): pressure sores/ skin injuries (n=7): 29.7% 95% CI 26.2-33.2 invasive devices: - removal of lines (n=7): 0.9% 95% CI 0 – 1.7 - unscheduled extubation (n=5): 7.7% 95% CI 5.2 – 10.3 - displacement of endotracheal tubes (n= 4): 1.9% 95% CI 0.7 – 3.2 - airway obstruction (n=2): 4% 1.7 – 6.4 respiratory system: - severe desaturation (n=3): 37.9% 95% CI 33.3 – 42.4 - VAP (n=2): 28.2 95% CI 23.5 – 33.0 - pneumothorax (n=2): 2.9% 95% CI 0 – 6.1 - barotrauma (n=1): 30.6% 95% CI 15.5 – 45.6 cardiovascular system: - cardiac arrest (n=5): 3.4% 95% CI 1.9 – 4.9 - hypotension (n=3): 10.2% 95% CI 7.2 – 13.2 - arrhythmia (n=2): 15.4% 95% CI 11.1 – 19.7 peripheral nerve injuries (n=4): 8.1% 95% CI 4.2 – 12.0 visual system: eye hemorrhage or edema (n=3): 3.5% 95% CI 1.1 – 5.9 gastrointestinal system: - vomit (n=1): 1.5% 95% CI 0 – 4.5 - hemoptysis (n=1): 2.5% 95% CI 0.5 – 4.5 nervous system: - transient intracranial pressure (n=2): 2% 95% CI 0 – 4.7	5

AE = adverse event, ARDS = acute respiratory distress syndrome, CI = confidence interval, pts = patients, RCT = randomized controlled trial, VAP = ventilator-associated pneumonia

The most common adverse events associated with prone positioning are in the domain of the respiratory system and pressure sores.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2056 Petit 2022 PMID: 34259655 10.1097/CCM.000 000000005145 <b>Specification of</b> <b>study:</b> Retrospective, single-center study	1 center from January 2012– 2020 → 298 pts. Inclusion criteria: -severe ARDS patients given VV- ECMO support Exclusion criteria: -venoarterial-ECMO Per Branch 64 234	n/a	PP - ECMO	No-PP- ECMO	No sample size calculation due to study design (retrospective) <b>Primary Endpoint:</b> -time to successful ECMO-weaning within the 90-day post- randomization <b>Secondary Endpoints:</b> -90-day survival status -ECMO and PP-related complications -respiratory system static compliance gain post- PP -quantitative lung CT profile	Primary Results: -PP-ECMO patients' 90-day probability of being weaned- off ECMO and alive higher (0.75 vs 0.54; sHR [95% CI], 1.54 [1.05–2.58]) Secondary Results: -PP-ECMO patients' lower 90-day mortality (20% vs 42%) (p<0.01) -PP- and no-PP-ECMO groups' complication rates were comparable (n.s.) -Respiratory system static compliance increased greater than or equal to 3mL/cm H2O after 16 hours of PP for 34 patients (53%), whose static compliance rose by 6mL/cm H2O (3.5–10.3mL/cm H2O) post-PP, whereas static compliance changed by 0mL/cm H2O (–0.85 to 0.82mL/cm H2O) for the 30 other PP patients, already observed after 4 hours of PP (p < 0.01) -PP nonresponders had higher percentages of nonaerated or poorly aerated lung than PP responders (57% [15–76%] vs 29% [10–46%], respectively, p = 0.047), in ventral and medial-ventral regions.	4

pts. = patients; ARDS= acute respiratory distress syndrome; ECMO= extracorporeal membrane oxygenation; VV-ECMO= venovenous-ECMO; PP=prone positioning; CT=computer tomography; CI=confidence interval; sHR= Subdistribution hazard ratio; n.s.= not significant;

PP during VV-ECMO was safe and effective and was associated with a higher probability of surviving and being weaned-off ECMO at 90 days.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2057 Binda 2021 PMID: 34244027 https://doi.org/10. 1016/j.iccn.2021.1 03088 <b>Specification of</b> <b>study:</b> A cross-sectional study	63 pts., 219 proning cycles, from March to June 2020 Inclusion criteria: -laboratory-confirmed SARS- CoV-2 infection -admitted to ICU -on invasive MV -treated with PP Exclusion criteria: -noninvasive ventilation -intubated but not treated with PP Per Branch 63	n/a	PP	n/a	No sample size calculation No primary endpoint defined <b>Extracted Endpoints:</b> -prevalence of complications - development of pressure ulcers	Results:-32 pts. had at least one complication-15 PP cycles were interrupted (6.8%,15/219)-Episodes of bleeding 25.4% (16/63)-Rate of displacement of medical devices duringPP 12.7% (8/63)-no unplanned extubation nor chest drainagetube accidental removal-prevalence of pts. with PU: 42.9% (95% CI: 30.6–55.1) whereas 30.2% (95%CI: 18.8–41.5) wereprone related $\circ$ With PU higher level of correlation (q =0.47, P = 0.042) between days of MV andPP-time, compared to pts. without PU (q $= 0.29, P = 0.052$ ) $\circ$ PP-time, predictor for prone related PU(P = 0.039) $\circ$ effect of increasing mean PP-time from24 to 48 hours was to increase the oddsby a factor of 1.4 (95%CI: 1.02 to 1.91) $\circ$ increasing weight from 22 to 28 kg/m2increased the odds by a factor of 1.3(95%CI 0.6–2.8, P = 0.498)	3 → 4

pts. = patients; SARS-CoV-2= severe acute respiratory syndrome coronavirus 2; ICU=intensive care unit; MV=mechanical ventilation; PP=prone position; PU=pressure ulcers; CI=confidence intervall

The use of PP in patients with COVID-19 was a safe and feasible treatment.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2059 Rosén 2021 PMID: 34127046 DOI: 10.1186/s130 54-021- 03602-9 Specification of study: multicenter randomized clinical trial	75 pts in 2 tertiary and 1 county hospital in         Sweden         Inclusion criteria:         - adults ≥ 18 years of age         - COVID-19 infection with SARS-CoV-2 and         hypoxemic respiratory failure         - HFNO or NIV respiratory support and a         PaO2/FiO2-ratio ≤ 20 kPa or corresponding         values of SpO2 and FiO2 for > 1 hour         Exclusion criteria:         - oxygen supplementation with a device         other than HFNO or NIV         - inability to assume prone or semi-prone         position         - immediate need for endotracheal         intubation         - severe hemodynamic instability         - pregnancy         - terminal illness with less than one year life         expectancy         - do-not-intubate order         - inability to understand oral or written         study information		<ul> <li>APP:</li> <li>at least 16 h APP per day</li> <li>prone and semi-prone positioning was allowed</li> <li>flat supine positioning was discouraged and patients were instructed to place themselves in the semi-recumbent or lateral position in between proning sessions.</li> </ul>	Standard of care	<ul> <li>Primary endpoint: <ul> <li>intubation within 30 days</li> </ul> </li> <li>Secondary outcomes: <ul> <li>duration of APP</li> <li>30-day mortality</li> <li>NIV</li> <li>ventilator-free days</li> <li>ICU and hospital LOS</li> <li>organ support</li> </ul> </li> <li>Sample size calculation: <ul> <li>estimated based on previous studies with 240 pts to detect a decrease in intubation rate of 20%</li> </ul> </li> </ul>	<ul> <li>Primary outcome: <ul> <li>intubation within 30 days: 13 pts (33%)</li> <li>in the control group and 12 pts (33%) in the prone group were intubated [HR 1.01 (95% CI 0.46–2.21), P = 0.99]</li> </ul> </li> <li>Secondary outcomes: <ul> <li>duration of early APP and total APP was longer in the prone group compared with the control group (P = 0.0001; P = 0.014, respectively).</li> <li>3 pts (8%) died in the control group compared with 6 pts (17%) in the prone group [HR 2.29 (95% CI 0.57–9.14), P = 0.30]</li> <li>no significant differences between groups in ventilator-free days for intubated pts, days free of NIV/HFNO for not intubated pts, hospital or ICU LOS, use of organ support between groups</li> <li>9 pts in control and 2 pts in intervention group had pressure sores</li> <li>3 cardiac arrests not related to APP (n = 1 control, n = 2 intervention)</li> </ul> </li> </ul>	2

APP = awake prone positioning, FiO2 = fraction of inspired oxygen, HFNO = high-flow nasal oxygenation, HR = hazard ratio, ICU = intensive care unit, LOS = length of stay, NIV = non-Invasive ventilation, PaO2 = partial pressure of oxygen, pts = patients, SpO2 = oxygen saturation

# Awake prone positioning did not reduce rate of intubation in patients with hypoxemic respiratory failure but seemed to increase mortality, whilst not increasing prevalence of pressure sores.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2088 Longobardo 2021 PMID: 33594874 DOI: 10.23736/S0375- 9393.21.15254-X Specification of study: Systematic review and meta-analysis	<ul> <li>8 RCTs including 2235 add ARDS pts<sup>1-8</sup></li> <li>Inclusion criteria: <ul> <li>RCTs</li> <li>studies with prone positioning as intervention</li> </ul> </li> <li>Exclusion criteria: <ul> <li>studies involving ARDS therapies requiring transfer to a tertiary level referral center</li> <li>patients outside the IC</li> <li>pediatric patients</li> </ul> </li> <li>Per Branch <ul> <li>1144</li> </ul></li></ul>		Prone positioning	Standard care	Primary endpoint: - mortality (28-day or 30-day) Secondary outcome: - improvement in oxygenation measured by the P:F ratio at 24h	Significant differences between groups in: - prone positioning duration >12h improves mortality: (33.1% vs. 44.4%; RR 0.75 [0.59-0.95]; P=0.02; I <sup>2</sup> =49%) No significant differences between groups in: -improvement in mortality: (39.3% vs. 44.5%; RR 0.83 [0.68-1.01]; P=0.06; I <sup>2</sup> =67%) - improvement in P:F ratio(n=3): MD 26.81 [-5.93-59.54]; P=0.11; I <sup>2</sup> =86%	1

ARDS = acute respiratory distress syndrome,  $P:F = PaO_2/FiO_2$ , pts = patients

Prone positioning only improves mortality when it is performed for 12 hours or more.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2094 Wright 2021 PMID: 33481406 DOI: 10.1097/CCM.00000 00000004820 Specification of study: Systematic review and Proposed Protocol	10 publications (1 RCT, 4 cohort studies, 1 case series, 4 case reports) Inclusion criteria: - neurologically ill patients with ARDS Exclusion criteria: - nonhuman studies - basic science research - pediatric patients Per Branch		Prone Position	Supine Position	No primary endpoint defined Extracted endpoints: - protocols for prone positioning - safety - ICP - CPP - MAP - PbtO2 - PaO2	no meta-analysis <b>Significant differences between groups in:</b> - ICP increase: 3 studies p<0.05 - CPP increase: 1 study p<0.05, - CPP decrease: 1 study p<0.05 - MAP increase: 1 study p<0.05 - MAP decrease: 1 study p<0.05 - PbtO2 increase: 1 study p<0.05 - PaO2 increase: 1 study p<0.05	1 → 3 (not only RCTs, no MA)

ARD = acute respiratory distress syndrome, CPP = cerebral perfusion pressure, ICP = intracranial pressure, MA = meta-analysis; MAP = mean arterial pressure, PbtO2 = brain tissue oxygen tension, RCT = randomised controlled trial

#### Prone position is safe and feasible in neurologically ill patients with acute respiratory distress syndrome. Increased intracranial pressure and compromised cerebral perfusion pressure may occur with prone positioning.

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Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2105 Akbiyik 2021 PMID: 33230628 DOI: 10.1007/s10096- 019-03789-4 Specification of study: RCT	<ul> <li>relatives approved to particulation of the particulation of the particulation of the particulation of the presence of the first 48 h following M</li> <li>positive sputum culture</li> <li>MV support or within the support</li> <li>diabetes mellitus</li> <li>contraindications for ro</li> </ul>	cracheal tube cted to mechanical ged every 4 h in a day articipate in the study prior to MV support within IV support		Oropharyngeal aspiration - using a pressure of 100– 120mmHg for 10s - prior to each position changes	Routine nursing care in the ICU - endotracheal aspiration and oropharyngea l aspiration - oral care - routine (every 4 h in a day) and non- routine position changes	<b>Primary endpoints:</b> - ICU LOS - mechanical ventilation support - VAP mortality	Primary endpoints: - median ICU LOS 27.28 $\pm$ 30.69 and 18.00 (min 4 days; max 168 days) days- median of mechanical ventilation support 26.72 $\pm$ 30.65 and 18.00 (min 4 days; max 168 days) days- VAP development significantly different with respect to OA before the change of position ( $\chi$ 2 = 11.905; p = 0.001)- mean age of the pts who developed VAP 66.2 $\pm$ 17.71 (min 22; max 89)- no significant difference in the development of VAP according to the mean of age (t = 0.843; p = 0.405)- VAP development increased the death rate ( $\chi$ 2 = 13.112; p = 0.002)	2 → 3

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, OA = oropharyngeal aspiration, pts = patients, RCT = randomized controlled trial, VAP = ventilated associated pneumonia

Oropharyngeal aspiration prior to each position change reduced the incidence of VAP significantly.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2112 Monsees 2022 PMID: 35649531 DOI: 10.1111/nicc.12785 Specification of study: Systematic review + MA	10 RCTs including 1291 adult ICU pts <sup>1-10</sup> Inclusion criteria: - RCT - language English - critically ill adult patients - inclusion within 4 days of admission or intubation - utilization of EM - report of ICU LOS Exclusion criteria: - utilization of Passive exercise only - utilization of cycle ergometry as only intervention Per Branch		EM that promotes active exercise	Usual care or no EM intervention	Primary endpoint: - ICU LOS Secondary outcomes: - duration of MV - mortality - hospital LOS - FI	<ul> <li>Significant differences between groups in: <ul> <li>reduction in duration of MV: p= 0.0002, l<sup>2</sup>= 82%</li> </ul> </li> <li>No significant difference between groups in: <ul> <li>ICU LOS (n=4 studies): Study MD -0.18 (95% CI -0.53 - 0.18)</li> <li>mortality: No significance. Risk Ratio of 1.01 (95% CI 0.2-1.26), l<sup>2</sup> = 0%.</li> <li>hospital LOS: Results favored intervention treatment, except for one study. Results were not significant, except for one study reporting a reduction of 6.5 median days (p = 0.011).</li> <li>FI: no meta-analysis possible</li> </ul> </li> </ul>	1

EM = early mobilization, FI = functional independence, ICU = intensive care unit, LOS = length of stay, MD = mean difference, MV = mechanical ventilation, pts = patients, RCT = randomised controlled trial

### Early mobilisation shortens the duration of mechanical ventilation and shows a trend towards reduced ICU LOS and hospital LOS.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2114 Cartotto 2022 PMID: 35639543 DOI: 10.1093/jbcr/irac00 8 Specification of study: Comprehensive Literature Search and Review	3 case-control studies <sup>1-3</sup> Inclusion criteria: - burn pts in ICU - EMR intervention - with a control group - at least one outcome of predefined PICO outcomes - MV - publications in English - from the inception of the database to April 29, 2021 Exclusion criteria: - abstracts - surveys - case reports - unrelated articles		EMR	Non- standardized or late mobilization and rehabilitation	<ul> <li>Primary endpoints:</li> <li>1. Does EMR (a) shorten the duration of MV and (b) reduce the development of ICUAW?</li> <li>2. Does EMR result in fewer hospital- acquired pressure injuries?</li> <li>3. Does EMR result in loss of skin grafts or skin substitutes?</li> <li>4. Does EMR reduce the prevalence of delirium?</li> </ul>	<ol> <li>Does EMR (a) shorten the duration of MV and (b) reduce the development of ICUAW?         <ul> <li>recommendation:</li> <li>(a): none. insufficient evidence.</li> <li>(b): conditional recommendation (based on low- to very low quality evidence) for implementation of EMR to reduce ICUAW with open dialogue between medical, nursing, and rehabilitation staff to identify any specific safety concerns or medical/surgical limitations.</li> </ul> </li> <li>Does EMR result in fewer hospital-acquired pressure injuries?         <ul> <li>recommendation: none. no evidence identified.</li> </ul> </li> <li>Does EMR result in loss of skin grafts or skin substitutes?         <ul> <li>recommendation: none. no evidence identified. suggestion that surgeons and rehabilitation therapists consider whether EM is feasible and warranted in a critically ill burn pts with recent grafting.</li> </ul> </li> <li>Does EMR reduce the prevalence of delirium?         <ul> <li>recommendation: no evidence identified</li> <li>conditional recommendation for implementation of EMR to reduce delirium recommended, based on literature that was not included in the search results of this database search.</li> </ul> </li> </ol>	1

BI = Barthel index, EMR = early mobilization and rehabilitation, FIM = functional independence measure, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients

Underlying evidence is not sufficient to recommend EMR to reduce the duration of MV in the burn ICU or development of hospital-acquired pressure injuries. Conditional recommendation for the use of EMR to reduce development of ICUAW and delirium in critically ill burn patients in the ICU.

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2780 - multicomponent non-pharmacological intervention (i.e. Assessment of SP, CS, EM, PC, and CTS interventions of SP, CS, EM, PC, and PC, an	Reference, Study Type	Cases and Cases	naracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Matsuura 2022 PMID: 35624556 DOI: 10.1111/nicc.1 2780 Specification of study: A systematic review and	randomized, 8 controlled studies, n = 2.549 pts) <sup>1-11</sup> Inclusion criteria: - ICU pts aged 18 year or - occurrence of delirium valid tools - RCTs, CCTs, CBAs - evaluated the effects of pharmacological interve delirium - multicomponent non-p interventions - delirium occurrence as - published in English. Exclusion criteria: - unoriginal studies - not an ICU setting - pediatric participants - pharmacological interve Per Bra	d before and after <sup>1</sup> r older via reliable and of non- entions to prevent oharmacological primary outcome <u>rentions</u>		pharmacological multicomponent intervention (i.e. Assessment of SP, CS, EM,		endpoints: - the efficacy of non- pharmacological interventions, - combination of care - effectiveness of combinations of non- pharmacological interventions in preventing	<ul> <li>rate of delirium occurrence in non- pharmacological multicomponent interventions performed to prevent delirium (OR 0.58, 95% CI 0.44-0.76, p &lt;0.001)</li> <li>two effective bundles compared to control for the incidence of delirium: a) the combination of SP, CS, EM, PC, and AS (OR 0.47, 95% CI 0.35–0.64, p &lt; 0.002) b) the combination of SP and CS (OR 0.46, 95% CI 0.28–0.75, p &lt; 0.001)</li> <li>SUCRA analysis suggests with 76.8% that SP-CS was the highest among multicomponent interventions for</li> </ul>	(not only

AS = assessment, CBA = controlled before and after trial, CCT = controlled clinical trial, CS = cognitive stimulation, EM = early mobilization, PC = pain control, pts = patients, RCT= randomized controlled trial, SP = sleep promotion, SUCRA = surface under the cumulative ranking

This study revealed that non-pharmacological interventions, particularly multicomponent interventions, helped to prevent delirium in critically ill patients. In the network meta-analysis, the most effective care combination for reducing incidence of delirium was found to be multicomponent intervention, which comprises SP-CS-EM-PC-AS, and SP-CS.

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2116 Rahiminezhad 2022 PMID: 35619171 DOI: 10.1186/s1310 2-022-00489-z Specification of study: a single- blinded randomized controlled clinical trial	90 pts Inclusion criteria: - above 18 years - 1st day of ICU admission (pts under invasive MV, non-invasive MV, and not MV pts) - FOUR score ≥ 14 - no amputation - no fractures in the lower or upper extremities - no neuromuscular diseases (myasthenia gravis, Guillain–Barre syndrome, botulism and pesticide poisoning - no deep vein thrombosis - no metabolic disorders (including hypokalemia, hypophosphatemia, hypomagnesemia) - no allergy to olive oil in the massage group Exclusion criteria: - transferred to the ward during the intervention Per Branch n = 38 n = 36 n = 35 massage ROM control	<ul> <li>Control n=5 <ul> <li>a. ICU LOS &lt; 7</li> <li>days n = 3,</li> <li>b. inadequate</li> <li>loc n = 2</li> </ul> </li> <li>Massage n=8 <ul> <li>a. decline to</li> <li>participate n = 5</li> <li>b. ICU LOS &lt; 7</li> <li>days n = 2</li> <li>c. inadequate</li> <li>loc n = 1</li> </ul> </li> <li>ROM n=6 <ul> <li>a. decline to</li> <li>participate n = 3</li> <li>b. ICU LOS &lt; 7</li> <li>days n = 2</li> <li>c. inadequate</li> <li>loc n = 1</li> </ul> </li> </ul>	Group 1: ROM exercises (on pts extremities once a day for 7 consecutive days) Group 2: Massage	Routine care as usual	Primary endpoint: - muscle strength measured with a hand-held dynamometer before, before the intervention (T1), on the 4 <sup>th</sup> (T2) and 7 <sup>th</sup> (T3) day of intervention at 8 p.m.	Primary endpoints: - muscle strength of the right arm - before intervention lower strength in massage group than that of the control ( $p < 0.001$ , mean difference = -2.4) - mean difference of increase of muscle strength T3-T1 (mean+SD): a) ROM: 0.63 ± 0.17 b) massage: 0.29 ± 0.23 c) control: -0.55 ± 0.28 significant difference between the three groups (ANOVA, $p < 0.001$ , $F = 205.54$ ) Bonferroni post hoc test for mean difference between: a) massage and Rom (-0.34): $p < 0.001$ ) b) massage and control (0.84): $p < 0.001$ c) ROM and control (1.18): $p < 0.001$ c) ROM and control (1.18): $p < 0.001$ c) ROM and control (1.18): $p < 0.001$ c) and difference $= -2.45$ rean difference $= -2.45$ reand difference $= -2.45$ reand difference $= -2.45$ control: -0.56 ± 0.28 c) control: -0.56 ± 0.28 c) control: -0.56 ± 0.29 c) control: -0.56 ± 0.29 c) control: -0.56 ± 0.28 c) control: -0.56 ± 0.28 control: -0.76 ± 0.33 control: -0.76 ± 0.33 control: -0.76 ± 0.33 control: -0.75 ± 0.21 b) massage and ROM (-0.33): $p < 0.001$ c) ROM and control (1.18): $p < 0.001$ c) ROM and control (1.18): $p < 0.001$ c) ROM: -0.51 ± 0.21 b) massage 0.27 ± 0.18 c) control: -0.70 ± 0.33 c) control: -0.70 ± 0.33 c) control: -0.70 ± 0.33 c) control: -0.70 ± 0.33 c) control: -0.71 ± 0.29: $p < 0.001$ b) massage and ROM (-0.25): $p < 0.001$ c) ROM and control (0.27): $p < 0.001$ c) ROM and con	2

ICU = intensive care unit, loc = level of consciousness, LOS = length of stay, pts = patients, ROM = range of motion, T = timepoint

# The results of the present study showed that ROM exercises and massage were effective interventions in increasing muscle strength of the critically ill patients admitted to intensive care units.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2118 Zhou 2022 PMID: 35617287 DOI: 10.1371/journa I.pone.0268599 Specification of study: a prospective dual-center randomized controlled trial	150 pts Inclusion criteria: ->18 years of age - admitted to the ICU for the 1st time - expected ICU stay >72 h - conscious within the subsequent 24 h to respond to at least three of the following orders: "open and/or close your eyes," "look at me," "put out your tongue," "nod your head," and "raise your eyebrows" - BI >70 at 2 weeks before ICU admission Exclusion criteria: - pregnancy - deformity, paralysis, fracture, or surgery of limbs - pre-existing primary systemic neuromuscular disease that affects muscle strength - intracranial or spinal processes affecting motor function; - gastrointestinal surgery within 1 month - no expectation of any nutritional intake within the subsequent 48 h - terminal cancer, expected death, or extremely poor prognosis. Per Branch EM Group = 50 EMN Group = 50 EMN Group = 50		EM Group: early, individualized, progressive mobilization within 24 h of ICU admission EMN Group: early mobilization + guideline-based early nutrition (within 48 h of ICU admission)	Routine care	Primary endpoint: - occurrence of ICU- AW at discharge from the ICU Secondary outcomes: - muscle strength - functional independence - organ failure (SOFA) - nutritional status - duration of MV - ICU LOS - ICU mortality at ICU discharge.	Primary endpoint: - control had more incidents of ICU-AW at discharge than EM or EMN groups (16% vs. 2%; p = 0.014 for both) -ICU-AW (EM vs. control: p = 0.027, OR [95% CI] = 0.066 [0.006– 0.739], EMN vs. control: p = 0.016, OR [95% CI] = 0.065 [0.007– 0.607]). Secondary outcomes: -Barthel Index (control vs. EM/EMN: 57.5 vs 70.0; p = 0.022) - muscle strength, EMN vs control (p = 0.028) - nutritional status EMN vs control (p = 0.031) - organ failure EMN vs control 0 vs 0 (p = 0.614) - duration of MV control vs EM/EMN 0 vs 0 vs 0 (p = 0.753) - ICU LOS control vs EM/EMN 4.1 vs 4.5 vs 3.4 (p = 0.040) - ICU mortality control vs EM/EMN 2 vs 3 vs 2 (p = 1)	2→3 (high risk of bias)

EM = early mobilisation, EMN = early mobilisation with early nutrition, ICU-AW = ICU-acquired weakness, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients

### EM and EMN had positive effects. There was little difference between the effects of EM and EMN, except for muscle strength improvement. Both EM and EMN may lead to a lower occurrence of ICU-AW and better functional independence than standard care. EMN might benefit nutritional status more than usual care and promote improvement in muscle strength.

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Drop- out	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	Total	Rate					
#2119 Balke 2022 PMID: 35615672 DOI: 10.3389/fphys.2 022.865437 Specification of study: systematic review	26 RCTs <sup>1-26</sup> Inclusion criteria: - full text articles - RCTs - pts aged >18 years Exclusion criteria: - focused on histological and morphological changes only - investigated the acute effects of EMS - not written in English - grey literature or website articles - did not clearly report on included subjects, type of intervention or applied treatment, outcome measures, and statistical analysis - included healthy subjects - focused on other conditions - did not include humans - not original research Per Branch		EMS	Conventional care	Endpoints: - stimulated muscles/muscle area (quadriceps muscle only; two to four leg muscle groups; legs and arms; chest and abdomen) - treatment duration (<10 days, >10 days). -stimulation parameters (impulse frequency, pulse width, intensity, duty cycle) - the net EMS treatment time	No meta-analysis or comparative statistical analysis was performed - isolated stimulation of quadriceps muscles(n=10), 60% reported significantly larger improvement in the EMS group - combined stimulation of two to four leg muscle groups(n=8) All eight studies reported on muscle parameters and three (37.5%) detected significant positive EMS effects compared to control. - combined stimulation of legs and arms(n=3), Three studies of this group reported on muscle parameters, of which two reported significantly greater improvements compared to control, with one study applying EMS for ≤10 days, and two studies applying EMS for >10 days. - 2–4 Leg muscle groups and abdomen (n= 1) Improved muscle volume and functional independence without any significant differences in ICU LOS - abdomen and chest (n=2) significant reduction of ICU LOS.	1 → 3 (qualitative approach, no meta- analysis)

EMS = electrical muscle stimulation, LOS = length of stay, pts = patients

The overall efficacy of EMS was inconclusive and neither treatment duration, stimulation site nor net EMS treatment time had clear effects on study outcomes.

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103 pts		Control	Optimal Population	Primary Results	Evidence Grade
-> 18y         -> submitted to myocardial         #2120         Cordeiro         2022         PMID:         Exclusion criteria:         - previous cardiac surgery         - physical limitations         DOI: not         avilable	s that achieved d to chair <b>NM</b> nsfer on first (par y post-op and kine ibulation on in b cond day post-	<b>MG</b> assive nesiotherapy bed)	<b>Outcomes:</b> - duration of MV - ICU LOS - mortality - MRC (admission vs. discharge) - FIM (admission vs. discharge) - 6-MWT	Significant differences between the groups: - duration of MV (hours): MG: $6 \pm 2$ vs. NMG $10 \pm 3$ ; $p = 0.02$ - ICU-LOS (days): MG: $2 \pm 2$ vs. NMG: $4 \pm 3$ ; p < 0.001 - $6$ -MWT (admission vs. discharge) ( $\Delta$ ): MG: - $37 \pm 10$ vs. NMG: $-78 \pm 11$ ; $p < 0.001$ No significant differences between the groups: - mortality: n.s. - MRC (admission vs. discharge): n.s. - FIM (admission vs. discharge): n.s.	3

ALS = amylotrophe lateral sclerosis, COPD = chronic obstructive pulmonary disease, FIM = functional independence measurement, LOS = length of stay, MG = mobilisation group, MRC = medical research council, MV = mechanical ventilation, NMG = non-mobilization group; pts = patients; 6MWT = 6-minute walking test

Cardiac surgery patients in the early mobilization group had a reduced duration of MV and length of stay, better physical function, and had a lower decrease in distance walked during 6-MWT.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2123 Wanabe 2022 PMID: 35566716 DOI: 10.3390/jcm 11092587 Specification of study: A Multi- Center Prospective Cohort Study	N = 192 Inclusion criteria: - ICU stay for more than 48 h Exclusion criteria: - less than 18 years of age - unable to walk independently before admission - neurological complication - lacking communication skills due to pre-existing mental diseases - terminal state - history of psychiatric disorders - died or did not complete the assessment at 3 month follow-up after hospital discharge Per Branch 107 85	N=47 in Non EM (death, lost to follow-up after ICU discharge) N=47 in Non-EM (death, lost to follow-up after ICU	EM	Non-EM	Primary Endpoint: - incidence of psychiatric symptoms at 3 months after hospital discharge (using HADS, IES-R) Secondary Endpoints: - HADS subsets (depression, anxiety) and IES-R score (PTSD) at hospital discharge and 3 months after and changes between 3 months and hospital discharge - EQ-5D-5L at 3 months follow- up and at hospital discharge - walking independence at discharge - duration of MV - LOS ICU and hospital - incidence of delirium during ICU stay - incidence of ICU-AW at ICU discharge	<ul> <li>Primary Endpoint: <ul> <li>incidence of psychiatric symptoms: significantly lower in the EM group (odds ratio (OR): 0.27, adjusted p = 0.032]</li> <li>significantly lower incidence of PTSD (OR: 0.06, adjusted p = 0.026) and significantly lower HADS subset score for anxiety (adjusted p = 0.004) and IES-R (adjusted p = 0.009) in EM-group</li> <li>risk for developing psychiatric symptoms [RR: 0.49, confidence interval (CI): 0.29–0.83, p = 0.010], depression (RR: 0.52, CI: 0.27–0.99, p = 0.006), anxiety (RR: 0.27, CI: 0.10–0.71, p &lt; 0.001), and PTSD (RR: 0.07, CI: 0.01–0.54, p &lt; 0.001) at 3 months follow-up</li> </ul> </li> <li>Secondary Endpoints: <ul> <li>3 months follow-up, EM group lower incidence of PTSD (OR: 0.06, adjusted p = 0.026) and IES-R (adjusted p = 0.009)</li> <li>incidence of depression, anxiety, and PTSD, the HADS subset scores for depression and anxiety, and the IES-R score at the time of hospital discharge (n.s)</li> <li>comparing hospital discharge and at 3 months follow-up, changes in the HADS subset scores for anxiety in the EM group were significantly higher (adjusted p = 0.032)</li> <li>EQ-5D-5L 3 months follow-up (p=0.235) hospital discharge (p=0.384)</li> <li>walking independence at discharge higher in EM (p=0.032)</li> <li>duration of MV shorter in EM (p&lt;0.001)</li> <li>LOS ICU and hospital shorter in EM (ICU: p &lt;0.001 and hospital: p= 0.004)</li> <li>incidence of delirium during ICU stay lower in EM (p=0.013)</li> <li>incidence of ICU-acquired weakness (ICU-AW) at ICU discharge lower in EM (p= 0.006)</li> </ul> </li> </ul>	3

ICU = Intensive Care Unit, EM = Early Mobilization, HADS = Hospital anxiety and depression scale, IES-R = Impact of event scale-revised, PTSD = posttraumatic stress disorder, MV = Mechanical ventilation, LOS = Length of stay, ICUAW = Intensive Care Unit acquired weakness; OR= Odds ratio

EM in the ICU is significantly associated with lower rates of psychiatric symptoms, including depression, anxiety, and PTSD, at 3 months follow-up after hospital discharge.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2124 Vollenweider 2022 PMID: 35552550 DOI: 10.1371/jour nal.pone.026 7255 <b>Specification</b> of study: a systematic review	5 publications (1x within-patient randomized trial, 1x controlled randomized open clinical trial, 1x within- patient randomized trial, 1x randomized controlled cross-over trial, 1x controlled randomized pilot study) Inclusion criteria: -RCTs -in English or German language - mechanically and invasively ventilated and sedated critically ill pts > 18 years - evaluated the effect of passive motion of the lower extremities carried out in bed, either manually or through a therapy device, on musculature, inflammation, the immune system -development of ICUAW -included a comparison		Passive early motion interventions	Standard therapy -respiratory therapy -nursing measures and positioning	<b>Outcomes:</b> Effects of early passive motion -on musculature -on inflammation and immune system -on development of ICUAW	No p-values stated No significant difference between groups in: -muscle degradation -development of ICUAW Significant difference between groups in: - effect on musculature by passive bed cycling o preservation of muscle thickness o increase of microcirculation - application of a cuff with additional passive exercise and the high-dose passive exercise on a CPM splint led to significantly lesser muscle loss - Significant reduction of TNF-α Unclear effects on inflammation and immune system: - unclear effects on cytokines - Increase of pro-inflammatory IFN- γ	1 → 3 (no meta- analysis)

Pts = patients, ICU-AW = intensive care unit acquired weakness

Multicomponent strategy was the most effective non-pharmacological intervention in reducing the incidence of ICU delirium. Early mobilization and family participation involvement in non-pharmacological interventions seemed to be more effective in reducing the incidence of ICU delirium.

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Reference, Study Type	Cases and C (Participant #, Ch Tota	naracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2126 Bordas-Martinez 2022 PMID: 35479948 DOI: 10.3389/fmed.2022.8660 55 Specification of study: retrospective cohort study	159 patients admitted the intermediate respin (IMCU) from March 13 of 2020 Inclusion criteria - survival of severe COV - requirement of high of required [inspired oxyg >0.5] with HFNC , and/ (IOT-MV) or NIV-MV no exclusion criteria m Per Bra N=108	ratory care unit th until May 15th VID-19 pneumonia oxygen support gen fraction (FiO2) or either invasive		Physiotherapy group With : n=32 early PT, n=76 non- early PT	Non- physiotherapy group	Primary outcome - hospital LOS - subject and therapist safety Secondary outcome - multivariate analysis of MV obesity	Primary outcome - hospital LOS: 19 [ IQR 36.25] and 34 days (IQR 27.25) (p = 0.001) for early and non-early PT groups - no physiotherapist was infected, no subject adverse effect was identified - early-PT group: identified obesity [OR 3.21; p-value 0.028], invasive mechanical ventilation (OR 6.25; p-value<0.001) - non-early-PT-group:(OR 3.54; p- value 0.017) as independent factors associated with a higher risk of prolonged hospital stay	4

HFNC = high-flow nasal cannula, IQR = interquartile range, MV = mechanical ventilation, NIV = non-invasive, OR = odds ratio, PT = physio therapy

Rehabilitation in acute severe COVID-19 pneumonia is safe for subjects and healthcare workers and could reduce the length of hospitalization stay, especially in those that start early.

Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2127 Liu 2022 PMID: 35468868 DOI: 10.1186/s40560- 022-00613-8 Specification of study: retrospective cohort study	<ul> <li>progressive neurom</li> <li>post-cardiac arrest s</li> <li>unstable pelvic fract</li> <li>spinal injury with fractor</li> <li>or multiple absent ling</li> </ul>	ased on the Sepsis-3 lar disease nuscular disease syndrome ture acture of the spine,		<b>EM group</b> (rehabilitation at the level of sitting on the edge of the bed or more within the frst 3 days of the patients' ICU stay	Non-EM group	Primary outcome - in-hospital mortality - ambulatory dependence at the hospital discharge Secondary outcome - ICU-LOS - hospital stay - total hospital costs	Primary outcome - mortality : 7 (n=96) vs. 48 (n=200), OR= 0.22 [95% Cl 0.06–0.88]; p<0.01 - dependence at discharge: 26 (n=96) vs. 113 (n=200), OR=0.24 [95% Cl 0.09–0.61]; p<0.01 Secondary outcome - ICU-LOS (days) : Intervention= 5.3 [4.2–6.8] vs. control= 6.5 [5.0–10.7];p<0.01 - LOS hospital (days): intervention= 28.3 [16.8–46.1] vs. control= 34.0 [19.5–61.1]; p=0.10 - total costs: intervention= 24,823 [14,778– 39,703], control= 32,515 [20,060– 51,854]; p<0.01	4

CI = confidence interval, ICU = intensive care unit, LOS = length of stay, OR = odds ratio

Achieving mobilisation within the first 3 days of ICU stay was significantly associated with better outcomes. Patients with sepsis might benefit most from achieving mobilization within 2–4 days.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2128 Chen 2022 PMID: 35468538 DOI: 10.1016/j.ijnurstu. 2022.104239 <b>Specification of</b> <b>study:</b> a systematic review and network meta-analysis	29 RCTs, 7005 pts <sup>1-29</sup> Inclusion criteria: -pts (age >18 years) in ICU -non-pharmacological interventions as the intervention group - non-pharmacological interventions or routine care as the control group - reporting delirium incidence assessed by valid assessment tools -delirium duration -adopting RCT design Exclusion criteria: -subacute critical care unit Per Branch		non- pharmacological interventions	routine care	<b>Outcomes:</b> - incidence of delirium - duration of delirium	Results: -multicomponent strategy was the most effective non-pharmacological intervention compared to usual care in reducing incidence of ICU delirium (OR=0.43, 95% CI= 0.22–0.84) but not ICU delirium duration - specific multi-treatment interventions reduced the ICU delirium incidence and duration, particularly involvement of EM and family participation (OR = 0.12 with 95% CI = 0.02 to 0.83; mean difference = - 1.34 with 95% CI = -2.52 to -0.16)	1

Pts = patients, RCT = randomized controlled trial, ICU = intensive care unit, OR = Odds Ratio, CI = Confidence interval, EM = early mobilization

The study suggests that the multicomponent strategy was the most effective nonpharmacological intervention in reducing the incidence of ICU delirium. Early mobilization and family participation involvement in non-pharmacological interventions seemed to be more effective in reducing the incidence of ICU delirium.

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+2129 Kagan 2022 PMID: 35458151 DOI: 10.3390/nu140 81589 Kagan - age 1 - MV f - expe Exclus - cond - traur lumba - open compa - antic - artic - artic	<b>lusion criteria:</b> ge 18–90 years V for at least 48 h spected period of venti <b>lusion criteria:</b> onditions that impaired	lation ≥ 7d the cycling movement ery of the leg, pelvis, or	Group 1: Cycle ergometry with		Primary		
of study: function RCT severe	oen abdominal wounds npartment syndrome nticipated fatal outcom e-existing diagnosis of akness, acute stroke, o rdiorespiratory instabi ontra-indication for EN,	e of ICU neuromuscular r status epilepticus lity including mechanical or ion, high output fistula, atitis	standard EN (Jevity®, Abbott, Chicago, IL, USA) Group 2: Cycle ergometry with protein-enriched EN (veryhigh- protein formula Promote®, Abbott)	Conventional PT with EN: - (MOTOmed viva2, Medimotion, Carmarthenshire, Wales, United Kingdom, SA39 9AZ)	endpoint: - MV duration Secondary outcomes: - ICU mortality - ICU LOS - hospital LOS - reintubation rate	Primary endpoint: - MV duration n.s. Secondary outcomes: - no significant differences	2

EN = enteral nutrition, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, n.s. = not significant, PT = physiotherapy, pts = patients

Cycle ergometry combined with either standard enteral nutrition or with protein-enriched enteral nutrition seems to have no effect on MV duration.

Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2130 Watanabe 2022 PMID: 35415279 DOI: 10.2490/prm.20220 013 Specification of study: Retrospective single-center study	177 patients admitte January 2016 to Mar Inclusion criteria - pts > 18 years Exclusion criteria - ICU discharge withi - unable to walk inde hospitalization, were impaired - difficulty communi - mobility-limiting co unstable pelvic fract - considered termina life/ died during the Per Br	rch 2019 in 48h ependently before e neurologically cating onditions (e.g., ures) al or at the end of ICU stay	-	EM	Late mobilisation	Primary outcome - independent gait at discharge Secondary outcome - medical costs - 90-day survival and durations of ICU - hospital stays	Primary outcome         - independent gait at         discharge:         (OR: 4.47, 95% CI: 1.39–         17.43, P=0.011)         Secondary outcome         - medical costs:         Intervention= 19,210         [11,107– 26,620], control=         28,789 [20,969– 41,853];         p>0.0001         - 90-day survival(%):         intervention=80 (94),         control= 70 (76) ; p<0.0001	4

CI = confidence interval, EM = early mobilization, ICU = intensive care unit, LOS = length of stay, OR = odds ratio, pts = patients

EM, which refers to achieving the strength to sit on the edge of the bed within the first 5 days of the ICU stay, might be an adequate target to improve clinical outcomes.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2131 Campos 2022 PMID: 35412472 DOI: 10.1097/CCM .000000000 005557 Specification of study: RCT	ventilated for >4 Exclusion criteri - inability to wal admission -neur disease - spinal cord inju - epilepsy - risk of death w - musculoskelet conditions	ay mechanically 48h i <b>a:</b> ik prior to omuscular uries	92 drop-outs: (49 I, 43 C) reasons: - death - transferred to other hospital - palliative care - could not be assessed with FSS-ICU at ICU discharge	EM+ NMES - on quadriceps and tibialis anterior - once a day 60 min, 5d/week until ICU discharge	EM	Primary endpoint: FSS-ICU at ICU- discharge, hospital discharge and day of awakening Secondary outcomes: - MRC-SS - PFIT - Bathel index	Primary endpoint: - FSS-ICU at ICU discharge: I: 28 vs C: 18 p=0.004 on the first day awake: I: 22 vs C: 12 p=0.019 at hospital discharge: I: 33 vs C: 25 p=0.014 Secondary outcomes: at ICU discharge: - MRC-SS: 58.5 vs 50 p=0.001 - PFIT: 11 vs 7 p=0.001 - Barthel index: n.s. at first day awake: - MRC-SS: 54 vs 42 p=0.011 - PFIT: 9 vs 5 p=0.025 at hospital discharge: - MRC-SS: 59 vs 52 p=0.010 - PFIT: 11 vs 9 p=0.005 - Barthel index: n.s.	2

C = control, EM = early mobilisation, FSS-ICU = functional status score for ICU, I = intervention, ICU = intensive care unit, MRC-SS = medical research council sum-score, NMES = neuro-muscular electrical stimulation, PFIT = the physical function test in the ICU, pts = patients

Early neuromuscular electrical stimulation in addition to early mobilisation improves functional status and improves muscle strength in ICU patients.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2032 Sumin 2022 PMID: 35410009 DOI: 10.3390/ijerp h19074329 Specification of study: Observational study	60 pts Inclusion criteri - elective heart of vessel surgery w complications (i stay by 3 d or pr Exclusion criteri - patient refusal - severe comorb (neurological or - cognitive dysfu - post-op deliriu - agonizing patie - fatal post-op co (hospital death) Per B n = 31	or intrathoracic vith ncreasing ICU rolonged MV) ia: bidity orthopedic) unction m ents omplications		<b>Group 1:</b> achieved > 300m in 6MWT before discharge	<b>Group 2:</b> achieved < 300m in 6MWT before discharge	<b>Outcome:</b> factors determining functional status at discharge	Factors that determined functional status: - lower-extremity muscle strength 3d post-op: G1: 16.7 [13.2; 25.1] vs. G2: 12.6 [9.1; 14.9]; p = 0.001 - lower handgrip strength 3d post-op: G1: 28.0 [24.0; 35.0] vs. G2: 18.0 [15.0; 27.0]; p = 0.002 - foot extensor strength (MD 0.308; p= 0.019) - longer aortic clamping time (MD -0.401; p= 0.001) - longer ICU-LOS: G1: 5.5 [3.0; 6.0] vs. G2: 7.5 [3.0; 12.0]; p <0.001	3

ICU = intensive care unit, MV = mechanical ventilation, 6MWT = 6-minute walking test

Lower muscle strength, longer aortic clamping time and longer ICU stay are independent factors for reduced functional status after cardiac surgery.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2134 Sakai 2022 PMID: 35358285 DOI: 10.1371/jour nal.pone.026 6348 Specification of study: Retrospective cohort study	257 pts Inclusion criteria: - <18 years - received intens - sepsis diagnose - Bl score > 69 Exclusion criteria: - head injuries - burns - spinal injuries - lower limps with fractures - septic shock - unresponsive to - expected morta Per E	h multiple treatment		After assigning a specialized physical therapist	Before assigning a specialized physical therapist	Primary outcome: ADL recovery (BI ≥ 70 considered as ADL independence) Secondary Outcome: - hospital LOS - discharge Outcome Sample size calculation: 64 per group with an effect size of 0.5 and 80% power	Primary outcome: - independence in ADLs: BI ≥ 70: 39 (45%) vs. 39 (66%), p = 0.022 Secondary outcome: - hospital LOS: 28 (16-46) days vs. 18 (10-39); p = 0.016 - discharge to home: 41 (48%) vs. 32 ( 54%) p = 0.44)	4

ADL = activities of daily living, BI = Barthel index

Assigning a physical therapist to a patient with sepsis shortened the number of days until begin of rehabilitation.

Reference, Study Type	Cases and (Participant #, ( To	Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2135 Han 2022 PMID: 35301878 DOI: 10.1177/030 00605221087 031 Specification of study: RCT	140 pts Inclusion criteria: - 50 years or older - elective CABG for t between January 20 Exclusion criteria: - exercise-induced sy ventricular arrhythm - inability to exercise and walk owing to co - MV > 24h - fraction of inspired - new ischemic elect changes Per Ba SGR-Group	he first time 19 and June 2018 yncope or nias e omorbidities I oxygen >55% crocardiographic	16 pts (9 due to pain, 7 due to lack of motivation)	SGR (+UC) = respiratory exercises and daily walking exercises IGR (+UC) = early CR + general ward rehabilitation	Usual care	Primary outcome: - activities of daily living (Barthel Index score) Secondary outcomes: - post-operative LOS - PPC - atrial fibrillation during hospitalization - complications within 30 days of discharge (i.e., death, need for reoperation, atrial fibrillation, deep sternal infection, stroke, and re-admission to the hospital)	Secondary outcomes: - ICU and post-operative hospital LOS for IGR group statistically shorter compared with UC group and SGR group (p<0.05) - PPC (p1 = 0.740, p2 = 0.740, p3 = 1.000) and atrial fibrillation (p1 = 0.538, p2 = 0.682, p3 = 0.437): n.s. - complications higher in UC than SGR	2 → 3 (high risk of bias)
	(n = 47) IGR group (n =47)	UC group ( n = 46)					and IGR (p1 = 0.011, p2 = 0.011, p3 = 1.000)	

CABG = coronary artery bypass grafting, CR = cardiac rehabilitation, IGR = intensive care unit group rehabilitation, LOS = length of stay; post-operative pulmonary complications, MV = mechanical ventilation, n.s. = not significant, pts = patients, p1 = p-value of the SGR group vs. the UC group, p2 = p-value of the IGR group vs. the UC group, p3 = p-value of the IGR group vs. the SGR group vs. the SGR group vs. the SGR group vs. the SGR group, SGR = single general ward rehabilitation, UC = usual care

Early rehabilitation during the ICU stay and on the general ward results in significant improvements in functional independence.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2136 van den Oever 2022 PMID: 35285178 DOI: 10.14814/phy2.1 5213 Specification of study: prospective, observational study	10 pts. Inclusion criteria: - > 18y - mechanically ventilate - capable of active in-becycling Exclusion criteria: - contra indications for physical exercise Per Branch 2 8		Motorized cycling ergometer (MOTOmed Letto2) 5 min rest, 1min passive cycling, 2 min unloaded cycling	Non- motorized cycle ergometer (Lode) no passive cycling, resistance increased by 2 W every minute	Outcomes: - VO <sub>2</sub> , VCO <sub>2</sub> and workload versus time - HR, SpO <sub>2</sub> - VCO <sub>2</sub> removal and workload versus time - VCO <sub>2</sub> and heart rate versus VO <sub>2</sub> - EqO <sub>2</sub> and EqCO <sub>2</sub> versus time - VE versus time - VE versus VCO <sub>2</sub> - PaO <sub>2</sub> and PaCO <sub>2</sub> vs time - respiratory exchange ratio vs time - tidal volume versus expiratory minute volume	<ul> <li>- VO₂ max was not achieved by any patients</li> <li>- all remaining parameters increased during exercise, but no statistical analysis was performed</li> </ul>	3 → 4

EqCO<sub>2</sub> = ventilatory equivalents for CO2, EqO<sub>2</sub> = ventilatory equivalents for O2, VE = expiratory minute volume, W = watt

### Exercise by motorized and non-motorized cycle ergometer was feasible even though it did not reach maximal exercise capacity.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2139 Borges 2022 PMID: 35244377 DOI: 10.21470/1678- 9741-2021-0140 Specification of study: Systematic review without meta analysis	14 RCTs from 2020 (n = 1170 pts) <sup>1-14</sup> Inclusion criteria: - RCTs describing EM protocols - Pts following cardiac surgery  Per Branch		<b>Early mobilisation:</b> immediate postoperative period or 1 <sup>st</sup> postoperative day	Standard of care	Prescription of early mobilization	<ul> <li>Prescription of early mobilization: <ul> <li>n = 14 studies prescribed early mobilization in patients undergoing cardiac surgery</li> <li>EM is performed once or twice daily</li> <li>EM duration 10-30 minutes</li> <li>intensity of mobilization: <ul> <li>a) n = 2 studies aim for a low value using the borg scale</li> <li>b) n = 2 studies aim for a maximal increase in heart rate of 20 bpm</li> <li>c) n = 1 study aims for the highest possible intensity</li> <li>d) n = 9 studies did not report intensity</li> </ul> </li> </ul></li></ul>	1 → 3 (qualitative analysis only without meta- analysis)

EM = early mobilisation, pts = patients, RCT = randomized controlled trial

Early mobilisation in patients undergoing cardiac surgery is performed with different intensities up to twice daily for a maximum of 30 min.

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Reference, Study Type	(Participant #,	d Controls Characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidenco Grade
#2142 Nakamura 2022 PMID: 35182302 DOI: 10.1007/s11748- 022-01786-7 Specification of study: Retrospective cohort study	of aortic surgery	aortic surgery and le ICU surgery		<b>Early rehabilitation</b> (rehabilitation program prescribed by physicians, physical therapists, or occupational therapists within 3 days of aortic surgery)	Usual care	Primary outcome - physical function at discharge measured by the Barthel index score Secondary outcome - in-hospital mortality, -ICU LOS - hospital LOS - total hospitalization costs	Primary outcome - Barthel index score: difference= $4.0 (95\%Cl: 2.8$ to $5.2$ ), p<0.001 Secondary outcome - in-hospital mortality (%): difference= $-2.5 (95\% Cl:$ -3.0 to $-2.0$ ); p<0.001 - ICU LOS (days): difference= $-1.7 (95\%$ Cl-2.0 to $-1.4$ ); p<0.001 - hospital LOS (days): difference= $-5.2 (95\% Cl:$ -6.8 to $-3.7$ ) <0.001 - total hospitalization costs	4
conort study	N=44746	N=76278					(x100000 yen) : difference= -4.9 (95% CI: -6.6 to -3.1); p<0.001	

CI = confidence interval, ICU = intensive care unit, LOS = length of stay

Early rehabilitation within 3 days of aortic surgery was associated with improved physical functions at discharge, shorter ICU and hospital stays, and lower hospitalization costs without increased mortality.

#2145Inclusion criteria: - age > 18 years - ARDS pts in ICU - MV > 24 hoursEarly physiotherapy (including respiratory and rehabilitation activities; not further described): - in ICU/IMCU: o twice a day, ≥ 40Primary outcome: - number and type of physiotherapy treatments performed during hospitalization - number of physiotherapy-related AEsPrimary outcome: - number and type of physiotherapy treatments performed during hospitalization: - number of physiotherapy-related AEsPrimary outcome: - number of physiotherapy reatments performed during hospitalization - number of physiotherapy treatments performed during hospitalization - in ICU/IMCU: o twice a day, ≥ 40Primary outcome: - number of physiotherapy - number of physiotherapy - number of physiotherapy - in ICU/IMCU: o twice a day, ≥ 40Primary outcome: - number of physiotherapy - number of physiotherapy - number of physiotherapy - in ICU/IMCU: o twice a day, ≥ 40Primary outcome: - number of physiotherapy - number of physiotherapy - inticuring hospitalization - first time sitting out of head standPrimary outcome: - number of physiotherapy - inticuring hospitalization - inticuring hospitalizatio	Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
DOI:       10.1011/2       Exclusion criteria:       - cognitive impairment       - orgitive impairment       - orgitive impairment       - neuromuscular, orthopaedic, or any other disease hindering ambulation       - ostarting as soon as sedation was reduced and clinical conditions were stable ( <i>not further described</i> )       - functional independence in ADL assessed by Barthel Index       - number of AEs (n [%]): 32 (0.58%)       - number of AEs (n [%]): 32 (0.58%)       - n = 5 in ICU       - n = 5 in ICU       - n = 0 in general ward         Yudy       Per Branch       - in-hospital deaths for any cause       - in-hospital deaths for any cause       - MMS       - No detailed assessment was carried out because higher-quality evidence is available on this topic.       - n = 0 in general ward	Rossi 2022 PMID: 35086328 DOI: 10.4081/mon aldi.2022.208 7 Specification of study: Retrospective observational	Inclusion criteria: - age > 18 years - ARDS pts in ICU - MV > 24 hours - laboratory-confirmed COVID-19 diagnosis - treatment by respiratory physiotherapist during ICU stay Exclusion criteria: - cognitive impairment - neuromuscular, orthopaedic, or any other disease hindering ambulation		<ul> <li>(including respiratory and rehabilitation activities; not further described):</li> <li>in ICU/IMCU: <ul> <li>twice a day, ≥ 40</li> <li>minutes per session</li> <li>starting as soon as sedation was reduced and clinical conditions were stable (not further described)</li> <li>in general wards: <ul> <li>one session per day</li> <li>assignment of</li> </ul> </li> </ul></li></ul>		<ul> <li>number and type of physiotherapy treatments performed during hospitalization</li> <li>number of physiotherapy-related AEs</li> <li>Secondary outcomes: <ul> <li>physiotherapy treatments</li> <li>performed during hospitalization</li> <li>first time sitting out of bed, stand and walking</li> <li>6MWT</li> <li>1m-STST</li> <li>MRC-SS of upper and lower extremities</li> <li>functional independence in ADL assessed by Barthel Index</li> <li>ICU LOS</li> <li>hospital LOS</li> <li>duration of MV</li> <li>discharges at home, to in-patient rehabilitation or transferred to other hospital</li> <li>in-hospital deaths for any cause</li> </ul> </li> </ul>	<ul> <li>number and type of physiotherapy treatments performed during hospitalization:         <ul> <li>number of physiotherapy entries registered during the hospital stay (Median [IQR]): 60.5 [36-93]</li> <li>type of physiotherapy treatments at first assessment:                 <ul> <li>12% sitting on the edge of bed</li> <li>88% In-bed interventions</li></ul></li></ul></li></ul>	

ADL = activities of daily living, AE = adverse events, ARDS = acute respiratory distress syndrome, ICU = intensive care unit, IMCU = intermediate care unit, LOS = length of stay, MMS = Manchester mobility score, MRC = medical research council sum score, MV = mechanical ventilation, pts = patients, 1m-STST = 1-minute sit-to-stand test, 6MWT = 6minute walking test

Early physiotherapy is feasible and might be safe in critically ill COVID-19 patients.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Watanabe 2021 DOI: 10.2490/prm.2 0210054 PMID: 35083381 <b>Specification</b> of study: Single-Center, retrospective, cohort study	patients at ICU between April 2019 and March 2020 → 54 pts Inclusion criteria: - age > 18 years - mechanical ventilation in ICU >48 hours Exclusion criteria: - BI <70 before admission - unable to walk independently before hospitalization - neurological complications - Lack of communication skills because of diseases - Terminal / end of life care Per Branch		High doses of rehabilitation via the median of the daily mean RATs	Low dose of rehabilitation via the median of the daily mean RATs	No sample size calculation (retrospective study) <b>Primary Outcome:</b> - rate of ADL dependence at discharge (BI < 70) <b>Secondary</b> <b>Outcomes:</b> - medicals costs duration of MV - lengths of ICU and hospital stay - rate of discharge to home - hospital survival rate - incidence of delirium during ICU - incidence of ICU- AW at ICU discharge	<ul> <li>Baseline Characteristics: <ul> <li>median of daily mean RATs during entire ICU</li> <li>admission period was 3.6 (IQR 1.4 – 9.6) -&gt; pts were</li> <li>divided into high-dose (&gt;3.6) and low-dose (&lt;3.6)</li> <li>rehabilitation group</li> </ul> </li> <li>Primary Outcomes: <ul> <li>rate of ADL dependence at discharge was significantly</li> <li>lower in the high-dose rehabilitation group (81%) than in the low-dose rehabilitation group (22%), p &lt; 0.001</li> </ul> </li> <li>Secondary Outcomes: <ul> <li>incidence of ICU-AW at ICU discharge was significantly lower in high-dose rehabilitation group (70%) in low-dose rehabilitation group (37%), adjusted p = 0.016</li> <li>no significant differences in other secondary outcomes</li> </ul> </li> <li>Post-hoc Sensitivity Analysis <ul> <li>increased RATs during entire ICU admission period and ICU admission after meeting criteria for physiological stability was significantly associated with lower ADL dependence at discharge (p &lt; 0.001)</li> <li>higher RATs from low-level activity before meeting the criteria for physiological stability showed significant association with lower ADL dependence at discharge (p &lt; 0.001)</li> </ul> </li> </ul>	4

ICU = intensive care unit, pts = patients, BI = Barthel Index, RATs = Rehabilitation Activity Time score, MV = mechanical ventilation, ICU-AW = intensive care unit-acquired weakness, IQR = interquartile range; ADL= activities of daily living

ADL dependence was lower among those who underwent high-dose rehabilitation.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type		ses and Contr pant #, Charac Total		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2148 Dos Santos Moraes 2021 PMID: 35076492 DOI: 10.3390/clinpract1 2010002 Specification of study: retrospective observational study	mobility leve Inclusion crit - aged ≥18 ye the ICU for m reason Exclusion crit patients with - neurodeger - spine and/c amputation c - diagnosis of in the acute c which any co	at ICU with di at ICU with di arears who were bedical or elect teria teria transitive diseas for lower limb f of one or both for one or both for cerebrovascu or chronic pha onditions that te or make it in	e admitted to tive surgical se ractures, lower limbs ilar accident se or in	Kate	- low mobility (n=28) - moderate mobility(n=33) - high mobility (n=60)	No control group	Endpoints (not more precisely defined) - ICU discharge - mortality	Outcomes - low mobility (n=28): 45 times more likely to die (OR = 45.3; 95% CI = 3.23–636.3) and 88 times less likely to be discharged from the ICU (OR = 0.22; 95% CI = 0.002–0.30); both p<0.05 - moderate and high mobility levels were not associated with the investigated outcomes	4
	N=28	N=33	N=60						

CI = confidence interval, ICU = intensive care unit, OR = odds ratio

Patients with low mobility had a higher chance of death and a lower chance of discharge from the ICU. Moderate and high mobility were not associated with the investigated outcomes.

Reference, Study Type	(Part	icipant #,	d Controls Characteri tal	stics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2150 Kinoshita 2022 PMID: 35054051 DOI: 10.3390/jcm110 20357 Specification of study: retrospective cohort study	(COVID-1 university rehabilita until 31 M Inclusion - patients - received Exclusion - age< 18 - low ADL before ad	9) in the IC v hospital v tion under lay 2021 criteria admitted l rehabilita vears independen mission iving venti		IV from a ed control	3 (non- survivor)	Early rehabilitation A: from the third day of admission under deep sedation, ROM training, 20 min of sitting on the edge of the bed B: next day after admission, ROM training, 20 min of sitting on the edge of the bed C: next day after admission, ROM, 20 min of sitting on the edge of the bed D: with a 6-L reservoir mask on admission day, ROM, 20 min of sitting on the edge of the bed	No control group	Endpoints (not more precisely defined) - period from intubation to extubation - ICU LOS - the extent of ADL improvement during ICU admission - mortality rate - the number of severe adverse events during rehabilitation	Outcome - time from intubation to extubation (days): 4.9 ± 1.1 - ICU stay (days): 11.8 ± 5.0 - ADL: was severely impaired (FIM=36.5 (28.0–40.5), BI=22.5 (3.75–40.0)) - mortality: 42.8% (3 non- survivor) - no serious adverse events during rehabilitation	4

ADL = activities of daily living, BI = Barthels index, CI = confidence interval, FIM = functional independence measure, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, OR = odds ratio, ROM = range of motion

Early rehabilitation in the acute disease stage is essential for improving physical functions.

Reference, Study Type	Cases and (Participant #, C		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Tot	tal					Primary outcome	
#2152 Elkbuli 2022 PMID: 35026443 DOI: 10.1016/j.jss.2021.11. 011 Specification of study: retrospective cohort analysis	<ul> <li>11.937 patients</li> <li>Inclusion criteria <ul> <li>adult patients (age</li> <li>suffered traumatic</li> <li>evaluated/treated</li> <li>centre</li> <li>received PT service</li> <li>hospital stay</li> </ul> </li> <li>Exclusion criteria <ul> <li>paediatric patients</li> <li>patients who were</li> <li>another facility or di</li> <li>hospital discharge</li> </ul> </li> </ul>	injury in our trauma es during their (aged <18 years) transferred to ied prior to	N=138 (did not meet the inclusion criteria	TBI trauma patients Early PT : n=311 - early- intermediate(24- 48h) : n=280 - late intermediate(48- 72h): n=133 - late (>72h): n=411	Non-TBI trauma patients early PT : n=4782 - early- intermediate (24-48h) : n=2416 - late intermediate (48-72h): n=1035 - late (>72h): n=2431	Primary outcome - hospital discharge disposition Secondary outcome - hospital LOS - ICU LOS Tertiary outcome measures were complication rates	- intervention: (n=1035) 60% lower odds of being discharged home without services (P < 0.05), significantly increased hospital and ICU length of stay (Hospital LOS, ICU-LOS) (P < 0.05), significantly higher odds of complications (VTE, pneumonia, pressure ulcers, ARDS) (P < 0.001). – control: (n=411) 76% lower odds of being discharged home without services (P < 0.05), significantly longer Hospital LOS /ICU-LOS (P < 0.05) <b>Secondary outcome</b> - hospital LOS (days): $3.6 \pm 4.3$ (n=4782), $4.7 \pm 4.9$ (n=2416), $5.9 \pm 4.7*$ $18.6 \pm 28.7* < 0.001$ - ICU-LOS (days): $0.79 \pm 2.71$ (n=4782), $1.2 \pm 3.3$ (n=2416), $1.4 \pm 3.2$ (n=1035), $8.16 \pm 18.33$ (n=2431); p<0.001 <b>Tertiary outcome</b>	4
	N=10.664	N=1.135				rates	- delayed PT initiation: higher complication rates of DVT (P < 0.001), pneumonia (P < 0.001), pressure ulcers (P < 0.001), PE (P < 0.001), ARDS (P < 0.001), and VAP (P < 0.001)	

ARDS = acute respiratory distress syndrome, DVT = deep vein thrombosis, ICU = intensive care unit, LOS = length of stay, PE = pulmonary embolism, PT = physical therapy, TBI = traumatic brain injury

Among traumatically injured patients, early PT is associated with decreased odds of complications, shorter H-LOS and ICU-LOS, and a favourable discharge disposition to home without services

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2153 Sasano 2022 PMID: 35018344 DOI: 10.1097/CCE.0000000 000000604 Specification of study: retrospective cohort study	99 adult patients ad the Nagoya City Univ Medical Center from to December 31, 202 Inclusion criteria - Pts expected to sta least several days Exclusion criteria - elevated intracrani instability, neuromu - active bleeding, be - score on the Richm Sedation Scale of +2	versity West n January 1, 2015, 20 ny in the ICU for at al pressure, spinal scular paralytics rd-rest order nond Agitation- or higher		out-of-the-ICU activities include visiting indoor area, visiting our outdoor garden, and bathing	No control group	<ul> <li>primary outcome         <ul> <li>the occurrence rate of physical safety events, (unintentional removal of medical devices, patient agitation requiring the discontinuance of the session, falling, and injury requiring medical treatment)</li> </ul> </li> <li>secondary outcome         <ul> <li>the occurrence rate of adverse physiologic change(defined as the occurrence of the following after the mobility session)</li> </ul> </li> </ul>	Primary outcome - rate of physical events: 27 potential safety events detected in 24 sessions across 14 patients - one event (0.2%; 95% Cl, 0.006–1.3%) of dislodgement of a tracheostomy tube occurred when the patient transitioned to sitting on the edge of bed Secondary outcome - in 23 sessions (5.7%; 95% Cl, 3.6–8.4%) out of the 406 sessions: 26 adverse physiologic changes occurred among 13 patients	4

CI = confidence interval, ICU = intensive care unit, LOS = length of stay, OR = odds ratio, pts = patients

An out-of-the-ICU program can be provided safely to adult ICU patients, provided that it is supervised by a dedicated intensivist with an appropriately trained multiprofessional staff and equipment on-site.

Cases and Controls (Participant #, characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Eviden ce Grade	
Total							
80 ICUs were screened in Spain -> 668 pts were included Inclusion criteria: - IMV >48 hours Exclusion criteria: - pregnant women - those referred to the ICU from other Hospitals - primary neurologic or neuromuscular pathology - unable to walk (mobility aids allowed) - recent limb amputees - users of orthopaedic devices - BMI > 35 Per Branch	n = 63 (lost to follow up)	ABCDE-Bundle	standard of care	Sample Size Calculation: 531 pts Primary Outcomes: - pain level - Level of cooperation via Hermans' five commands - patient days with delirium - Patient days with delirium - Patient days with physical restraint - Level of mobility via IMS - implementation of bundle components ABC, D and E Secondary Outcome: - cumulative drug dosing by IMV Tertiary Outcomes: - need for reintubation / tracheostomy - ICU LOS - IMV days - bed rest days - ICU mortality - development of ICUAW via MRC-score base at first awakening Independent variables - Protocols with analgosedation algorithms (ABC in the bundle) - Delirium prevention and management protocols (D in	<ul> <li>- 605 patients were studied from 80 ICUs resulting in 5214 days with IMV.</li> <li>Primary Outcomes: <ul> <li>pain level: not assessed on 83.6% of days (95% CI 81.1-86.1), found to be zero on 11.1% days (95% CI 8.1-3.1), mild to moderate on 3.2% (95% CI 2.1-4.2), moderate to severe 1.9% (95% CI 0.8-2.8) and very intense on 0.2% days (95% CI 0.08-0.5)</li> <li>level of cooperation: sufficient to make the MRC feasible on 20.7days (95% CI 17.9-23.4)</li> <li>pts days with delirium: 4.2% of days (95% CI 2.8-5.5)</li> <li>physical restraint applied on 25.2% of days (95% CI 2.2-28.1)</li> <li>immobility (IMS of 0) on 69.6% of days (95% CI 2.2-28.1)</li> <li>133 (22.0%) were admitted to an ICU that implemented a protocol with analgosedation algorithms</li> <li>delirium prevention and management protocol (D) was applied in 68 (11.2%) patients, and these patients had more pain assessments, a higher level of cooperation, and more MRC assessments; they had</li> <li>no lower incidence of delirium or greater mobility</li> <li>early mobilization protocol (E) was applied in 51 (8.4%) pts. These patients received more pain assessments, registering no differences in level of cooperation, but more days of mobility with an IMS score of 1 to 2</li> </ul> </li> <li>Seconday Outcome: <ul> <li>patients who were admitted to an ICU that implemented a protocol with analgosedation algorithms for dose management and adjustment (ABC) received more opioids (remifentanil IVI, and fentanyl bolus and tramadol in divided doses) and more metamizole as a bolus and divided dose alike. Likewise, they received more dexmedetomidine IVI, more midazolam boluses, and also cisatracurium IVI and rocuronium boluses</li> <li>pts admitted to an ICU that implemented a elirium prevention and management protocol received more propofol and dexmedetomidine IVI</li> <li>pts admitted to an ICU that implemented early mobilization protocol received more remifentanil, propofol and dexmedetomidine IVI</li> <li>pts admitted to an ICU that implemented early mobi</li></ul></li></ul>	4	
	characteristics) Total 80 ICUs were screened in Spain -> 668 pts were included Inclusion criteria: - IMV >48 hours Exclusion criteria: - IMV >48 hours Exclusion criteria: - pregnant women - those referred to the ICU from other Hospitals - primary neurologic or neuromuscular pathology - unable to walk (mobility aids allowed) - recent limb amputees - users of orthopaedic devices - BMI > 35	(Participant *, characteristics)     out Rate       Total     Out Rate       Total     Rate	(Participant #, characteristics)out RateInterventionTotalInterventionB0 ICUs were screened in Spain -> 668 pts were includedInterventionB0 ICUs were screened in Spain -> 668 pts were includedInterventionInclusion criteria: - IMV >48 hoursInterventionExclusion criteria: - pregnant women - those referred to the ICU from other Hospitals - primary neurologic or neuromuscular pathology - unable to walk (mobility aids allowed)n = 63 (lost to follow up)recent limb amputees - users of orthopaedic devices - BMI > 35ABCDE-Bundle	(Participant #, characteristics)out RateInterventionControlTotalInterventionControl80 ICUs were screened in Spain -> 668 pts were includedInclusion criteria: - IMV >48 hoursInclusion criteria: - IMV >48 hoursInclusion criteria: - pregnant women - those referred to the ICU from other Hospitals - primary neurologic or neuromuscular pathology - unable to walk (mobility aids allowed)n = 63 (lost to follow up)ABCDE-Bundlestandard of careMathematical Section Sect	Characteristics)out RateInterventionControlOptimal PopulationTotalTotalPrimary Dutcomes: - pain level - Level of cooperation via Hermans' five commands - patient days with delirium - restraint - Level of mobility via IMS - implementation of bundle components ABC, D and EExclusion criteria: - primary neurologic or neuromuscular pathology - unable to walk (mobility aids allowed) - recent limb amputes - users of orthopaedic devices - BMI > 35n = 63 (lost to follow up)ABCDE-Bundlestandard of careTertiary Outcomes: - need for reintubation / tracheostomy - ICU LOS - IMV days - bed rest days - ICU mortality - development of ICUAW via MRC-score base at first awakeningPer BranchIndependent variables - Protocols with analgosedation algorithms (ABC in the bundle)Independent variables - Protocols with analgosedation algorithms	Intervention characteristics         out Rate         Intervention Rate         Control         Optimal Population         Primary Results           Total	

Pts = patients, ICU = intensive care unit, IMV = invasive mechanical ventilation, BMI = Body Mass Index, MRC = Medical Research Council, IMS = ICU mobility scale, LOS = length of stay, ICUAW = intensive care unit acquired weakness, BI = Barthel Index, SOFA = Sequential Organ Failure Assessment, APACHE II = Acute Physiology and Chronic Health Evaluation II, IVI = intravenous injection

# The implementation rate of ABCDE bundle components was very low, but when implemented, patients had a shorter ICU stay, more analgesia dosing, and lighter sedation.

Reference, Study Type	(Partic Charact	d Controls ipant #, eristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2155 Cordeiro 2021 (PMID: 34988326) DOI: not available Specification of the study: Prospective cohort study	and/or mitral <b>Exclusion crit</b> - patients with impairment th functional eva - death - > 4 p.o. days	eria: rs e surgery (aortic ) eria: n cognitive nat prevented aluation		<b>Cohort A:</b> walking at least 15 m in the ICU until discharge	<b>Cohort B:</b> not able to walk ≥ 15 m	Primary outcome: - functionality assessed with FMI scale and Perme scale Secondary outcomes: - adverse events during walking	Primary outcome:         - cohort A showed a smaller decrease in FIM scale         than cohort B (27 ± 3 vs. 36 ± 5, p < 0.001)	3

FIM = functional independence measurement, ICU = intensive care unit, Perme = Perme intensive care unit mobility score, p.o. = post-operative

Early ambulation in patients undergoing elective valve replacement surgery might be associated with greater functionality at ICU and hospital discharge.

Reference, Study Type	(Partic Charact	d Controls ipant #, ceristics) ital	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2158 O'Neil 2022 PMID: 34978322 DOI: 10.1093/jbcr /irab248 Specification of study: retrospective cohort study	127 pts from 24 a burn ICU whi early mobilizat Inclusion criter - mechanically Exclusion crite - extubation or therapy evalua Per B 95	le using an ion algorithm r <b>ia:</b> ventilated pts. <b>ria:</b> r death before		Active group (sitting on edge of bed or higher)	Inactive group (in bed mobility or dependent transfer)	<b>Outcomes:</b> - %TBSA - tracheostomy rate - LOS - mortality	<b>Outcomes (no significance level given):</b> - %TBSA burnt: AG: 14.11 vs IG: 25.31 - tracheostomy rate: AG: 25% vs. IG: 26% - LOS (d): AG: 20.95 vs. IG: 27.58 - mortality: AG: 9% vs. IG: 23%	4

AG = active group, ICU = intensive care unit, IG = inactive group, LOS = length of stay, %TBSA = percentage of total body surface area

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	Cases and Co (Participant #, Cha Total	aracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2159 Mayer 2021 DOI: 10.1093/ptj/ pzab301 <b>Specification</b> of study: Retrospective cohort study	315 pts from 2010 to 2 Inclusion criteria: - >18y - requiring ECMO > 72 Exclusion criteria: -pediatric pts. -pregnant individuals -prisoners -requiring ECMO < 72 h Per Bran during ECMO: 218 after ECMO: 70	h our		Rehabilitation during ECMO OR Rehabilitation received after ECMO	No rehabilitation	Primary outcome: in-hospital mortality Secondary endpoint: - hospital LOS - discharge destination - 30-day readmission rates	Primary outcome: - in-hospital mortality: during ECMO: 103/218 (47%) vs. after ECMO: 26/70 (37%) vs. no rehabilitation: 27/27 (100%); p < 0.001 Secondary outcomes: -hospital LOS: rehabilitation during ECMO (44.8/SD 49.4) vs. rehabilitation after ECMO (40/SD 39) vs. no rehabilitation (10/SD 8.3), p<0.001 - no significant differences at discharge destination and 30- day-readmission rates	4

ECMO = extracorporeal membrane oxygenation; LOS=Length of stay

The patient functional response during physical rehabilitation is an important indicator of illness and potential recovery.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2163 Afxonidis 2021 PMID: 34946461 DOI: 10.3390/heal thcare91217 35 Specification of study: RCT	<ul> <li>hemodynamic ins</li> <li>dyspnea/invasive</li> <li>support/oxygen sa</li> <li>neurological diso</li> <li>mobile disabilitie</li> </ul>	e perform s elective surgery stability e ventilator aturation <90% rders		Early and enhanced physiotherapy care: 1 early PT session on the day of the operation + 3 daily PT sessions during the first 3 days of ICU or until discharge.	Standard of care (twice per day, from first post- operative day until discharge)	Primary endpoints: - ICU-LOS - hospital LOS Secondary outcomes: - hemodynamic measurements - laboratory measurements	Primary endpoints: - ICU- LOS: 23.2d intervention group vs 25.4d control(MD: 2.2h, 95% CI 1.3- 3.2 h, p<0.001) - hospital LOS: 8.1d intervention groups vs 8.9d control (MD: 0.8d, 95% CI 0.6- 1d, p<0.001) Secondary outcomes: - hemodynamic measurements: n.s. - laboratory measurements: n.s.	2

CABG = coronary artery bypass grafting, GCS = Glasgow coma scale, LOS = length of stay, PT = physio therapy, pts = patients, RCT = randomized controlled trial

#### Early and enhanced physiotherapy care decreases the length of ICU stay and hospital stay.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total		Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2164 Thiolliere 2021	276 patients							
PMID: 34844035 DOI:	Inclusion criteria: - patients >70 years - admitted to the ICU for more than 48h Exclusion criteria: - death before day 180 - lost to follow-up - ADL - score not available			Out-of-bed mobilisation       No out-of- bed mobilisation       mobilization on the decreased 6- month       OoB 4.5 [3-6]) p=0.001	No out-of-	impact of OoB	- 6-month ADL score: (OoB 6 [4.5-6] vs. no-	
10.1016/j.jcrc.202 1.11.007					3			
Specification of study: a cohort study			-			autonomy	greater risk of 6-month decreased autonomy (aOR 2.43 [1.18; 4.98])	
(ancillary study of RCT)	Per Bra 226 intervention	50 control						

ADL- Score = activities of daily living score, OoB = out-of-bed

Conclusions: Mobilisation during the ICU stay of elderly ICU patient survivors was associated with a lower decreased autonomy at 6 months.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2167 De Azevedo 2021 (PMID: 34773985 DOI:	211 pts Inclusion criteria: - expected ICU stay Exclusion criteria: - pregnant - moribund - under ventilation : enrolment - unable to walk wit before the acute illr - severe cognitive ir hospitalization - neuromuscular dis - acute pelvic fractu - unstable spinal tra - severe liver diseas - death <48h - early extubation - fiO2 > 60% - cannot provide nu - physical limitation	4 days > 96h before hout assistance hess npairment before seases ire huma e	physical limitation, protocol violation)	-2 daily sessions of cycle ergometry exercise (15 min each) - immediately	physiotherapy + Protein 1.19g/kg/day:	Primary endpoint: - PCS score at 3 and 6 months	Primary endpoint: - PCS was higher in the intervention group at 3 months (p = 0.01) and 6 months (p = 0.01) Secondary outcome: - ICU-acquired weakness was identified in 16 (28,5%) and 26 (46,4%) pts in intervention and control groups (p=0.05) - ICU mortality rates in intervention and control groups were 23 (26.4%) and 41 (43,6%) (p = 0.01) - hospital mortality rates were 31.2% and 53.4% (p=0.002) - 6-months mortality rates were 33.3% and 54.2 % (p=0.005) in intervention and control group - no difference in LOS/	2
	99	112					duration of MV	

h = hours, LOS = length of stay, MV = mechanical ventilation, PCS = physical component summary, pts = patients

#### This study showed that a high-protein intake and resistance exercise improved the physical quality of life and survival of critically ill patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristic Total	5) Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2171 Prasobh 2021 PMID: 34535456 DOI: 10.1136/bmjo q-2020- 001256 Specification of study: Retrospective analysis	<ul> <li>1.320 pts from 2015 to 2019</li> <li>Inclusion criteria: <ul> <li>&gt; 14y</li> <li>undergoing CABG, valve repa</li> <li>replacement, or aortic dissections</li> <li>surgery</li> <li>admitted to the CTICU</li> </ul> </li> <li>Exclusion criteria: <ul> <li>requiring mechanical or</li> <li>circulatory devices to maintain</li> <li>haemodynamic stability</li> <li>GCS &lt; 13</li> <li>complications that limited</li> <li>mobility (stroke, open sternum)</li> <li>limited preoperative mobility</li> </ul> </li> <li>Per Branch <ul> <li>1320</li> </ul> </li> </ul>	on I	<ul> <li>mobility-level checklist</li> <li>initiating PT referrals</li> <li>patient and family</li> <li>engagement (booklet</li> <li>with mobilisation advice)</li> <li>enhancing the</li> <li>mobilisation experience</li> <li>(pain control)</li> <li>color-coded risk</li> <li>categories</li> <li>adopting technology</li> <li>(telemonitoring)</li> <li>protocol for initiation</li> <li>and termination of</li> <li>mobilisation</li> <li>visual reminders</li> <li>communication of</li> <li>mobility level (during</li> <li>multidisciplinary rounds)</li> </ul>		<b>Outcomes:</b> - patients who progressed (%) - time to out-of- bed-mobilisation - IMS - FIM	<b>Outcomes:</b> - patients who progressed (%): initially 55%, after 1 year 95% - time to out-of-bed-mobilisation: postintervention 11.74h vs. preintervention: 22.77h (p<0.05) - IMS: postintervention: 7.23 vs. Preintervention: 3.96 (p = 0.00) - FIM: postintervention: 58.62 vs. Preintervention: 54.23 (p = 0.00)	4

CABG = coronary artery bypass graft, CTICU = cardiothoracic intensive care unit, FIM = functional independence measure, GCS = Glasgow coma scale, IMS = ICU mobility scale

The implementation of an early mobiliastion protocol reduces the time to out-of-bed mobilisation and increases the IMS level reached and functional independence.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2172 Wang 2021 (PMID: 34406169 DOI: 10.1097/CC M.00000000 00005285 ) Specification of study: systematic review with meta- analysis	60 publications (57 RCTs, 3 controlled clinical trials) <sup>1-60</sup> 5352 pts Inclusion criteria - RCTs and CCTs - adults ≥18y admitted to an ICU - English language Exclusion criteria - pts with head injuries, cerebrovascular accidents, burns, and spinal injuries		Physical rehabilitation	Standard care	Outcomes: - muscle strength - physical function - mortality - health-related quality - duration of MV - MV free days at day 28 - ICU and Hospital LOS	Significant outcomes:         1) MV (46 studies)         - overall: MD -0.18d (95% Cl: -0.37 to 0.02)         - low dose CG: MD -1.6d (95% Cl: -2.49 to -0.71) for         - functional intervention: MD -1.15d (95% Cl: -1.99 to -0.30)         2) ICU LOS (47 studies)         - overall: MD -0.80d (95% Cl: -1.37 to -0.23)         - low dose CG: MD -1.87d (95% Cl: -3.16 to -0.58)         - functional intervention: MD -1.31d (95% Cl: -2.46 to -0.16)         3) hospital LOS         - overall: MD -1.75d (95% Cl: -3.03 to -0.48)         - low dose CG: MD -2.45d (95% Cl: -4.05 to -0.84)         - functional intervention: MD -1.90d (95% Cl: -3.74 to -0.06)         Non-significant outcomes:         4) mortality n.s.         5) muscle strength n.s.         6) physical function         - at ICU discharge n.s.         - at G months n.s.         7) MV free days n.s.         8) HRQL at 6 months n.s.         9) HRQL at 6 months n.s.         5) muscies by dosage was not possible	1

CCT = controlled clinical trial, d = days, ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, pts = patients, RCT = randomized controlled trial, y = years

Physical rehabilitation seems to have a benefit in relation to ICU LOS, hospital LOS and physical function.

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Reference, Study Type	(Partici Charact	d Controls ipant #, ceristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2173 Iwai 2021 PMID: 34395932 DOI: 10.2490/prm.202 10030) Specification of study: single- center retrospective before/after study	713 consecu admitted to Exclusion cri - <18y - LOS < 48h - cardiac sur Per B 330	ICU iteria:		Phase II: dedicated PT allocated to ICU (1x/day 20-60 min)	<b>Phase I:</b> no dedicated PT	<ul> <li>days to first</li> <li>rehabilitation</li> <li>number of</li> <li>Interventions</li> <li>duration of MV</li> <li>LOS</li> <li>extubation</li> </ul>	Significant differences between the groups: days to first rehabilitation: phase I: 4.0 (2.5– 8.0) vs. phase II: 1.0 (1.0–1.0); p <0.001 number of interventions: phase I: 29 (25.4%) vs. phase II: 90 (67.2%); p <0.001 No significant differences between the groups: - duration of MV - ICU-LOS - hospital LOS - extubation	4

LOS = length of stay, MV = mechanical ventilation, PT = physical therapy

#### No detailed assessment was carried out because higher-quality evidence is available on this topic

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Populatio n	Primary Results	Evidence Grade
#2174 Koyuncu 2022 PMID: 34346134 DOI: 10.1111/jocn.15986 Specification of study: a quasi- experimental non- randomized study with historic control	51 patients Inclusion criteria: - adults >18 years - underwent major abdominal surgery - had an American Society of Anesthesiologists score of less than 4 - did not have a communication disorder - had no diagnosis to limit mobilization Exclusion criteria: - emergency surgery - postoperative complications - no toleration of mobilization	N = 9 (excluded in control group 2x emergency surgery, 2x post-surgical complications) (excluded in intervention group 2x emergency surgery, 2x post-surgical complications, 1x receiving inotropic support in the postoperative period)	Mobilisation training by research nurse the evening before operation + application of a mobilization protocol on the 0th postoperative day	Mobilisation postoperative ly by the nurses according to the decision of the nurse and physician in the intensive care unit (ICU) on the day of the operation	Endpoints: - time to mobilizati on after ICU admission - ICU LOS - hospital LOS - higher sleep quality	Significant differences between the groups in: - time to mobilization after ICU admission (6.22 ± 1.95 hours vs 12.21 ± 3.76 hours) p<0.05 - ICU LOS (2(1-2) vs 4(1-7)) p<0.001 - hospital LOS (7 (5-11) vs 12 (7-24)) p<0.001 - higher sleep quality (8 (5 – 10) vs 4 (1 – 8) p<0.001	4
	21 intervention 25 control						

LOS = length of stay

Conclusions: The structured mobilization protocol is effective in the management of early mobilization and improvement of patient care outcomes.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2175 Patrick 2021 PMID: 34333616 DOI: 10.4037/ccn20216 89 Specification of study: Retrospective review	9 patients 242 therapy sessions Inclusion criteria: - mobilized patients (agitation sedation scale of -1 to 0) - no fluctuation ECMO flow from 3- 5 L/min - stable hemoglobin levels for the previous 12 hours Exclusion criteria: - patients receiving ≥ 2 vasopressors - significant bleeding Per Branch 9 intervention		Implementation of standardized mobility protocol	No control	<b>Endpoints:</b> - safety	Outcome: patients experienced the following complications: - chugging (1 patient) - decrease in flow rate (2 patients) - bleeding at the cannula site (2 patients) - neck hyperextension (1 patient) - fear/anxiety (1 patient) - shortness of breath (2 patients)	4

ECMO = extracorporal membrane oxygenation

Conclusions: Patients receiving extracorporeal membrane oxygenation before lung transplant, including those with femoral cannulation, can be mobilized safely with the use of an interprofessional ambulation protocol. Further evaluation is indicated, including research on clinical outcomes.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2178 Nakamura 2021 PMID: 34229920 DOI: 10.1016/j.jjcc.20 21.06.004 Specification of study: retrospective nationwide study	units - admitted for AMI - received PCI on th - admitted to the IC admission <b>Exclusion criteria:</b> - younger than 18 y - received cardiopur resuscitation - received ECMO	ne day of admission CU on the day of years		Early rehabilitation	Standard of care	Primary endpoints: - ADL at discharge (Barthel index) Secondary endpoints: - in Hospital mortality - ICU LOS - Hospital LOS - total hospialization cost	Primary outcome: no significant differences between the groups in: - ADL at discharge (control 78.9±37 vs intervention 83.2±33) p=0.3 Secondary outcomes: significant differences between the groups in: (control vs intervention) -in Hospital mortality (9.4 vs 5.5) p<0.001 -hospital LOS (27.2±24 22.5±20) p<0.001 -hospital LOS (7.7±6 vs 6.7±6) p=0.001 -hospitalization cost (31.5±20 26.9±15) p=0.001	4 → 3 (large cohort – national database)

ADL = activities of daily living, AMI = acute myocardial infarction, LOS = length of stay, PCI = percutaneous coronary intervention

Conclusions: No correlations were observed between early rehabilitation and ADL at discharge. However, the present results suggest that early rehabilitation is safe and associated with lower hospital costs and shorter hospital stays after AMI.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2180 Katsukawa 2021 (PMID: 34199207 DOI: 10.3390/jcm10122607) <b>Specification of study:</b> Multi-center retrospective observational study	390 pts Inclusion criteria: - adult tracheal intubated pts - on MV on ICU Exclusion criteria: - MV <48h - <18 year - no activity of daily living independence before hospitalization - receiving end-of-life care - neurological pts - bed rest Per Branch	n = 251 (discharge from ICU with in-bed exercise only), n = 52 (extubated before mobilization)	Active mobilisation		Sample size calculation: No power calculation reported. Endpoint: -occurrence of PSE	Primary endpoint: - PSE occurred in 11,5% of cases (62% systolic blood pressure instability, 23% heart rate instability, 15% desaturation) - occurrence of PSE was higher if mobilization was carried out on 1 <sup>st</sup> day of ICU admission (p <0.05) - more pts with PSE were administered vasopressors before mobilization (p<0.05). - rate of participation of a physical therapist in mobilization was lower in group with PSE (p <0.05) - highest occurrence rate of PSE was for standing (event rate = 205.1 per 1000 sessions). - adverse events: no accidents, such as line/ tube removal or falls or any severe, life-threatening event	4

ICU = intensive care unit, MV = mechanical ventilation, PSE = patient-related safety event, pts= patients

The highest activity level was identified as a risk factor for PSE occurrence, and close vigilance is required during mobilization in the standing position regarding circulatory dynamics.

Reference, Study Type	(Participant #,	d Controls Characteristics) ttal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2181 Jin 2021 PMID: 34150113 DOI: not available Specification of study: prospective cohort	172 pts Inclusion criteria - pts with RF req - > 18y - MV duration > - no treatment a Exclusion criteri - inability to com - unstable hemo - elevated ICP - fractures - contraindicatio mobilization - instable pulmo function Per B RG = 92	24h offecting ERN a: nmunicate odynamics		Early rehabilitation nursing (exercise plan, in-bed mobilization, respiratory care, respiratory muscle training)	Routine nursing	Outcomes: - vital signs 1 week after intervention - ABG - spirometry - ICU-LOS - duration of MV - hospital LOS - complications - SAS and SDS - QoL (SGRQ negatively correlated)	Outcomes:- vital signs 1 week after intervention: temp.: $37.38\pm 0.63$ vs. $38.05\pm 0.6$ ; $p < 0.001$ RR: $24.12\pm 2.86$ vs. $28.05\pm 2.23$ ; $p < 0.001$ HR: $90.75\pm 8.61$ vs. $103.12\pm 8.15$ ; $p < 0.001$ - ABG: PaO <sub>2</sub> (mmHg): $94.15\pm 3.78$ vs. $88.62\pm 3.45$ ; $p < 0.001$ - PaCO <sub>2</sub> (mmHg): $39.15\pm 4.05$ vs. $43.75\pm 3.18$ ; $p < 0.001$ - SpO <sub>2</sub> (%): $97.56\pm 4.85$ vs. $85.63\pm 2.72$ ; $p < 0.001$ - spirometry: increased FEV1, FEV1/FVC and FEV1% in intervention ( $p < 0.05$ ), values only in graph ICU-LOS (d): $6.52\pm 1.66$ vs. $8.76\pm 1.45$ ; $p < 0.001$ - duration of MV (d): $4.35\pm 1.85$ vs. $5.88\pm 2.17$ ; $p < 0.001$ - hospital LOS (d): $11.78\pm 2.89$ vs. $14.96\pm 3.53$ ; $p < 0.001$ - SGRQ: $69.39\pm 7.15$ vs. $80.18\pm 4.85$ ; $p < 0.001$ - complications: n.s SAS and SDS: n.s.	3

ABG = arterial blood gas analysis, ERN = early rehabilitation nursing, GG = general group, HR = heart rate, ICP = intracranial pressure, MV = mechanical ventilation, QoL = quality of life, RF = respiratory failure, RG= recovery group, RR = respiratory rate, SAS = self-rating anxiety scale, self-rating depression scale; SGRQ = St. George's respiratory questionnaire

Early rehabilitation nursing improves physiological values as well as hospital and ICU length of stay and reduces duration of mechanical ventilation.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2182 Abrams 2021 PMID: 34077700 DOI: 10.1513/Annal sATS.202102- 1510C Specification of study: single-center, retrospective study	<ul> <li>177 patients</li> <li>2.706 active physical therapy sessions</li> <li>Inclusion criteria: <ul> <li>patients &gt; 18 years</li> <li>active physical therapy</li> <li>receiving ECMO for cardiopulmonary failure</li> </ul> </li> <li>Exclusion criteria: <ul> <li>significant hemorrhaging</li> <li>unstable arrhythmia</li> <li>hemodynamic instability despite high-dose vasopressors</li> <li>severe hypoxemia</li> <li>sedation precluding active patient participation</li> <li>use of neuromuscular blockade</li> </ul> </li> <li>177 intervention</li> </ul>		Physical therapy	No control	Endpoints: - factors predicting possible intensity of physical therapy - safety - feasibility	Outcomes: - 138 (78%) achieving out-of-bed activity Increased odds of achieving OoB associated with: - bridge-to-transplant (odds ratio [OR], 17.2; 95%confidence interval [CI], 4.12–72.1) - venovenous ECMO (OR, 2.83;95% CI, 1.29– 6.22) - later cannulation year (OR, 1.65; 95% CI,1.37–1.98) - higher Charlson comorbidity index (OR, 1.53; 95% CI,1.07–2.19) Decreased odds of OoB activities: - invasive mechanical ventilation (OR, 0.11; 95% CI, 0.05–0.25) - femoral cannulation (OR, 0.19; 95%CI, 0.04–0.92) - AEs in 2% of sessions	4

AE = adverse event, MV = mechanical ventilation, OoB = out-of-bed

Several patient- and ECMO-related factors were associated with achieving higher intensity of early mobilization inpatients participating in rehabilitation. Physical therapy with femoral cannulation was safe and feasible, and complications related to mobilization were uncommon.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Interve ntion	Control	Optimal Population	Primary Results	Evidence Grade
2021 PMID: 33260011 DOI:	18 articles <sup>1-18</sup> up to 5 November 2020 (13 RQ1, 5 RQ2) Inclusion criteria: -concerned family participation on the ICU -one or more physiotherapy-related tasks (i.e., passive/active exercises such as range of motion, foot flexion, limb exercises, positioning, mobilization/transfer/ambulation, or respiratory techniques/breathing training) as part of their family participation intervention -reported results on relative involvement in physiotherapist-related tasks Exclusion criteria: -Studies solely focusing on family involvement in conversations, medical decisions, ICU rounds, nursing tasks (e.g., washing, bathing, feeding), occupational tasks, or studies on family visiting hours Per Branch				No sample size calculation due to study design No endpoints defined <b>Defined RQ:</b> -RQ 1: What are the perceptions of patients, their relatives and staff on family participation in physiotherapy-related tasks of critically ill patients? -RQ 2: What are the effects of interventions involving ICU family participation in physiotherapy- related tasks on patient outcomes, their relatives and/or staff?	<b>Results:</b> - Passive tasks like massage and passive exercises were acceptable for family participation, active tasks less positively received. -Quantitative evidence: majority of patients, relatives, and staff value family participation in physiotherapy care, with 77% of patients in favor of it. - involving ICU family members in physiotherapy-related tasks can lead to positive outcomes for the family, such as improved psychological well-being, but did not show significant effects on patient physical functioning.	1 → 5 (no quantitative analysis, no RCTs)

RQ = research question; ICU = Intensive Care unit

Patients, relatives, and staff had positive attitudes towards family participation in physiotherapy-related tasks for critically ill patients.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

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Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2215 Amundadottir 2019 PMID: not available DOI: 10.1080/21679169. 2019.1645880 Specification of study: a randomized controlled trial	50 patients Inclusion criteria: - ICU patients 18-80 y - requiring MV >48 hd - ambulate independ onset of acute illness - cooperate and com assessment and inter year after the ICU dis Exclusion criteria: - poor survival outcor - admission to the ho two weeks prior to IC - contraindication for mobilsation Per Br 29 intervention	ours lently before the ply with rvention for one scharge me ospital more than CU admission r upright	At 12 months after ICU discharge 5 pts in interventio n (3 deceased, 2 lost to follow up), 3 pts in control group (2 deceased, 1 lost to follow up)	Intensive twice-daily mobilization	Daily mobilisation	Endpoints: - duration of MV - ICU LOS - hospital LOS Secondary endpoints: - health- related quality of life - physical function	Primary outcomes: no significant differences between the groups in: (intervention vs control) - duration of MV (8.8 vs 7.8) (p=0.89 - ICU LOS (12.4 vs 11) p=0.86 - hospital LOS (36.9 vs 24.6) p=0.29 Secondary outcomes: no significant differences between the groups in: (intervention vs control) ICU discharge, 3, 6, 12 months - health-related quality of life (SF-36v2 score) 4 weeks before ICU: (44.1 vs 46.1) p=1 3 months: (36.3 vs 37.4) p=1 6 months: (38.5 vs 37.3) p=1 12 months: (38.3 vs 40.2) p=1 - physical function (MRC-SS) ICU discharge: (40.2 vs 42.4) p=0.99 3 months: (52.9 vs 54.5) p=1 6 months: (55 vs 54.4) p=1 12 months: (56.9 vs 55.9) p=1	2

LOS = length of stay, MRC-SS = medical research council sum-score, MV = mechanical ventilation, SF-36v2 = short form-36 health survey version 2

The intensive twice-daily mobilisation group neither started upright mobilization early nor yielded superior short- or long-term outcomes compared to the daily mobilisation group. Both groups showed poor physical health-related quality of life and exercise capacity one year after ICU discharge.

Study Type	(Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#2239 Wappel 2021 PMID: 32817444 DOI: 10.4187/respcare. 07840 Specification of study: retrospective analysis	32 patients Inclusion criteria: - age >50 years - tracheostomy on PMV for at least 14 d during acute hospitalization - requiring PMV for >6 h/d - able to participate in MRP activities - preadmission Barthel Index>70 - all extremities intact and mobile - meeting clinical criteria for ICU-acquired weakness Exclusion criteria: - acute superimposed cardiopulmonary disease - cognitive impairment - severe functional impairment related to neuromuscular dysfunction Per Branch	1 withdrew before randomization	MRP+HPRO (n=10) MRP+LPRO (n=5) UC+HPRO (n=8) UC+LPRO (n=8)		<b>Endpoints:</b> effects of MRP on - weaning - discharge home	Outcome: significant differences between the groups in: MRP+HPRO vs UC+LPRO - weaning (90% vs 38%) p=0.045 - discharge home rate (70% vs 13%) p=0.037 No significant differences between the groups in: MRP+HPRO vs MRP+LPRO - rate of discharge home (70% vs 20%) p=0.10	4 → 5

HPRO = high protein, LPRO = low protein, MRP = mobility-based rehabilitation programs, PMV = prolonged mechanical ventilation, UC = usual care

Combining high protein with mobility-based rehabilitation was associated with increased rates of discharge home and ventilator weaning success in survivors of critical illness. Further studies are needed to evaluate the role of combined exercise and nutrition interventions in this population.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3000 Reinprecht, 2003 (PMID: 12794427 DOI: 10.1097/01.CCM.00 00063453.93855.0A ) Specification of study: Retrospective analysis	Exclusion crite Not specified	is prone position	1: missing data	PP	SP	Outcomes: measured during PP and SP on the same patient: - hemodynamics - arterial oxygenation measured in torr - ventilatory setting - ICP + CPP - brain tissue oxygen partial pressure	Significant differences between groups in: - increase in PaO2 from 97.3 $\pm 20.7$ torr (mean $\pm$ SD) in the SP to 126.6 $\pm$ 31.7 torr in the PP (p < .0001) -increase in brain tissue oxygen partial pressure from 26.8 $\pm$ 10.9 torr to 31.6 $\pm$ 12.2 torr (p < 0.0001) - ICP increased from 9.3 $\pm$ 5.2 mm Hg to 14.8 $\pm$ 6.7 mm Hg (p < 0.0001) -CPP decreased from 73.0 $\pm$ 10.5 mm Hg to 67.7 $\pm$ 10.7 mm Hg (p < 0.0001)	4

ARDS = acute respiratory distress syndrome, CPP = cerebral perfusion pressure, ICP = intracranial pressure, PP = prone position, pts = patients, SAH = subarachnoid hemorrhage, SP = supine position

Prone positioning in patients with SAH and ARDS led to improved arterial oxygenation and brain tissue oxygen partial pressure, but also increased ICP and decreased CPP.

Reference, Study Type	(Partic Charac	d Controls ipant #, teristics) otal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3001 Beuret 2002 (PMID: 12029403 DOI: 10.1007/s0013 4-002-1266-x) <b>Specification</b> of study: prospective, randomized, controlled study	150) - hemodynami - anterior flail - vertebral or l fracture - orthopedic tr - ICP ≥ 20mm⊢	ria: h ing kia (PaO <sub>2</sub> /FIO <sub>2</sub> < ic failure chest ong bone raction	SP: 2 death within 24h	<b>PP:</b> 4h/day beginning within 24h of intubation	<b>SP:</b> continuously with head elevated at 20°	<ul> <li>Primary endpoint: <ul> <li>incidence of lung worsening</li> <li>defined by increase of lung Injury</li> <li>Score of at least 1 point</li> </ul> </li> <li>Secondary Outcome: <ul> <li>incidence of VAP</li> </ul> </li> <li>Sample size calculation: <ul> <li>reduction in incidence from 60 to</li> <li>25% with 66 pts. per arm (alpha= 5%, power= 80%)</li> </ul> </li> </ul>	Primary endpoint: - incidence of deterioration of pulmonary funciton was lower in the PP group (12%) than in the SP group (50%) (p=0.003) Secondary outcome: - incidence of VAP was 20% in the PP group and 38.4% in the SP group (p=0.14)	2

GCS = Glasgow coma scale, ICU-LOS = intensive care unit length of stay, ICP = intracranial pressure, MV = mechanical ventilation, PP = prone positioning, pts = patients, SP = supine positioning, VAP = ventilator-associated pneumonia

#### Prone positioning reduced the incidence of deterioration of pulmonary functionand showed a reduction of VAP.

Study Type	· · ·	Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
(PMID: 15372177	52 pts Inclusion criteria: - > 18 years - ARDS (paO2/FIO2 r - Bilateral infiltration Exclusion criteria: - cardiac pulmonary - acute brain injury - acute shock syndro - contraindication PF Per E 27 pts. in 135° PP	oedema	7 (5 IPP, 2 CPP) due to acute complications	Incomplete PP (135° PP)	Complete PP (180° PP)	Primary endpoint: - oxygenation (after 6h) Secondary outcomes: - AE - PaCO2 No sample size calculation	Significant differences between groups in: - significant increase of PaO2/FiO2 ration in complete PP 139±54mmHg to 206±75mmHg incomplete PP) vs (142±46mmHg to 253±107mmHg CPP), p< 0.05 No significant difference between groups in: - PaCO2 - safety: the incidence of side effects tended to be increased during the CPP	2

ARDS = acute respiratory distress syndrome, ICP = intra cranial pressure, IPP = incomplete prone position, MAP = mean arterial pressure, PEEP = positive end expiratory pressure, PP = prone position, pts = patients

#### Incomplete prone positioning improves oxygenation but is inferior to complete prone positioning.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade	
3003 Hering 2001,	16 pts on MV wi within 24h. Ever and SP <b>Exclusion criteri</b> - unstable cardi	y pt. received PP					<b>Outcomes:</b> intraabdominal pressure: PP: 14 ± 5 mmHg vs SP: 12 ± 4 mmHg (p < 0.05)		
(PMID: 11323351 DOI:	function - diuretics - renal transplar replacement the			Prone	Supine positioning for	<b>Outcomes:</b> - intraabdominal pressure	cardiovascular function: - Cl: 4.4 vs. 4.1 L/min⋅m <sup>2</sup> (p < 0.05) - MAP: 82 vs. 77 (p < 0.01)		
10.1097/000 00539- 200105000- 00027)	- cerebral injury -unstable spine - peritonitis			<b>positioning</b> for 180 min.		<b>positioning</b> for 180 min.	- cardiovascular function - renal function	- PaO <sub>2</sub> /FiO <sub>2</sub> : 267 vs 220 (p < 0.05) - HR, ITBVI, CVP, SVRI, pH: n.s.	3
Specification	Per B	Franch				renal function:			
<b>of study:</b> Cross-over study	16	16					- RF: 15.5 vs 19.1 (p < 0.05) - RVRI: 15078 vs 11762 (p < 0.05) U <sub>vol</sub> , ERPFI, ERBFI, GFRI: n.s.		

ALI = acute lung injury, CI = cardiac index, CVP = central venous pressure, ERPFI = effective renal plasma flow Index, HR = heart rate, ITBVI = intrathoracic blood volume index, MAP = mean arterial pressure, PP = prone positioning, RF = renal function, RVRI = renal vascular resistance index, SP = supine positioning, SVRI = systemic vascular resistance index, U<sub>vol</sub> = urine volume,

Prone positioning increases intraabdominal pressure, cardiac index, mean arterial pressure and oxygenation while reducing renal function.

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Primary Results	Evidence Grade
	Total		
#3004 Kirkpatrick 2013 PMID: 23673399 DOI: 10.1007/s00134- 013-2906-z Specification of study: Clinical Practice Guideline	n = 5 publications <sup>1-5</sup> Inclusion criteria: - patients with abdominal compartments syndrome (No data available) Definition of EM No data available	<ul> <li>Recommendations <ul> <li>no recommendations regarding mobilization</li> </ul> </li> <li>Suggestions regarding mobilisation: <ul> <li>3. potential contribution of body position to elevated IAP to be considered among patients with, or at risk of, IAH or ACS suggested [GRADE 2D]</li> </ul> </li> <li>Grading of quality level of evidence following GRADE recommendations (1 = high recommendation, 2 = weak recommendation; A to D = Quality level of evidence)</li> </ul>	1

ACS = abdominal compartment syndrome, EM = early mobilisation, GRADE = grading of recommendations, assessment, development and evaluations, IAH = intraabdominal hypertension, IAP = intraabdominal pressure, pts = patients

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3005 Cheatham 2009 (PMID: 19487946 DOI: 10.1097/CCM. 0b013e3181a0 21fa] Specification of study: A prospective, cohort study	<ul> <li>- unable to tolerate changes in body position (because of spinal precautions, intracranial hypertension, hemodynamic instability, etc)</li> <li>- intravesicular pressure measurements</li> </ul>		Triplicate intravesicular pressure measurments at least 4h apart with patients in: - 15° degree - 30° degree head of bed elevated position	Triplicate intravesicular pressure measurments at least 4h apart with patients in: - supine position	Primary endpoints: - measured IAP values	Primary outcome: significant differences between the groups in: (control vs intervention) - IAPsupine and IAP15° was 1.5 mm Hg (1.3– 1.7) p<0.0001 - APsupine and IAP30° was 3.7 mm Hg (3.4 – 4.0) p<0.0001	3

ACS = abdominal compartment syndrome, APP = abdominal perfusion pressure, IAH = intra-abdominal hypertension, IAP = intra-abdominal pressure, ICU = intensive care units, VAP = ventilator-associated pneumonia

Conclusions: Head of bed elevation results in clinically significant increases in measured IAP. Consistent body positioning from one IAP measurement to the next is necessary to allow consistent trending of IAP for accurate clinical decision making. Studies that involve IAP measurements should describe the patient's body position so that these values may be properly interpreted.

Reference, Study Type	Cases and C (Participant #, Ch Tota	aracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3006 Ehrmann 2021 (PMID: 34425070 DOI: 10.1016/S2213- 2600(21)00356-8) <b>Specification of</b> <b>study:</b> randomised, controlled, multinational, open- label meta-trial	1126 pts Inclusion criteria: - > 18 years - acute hypoxaemic failure due to prove pneumonia Exclusion criteria - consent - haemodynamica u - BMI > 40 - pregnancy - contraindication for Per Brain 567 awake PP	n COVID-19- nstable or awake PP	n=5 (withdrew consent)	Awake prone position - (patients in the awake prone positioning group were instructed and assisted to lie in the prone position for as long and as frequently as possible each day. The duration of each proning session was recorded by bedside nurses)	Standard of care	<ul> <li>Primary endpoint: <ul> <li>treatment failure (defined as intubation or death)</li> </ul> </li> <li>Secondary outcome: <ul> <li>mortality</li> </ul> </li> <li>Sample Size calculation: <ul> <li>based on previews reports primary outcome incidence was estimated between 60-70% in standard care group, 90% power</li> <li>Sample size was 1000 pts</li> </ul> </li> </ul>	Primary endpoint: treatment failure within 28 days: - awake proning: 223 (40%) vs SOC: 257 (46%); p=0.025 Secondary outcome: - no difference in mortality	2

BMI = body mass index, h = hours, PP = prone position, Pts = patients, SOC = standard of care

# Awake prone positioning of patients with hypoxemic respiratory failure due to COVID-19 reduces the incidence of treatment failure and the need for intubation without any sign of harm.

Reference,	Cases and (Participant #, cl		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	Tota	al						erude
	40 patients at 1 quaterna	ary referral center						
	Inclusion criteria:							
	<ul> <li>adult patients</li> </ul>							
	- submitted to ICU by on	e of the study teams						
	- positive SARS-CoV-2 tes	st within 7 days						
3007 Taylor 2021	<ul> <li>suspected COVID-19 pn experienced:</li> </ul>	neumonia and						
PMID: 33356977	1) room air oxygen satu	iration <93%				<b>- .</b>	Results:	
DOI: 10.1513/AnnalsA TS.202009-	<ol> <li>oxygen requirement greater without the need ventilation</li> </ol>	•	1 intervention patient did	APPS + UC	Usual	Endpoints: Clinical outcomes: - S/F ratio - S/F ratio below 315 - hospital LOS	Differences in (no p value given): (Control vs intervention) -S/F ratio (216 vs 253) -S/F ratio below 315 (42h vs 20h)	2 → 3 (pilot trial, bias risk)
1164OC	Exclusion criteria:		leave the study hospital		care			
	- unable to self-turn					Safety:	-Hospital LOS (5 vs 6)	
Specification of	- spinal instability					- AEs	-AE (0 vs 1)	
study:	- facial or pelvic fractures	S						
A cluster	- open chest or abdomer	า						
randomized pilot trial	- altered mental status							
that	- anticipated difficult airv	- anticipated difficult airway						
	- signs of respiratory fati	gue						
	- receiving end-of-life car	re						
	Per Bra	anch						
	28 APPS + UC	13 UC						

PP = prone position, UC = usual care, APPS = awake prone positioning strategy, LOS = length of stay

A definitive trial evaluating the effect of prone positioning in non-intubated patients with COVID-19 is warranted, but several barriers must be addressed to ensure that the results of such a trial are informative and readily translated into practice.

(10.1080/1110)       -<200, respiratory rate > 24 b/m       3 days of critical care admission (arterial blood gas at admission (arterial blood gas at admission (arterial blood gas at admission then daily after the procedure for frequent 3 days)       mmHg PP group       - mean arterial pCO2 was decreased significantly in NIV group 239.34 ± 5.12       2 → 3         Specification of study:       Exclusion criteria:       - need invasive and immediate ventilation       - RR>40b/m       - systolic pressure <100 mmHg, -unable or unwilling trail of PP and NIV       Secondary outcomes:       - reducing in hospital stay       - regarding ICU or hospital duration of stay (n.s)       Secondary outcomes:       - regarding ICU or hospital duration of stay (n.s)       - regarding ICU or hospital duration of stay (n.s)	Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Interven tion	Control	Optimal Population	Primary Results	Evidence Grade
	Gad 2021 https://doi.org /10.1080/1110 1849.2021.188 9944 Specification of study: prospective randomized comparative	Inclusion criteria: - positive nasopharyngeal/oropharyngeal covid-19 swab is confirmed, - >18 years old - SaO2 <90% (5–10O2l/min simple face mask) - PaO2/FiO2 <200 - <200, respiratory rate > 24 b/m - bilateral lung infiltration in CT chest - not explained by cardiac failure - ready to co-operate pp or NIV Exclusion criteria: - need invasive and immediate ventilation - RR>40b/m - use accessory muscle - systolic pressure <100 mmHg, -unable or unwilling trail of PP and NIV		PP	NIV	<ul> <li>- improved in oxygenation and avoiding intubation within the first 3 days of critical care admission (arterial blood gas at admission then daily after the procedure for frequent 3 days)</li> <li>Secondary outcomes: - reducing in ICU stay</li> </ul>	<ul> <li>mean SaO<sub>2</sub> (on simple face mask 5–10 l/min) at admission 79 ± 8.47%in PP group, 82 ± 7.05% in NIV group</li> <li>-SaO<sub>2</sub> and tension was significantly increased mean SaO2 93 ± 5.9%, mean PaO2 107 ± 12 mmHg PP group</li> <li>mean arterial pCO<sub>2</sub> was decreased significantly in NIV group 239.34 ± 5.12 mmHg compare to PP group 43.41 ± 3.2 mmHg (day3) p-value &lt;0.001</li> <li>-PH (n.s)</li> </ul>	2 → 3

CT = computer tomography, ICU = intensive care unit, NIV = non-invasive ventilation, n.s. = not significant, PP = prone position, pts =patients

Awake prone positioning and non-invasive ventilation showed marked improvement in SaO2 and PaO2 in COVID-19 patients with improvement in clinical symptoms with reduced rate of intubation and superiority of NIV in hypercapnic patients.

Reference, Study Type	(Parti chara	nd Controls icipant #, cteristics) Fotal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3019 Drakulovic 1999 PMID: 10584721 DOI: 10.1016/S0140- 6736(98)12251-1 <b>Specification of</b> <b>study:</b> RCT	90 pts from J until May 31, Inclusion crit - mechanicall Exclusion crit - abdominal - neurosurgio (<7d) - shock refrac vasoactive dr - endotrache (<30d)	une 1, 1997, , 1998 <b>eeria</b> : ly ventilated pts. <b>teria</b> : surgery (<7d) cal intervention	4 (intervention group): 1 died, 3 withdrawn due to reintubation (protocol violation)	Semirecumbent body position (45°)	Supine body position (0°)	Primary Endpoint: - frequency of clinically suspected pneumonia Secondary outcomes: - frequency of microbiologically confirmed pneumonia	Primary Endpoint:         - frequency of clinically suspected pneumonia: Intervention 8% vs control 34% (95% Cl for difference 10-4, p=0.003)         Secondary outcome:         - frequency of microbiologically confirmed pneumonia: Intervention 5% vs control 23% (95% Cl for difference 4-33, p=0.018)	2

Pts = patients, RCT = randomized controlled trial, d = days, CI = confidence interval

The semirecumbent body position reduces the risk of pneumonia in mechanically ventilated patients.

Reference, Study Type	(Participant #,	l Controls characteristics) tal	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3020 Borges, 2016 PMID: 27170538 DOI: 10.1123/jpah.2 015-0614 Specification of study: RCT	pump or other ir devices - surgical reinter - death - prolonged hosp	a: 3G a: dominal balloon tvasive femoral		Conventional physiotherapy + aerobic exercise with cycle ergometer	Conventional physiotherapy	Primary Endpoint: - mortality risk (InsCor score) Secondary Endpoints: - Spirometry /pulmonary function (FVC, FEV1, PEF) - respiratory muscle strength / manovacuometry (MIP, MEP) - 6-MWT - MV duration (hours) - ICU stay (days) - Hospital discharge (days)	Primary Endpoints: - mortality risk n.s. (P=0.49) Secondary Endpoints: -pulmonary function from preoperative to hospital discharge (FVC P=0.001; FEV1 P=0.001; PEF P=0.02 for Intervention and P=0.01 for Control) - MEP decreased (P=0.006 for intervention and P=0.004 for Control) - 6-MWT decreased in control group (P = 0.01) - difference in intergroup at hospital discharge (P = 0.03) -difference in MIP, MV duration and ICU stay(n.s.)	2

CABG = coronary artery bypass grafting, RCT = randomized controlled trial, pts = patients, 6-MWT = 6-Minute Walk Test, FVC = forced vital capacity, FEV1 = forced exspiratory volume, PEF = Peak Expiratory Flow, MIP = maximal inspiratory pressure, MEP = maximal expiratory pressure, ICU = Intensive Care Unit, MV = mechanical ventilation,

Aerobic exercise after CABG may help maintain functional capacity but had no impact on pulmonary function and respiratory muscle strength when compared with conventional physiotherapy.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3032 Kimmoun 2015 (PMID: 26538308 DOI: 10.1186/s13613- 015-0078-4 <u>)</u> <b>Specification of study:</b> Retrospective study	17 patients who received PP during VV-ECMO between January 2012 and January 2014 Inclusion criteria - patients with severe ARDS as defined by the BERLIN consensus Exclusion criteria - patients under vasopressor treatment - pts after open chest cardiac surgery Per Branch		Pre-PP parameters compared with post- PP (27 sessions were performed, identical duration of 24 h)	no control	Endpoints (not defined in detail) - PaO2/FiO2 ratio (Horowitz-Index) - respiratory system compliance - tidal volume	Endpoints - PaO2/FiO2 : significantly increased from 111 (84–128) to 173 (120– 203) mmHg ; (p < 0.0001) - PaO2/FiO2 ratio increased by over 20 % in 14/14 sessions for late sessions (≥7 days) and in 7/13 sessions for early sessions (< 7days); p=0.01 - respiratory system compliance: increased from 18 (12–36) to 32 (15–36) ml/cmH2O; (p < 0.0001) - tidal volume: increased from 3.0 (2.2–4.0) to 3.7 (2.8–5.0) ml/kg; (p < 0.005)	4

ARDS = acute respiratory distress syndrome, FiO2 = inspiratory oxygen concentration, ICU = intensive care unit, pts = patients, PP = prone position, PaO2 = partial oxygen content, VV-ECMO = veno-venous extra-corporal membrane oxygenation

When used in combination with VV-ECMO, 24 h of prone positioning improves both oxygenation and respiratory system compliance.

Reference, Study Type	(Participant #, (	l Controls Characteristics) tal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3035 Giani 2021 (PMID: 32941739 DOI: 10.1513/AnnalsATS.2 02006-625OC) <b>Specification of</b> <b>study:</b> Multicenter retrospective cohort study	240 patients treated ECMO referral center January 2014 and D Inclusion criteria - adult patients with ARDS according to t - treated with VV- E no exclusion criteria Per B N=107	ers between ecember 2018 n a diagnosis of the Berlin definition ECMO support a mentioned		<b>Prone group</b> (start of first PP session = 4 (2– 7) days; 326 PP maneuvers, mean duration of pronation cycles = 15 (12–18) hours	Supine group	Primary outcome - efficacy and safety of the application of PP in patients with ARDS supported with V-V ECMO (duration of ECMO support, length of stay in the ICU, ICU mortality) Secondary outcome - association of PP and hospital mortality	Primary outcome - ECMO duration (days): intervention = 16 vs. control = 10; p=0.0344) - ICU LOS (days): intervention=35 (21–50), control=26 (15–51); p=0.0102 - alive at ICU discharge: intervention= 33 (21–48), control=30 (19–57); p=0.4352 Secondary outcome - hospital mortality: intervention= 36 (34%) vs. control= 61 (49.6%); P = 0.017) - PP during ECMO: Odds ratio (95% CI) = 0.499 (0.285–0.872); p=0.0147	4

ARDS = acute respiratory distress syndrome, CI = confidence intervall, ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit, PP = prone positioning, VV-ECMO= veno-venous ECMO

PP during ECMO improved oxygenation and was associated with a reduction of hospital mortality.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3039 Rilinger 2020 (PMID: 32641155 DOI: 10.1186/s13054-	158 patients with se requiring VV ECMO October 2010 and M Interdisciplinary Me Care Unit at the Me University of Freibur No inclusion/exclus defined	support between Aay 2018 at the dical Intensive dical Centre, rg, Germany				Primary outcome - successful ECMO weaning (defined as being free from	Primary outcome - weaning successful: 74 (46.8%, n=158) , intervention= 18 (47.4%) and control= 56 (46.7%); p= 0.940 - ICU survival: 58 (n=158, 36.7%), intervention= 14 (36.8%) and control= 44 (36.7%); p=0.984 - hospital survival: 58 (n=158, 36.7%), intervention=14 (36.8%) and control= 44 (36.7%); p=0.984	
020-03110-2) <b>Specification of</b> <b>study:</b> retrospective data report of a single- centre registry	N=38	N= 120		Prone position	Supine position	ECMO and alive for at least 48 h after decannulation) - ICU and hospital survival	<ul> <li>no significant differences in VV ECMO weaning rate (pp= 47.4% vs. sp= 46.7%, p = 0.94) and hospital survival (pp= 36.8% vs. sp=36.7%, p = 0.98)</li> <li>no difference in hospital survival (pp=36.8% vs. sp=36.8%, p = 1.0) or VV ECMO weaning rate (pp=47.4% vs. sp=44.7%, p = 0.82)</li> </ul>	4

ICU = intensive care unit, PP = prone position, SP = supine position, VV-ECMO = veno-venous extracorporal-membrane oxygenation

In this propensity score matched cohort of severe ARDS patients requiring VV ECMO support, prone positioning at any time was not associated with improved weaning or survival.

Reference, Study Type	Cases and (Participant #, C		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
	Tot	al						
3041 Jagan 2020 (PMID: 33063033 DOI: 10.1097/CCE.0000000 000000229)	105 non-intubated, o disease-infected pat March 24, 2020, and CHI Health St. Franci Nebraska Inclusion criteria - ≥19 years - COVID-infeo Exclusion criteria - Pregnancy	ients 9 between I May 5, 2020, to s in Grand Island, cted		Prone group (tolerated awake	Supine group	<ul> <li>primary outcome         <ul> <li>need for intubation during the hospital stay</li> </ul> </li> <li>secondary outcome         <ul> <li>serial peripheral capillary oxygen saturation measured by pulse oximetry to the Fio2 ratios             <ul>                      in-hospital mortality</ul></li>                     hospital discharge disposition(home, died, nursing home)</ul></li> </ul>	<pre>primary outcome - risk of intubation: lower in proned group after adjusting for disease severity using SOFA scores (adjusted hazard ratio, 0.30; 95% CI, 0.09–0.96; p = 0.043) or APACHE II scores (adjusted hazard ratio, 0.30; 95% CI, 0.10–0.91; p = 0.034) secondary outcome</pre>	4
,	Per Br	ubation/ventilation		self-proning)			- <u>discharge disposition(%)</u> home: supine = 41.5, proned=	
Specification of study: Retrospective analysis of prospectively collected clinical data	N=40	N=65					72.5; p < 0.001 died: supine= 24.6, proned=0.0 nursing home: supine=9.2, proned=5.0 - pulse oximetry to the Fio2 ratios were statistically similar for both groups - mortality: intervention=0% vs control= 24.6% (p < 0.001; NNT = 5; 95% Cl, 3–8)	

APACHE = acute physiology and chronic health evaluation, CI = confidence interval, FiO2 = inspiratory oxygen concentration, NNT = number needed to treat, SOFA = sequential organ failure assessment

#### Awake self-proning was associated with lower mortality and intubation rates in coronavirus disease 2019-infected patients.

Reference, Study Type		es and Controls ant #, Characteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3043 Perez-Nieto 2022 ( PMID: 34266942 DOI: 10.1183/13993003.0 0265-2021) Specification of study: retrospective, multicentre observational study	827 non-intubated par 27 hospitals in Mexico 2020 and 12 June 2020 Inclusion criteria - age over 18 years - positive test for SARS compatible with COVII - clinical record availal Mexican standard or e - room air SpO2 <94% - two or more of the for cough, fever, dyspnoe or odynophagia Exclusion criteria - voluntarily discharge - pts referred to anoth ascertainment - those with incomplet information to calcula	S-CoV-2 or imaging study D-19 ble in accordance with the official equivalent in Ecuador ollowing symptoms: eye pain, a, headache, myalgia, arthralgia		Prone position	Supine position	<pre>primary outcome - successful orotracheal intubation for invasive mechanical ventilation secondary outcome - death during in- hospital follow-up</pre>	Primary outcome - intubation: control=130 (40.4%), intervention= 119 (23.6%); p<0.0001 - pp= protective factor for intubation even after multivariable adjustment (OR 0.35, 95% CI 0.24–0.52; p<0.0001) Secondary outcome - control=120 (37.3%), intervention= 100 (19.8%); p<0.0001 (adjusted OR 0.38, 95% CI 0.26–0.55)	4
	Per Branch	-						
	N=505	N=322						

CI = confidence interval, OR = odds ratio, pp = prone position, pts = patients, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

# Awake prone positioning in hospitalized non-intubated patients with COVID-19 is associated with a lower risk of intubation and mortality.

Reference, Study Type	Cases and C (Participant #, Ch Total	aracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3048 Patman 2001 (PMID: 11552858 DOI: 10.1016/s00 04- 9514(14)602 94-4) Specificatio n of study: RCT	236 pts Inclusion criteria: - elective or semi-urgent Exclusion criteria: - severe asthma, chronic bronchiectasis or ankylos - post-operatively: unsta status (systolic blood pre 180mmHg or MAP < 60 c - arrhythmias that compr cardiovascular function, loss from subcostal cathe - perioperative neurologi Per Bran	airflow limitation, sing spondylitis ble cardiovascular ssure < 100 or > or > 110mmHg) romised or excessive blood eters (> 100mL/hr) ical complication	26 pts treatment group: 7 control group: 19 (Reason: 18 prolonged ventilation for more than 24 hours; 3 died in ICU; 5 slow awake from anaesthesia)	Physiothe- rapy during intubation and after extubation	<b>Physiotherapy</b> only after extubation	Primary endpoints: - length of intubation period - ICU LOS - hospital LOS - maximal daily incentive spirometry values - incidence of post- operative pulmonary complications	Primary endpoints: - no significant difference in any outcome parameter - Intubation (hours): 13.0 (SD:4.8) vs. 12.7 (SD:4.7) p=0.85 - ICU stay (hours): 42.7 (SD:42.4) vs. 36.7 (SD:26.8) p=0.56 - Hospital stay (days): 9.2 (SD:4.5) vs. 9.6 (SD:4.7) p=0.25	2
	101	109						

ICU = intensive care unit, LOS = length of stay, MAP = median arterial pressure, pts = patients

In this study physiotherapy interventions during the intubation period did not improve outcomes in patients after cardiac surgery.

Reference, Study Type	Cases and Cont (Participant a Characteristic Total	#, Dron-out Pate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3050 Van der Peijl 2004 (PMID: 15111138 DOI: 10.1016/j.a thoracsur.2 003.10.091) Specificatio n of study: RCT	Per Branch	zedthoracotomy, 1 death, 9, nothemodynamic instability, 3serious rhythmicdisturbances, 2 combinationswith other surgery, 1cerebrovascular accident)LFE: 31 (2 pulmonarycomplications, 8 othercardiac surgery, 1 re-thoracotomy, 3 death, 12hemodynamic instability, 1serious rhythmic	coordination, walking and stair climbing. -2x/day incl. weekend, starting on day 1 post- surgery	Low frequency exercise: - RoM, muscle strength and coordination, walking and stair climbing. -1x/day excl. weekend, starting on 1. Weekday after surgery	Primary outcomes: - functional milestones: sitting, walking, group exercise therapy, climbing stairs - fatigue and dyspnoe (RPE scale) - semistructured interview day before surgery (selfcare, locomotion, FIM) - quantity of physical activity (portable activity monitor) - satisfaction	Primary outcomes: - functional milestones: sitting, walking and group exercise were achieved faster by HFE (p = 0.0048, p = 0.0072, p<0.00005), stairs: n.s. - RPE: n.s. - FIM: n.s. - quantity of physical activity: n.s. - pts satisfaction: HFE more satisfied (p < 0.05)	$2 \rightarrow 3$ (indirectness)

CABG = coronary artery bypass graft, FIM = functional independence measure, HFE = high frequency exercise, LFE = low frequency exercise, pts = patients, RoM = range of motion, RPE = rating of perceived exertion

High frequency exercise programs lead to a faster achievement of functional milestones while not increasing the perceived exertion.

Reference, Study Type	(Participant #	nd Controls #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3053 Routsi 2010 DOI: 10.1186/cc89 87) <b>Specification</b> of study: RCT	and June 2009 Inclusion criteria: - all pts admitted to ICU - APACHE II at admission Exclusion criteria: - <18 years - pregnancy - obesity (BMI >35 kg/r - preexisting neuromus myasthenia Gravis, Gui - diseases with systemi such as systemic lupus - technical obstacles th implementation of EMI skin lesions (e.g., burns - end-stage malignancy - cardiac pacemakers - brain death Per EMS group (n=70)	$n \ge 13$ n2) scular disease (e.g., illain-Barré disease) c vascular involvement erythematosus at did not allow the S such as bone fractures or s) T Branch control group (n=72)	90pts/63.3% EMS group: 2 withdrew their consent, 28 died, 3 prolonged neuromusclular blocking agents, 2 no EMS sessions Control group: 22 died, 22 impaired cognitive state	daily EMS sessions	No EMS	Primary outcome: - diagnosis of CIPNM as assessed with the MRC scale for muscle strength Secondary outcomes: - duration of weaning from MV - ICU LOS	<ul> <li>Primary outcome: <ul> <li>CIPNM was diagnosed in 3 patients</li> <li>in EMS group compared to 11 patients</li> <li>in control group (OR = 0.22; CI: 0.05 to 0.92, p=0.04)</li> <li>MRC score was significantly higher in patients of EMS group compared to control group [58 (33 to 60) vs. 52 (2 to 60) respectively, median (range), p=0.04)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>weaning period shorter in pts of EMS group vs. control group [1 (0 to 10) days vs. 3 (0 to 44) days, respectively, median (range), p=0.003]</li> <li>ICU LOS not significantly different (mean (range), 14 (4 to 62) vs. 22 (2 to 92), days, respectively, log rank test, p=0.11)</li> </ul></li></ul>	2
	(24 analyzed)	(28 analyzed)						

ICU=intensive care unit; APACHE II= Acute Physiology and Chronic Health Disease Classification System II, BMI = body mass index, CI = confidence interval, CIPNM= Critical illness polyneuromyopathy, EMS = electrical muscle stimulation, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, OR = odds ratio, pts = patients

#### EMS prevents the development of CIPNM and results in shorter MV duration.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3060 Gerovasili, 2009 (PMID: 19814793 DOI: 10.1186/cc8123) <b>Specification of</b> <b>study:</b> randomized study	49 pts         Inclusion criteria:         - all pts admitted to ICU during study period         Exclusion criteria:         - age under 18 years         - pregnancy         - obesity (BMI >35 kg/m2)         brain death         - preexisting neuromuscular disease (e.g. myasthenia gravis)         - diseases with systemic vascular involvement such as lupus erythematosus         - technical obstacles that did not allow the implementation of EMS such as bone fractures or skin lesions (e.g. skin burns)         - end- stage malignancy         - pacemakers         - ICU stay of less than 48 hours         EMS group (n=24)       Control group (n=25)	EMS: 5 pts excluded due to oedema, 6 pts died or were discharged before 2nd measurement Control: 6 pts excluded due to oedema, 5 pts died or were discharged before 2nd measurement and 1 patient could not be measured due to technical problems	daily EMS sessions of both lower extremities	No EMS	Primary outcome: - muscle mass (evaluated with US, by measuring the CSD of vastus intermedius and the rectus femoris of the quadriceps muscle)	Primary outcome: - 26 pts evaluated - CSD of the right rectus femoris decreased significantly less in EMS group (-0.11 ± 0.06 cm, -8 ± 3.9%) compared to control group (-0.21 ± 0.10 cm, -13.9 ± 6.4%; p<0.05) - CSD of the right vastus intermedius decreased significantly less in EMS group (-0.10 ± 0.05 cm, -12.5 ± 7.4%) compared to control group (-0.29 ± 0.28 cm, -21.5 ± 15.3%; p<0.05)	2

CSD = cross sectional diameter, EMS = electrical muscle stimulation, pts = patients, US = ultrasonography

EMS was able to preserve muscle mass in critically ill patients.

Reference, Study Type	(Partic Charact	d Controls ipant #, teristics) otal	Drop-out Rate	Interventi on	Contr ol	Optimal Population	Primary Results	Evidence Grade
3065 Karic 2016 (PMID: 27058204 DOI: 10.3171/2015. 12.JNS151744) Specification of study: Prospective interventional study	-neurodege disorder	o- te ward <b>riteria:</b> ears SAH brain injury	2 pts: (1 thrombo- embolic complication, 1 death)	EM and rehabilita tion in addition to SOC	SOC	Endpoints: - treatment variables - frequency and severity of cerebral vasospasm - cerebral infarction acquired in conjunction with the aSAH - acute and chronic hydrocephalus - pulmonary and thromboembolic complications	Significant Outcomes: treatment variables the intervention group had a significantly - earlier mobilization for days 1-7 (p < 0.01) - higher mobilization level at discharge (Step 5 vs. Step 4, p = 0.004) - significantly less clinical vasospasm in the early rehab group (p=0.03) Not significant outcomes: - cerebral vasospasm: 5 in control, 10 in intervention - time from ictus to vasospasm (median 8 days (range 3-18) vs. 7 (range 4-22)) - cerebral infarction acquired after the ictus (40% vs. 29%) - LOS (13.9 (3-37) vs. 14.5 (2-61)) - no unintended removal of lines/tubes - clinical status at discharge (GCS score 13.9 ± 1.9 vs. 14.1 ± 1.5))	3 → 4 (indirectness)

aSAH = after aneurysmal subarachnoid hemorrhage, EM = early mobilization, LOS = length of stay, pts = patients, SOC = standard of care

Early rehabilitation of patients after aSAH is safe and feasible in intermediate care patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3066 Karic 2016 (PMID: 27494170 DOI: 10.2340/1650 1977-2121) <b>Specification</b> of study: Prospective, controlled, interventional study	168 aSAH pts in the neuro-intermediate ward being poor-grade WFNS (3-5)Inclusion criteria:- adults (>18 years)- South-East health region- with aSAH- admitted to the NIW at Oslo University Hospital after aneurysm repairExclusion criteria:- history of SAH- traumatic brain injury- neurodegenerative disorder that could interfere with aSAH-aquired disabilityPer Branch9477		EM and rehabilitation: - in addition to standard treatment	Standard of care	Primary endpoints: - global functional outcome (Rankin Scale, Glasgow Outcome Scale Extended) Secondary endpoints: - clinical data - LOS - intervention data	Significant differences between groups: - initiation of early rehabilitation (WFNS 3-5 median 7.4 days (range 1- 23), WFNS 1-2 0.9 (0-20) - application of early rehabilitation (WFNS 1-2 median 9 days (range 1- 36), WFNS 3-5 10 (1-26)) No significant differences between groups in: - mRS and GOSE (univariate: 0.982 (0.69-1.39), p=0.922 multivariate 1.30 (0.836-2.037), p=2.42) - LOS (control 14.5 (range 2-61) vs. intervention 14.4 (3-37))	3 → 4 (indirectness)

aSAH = after aneurysmal subarachnoid hemorrhage, EM = early mobilization, GOSE = Glasgow outcome scale extended, LOS = length of stay, mRS = modified ranking scale, pts = patients, WFNS = World Federation of Neurosurgery Scale

# Early mobilisation and rehabilitation probably increase the chance of a good functional outcome in poor-grade aneurysmal subarachnoid hemorrhage patients admitted to intermediate care.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3067 Pun 2019 (PMID: 30339549 DOI: 10.1097/CCM. 00000000000 3482) Specification of study: Prospective, multicenter, cohort study	17.228 pts Inclusion criteria: - > 18 years - admitted to participating medical, surgical, cardiac, or neurologic ICU Exclusion criteria: - death or discharge from the ICU within 24 hours of ICU admission - undergoing active life support withdrawal and/or "comfort care- only" within 24 hours of ICU admission Per Branch 17.228	2002 (no full 24 hours in ICU)	Complete performance of ABCDEF Bundle: - pts receive every eligible bundle element on any given day)	Proportional performance: - percentage of eligible bundle elements performed on any given day	Endpoints: - mortality - ICU discharge - hospital discharge - mechanical ventilation - coma - delirium - pain - restraint use - ICU readmission - ICU discharge destination	Significant differences between groups in: complete ABCDEF Bundle performance was associated with lower likelihood of: - hospital death within 7 days (AOR, 0.32; Cl0.17-0.62) - next-day MV (AOR, 0.28; Cl, 0.22-0.36) - coma (AOR, 0.35; Cl, 0.22-0.56) - delirium (AOR, 0.60; Cl, 0.49-0.72) - physical restraint use (AOR, 0.37; Cl, 0.30-0.46) - ICU readmission (AOR, 0.54; Cl, 0.37- 0.79) - discharge to a facility other than home (AOR, 0.64; Cl, 0.51-0.80) => all p < 0.002 - significant pain was more frequently reported as bundle performance proportionally increased (p = 0.0001)	3

AOR = adjusted hazard ratio, CI = confidence interval, ICU = intensive care unit, MV = mechanical ventilation, pts = patients

ABCDEF bundle performance showed significant and clinically meaningful improvements in outcomes including survival, mechanical ventilation use, coma, delirium, restraint-free care, ICU readmissions, and post-ICU discharge disposition.

Reference, Study Type		es and Controls int #, Characteristics) Total	Drop- out Rate	Interventio n	Control	Optimal Population	Primary Results	Evidence Grade
3069 Zeckey 2015 (PMID: 25391530 DOI: 10.3233/THC- 140869) Specification of study: Retrospective study	2009, 283 pts Inclusion criteria: - multiple trauma associated severe - primary admissic - plain radiographs and 24 h thereafte chest, abdomen, a Exclusion criteria: - penetrating thor - AIS <sub>Head</sub> > 2 - steroidal and nor medication - hormone replace - chronic diseases - liver or kidneys a	pts (ISS ≥ 16, age > 16y) with chest trauma (AIS <sub>Chest</sub> ≥ 3) on within 6 h after trauma s of the chest at admission er, CT of the head, spine, and pelvis acic trauma n-steroidal anti-inflammatory		<b>CLRT:</b> -5 to 7 days therapy with 62° rotation to each side was applied	Lung protective ventilation strategy	Endpoints: - mortality - ARDS - MODS - ALI - SIRS - Sepsis No sample size calculation (retrospective study)	Significant differences between groups in: Pts with CLRT had significantly increased - MV time (532.1 ± 320.7; 135.8 ± 245.8 hours, p < 0.0001) - ICU LOS (25.7 ± 13.4; 9.1 ± 11.0 days, p < 0.0001) - hospital LOS (38.4 ± 21.1, 24.4 ± 17.6 days, p < 0.0001) - blood replacement (PRBC 22.9 ± 26.6 vs. 10.5 ± 14.1, p < 0.01; FFP 16.6 ± 20.9 vs. 7.0 ± 11.4, p = 0.01; PRP 2.6 ± 5.7 vs. 0.9 ± 2.1 p = 0.01 Higher incidence of - SIRS (65% vs. 34% p = 0.001) - sepsis (53.1% vs. 19.5% p = 0.001) - mortality (12.5% vs. 5.7% p = 0.001) - mortality (12.5% vs. 5.7% p = 0.044) In CLRT group After multivariate logistic regression analysis for mortality revealed: - CLRT OR 0.96 [0.34; 2.74], p > 0.05 - age ( ≥ 40y): OR 2.71 [0.88; 8.41], p 0.05 - TTS OR 4.47 [1.68; 11.91], p = 0.0027) - PRP requirement OR 9.86 [3.04; 31.94] p = 0.0001)	4

AIS = abbreviated injury scale, CLRT = continuous lateral rotation therapy, FFP = fresh frozen plasma, ICU = intensive care unit, ISS = injury severity score, MV = mechanical ventilation, LOS = length of stay, PRP = platelet-rich plasma, PRBC = packed red blood cells, pts = patients, TTS = thoracic trauma severity score

#### CLRT shows signal of harm in several clinical endpoints.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3071 Altinay, 2022 (PMID: 34411633 DOI: 10.1016/j.bjan e.2021.07.029] Specification of study: retrospective cohort study	72 pts         Inclusion criteria:         ->18 years of age         - monitored and treated in the ICU for acute respiratory failure due to COVID-19 pneumonia         - received conventional oxygen therapy with nonrebreather mask oxygen         Exclusion criteria:         - supported with noninvasive or invasive MV to respiratory acidosis (pH <7.30 and PaCO2 >50 mmHg)         - PaO2/FiO2 ratio <150	APP: 24 (PP performed less than 12 hours a day due to non- compliance)	<b>APP</b> 12-18 hours	Non-APP	Endpoints: - SpO2, PaO2/FiO2, pH, PaCO2, and PaO2 (initial and at 24 <sup>th</sup> hour) - ICU stay period - ventilator free period (day) - mortality rate - Intubation requirements	Endpoints: - initial SpO2, pH, PaO2, and PaO2/FiO2 (n.s.); initial PaCO2 values in APP group higher (p < 0.001); APP group higher 24th- hour SpO2 and PaO2 values (p = 0.001 and p = 0.002); decrease in pH value higher in non-APP group (p = 0.002); PaO2 increased in APP and decreased in non-APP (p < 0.001); PaCO2 decreased in APP and increased in non-APP (p = 0.007); SpO2 increased in APP higher (p = 0.016) - ICU stay period (n.s.) - ventilator free period (day) (n.s.) - mortality rate lower in APP group (p = 0.020) - intubation requirements lower in APP group (p = 0.001)	4

APP = awake prone position, GCS = Glasgow coma scale, ICU = intensive care unit, n.s. = not significant, PP = prone position, pts = patients

Awake prone position application in patients receiving non-rebreather mask oxygen therapy for respiratory failure due to COVID-19 pneumonia improves oxygenation and decreases the intubation requirements and mortality.

Reference, Study Type	Cases and Cor (Participant #, Char Total		Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3074 Morris 2016 (PMID: 27367766 DOI: 10.1001/jam a.2016.7201) Specification of study: RCT	<ul> <li>- 300 pts</li> <li>Inclusion criteria: <ul> <li>admission to a medical ICU</li> <li>18 years or older</li> <li>MV or NIV and an arterial o pressure to fractional inspire</li> </ul> </li> <li>Exclusion criteria: <ul> <li>inability to walk without assimpairment prior to the acut</li> <li>acute stroke</li> <li>BMI &gt;50</li> <li>neuromuscular disease imp</li> <li>acute hip Fracture</li> <li>unstable cervical spine or p</li> <li>MV &gt; 80h or current hospitation of the study</li> </ul> </li> <li>Per Brance</li> <li>150</li> </ul>	ed oxygen < 300 sistance, cognitive te ICU illness pairing weaning pathologic fracture alization >7 days other research	- 0 for primary analysis - 135 for 6 month follow up (66 intervention: 69 control)	Standardized rehabilitation therapy: - PROM - PT - progressive resistance exercise - 3x/d for 7d/week until hospital discharge	Usual care	<ul> <li>Primary endpoint: <ul> <li>hospital LOS</li> </ul> </li> <li>Secondary outcomes: <ul> <li>physical function</li> <li>health related QoL</li> </ul> </li> <li>Power analysis: 326 pts to provide 80% power for 30% decrease in median hospital LOS using twosided 5% significance, 20% in-hospital mortality + 5% withdrawal lower mortality stopped at 300 pts.</li> </ul>	Primary endpoint: - hospital LOS n.s. (p=0.41) Secondary outcomes: - short physical performance battery score at 6 months (9.0 (8.3 to 9.7); 8.0 (7.2 to 8.7); p=0.04) - SF-36 physical functioning scale score at 6 months (55.9 (50.0 to 61.7); 43.6 (37.5 to 49.7); p=0.001) - functional performance inventory score (2.2 (2.1 to 2.4); 2.0 (1.9 to 2.2); p=0.02) - ventilator free days n.s. - ICU LOS n.s. - discharge destination n.s.	2

ICU = intensive care unit, LOS = length of stay, MV = mechanical ventilation, NIV = noninvasive ventilation, n.s. = not significant, PROM= passive range of motion, PT = physical therapy, pts = patients, RCT = randomized clinical trial

#### Standardized rehabilitation therapy seems to have a benefit in relation to physical functioning at 6 months.

Reference, Study Type	Cases and Co (Participan Characterist Total	t #, Drop	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3079 Cunha 2022 (PMID: 35475866 DOI: 10.36416/1806- 3756/e2021037 4) <b>Specification of</b> <b>study:</b> Retrospective Multicenter cohort study	574 pts Inclusion criteri - 18 years - suspected or confirmed dia of COVID-19 - invasive MV - PaO2/FIO2 ra 150 mmHg - PP Exclusion criter - awake PP wit mechanical ventilation Per Branc 412	agnosis atio < <b>'ia:</b> thout	Positive response to prone positioning (> 20 mmHg improvemen t in PaO <sub>2</sub> /FiO <sub>2</sub> ratio)	Negative response to prone positioning (< 20 mmHg improvemen t in PaO <sub>2</sub> /FiO <sub>2</sub> ratio)	Primary outcome: variables associated to a positive response Secondary outcome: predictive factors of mortality	Primary outcome:-SAPS III 63 [52-75] vs. 68 [56-79]; p = 0.01-SOFA score 9 [6-12] vs. 10 [7-13]; p = 0.04-D-dimer (ng/ml) 9.224 [891-4.452] vs. 10.534 [1.146 –6.376]; p = 0.04-RR (breaths/min) 28 [24-32] vs. 30 [25-34];p < 0.001	4

 $FiO_2$  = inspired fraction of oxygen, OR = odds ratio, PaO\_2 = partial pressure of arterial oxygen, PP = prone positioning, RR = respiratory rate, SAPS = simplified acute physiology score, SOFA = sepsis-related organ failure assessment

A positive response to prone positioning is predicted by SAPS III, SOFA score and initial PaO2/FiO2 ratio; mortality might be predicted by age, time to first PP session, number of sessions, proportion of pulmonary impairment and immunosuppression.

Reference, Study Type	(Participant #	nd Controls t, Characteristics) Fotal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3080 Abu- Khaber 2013 https://doi.org /10.1016/j.ajm e.2013.03.011 Specification of study: RCT	<ul> <li>receiving muscle</li> <li>diseases with sy involvement</li> <li>technical obstact the implementa bone fractures of burns)</li> <li>end-stage malig</li> <li>cardiac pacemal</li> <li>cervical spine fra quadriplegia of fra</li> </ul>	tilation > 24h romuscular disease e relaxant stemic vascular cles that do not allow tion of EMS such as or skin lesions (e.g. nancy kers actures, hemiplegia, neurological origin	2	NMES	No- NMES	Outcomes: - MRC - MV duration - ventilator free survival until day 28 - mortality Day 28	<ul> <li>MRC (mean ± SD; control vs. intervention): <ul> <li>a. day 2: 50.23 ± 5.51 vs. 49.28 ± 6.88, p = 0.465</li> <li>b. day 3: 46.43 ± 7.21 vs. 45.25 ± 9.64, p = 0.094</li> <li>c. day 4: 43.70 ± 9.32 vs. 46.86 ± 10.88, p = 0.041</li> <li>d. day 5: 40.69 ± 10.48 vs. 45.83 ± 11.39, p = 0.044</li> <li>e. day 6: 39.63 ± 10.30 vs. 43.00 ± 12.07, p = 0.046</li> <li>f. day 7: 37.27 ± 13.43 vs. 43.37 ± 9.85, p = 0.049</li> <li>g. day 14: 32.89 ± 16.89 vs. 37.91 ± 11.14, p = 0.047</li> <li>h. day 21: 19.60 ± 4.34 vs. 29.67 ± 8.87, p = 0.037</li> <li>i. day 28: 21.00 ± 9.76 vs. 20.60 ± 5.68, p = 0.091</li> </ul> </li> <li>Duration of MV (mean ± SD; control vs. intervention): 11.97 ± 8.07 vs 9.01 ± 8.01, p = 0.048</li> <li>Ventilator free survival until day 28 (mean ± SD; control vs. intervention): 14.73 ± 9.70 vs. 15.18 ± 9.65, p = 0.421</li> <li>Mortality Day 28, n (%) (control vs. intervention): 6 (15) vs. 4 (10), p-value not stated</li> </ul>	3 (downgraded for high risk of bias)

MRC = medical research council, MV = mechanical ventilation, NMES = neuromuscular electrical stimulation, pts = patients, RCT = randomized controlled trial

NMES increased muscle strength in critically ill patients.

Reference, Study Type		ses and Controls ant #, Characteristics) Total	Drop- out Rate	Interventio n	Contro I	Optimal Population	Primary Results	Evidence Grade
3082 Esperatti 2022 (PMID: 34996496 DOI: 10.1186/s13054 -021-03881-2) Specification of study: prospective multicenter cohort study	Inclusion criteria - ≥ 18 years with co - requiring HFNO Exclusion criteria - respiratory failu etiology - decreased level - presence of sho - immediate need	onfirmed COVID-19-related ARF for at least 4h :: ure secondary to a different of consciousness ck requiring vasopressors d for intubation pressure ventilation prior to		<b>AW-PP:</b> - ≥ 6 h/day	No PP	Primary endpoint: - endotracheal intubation - hospital mortality	Significant differences between groups in : - endotracheal Intubation: 44 (23%) of AW-PP vs 79 (53%) of no-PP were intubated OR 0,27 (95% CI 0.14-0.47) adjusted OR 0.36 (95% CI 0.2-0.7) - hospital mortality: 21 (11%) of AW-PP vs 47 (32%) No-PP died in hospital OR 0.58 (0.19-1.77) adjusted OR 0.50 (95% CI 0.19-1.31)	3

AW-PP = awake prone position, ICU = intensive care unit, PP = prone position, pts = patients

In the study population, AW-PP for  $\geq$  6 h/day reduced the risk of endotracheal intubation, and exposure  $\geq$  8 h/d reduced the risk of hospital mortality.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3083 Fazzini 2022 (PMID: 34774295 DOI: 10.1016/j.bja. 2021.09.031) <b>Specification</b> of study: Systematic review and meta-analysis	14 publications (2.352 pts), 8 prospective cohort studies, 4 retrospective cohort studies, 2 RCTs Inclusion criteria: - at least 20 adult pts with hypoxaemic respiratory failure secondary to ARDS or coronavirus - received PP with any oxygen delivery Exclusion criteria: - PP in intubated pts - PP combined or mixed to lateral positioning - follow-up < 7 days Per Branch 1041 (44%) 1311 (56%)		АРР	SP	Primary endpoint: - change in oxygenation pre and post PP reported as PaO2/FiO2 (P/F) ratio or SpO2/FiO2 (S/ F) ratio Secondary outcomes: - rate of tracheal intubation - mortality - adverse events	Significant differences between groups in: - improvements of PaO2/FiO2 ratio: MD -23.10; 95% CI: -34.80 to 11.39; p= 0.0001; I <sup>2</sup> =26%) after PP - mortality: OR 0.57 (95% CI: 0.36-0.93; P=0.02 I <sup>2</sup> =51%) No significant differences between groups in: - intubation rates - adverse events	1 → 2 (not only RCTs included)

ARDS = acute respiratory distress syndrome, PP = prone position, pts = patients, RCT = randomised controlled study

Prone positioning can improve oxygenation amongst non-intubated patients with acute hypoxaemic respiratory failure when applied for at least 4 h over repeated daily episodes. Awake proning appears safe, but the effect on tracheal intubation rate and survival remains uncertain.

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Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidenc e Grade
3085 Ibarra-Estrada 2022 (PMID: 35346319 DOI: 10.1186/s13054- 022-03950-0) <b>Specifikation of</b> <b>study:</b> RCT	<ul> <li>- 430 pts</li> <li>Inclusion criteria</li> <li>- aged≥18 years w</li> <li>- pulse oximetry &lt;</li> <li>receiving oxygen a</li> <li>through a non-reb</li> <li>- initiated on HFN</li> <li>Exclusion criteria:</li> <li>- severe respirato</li> <li>requiring immedia</li> <li>- do-not-intubate,</li> <li>orders</li> <li>- laparotomy with</li> <li>- pregnancy</li> <li>- vasopressor requimintain median</li> <li>&gt;65 mmHg</li> <li>Per B</li> <li>216</li> </ul>	<ul> <li>90% despite</li> <li>at 15 L/min</li> <li>breather mask</li> <li>C</li> <li>:</li> <li>ry failure</li> <li>ate intubation</li> <li>/resuscitate</li> <li>nin 2 weeks</li> <li>uirement to</li> </ul>		Awake prone positioning + HFNC	Usual care + HFNC	Primary endpoint: - intubation until day 28 Secondary outcomes: - being alive without intubation at day 28 - mortality at 28 days - HFNC duration - use of NIV - time to intubation - days of invasive ventilation - hospital LOS - physiological response to the 1 <sup>st</sup> prone session - AEs	Primary endpoint: - intubation until day 28: 65 of 216 (30%); 92 of 214 (43%); [CI95] 0.54– 0.90, p=0.006 Secondary outcomes: - hospital LOS (11 [IQR 9–14] vs 13 [IQR 10–17] days, p=0.001) - no significant differences in all other outcomes	2

CI = confidence interval, HFNC = high-flow nasal cannula, IQR = interquartile range, LOS = length of stay, NIV = non-invasive ventilation, pts = patients, RR = risk ratio

Awake prone positioning seems to have a benefit on intubation rate and hospital length of stay.

Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
#3087 Kwakman 2022 PMID: 35124345 DOI: 10.1016/j.jcrc. 2022.154000 Specification of the study: RCT	edge of the bed Exclusion criter - contraindicatio - inability to wa prior to ICU adr - ICU readmissio amputations or lower extremiti - cognitive impa imminent to de - traumatic brai Study duration ambulate with w minimal physica balance assistan	ia: instructions riceps muscle ording to the upported on the l ia: ons for pt lk independently mission on fractures in the es airments and ath n injury or stroke : till pts able to walking aids and al support for	6 pts(4 intervention :1 death, 3 other reason; 2 usual care: death)	Bodyweight supported treadmill training: -daily except on weekend - until the pts were able to ambulate with walking aids - duration of BWSTT individually determined by the performance of the 1 <sup>st</sup> training session - varied between walking just a few steps and walking for several minutes	Supervised physiotherapy sessions: - daily - including ambulation training, pulmonary physiotherapy, active strength exercises, transfer training, cycling, balance training, IMT and mobilizing out of bed	Primary endpoint: - number of days to independent ambulation Secondary outcomes: - maximum walking distance reached during hospital stay (2 Minutes Walking Test) - muscle strength 7 days after inclusion - functional mobility - hospital LOS; - symptoms of posttraumatic stress Sample size calculation: using data from two previous studies de- scribing the feasibility of BWSTT and usual care the required sample size was 88 (44 + 44) pts, assuming a 10% dropout rate	Primary endpoint: - median (IQR) time to independent ambulation 4 (3 to 7) days in the intervention group, vs 8 (4 to 23) days in the usual care group (p = 0.017), hazard ratio of 2,41 (95%Cl, 1.11 to 5.23) Secondary outcomes: - hospital LOS shorter (24 days) in the intervention group vs control (42 days) p=0.037 - all other outcomes n.s	2→ 3 (high risk of bias)

BWSTT = bodyweight supported treadmill training, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, pt = physio therapy, pts = patients

BWSTT seems a promising intervention to enhance recovery of ambulation and shorten hospital length of stay of ICU patients, justifying a sufficiently powered multicenter RCT.

Reference, Study Type	(Participant #,	d Controls Characteristics) otal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3088 Seo 2019 https://doi .org/10.14 474/ptrs.2 019.8.3.13 4 Specificati on of the study: RCT	upper limb joints - in the ICU for at lea - able to walk indep admission to the ICU <b>Exclusion criteria:</b> - chronic respiratory admission to the ICU - damage to the leg, trauma surgery - severe pressure uld diseases affecting m - signed a do not res form	es or limitations of the ast 5 days endently before J failure before J pelvis, and back, ceration, neurological uscle strength		<b>Exercise:</b> - postural and passive or active exercises - 5 days a week - for 30 min during ICU stay	Bedside ergometer exercise: - endurance and strength training - 5 days a week -for 30 min during ICU stay	Primary endpoints: - muscle strength via MRC - FSS - QoL via SF-36 Secondary outcomes: - ICU LOS - duration of MV no power analysis	Primary endpoint: - MRC Score [mean (SD)] (pre and post intervention), 10.87 (7.14) exercise vs 5.00 (1.69) ergometer, p = 0.041 - both groups had a significant increase in MRC Score (p<0.05) - FSS [mean (SD)], 6.12 (2.58) exercise vs 1.62 (1.06) ergometer, p = 0.001 - both groups had a significant increase in FSS (p<0.05) - QoL: 71.19 (7.93) exercise vs 41.11 (5.02) ergometer, p=0.001 - ICU LOS, 22.37 (8.86) exercise vs 24.00 (4.27) ergometer, p > 0.05 - duration of MV, 14.50 (7.23) exercise vs 13.50 (4.10) ergometer, p > 0.05	2 → 3 (pilot trial)

FSS = functional status scale, ICU = intensive care unit, LOS = length of stay, MRC = medical research council, MV = mechanical ventilation, pts = patients, QoL= quality of life, RCT = randomized controlled trial, SD = standard deviation, SF-36 = short form 36

#### Exercise seems to be more effective than bedside ergometer in loss of strength, function and HRQL.

Reference, Study Type	Cases and (Participant #, c Tot	haracteristics)	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3090 Lago 2022 PMID:	41 pts admitted to a Brazilian divided in two sub-studies us -Acute phase: septic shock < -Late phase: sepsis or septic	ing a cut-off of 72h: 72h	4 pts in group 1 (3 in the acute phase and 1 in the late phase) excluded due to IC- related issues	Group 1: intervention protocol followed by the control protocol <u>-Intervention</u> : pt kept in dorsal	Group 2:		Ouctomes: - <u>Intragroup comparison:</u> Within the acute phase group and the late phase group no statistically	
35176099 https://doi.or g/10.1371/jo urnal.pone.0 264068	<ul> <li>Inclusion criteria:</li> <li>-Sepsis or Septic shock.</li> <li>Exclusion criteria:</li> <li>-Age ≥ 85y or &lt; 18y, Pregnan</li> <li>-Neuromuscular disease or b</li> <li>-Fractures, burns, skin lesion</li> <li>diseases, severe lower extremation</li> </ul>	locker in the last 24h s, vascular impairment		<ul> <li>decubitus position</li> <li>with headboard</li> <li>lifted at 30° and</li> <li>lower limbs raised at</li> <li>20°, receiving a</li> <li>30min NMES on the</li> <li>gastrocnemius</li> <li>muscle to generate</li> <li>visible contraction</li> </ul>	control protocol followed by the intervention protocol, with a 4-6h wash-out period	Endpoints: measurement through IC during baseline, intervention and control of: - VO2 - EE - VCO2 - RQ	significant difference was found between baseline, intervention and control measures of VO2, EE and VCO2. The only statistically significant difference was in the acute phase group	2
Specification of study: Analysis of two randomized controlled	-Instability: vital parameters -Presence of chest tubes -Thrombocytopenia < 20.000 disease or deep vein thromb -Agitation						between RQ at baseline and during intervention (0,70 vs 0,68, p < 0,05) -Intergroup comparison: in the acute phase significantly higher VO2 and EE and	
crossover studies	Per Br Acute phase: 9 pts Late phase: 11 pts	anch Acute phase: 10 pts Late phase: 11 pts		NMES. Wash-out period: 4-6h between phases			significantly lower RQ compared to the late phase	

Pt = patient, SOFA = Sequential Organ Failure Assessment, MAP = Mean Arterial pressure, HR = Heart Rate, ICP = Intracranial Pressure, NMES = Neuromuscular Electric Stimulation, IC = Indirect Calorimetry, VO2 = Oxygen Consumption, EE = Energy Expenditure, VCO2 = Carbon Dioxide Production, RQ = Respiratory Quotient

# Both within and after the first 72h since diagnosis of sepsis or septic shock in the ICU, NEMS does not cause clinically relevant metabolic changes.

Reference, Study Type	(Participant #	nd Controls . Characteristics) otal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Eviden ce Grade
3092 Musso 2022 (PMID: 35488356 DOI: 10.1186/s13 054-022- 03937-x) Specification of the study: controlled non- randomized trial	Inclusion criteria: - acute moderate to serespiratory failure due to SARS-C - with NIV and prolon Exclusion criteria: - consent - pregnancy - hemodynamically un urgent endotracheal - palliative care	er 2h of last PP-session evere acute hypoxemic oV-2 pneumonia ged PP nstable or need of		<b>PP:</b> - initiated within 24h after ICU admission - at least 1 PP session lasting > 8h over night	SP	Primary endpoint: - occurrence of NIV failure within 28 days of enrolment (intubation/death) Secondary outcome: - clinical outcomes at day 28	Primary endpoint: - NIV failure occurred in 14 (17%) of PP pts vs 70 (43%) of controls , [HR=0.32, 95% CI 0.21–0.50; p<0.0001] Secondary outcome: - PP therapy was associated with improved oxygenation and an earlier decline in inflammatory markers and D-dimer	3

NIV = non invasive ventilation, PP = prone position, pts = patients, SP = supine position

Early prolonged PP is safe and is associated with lower NIV failure, intubation and death rates in noninvasively ventilated patients with COVID-19-related moderate-to-severe hypoxemic respiratory failure. Early dead space reduction and reaeration of dorso-lateral lung regions predicted clinical outcomes in the study population.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3098 Dantas 2012 DOI: 10.1590/S0103 - 507X20120002 00013 Specification of study: RCT	59 pts between February 2009 and         February 2011         Inclusion criteria:         MV and adequate cardiovascular reserve         < 50% variation in resting HR and SBP	<ul> <li>31 out of 59 pts dropped out due to death (47%)</li> <li>Intervent ion group n = 12</li> <li>Control group n = 19</li> <li>Leaving 14 pts per group</li> </ul>	5-stage mobilization protocol: - 2x a day - Daily	Passive mobilization: - Mobilization of all limbs - 5x week - Active- assisted exercises according to pts improveme nt and cooperation	Sample size calculation: 50 pts per group (Study is underpowered) No primary endpoint defined Extracted Outcomes: - Peripheral Muscle Strength (assessed as MRC) - Respiratory Muscle Strength (assessed as MIP and MEP)	Results:         - MRC Score (Control vs. Intervention):         a) Baseline $39.21 \pm 14.63$ vs. $49.29 \pm 11.02$ (p<0.001)	2 → 3 (under- powered, high risk)

Pts = Patients, HR = Heart Rate, SBP = Systolic Blood Pressure, SpO<sub>2</sub> = Saturation of partial oxygen, ICU = Intensive Care Unit, BMI = Body Mass Index, MV = Mechanical Ventilation, MIP = Maximal Inspiratory Pressure, MEP = Maximal Expiratory Pressure

Early Mobilization increases inspiratory and peripheral muscle strength.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3099 KURTOĞLU, 2015 <u>https://doi.org</u> /10.5152/tftrd. 2015.04378 <b>Specification</b> of study: observational- cohort study	30 pts         Inclusion criteria:         - COPD patients who developed         respiratory failure         - satisfying the criteria for the         need of ICU         - followed for at least 24 h in the         ICU         Exclusion criteria:         - unstable cardiovascular disease         (unstable angina, aortic valve         disease)         - uncontrolled hypertension         - malignancy         - liver and/or kidney failure         - severe systemic chronic         diseases         - orthopedic problems (fracture,         joint subluxation, etc.) that could         interfere with rehabilitation         programs         - with fever and who are under         the probable effects of acute         medication changes were not         included in the study         Per Branch         15       15		- same as control - additional NMES to auxiliary respiratory muscles applied 20min a day	- prescribed upper extremity ROM exercises - passively by a physician - controlled breathing techniques	<b>Endpoints:</b> - arterial blood gas measurements - peak heart rate per minute - breathing frequency per minute - oxygen saturation - quality of Life (SGRQ and SF-36) - functional capacity by FIM	Endpoints: - arterial blood gas measurements: no results stated - peak heart rate per minute: different between the group on the 15 <sup>th</sup> and 30 <sup>th</sup> days (p<0.001, p=0.008); between the baseline and 30 <sup>th</sup> day intragroup changes in both groups (p=0.03, p<0.001) - breathing frequency per minute: 30 <sup>th</sup> day between the groups (p=0.003); between the baseline and 30 <sup>th</sup> day intragroup changes in both groups (p<0.001) - oxygen saturation: between the groups on the 8th day (p=0.01); intervention group between the baseline and the end of the third day (p=0.005) - quality of Life (SGRQ and SF-36); SGRQ n.s. different at baseline and 30 <sup>th</sup> day between groups; SF-36, improved to the 30th day in control and intervention groups (p=0.02, p=0.021) - functional capacity by FIM: all subsets and overall scores improved significantly in both groups from the first day to the last (no p- value stated)	3

COPD = chronic obstructive pulmonary disease, FIM = functional independent measurement, ICU = intensive care unit, NMES = neuromuscular electrical stimulation, n.s. = not significant, pts = patients, ROM = range of motion, SF-36 = short form-36, SGRQ = St. George's respiratory questionnaire

# This study revealed positive effects of neuromuscular electrical stimulation in addition with therapeutic exercises on the cardiorespiratory system in the short run,

Reference, Study Type	Cases and Co (Participant #, Char Total		Drop-out - Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3100 Shen 2017 ( <u>https://www.sci</u> <u>encedirect.com/</u> <u>science/article/pi</u> <u>i/S18739598173</u> <u>00169</u> ) <b>Specification of</b> <b>study</b> : pilot RCT	25 pts Inclusion criteria: - adults with sepsis (20-90 yea - MV for longer than 72h Exclusion criteria: - skin defect or infection arour - acute myocardial infarction w - life-threatening cardiac arrhy - pregnancy - dying pts with life expectance month - severe encephalopathy with spontaneous breath drive - uncontrolled seizure - patient is fully awake and has power to cooperate active lim - air-born contagious diseases influenza) - moderate to severe adult ress syndrome with requirement of blocker - pts with ECMO EMS group (n=18)	nd the thighs within one week /thmia e shorter than 1 coma + no s adequate muscle b exercise (eg. tuberculosis, spiratory distress f neuromuscular	7 (6 EMS group: expired /dropped, 1 control group expired)	electric muscle stimulation (both quadriceps and biceps, 32 min with minimal voltage, 5x/week)	Passive mobilisation (arm biceps or thigh quadriceps limb)	Primary outcome: - duration of MV Secondary outcome: - mortality - hand grip strength	Primary outcome: - mean duration of MV was 6 days (IQR 6-15) in control group and 6.5 days (IQR 5-10) in EMS group (p = 0.85): n.s. Secondary outcomes: - hospital mortality was not different in both groups (p = 1.0) - 8/25 (32%) could perform hand grip strength test; 2-5 kg hand strength were measured; handgrip result much lower than normal reference (20-33 Kg for population older than 70 years-old)	$2 \rightarrow 3$ (pilot RCT)

ECMO = extracorporeal membrane oxygenation, EMS = electrical muscle stimulation, MV = mechanical ventilation, n.s. = not significant, pts = patients

EMS did not reduce duration of mechanical ventilation or mortality.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3101 McCaughey 2019 (PMID: 31340846 DOI: 10.1186/s130 54-019-2544- 0) <b>Specification</b> of study: RCT	20 pts <b>Inclusion Criteria:</b> - $\geq$ 18 years of age - dependent on MV due to critical illness <b>Exclusion Criteria:</b> - expected to be ventilated for < 24 hours - already ventilated for > 72 hours - pregnant - non- pharmacological paralysis (e.g. spinal cord injury) - physical obstacles that prevent abdominal FES (e.g. abdominal trauma, pacemaker), - diagnosed terminal illness - no response to abdominal FES (e.g. lower motor neuron impairment or obese) - abdominal surgery within 4 weeks prior to potential inclusion <b>Per Branch</b> 1010		Breath synchronized NMES: - of the abdominal muscles -30 min 2x day - 5 days a week	Sham	Primary endpoint: - feasibility Secondary outcomes: - change from baseline in rectus abdominis thickness (mm) - change from baseline in diaphragm thickness (mm) - change from baseline in rectus abdominis thickness (mm) - change from baseline in combined lateral abdominal muscle thickness (mm) - change from baseline in external oblique thickness (mm) - change from baseline in internal oblique thickness (mm) - change from baseline in internal oblique thickness (mm) - change from baseline in transversus abdominis thickness (mm) - duration of MV (days) - ICU LOS (days) - mortality	Primary endpoint: - feasibility (Session compliance in %, median [IQR]: control 97.2 [7.4] vs intervention 92.1 [5.77], p = 0.384 Secondary outcomes: - change from baseline in rectus abdominis thickness (mm): n.s - change from baseline in diaphragm thickness (mm): n.s - change from baseline in combined lateral abdominal muscle thickness (mm): n.s - change from baseline in external oblique thickness (mm): n.s - change from baseline in internal oblique thickness (mm): n.s - change from baseline in transversus abdominis thickness (mm): only significant difference on day 3: MD (95%CI): 1.04 (.10 – 1.98), p = 0.032 - duration of MV (days), median: control not estimable, intervention 11, p = 0.011 - mortality: values not stated, p = 0.629	2

FES = functional electrical stimulation, MV = mechanical ventilation, NMES = neuromuscular electrostimulation, pts = patients, RCT = randomized control trail

ICU length of stay and duration of mechanical ventilation duration were shorter in the abdominal FES than the control group.

Reference, Study Type	(Participant #,	l Controls Characteristics) tal	Drop-out Rate	Interven tion	Control	Optimal Population	Primary Results	Evidence Grade
3102 Abdellaoui 2011 (PMID: 21349913 DOI: 10.1183/0 9031936.0 0167110 ) Specificati on of study: RCT	15 pts Inclusion criteria: - acute exacerbation CC expiratory volume in on capacity ,70%) - ICU admission - < 75 years of age - BMI < 30 kg/m <sup>2</sup> - no locomotor or neurodisability that could limit - no pacemaker Per Batter B	e second/forced vital	17 pts included -> 2 dropouts due to 1 readmission to ICU and 1 withdrew consent	NMES	Sham- NMES	<b>Derived outcomes:</b> - MVC - 6MWD - muscle fiber size - adverse events	Derived outcomes: - MVC (kg), median [IQR]: control 3 $[1-5]$ vs intervention 10 $[4.7 - 11.5]$ , p = 0.02 -6MWD (meter), median [IQR]: control 58 [43 - 115] vs intervention 165 $[125 - 203]$ , p = 0.008 - muscle fiber size (Type I): p = 0.009 in favor of NMES - muscle fiber size (Type IIx): p = 0.16 - no adverse events	2

ICU = intensive care unit, MVC = maximal voluntary contraction, NMES = neuromuscular electrostimulation, pts = patients, RCT = randomized control trial, 6MWD = 6-min walking distance

Following COPD exacerbation, NMES is effective in counteracting muscle dysfunction and decreases muscle oxidative stress.

Reference, Study Type	(Participant	nd Controls #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3103 Gerovasili 2009 (PMID: 19814793 DOI: 10.1186/cc8 123) <b>Specificatio</b> <b>n of study:</b> Randomized study	myasthenia gravis, 6 - diseases with syste involvement such a -technical obstacles implementation of fractures or skin les - end- stage maligna - pacemakers - ICU stay < 48 hour	rg/m2) muscular disease (e.g. Guillain-Barré) emic vascular s lupus erythematosus t that did not allow the EMS such as bone ions (e.g. skin burns) ancy	23pts/46.9% (10 pts died, 12 excluded due to oedema, 1 technical reasons)	NMES	Sham- NMES	<b>Derived outcomes:</b> - cross sectional diameter change between randomization and day7/8 via ultrasound - duration of MV	Significant changes between groups in: - cross sectional diameter change M. rectus femoris right (cm), mean $\pm$ SD: control -0.21 $\pm$ 0.10 vs intervention -0.11 $\pm$ 0.06, p = 0.009 - cross sectional diameter change M. rectus femoris left (cm), mean $\pm$ SD: control -0.19 $\pm$ 0.16 vs intervention -0.13 $\pm$ 0.10, p = 0.07 -cross sectional diameter change M. vastus intermedius right (cm), mean $\pm$ SD: control - 0.10 $\pm$ 0.05 vs intervention -0.11 $\pm$ 0.06, p = 0.034 - cross sectional diameter change – M. vastus intermedius left (cm), mean $\pm$ SD: control -0.22 $\pm$ 0.26 vs intervention -0.09 $\pm$ 0.05, p = 0.018 No significant differences between groups in: - duration of MV (days), mean $\pm$ SD control: 9 $\pm$ 3 vs intervention 9 $\pm$ 2	3

ICU = intensive care unit, MNES = neuromuscular electrostimulation, MV = mechanical ventilation, pts = patients

#### NMES reduces muscle loss measured via ultrasound in the ICU.

Reference, Study Type	(Participant #,	nd Controls , Characteristics) otal	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3104 Karatzanos 2012 (PMID: 22545212 DOI: 10.1155/2012/4 32752) <b>Specification of</b> <b>study:</b> Secondary analysis of RCT	<ul> <li>brain death</li> <li>preexisting neuromus myasthenia gravis)</li> <li>diseases with systemi such as lupus erythema</li> <li>technical obstacles th implementation of EMS or skin lesions (e.g. skir</li> <li>end- stage malignance</li> <li>pacemakers</li> <li>ICU stay &lt; 48 hours</li> </ul>	n2) scular disease (e.g. c vascular involvement atosus at did not allow the S such as bone fractures n burns)	90 pts/63.3% EMS group - 28 died - 11 impaired cognitive state - 7 dropouts Control group - 22 died - 22 impaired cognitive state	NMES	Sham- NMES	<b>Derived outcomes:</b> - MRC score - hand grip strength	Derived outcomes: - MRC score, median [IQR]: control 52 [40-58] vs intervention 58 [51- 60], p = 0.04 - hand grip strength (kg), mean ± SD: control 14.8 ± 10.7 vs intervention 21.4 ± 10.8, p = 0.18	4

EMS = electrical muscle stimulation, ICU = intensive care unit, MRC = Medical Research Council, NMES = neuromuscular electrostimulation

#### NMES improves muscle strength in ICU patients.

Reference, Study Type	Cases and Controls (Participant #, Characteri Total	Dron-	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3106 Gruther 2010 (PMID: 20549166 DOI: 10.2340/165 01977-0564) Specification of study: RCT	<ul> <li>implantable cardioverter defibrillators</li> <li>neuromuscular disorders</li> <li>myopathy</li> <li>paresis of the stimulated m</li> <li>epilepsy</li> <li>allergic reactions to the election</li> <li>peripheral oedemas counter</li> <li>NMES</li> <li>heavy ischemia of the lowe extremities</li> <li>BMI &gt; 30</li> <li>incisions or open wounds on that might be stressed</li> </ul>	nuscles ctrodes eracting r	<ul> <li>NMES <ul> <li>M. vastus <ul> <li>intermedius and M.</li> <li>rectus femoris</li> <li>1 session/day</li> <li>5 session/week</li> <li>Total of 4 weeks</li> </ul> </li> <li>2 groups: <ul> <li>acute patients n = 8</li> <li>long-term patients n = 8</li> </ul> </li> </ul></li></ul>	Sham-NMES - low currency to avoid muscle contraction 2 groups: - acute patients n = 9 - long-term patients n = 9	<b>Outcome:</b> MLT difference between baseline and week 4 by ultrasound	Outcome: MLT at baseline (Mean, SD): - acute patient group a) intervention: 28.9 (6.6), p-value not stated b) control: 32.9 (9.7), p-value not stated - long-term patient group: a) 18.4 (4.2), p-value not stated b) 18.6 (5.9), p-value not stated MLT after 4 weeks (Mean, SD): - acute patient group a) intervention: 18.3 (3.2), p = 0.002 b) control: 20.1 (5.4), p < 0.001 - long-term patient group a) 19.3 (3.8), p = 0.036 within-group comparison, p = 0.013 between-group comparison b) 18 (5.8), p-value not stated	2 → 3 (down- graded)

BMI = body mass index, ICU = intensive care unit, MLT = muscle layer thickness, NMES = neuromuscular electrical stimulation, pts = patients, RCT = randomized controlled trial

#### NMES has a positive effect on muscle layer thickness when started late.

Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3107 Zanotti 2003 (PMID: 12853536 DOI: 10.1378/chest. 124.1.292) Specification of study: RCT	<ul> <li>24 pts</li> <li>Inclusion criteria: <ul> <li>chronic hypercapnic ratio COPD</li> <li>invasive MV via a tract</li> <li>presence of severe peratrophy</li> <li>clinically stable state</li> </ul> </li> <li>Exclusion criteria: <ul> <li>treated with systemic neuromuscular blockin while in the ICU</li> <li>history of diseases oth</li> <li>neurologic disease</li> <li>need for treatment wid during the rehabilitati</li> </ul> </li> <li>Per Brance 12</li> </ul>	cheostomy eripheral muscle c corticosteroids and ing agents for > 5 days her than COPD with systemic steroids ion period		ES + ALM - surface electrodes positioned bilaterally on the quadriceps femoris and vastus glutei muscles - stimulation duration 30 min	ALM	<ul> <li>Primary outcomes: <ul> <li>peripheral muscle</li> <li>strength assessed</li> <li>with MRC score</li> </ul> </li> <li>Secondary outcomes: <ul> <li>cardiorespiratory</li> <li>function: <ul> <li>a) SpO2</li> <li>b) HR</li> <li>c) RR</li> </ul> </li> <li>number of days needed to transfer from bed to chair</li> </ul></li></ul>	<ul> <li>Primary outcome: <ul> <li>no statistically significant differences in baseline strength between groups.</li> <li>MRC increase, mean ± SD (control vs. intervention): 1.25 ± 0.75 vs. 2.16 ± 1.02; p = 0.02</li> </ul> </li> <li>Secondary outcome: <ul> <li>no statistically significant differences in SpO<sub>2</sub>, HR and RR between groups.</li> <li>number of days needed to transfer from bed to chair, mean ± SD (control vs. intervention): 14.33 ± 2.53 vs. 10.75 ± 2.41; p = 0.001</li> </ul> </li> </ul>	2 → 3 (high risk of bias)
	12	12						

ALM = standard physical rehabilitation protocol of active limb mobilization, ES = electrical stimulation, HR = heart rate, MRC = medical research council, RR = respiratory rate, SpO<sub>2</sub> = saturation of inspired oxygen

NMES improves muscle strength in ICU patients and shortens the number of days needed to enable transfer from bed to chair.

Reference, Study Type	Cases and Co (Participant #, Cha Total	aracteristics)	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3108 Meesen 2010 (PMID: 21992890 DOI: 10.1111/j.1525- 1403.2010.00294.x) <b>Specification of</b> <b>study:</b> partially randomized controlled trial with intraindividual element	<ul> <li>25 pts</li> <li>Inclusion criteria: <ul> <li>day after admission</li> <li>expected prolonge ventilation</li> </ul> </li> <li>Exclusion criteria: <ul> <li>still able to move t despite the sedation</li> <li>signs of recent isch infarction &lt; 7 days</li> <li>severe orthopedic damage</li> <li>augmented risks for</li> <li>open wounds, hem arterial catheter at area</li> </ul> </li> <li>Per Brantal 11</li> </ul>	heir limb actively on ago or vascular or NMES nodialysis, or an the stimulation	6pts (no reasons stated)	NMES - electrod es placed on m. rectus femoris and m. vastus medialis - duration of stimulati on 30 min	No NMES	Outcomes: - muscle mass modeled from thigh circumference - cardio- respiratory parameters a) HR b) RR c) SpO <sub>2</sub> d) DBP	<ul> <li>Outcomes: <ul> <li>muscle mass, mean ± SD</li> <li>intervention group; stimulated leg:</li> <li>0.035 ± 0.015; p &lt; 0.0001</li> </ul> </li> <li>b) intervention group; non-stimulated leg: <ul> <li>-0.027 ± 0.015; p &lt; 0.0001</li> <li>c) control group:</li> <li>-0.025 ± 0.014; p &lt; 0.0001</li> </ul> </li> <li>muscle mass, type 3 test of fixed effects: <ul> <li>a) intervention group:</li> <li>stim. leg vs. non-stim. leg:</li> <li>0.062; p &lt; 0.0001</li> </ul> </li> <li>b) intervention vs. control: 0.060; p &lt; 0.0001</li> <li>cardiorespiratory parameters: no significant differences between groups</li> </ul>	2 → 3 (pilot and some concern risk)

DBP = diastolic blood pressure, HR = heart rate, NMES = neuromuscular electrical stimulation, Non-stim. = non-stimulated, RR = respiratory rate, SpO<sub>2</sub> = saturation of inspired oxygen, Stim. = stimulated

#### NMES increases muscle mass in ICU patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3109 Poulsen 2011 (PMID: 21150583 DOI: 10.1097/CCM.0b0 13e318205c7bc) <b>Specification of</b> <b>study:</b> Intraindividual RCT	8 pts Inclusion criteria: - septic shock - ICU pts Exclusion sriteria: - focus on infection in or trauma to the lower extremities - predicted ICU stay of < 7 days - severe respiratory or circulatory instability that precluded transportation to CT scan - BMI > 35 kg/m <sup>2</sup> - diabetic complications		NMES	No NMES	<b>Primary endpoint:</b> - muscle volume change via CT	Primary endpoint: - muscle volume change (%), median [IQR]: control - 2.3 [- 0.63.1] vs intervention-2.9 [- 0.43.6], p = 0.12	2 → 3 (pilot and some concern risk)

BMI = body-mass-index, ICU = intensive care unit, IQR = interquartile range, NMES = neuromuscular electric stimulation, pts = patients, RCT = randomized controlled trial

### NMES improves muscle mass in ICU patients.

Reference, Study Type		l Controls Characteristics) tal	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3110 Rodriguez 2012 (PMID: 21715139 DOI: 10.1016/j.jcrc. 2011.04.010) <b>Specification</b> of study: RCT - intraindividual	16 pts Inclusion criteria: - 18 years or older - sepsis - requiring MV ≥ 1 organ failure othe dysfunction within 44 according to a SOFA ≥ 3 Exclusion criteria: - previous or ongoing -orthopedic injuries t with evaluation of st - cardiac pacemakers - metallic prosthesis - previous immobiliza - pregnancy - need of neuromusc infusion - high risk of immine - previous poor perfo an Eastern Cooperati score > 2	8 hours of admission 3 neurologic diseases that could interfere rength ation for > 5 days ular blockers nt death ormance status with		NMES	No NMES	<b>Primary outcomes:</b> - MRC score - arm circumference change - thigh circumference change - M. biceps brachii thickness ultrasound	Primary outcomes: MRC score at awakening: - biceps, median [IQR]: control 3 $[1 - 4]$ vs intervention 3 $[2 - 4]$ , p = 0.014 - quadriceps, median [IQR]: control 2 $[2 - 3]$ vs intervention 3 $[2 - 3]$ , p = 0.025 - quadriceps + biceps, median [IQR]: control 5 $[3 - 6]$ vs intervention 6 $[6 - 7]$ , p = 0.009 MRC at last day of NMES: -biceps, median [IQR]: control 3 $[2 - 4]$ vs intervention 4 $[3 - 4]$ , p = 0.005 - quadriceps, median [IQR]: control 3 $[2 - 3]$ vs intervention 3 $[3 - 4]$ , p = 0.034 - quadriceps + Biceps, median [IQR]: control 6 $[4 - 7]$ vs intervention 7 $[5 - 8]$ , p = 0.009 - arm circumference change (cm): control and intervention values not stated, p = 0.615 - thigh circumference: control and intervention values not stated, p = 0.979 - M. biceps brachii thickness: control and intervention values not stated, p = 0.290	2 → 3 (pilot trial)

MV = mechanical ventilation, NMES = neuromuscular electric stimulation, pts = patients, RCT = randomized controlled trial

### NMES improves muscle strength in ICU patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3111 Hirose 2013 (PMID: 23561945 DOI: 10.1016/j.jcrc.2 013.02.010] Specification of study: Cohort Study	15 ptsInclusion criteria:- coma within the first 24 hours ofhospitalization- first-time stroke or TBI- no other associated thoracic orabdominal injury- age between 16 and 75 years- paralysis of one or both lowerlimbs- ability to live independentlybefore the acute- brain insult- no known muscle diseasePer Branch96		NMES	No NMES	<b>Primary endpoint:</b> - CT-CSA for the lower limb	Significant differences between groups in: - CT-CSA on day 14 (%) - M. quadriceps femoris, mean $\pm$ SD: control 87.5 $\pm$ 2.8 vs intervention 98.7 $\pm$ 2.4, p < 0.00 - M. biceps femoris, mean $\pm$ SD: control 87.5 $\pm$ 4.5 intervention 99.8 $\pm$ 2.7, p < 0.001 - M. tibialis anterior, mean $\pm$ SD: control 87.8 $\pm$ 5.8 intervention 101.2 $\pm$ 2.7, p < 0.001 - M. Gastrocnemius, mean $\pm$ SD: control – 89.1 $\pm$ 4.8 intervention 99.3 $\pm$ 2.0, p < 0.001	3 → 4 (small sample size)

CS = cross sectional area, NMES = neuromuscular electric stimulation, TBI = traumatic brain injury

#### NMES improves muscle mass in ICU patients.

Reference, Study Type	Cases and Controls (Participant #, Characteristics)	Recommendations
Study Type	Total	
3113 Berry A 2017 https://aci.health.nsw. gov.au/data/assets/pdf file/0005/239783/ ACI17131_PAM_Guideline.pd	SR of 35 studies in 2015: (3 case series, 10 cohort, 2 diagnostic, 3 observational, 4 QA, 7 SR, 6 RCT studies) <b>Inclusion criteria:</b> - adult pts in ICU receiving MV	<ul> <li>Assessment and clinical practice <ol> <li>A dedicated physical activity and movement program should be implemented to aid in the recovery of critically ill pts.</li> <li>Early physical activity and movement is feasible and safe for critically ill pts and should be incorporated into usual practice.</li> <li>All patients admitted to the ICU should be screened on a daily basis for inclusion in a PAM program. This assessment should be documented in the patient's medical record. Where feasible this screening should occur within 24 hours of admission.</li> <li>The program, based on the patient's current activity level, should be developed in consultation with a multidisciplinary team.</li> <li>In addition to the physical benefits PAM should be implemented to support patients' psychosocial needs and reduce concerns such as anxiety, depression and sleep disorders/disturbances that may impact the patient after discharge from the ICU.</li> <li>The minimum human resources for safely ambulating the ventilated patient must be three staff members, one of whom is experienced and will act as team leader. The actual number of staff will be based on pre-mobility assessment. A Medical Officer with accreditation in advanced airway skills must be available on site.</li> <li>The equipment that may be required includes a portable ventilator and/or manual resuscitator bag, portable suction and oxygen, IV pole, monitoring equipment, a walking frame and a wheelchair to follow.</li> <li>The development of a dedicated multidisciplinary team is essential for the successful implementation and maintenance of a patient physical activity and movement plan.</li> </ol> </li> <li>Infection prevention <ol> <li>Clinicians are to undertake a risk assessment to identify the risk of contamination and mucosal or conjunctival splash injuries during PAM activities. PPE (including goggles/face shield/gloves and gown/apron) as per NSW 2007 Infection Controp Policy are to be worn according to this risk assessment.</li> <li>Clinicians must adhere to</li></ol></li></ul>
Specification of study:		Infection Control Policy and ASA Standard 4187 prior to and following use. Work, health and safety
Clinical guideline		12. Clinical staff undertaking patient physical activity and movement must undertake a risk assessment of the intended
	Definition of EM	activity/ies to protect the health and safety of the patient and all staff involved.
	Development of a PAM program for critically ill adult ICU pts from the time of admission until discharge	<ul> <li>Governance</li> <li>13. Education and training should be given to key stakeholders regarding the benefits/importance of physical activities and movement in the ICU patient.</li> <li>14. Medical, nursing or physiotherapy ownership of a patient physical activity and movement plan should be determined.</li> <li>15. Hospital executive support, in terms of management/budgetary maintenance of a patient physical activity and movement program, should be available.</li> <li>16. Evaluation of a patient physical activity and movement program should occur following implementation, with regular audits for compliance conducted as a component of the ICU's routine quality improvement program. A number of valid and reliable ICU specific outcome measures are available to assist evaluation process.</li> </ul>

ICU = intensive care unit, MV = mechanical ventilation, PAM = physical activity and movement, pts = patients, QA = quality assurance, RCT = randomized controlled trial, SR = systematic review

Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3114 Prasobh 2021 (DOI: 10.1097/JAT.00000 0000000140) https://journals.lw w.com/jacpt/fulltex t/2021/01000/early mobilization_of_p atients_receiving.6. aspx Specification of study: Systematic Review	<ul> <li>5 publications (3 retrospective cohort, 2 prospective cohort, 528 pts)</li> <li>Inclusion criteria: <ul> <li>clinical trials and cohort studies</li> <li>outcome mobilization and safety of critically ill patients</li> <li>receiving vasoactive drugs (2010-2018)</li> </ul> </li> <li>Exclusion criteria: <ul> <li>did not report number of pts receiving vasoactive drugs or the number of mobilization sessions</li> </ul> </li> <li>Per Branch</li> </ul>		Early mobilisation	Bed rest or immobilized	Primary endpoint: - safety of early mobilization of patients on vasoactive drugs (adverse events) - relationship between dosage of vasoactive drugs and level of mobility achieved	Primary endpoint: - no severe adverse events (such as fall to the ground, cardiac arrest, unplanned extubation) - hypotension most commonly cited adverse event - no evidence on specific doses of vasoactive drugs allowing safe mobilization	1 → 3 (not only RCTs, no metaanalysis

# Evidence determining specific doses of vasoactive drugs that would allow safe mobilization of patients in critical care is lacking

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Reference, Study Type	Cases and Controls (Participant #, Characteristics) Total	Drop-out Rate	Intervention	Control	Optimal Population	Primary Results	Evidenc e Grade
3116 Nakamura 2020 (PMID: 32800385 DOI: 10.1016/j.cl nu.2020.07. 036) Specification of study: RCT	117 pts         Inclusion criteria:         - admitted to the ICU         Exclusion criteria:         - < 20 years	Without EMS: 9 pts. excluded after randomizatio n (death, discharged alive earlier) With EMS: 8 pts. Excluded after randomizatio n (death, discharged alive earlier)	Rehabilitation: - with belt-type EMS - either high protein or medium protein	Standard rehabilitation: - high protein or medium protein	Primary endpoint: - femoral muscle volume change Secondary outcomes: - FSS-ICU at hospital discharge - Barthel at ICU discharge - EQ-5D at hospital discharge - ICU and hospital LOS - MV days - ADL and quality of life scores - 28-day survival rate - duration of EN, oral intake restart, EN failure - diarrhea and vomiting events - PIICS criteria - pneumonia during stay	Primary endpoint: - femoral muscle volume loss 12.9 ± 8.5% in the high-protein group and 16.9 ± 7.0% in the medium- protein group (p = 0,0059) - muscle volume loss was significantly less in the high-protein group only during the EMS period (no declared p-value) Secondary outcomes: - no significant difference in ADL, FSS-ICU, Barthel- Index, QOL sore, survival rate, ICU and hospital LOS, duration of MV, EN failure, vomiting, diarrhea or pneumonia occurrence - proportion of PIICS lower in high-protein group compared to medium- protein group (11.7% vs. 26.3%, p = 0.041) (Based on protein differentiation)	2

ADL = activities of daily living, DNR = do not resuscitate, ECMO= extracorporeal membrane oxygenation, EMS = electrical muscle stimulation, EN = enteral nutrition, ICU = intensive care unit, LOS = length of stay, pts = patients, QOL = quality of life

A high protein delivery target provides greater benefit for muscle volume maintenance than medium protein delivery, but only with active early rehabilitation using belt-type EMS.

Reference, Study Type	Cases and Controls (Participant #, characteristics) Total	Drop- out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
2022 PMID: 34077700 https://doi.org/10. 1513/AnnalsATS.2 02102-1510C Specification of	1 center from April 2009 to January 2020 → 177 pts., 2706 APT session Inclusion criteria: -≥ 18 years old -APT while receiving VV- or VA ECMO Exclusion criteria: -not perform any APT while receiving ECMO support Per Branch 177	n/a	АРТ	n/a	activity (IMS score ≥4, including standing, marching on the spot or walking) vs. only IBPT activity during ECMO support Secondary Endpoints: -frequency and intensity of	Primary Results: - 138 patients (78%) achieving out-of-bed activity Secondary Results: -108 (61%) pts. ambulated (1284 sessions), 34 of whom had femoral cannulae (250 sessions) -Bridge-to-transplant (OR 17.2, 95% CI [4.12–72.1]), VV ECMO (OR 2.83, 95% CI [1.29–6.22]), later cannulation year (OR 1.65, 95% CI [1.37–1.98]) and higher CCI (OR 1.53, 95% CI [1.07–2.19]) associated with increased odds of achieving OOB vs. IBPT, whereas invasive MV (OR 0.11, 95% CI [0.05-0.25]) and femoral cannulation (OR 0.19, 95% CI [0.04–0.92) associated with decreased odds of performing OOB activities -AEs occurred in 2% of sessions	4
	1//						

pts. = patients; APT = active physical therapy; VV = veno-venous; VA = veno-arterial; ECMO = extracorporeal membrane oxygenation; ICU = Intensive Care unit; IMS = ICU Mobility Scale; IBPT = in-bed physical therapy; OR = odds ratio; CCI = charlson comorbidity index; OOB = out-of-bed; MV = mechanical ventilation; AE = Adverse events

Physical therapy with femoral cannulation is safe and feasible, and complications related to mobilization are uncommon.

No detailed assessment was carried out because higher-quality evidence is available on this topic.

Cases and Controls (Participant #, characteristics) Total	Recommendations
· · · · ·	<ul> <li>Key recommendations regarding rehabilitation:         <ul> <li>ensure the short-term and medium-term rehabilitation goals are reviewed, agreed and updated throughout the patient's rehabilitation care pathway.</li> <li>ensure the delivery of the structured and supported self-directed rehabilitation manual, when applicable.</li> <li>during the patient's critical care stay;</li> <li>as early as clinically possible, perform a short clinical assessment to determine the patient's risk of developing physical and non-physical morbidity, perform a comprehensive clinical assessment to identify their current rehabilitation needs. This should include assessments by healthcare professionals experienced in critical care and rehabilitation.</li> <li>for patients at risk, agree short-term and medium-term rehabilitation goals, based on the comprehensive clinical assessment. (The patient's family and/or carer should also be involved.)</li> <li>the comprehensive clinical assessment and the rehabilitation goals should be collated and documented in the patient's clinical records.</li> <li>for patients at risk, start rehabilitation as early as clinically possible, based on the comprehensive clinical assessment and the rehabilitation should include:</li></ul></li></ul>
No definition of EM	<ul> <li>information about the rehabilitation care particular.</li> <li>information about the rehabilitation care particular.</li> <li>information about the differences between critical care and ward-based care. This should include information about the differences in the environment, and staffing and monitoring levels.</li> <li>information about the transfer of clinical responsibility to a different medical team (this includes information about the formal structured handover of care recommended in the NICE guideline on acutely ill patients in hospital.</li> <li>if applicable, emphasise the information about possible short-term and/or long-term physical and non-physical problems that may require rehabilitation.</li> <li>if applicable, information about sleeping problems, nightmares and hallucinations and the readjustment to ward-based care.</li> </ul>
	(Participant #, characteristics) Total n = 15 publications Inclusion criteria: - adults with rehabilitation needs as a result of a period of critical illness that required level 2 and level 3 critical care Exclusion criteria: - adults receiving palliative care - clinical subgroups of patients whose specialist rehabilitation needs are already routinely assessed and delivered as part of their care pathway Definition of EM

EM = early mobilization

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Reference, Study Type	Cases and (Participant #, C Tot	Characteristics)	Drop -out Rate	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
3121 ECMO-PT Study Investigators, 2020 (PMID: 32179935 DOI: 10.1007/s0013 4-020-05994- 8) Specification of the study: Pilot RCT	20 pts Inclusion criteria - ≥18 years - functionally inc to current admis - va-ECMO or VV least 24h Exclusion criteria - in ICU > 5 days commencement - received ECMO - not expected to physical function - unable to comr English Per Br 10	dependent prior ssion /-ECMO for at prior to to fECMO 0 < 72h to recover n in 90 days municate in		Early goal- directed physiotherapy	Standard care physiotherapy	<ul> <li>Primary endpoint: <ul> <li>feasibility (increased duration of activity and higher IMS)</li> <li>safety (adverse and serious adverse events)</li> </ul> </li> <li>Secondary outcomes: <ul> <li>strength measured with MRC score</li> <li>KATZ ADL</li> <li>ICU and hospital LOS ICU and hospital mortality</li> </ul> </li> </ul>	Primary endpoint: - total time of EM higher in intervention (133 (82-220) vs. 27.5 (20.4-31) minutes, p = 0,002) - no increase in medium level of mobilization (IMS 2.67 (0 – 5.3) vs. 1.5 (1 – 4.7)) -two safety events in each group Secondary outcomes: - no difference for ICU LOS and mortality - increased functional independence in intervention (Katz activities of daily living 6 [6–6] vs. 5 [4, 5])	2 → 3 Small pilot RCT

ECMO = extracorporeal membrane oxygenation, ICU = intensive care unit, IMS = intensive care unit mobility scale, KATZ ADL = Katz index of independence in activities of daily living, LOS = length of stay, MRC = medical research council, pts = patients, VA = venous arterial, VV = venous venous

# Early mobilization was safe and feasible. In the intervention group, there was a signal for improved functional independence in the activities of daily living at hospital discharge

Reference, Study Type	Cases and Controls (Participant #, Characteris- tics) Total	Recommendations
3122 Murray 2016 (PMID: 27755068 DOI: 10.1097/CCM.000000 0000002027) <b>Specification of</b> <b>Study:</b> Clinical Practice Guideline	6 studies Inclusion criteria: patients receiving continuous infusions of a NMBA Definition of EM No definition of EM	Should patients receiving continuous infusions of a NMBA receive physiotherapy to improve mortality, quality of life, or exercise capacity? recommendation: we suggest that patients receiving a continuous infusion of NMBA receive a structured regimen of physiotherapy (weak recommendation, very low quality of evidence)

EM = early mobilisation, NMBA = neuromuscular blocking agent

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Reference,	Cases and Controls (Participant #, Characteristics)	Drop- out	Intervention	Control	Optimal Population	Primary Results	Evidence Grade
Study Type	Total	Rate			ropulation		Grade
Barnes-Daly 2016 (PMID: 27861180 DOI: 10.1097/CCM.0000 00000002149) Specification of study: prospective cohort study	6.064 ventilated and non- ventilated general medical and surgical ICU patients enrolled between January 1, 2014, and December 31, 2014 Inclusion criteria (not clearly defined) - surgical ICU patients - adults Exclusion criteria - active ethanol/drug withdrawal - open abdomen - significant hemodynamic or respiratory instability - new coronary ischemia - therapeutic neuromuscular blockade - intubation within the previous 6 hours without stabilization		Total and partial bundle compliance (daily measured) - ABCDEF bundle compliance accounting for total compliance (all or none) or for partial compliance ("dose" or number of bundle elements used) - A= Assess, prevent, and manage pain; B= Both spontaneous awakening trials (SATs) and spontaneous breathing trials (SBTs); C= Choice of Sedation/Analgesia; D= Delirium monitoring and management; E= Early mobility and exercise; F= Family engagement and empowerment	No control group	<b>Outcome</b> (not clearly defined) - hospital mortality -delirium-free days - coma-free days	hospital mortality: n = 586 [9.7%] - for every 10% increase in total bundle compliance: 7% higher odds of hospital survival (odds ratio, 1.07; 95% Cl, 1.04–1.11; p < 0.001) - for every 10% increase in partial bundle compliance: 15% higher hospital survival (odds ratio, 1.15; 95% Cl, 1.09– 1.22; p < 0.001) - delirium- and/or coma-free days mean (95% Cl): 1.61 (1.55–1.67) - with both total bundle compliance: incident rate ratio, 1.02; 95% Cl, 1.01–1.04; p = 0.004 - with partial bundle compliance: incident rate ratio, 1.15; 95% Cl, 1.09–1.22; p < 0.001	3
	N=6064						

CI = confidence interval, ICU= intensive care unit

Higher bundle compliance was independently associated with improved survival and more days free of delirium and coma after adjusting for age, severity of illness, and presence of mechanical ventilation.

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