Normovolemic hemodilution ancient or modern?

Prof. Dr. Jens Meier

Klinik für Anästhesiologie und Intensivmedizin
Kepler Universitätsklinikum Linz

JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

"Everything you always wanted to know about hemodilution

*But were afraid to ask"

ANH – ancient or modern?

JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

Europ. Surg. Res. *4:* 55–70 (1972)

Acute Normovolemic Hemodilution

Changes of Central Hemodynamics and Microcirculatory Flow in Skeletal Muscle[1]

K. Messmer, D. H. Lewis, L. Sunder-Plassmann, W. P. Klövekorn, N. Mendler and K. Holper

Institute for Surgical Research, Surgical University Clinic, Munich, and Department of Surgery I, University of Gothenburg, Gothenburg

Key Words
Oxygen transport capacity
Oncotic properties of dextran-60
In vivo viscosity
Capillary transport
^{51}Cr-EDTA clearance
Limited hemodilution

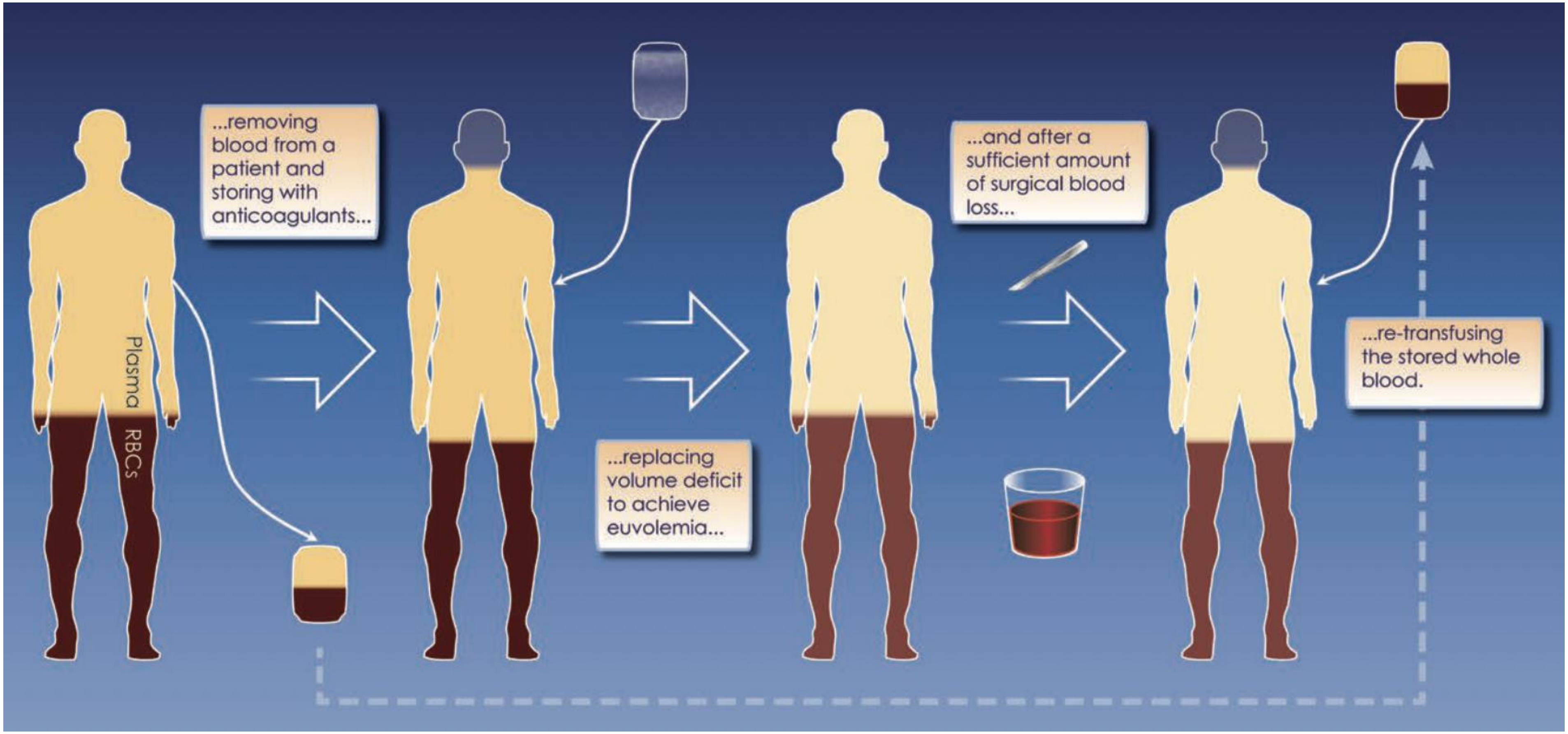
Abstract. Isovolemic hemodilution down to hematocrit values of 10% has been performed in splenectomized dogs during pentobarbital anaesthesia. Circulatory changes were followed in the systemic circulation; for the estimation of capillary flow and capillary transport in skeletal muscle a double isotope technic has been applied. Progressive hemodilution resulted in a significant increase of cardiac output and skeletal muscle flow; peripheral resistance decreased clearly parallel with the whole blood viscosity as measured at different shear rates. The transport capacity (PS) in skeletal muscle was not significantly changed. From this finding and from the lack of changes in the local effluent blood it is concluded that hypoxia does not occur when limited hemodilution is performed normovolemically. These data, therefore, add further support to the concept of limited hemodilution as a therapeutic tool in microcirculatory disorders.

The interest in the relationship of hematocrit and blood viscosity *in vivo* has been greatly stimulated by viscometric findings of recent years. By different groups it has been demonstrated that acute changes in hematocrit are followed by an increase in cardiac output [19, 21, 24]

[1] Paper presented at the 6th Congres of the European Society for Experimental Surgery, Hälsingborg, April 1971.

Received: September 10, 1971; accepted: September 28, 1971.

Acute Normovolemic Hemodilution

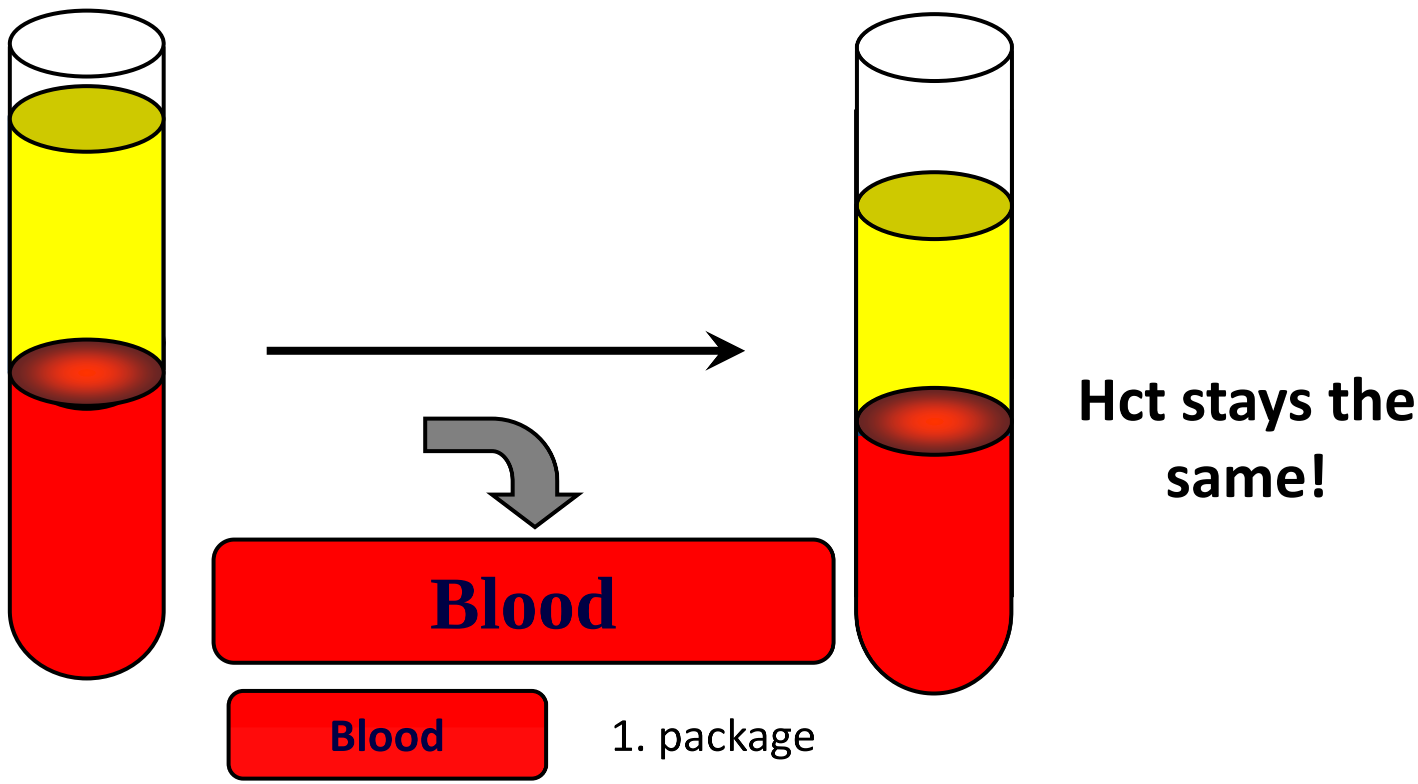


Wanderer, Anesth Analg, 2017

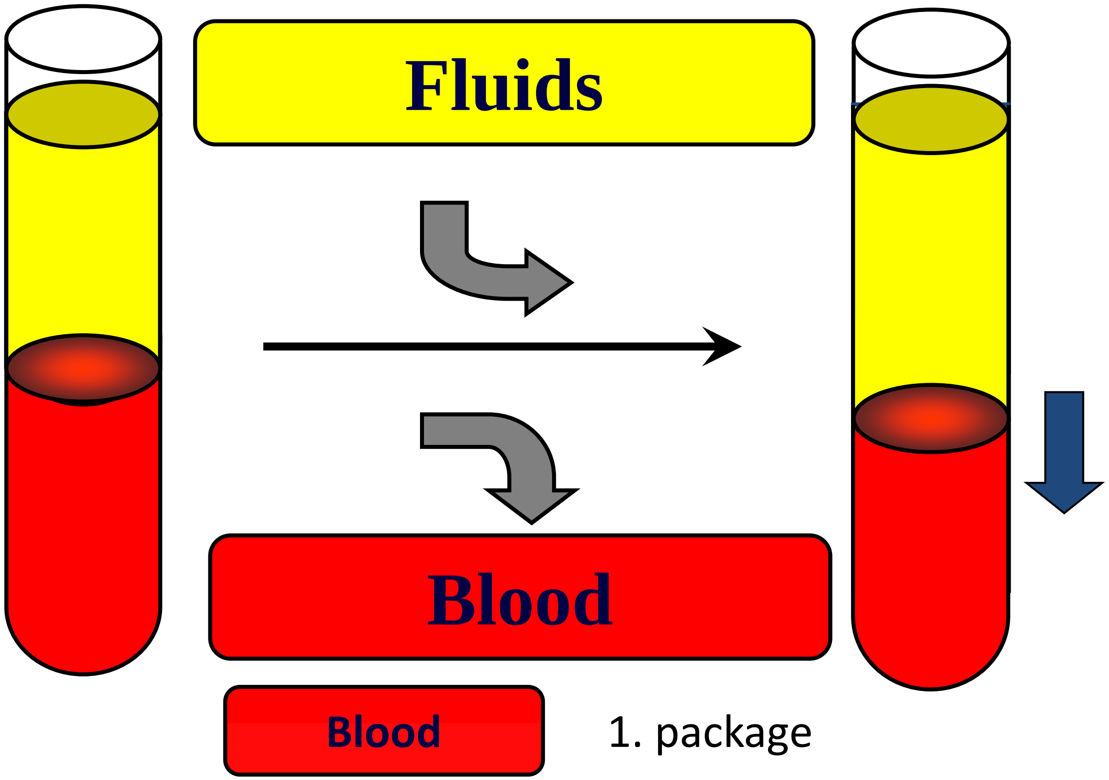
Acute Normovolemic Hemodilution

JOHANNES KEPLER UNIVERSITÄT LINZ

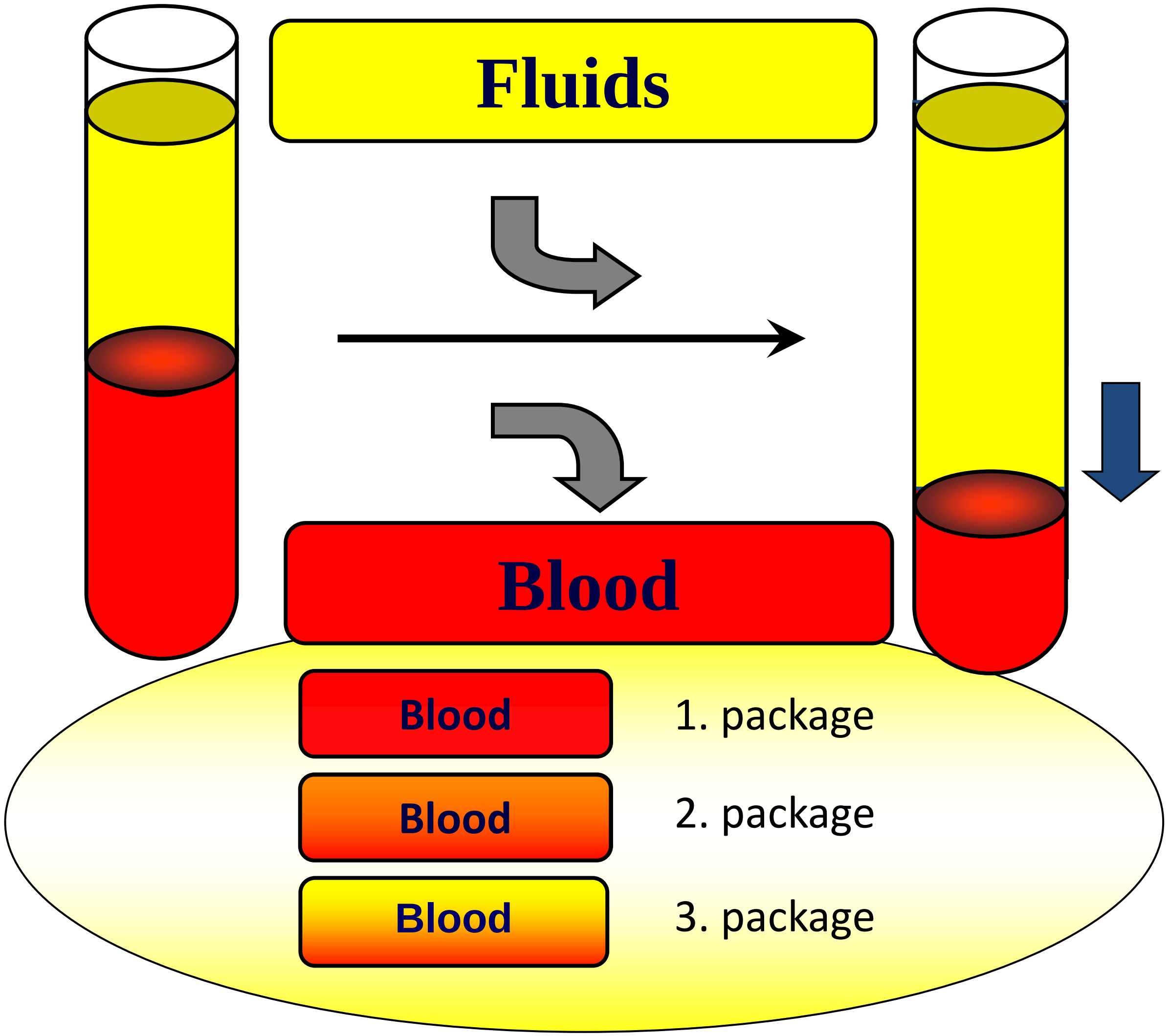
Kepler Universitäts Klinikum



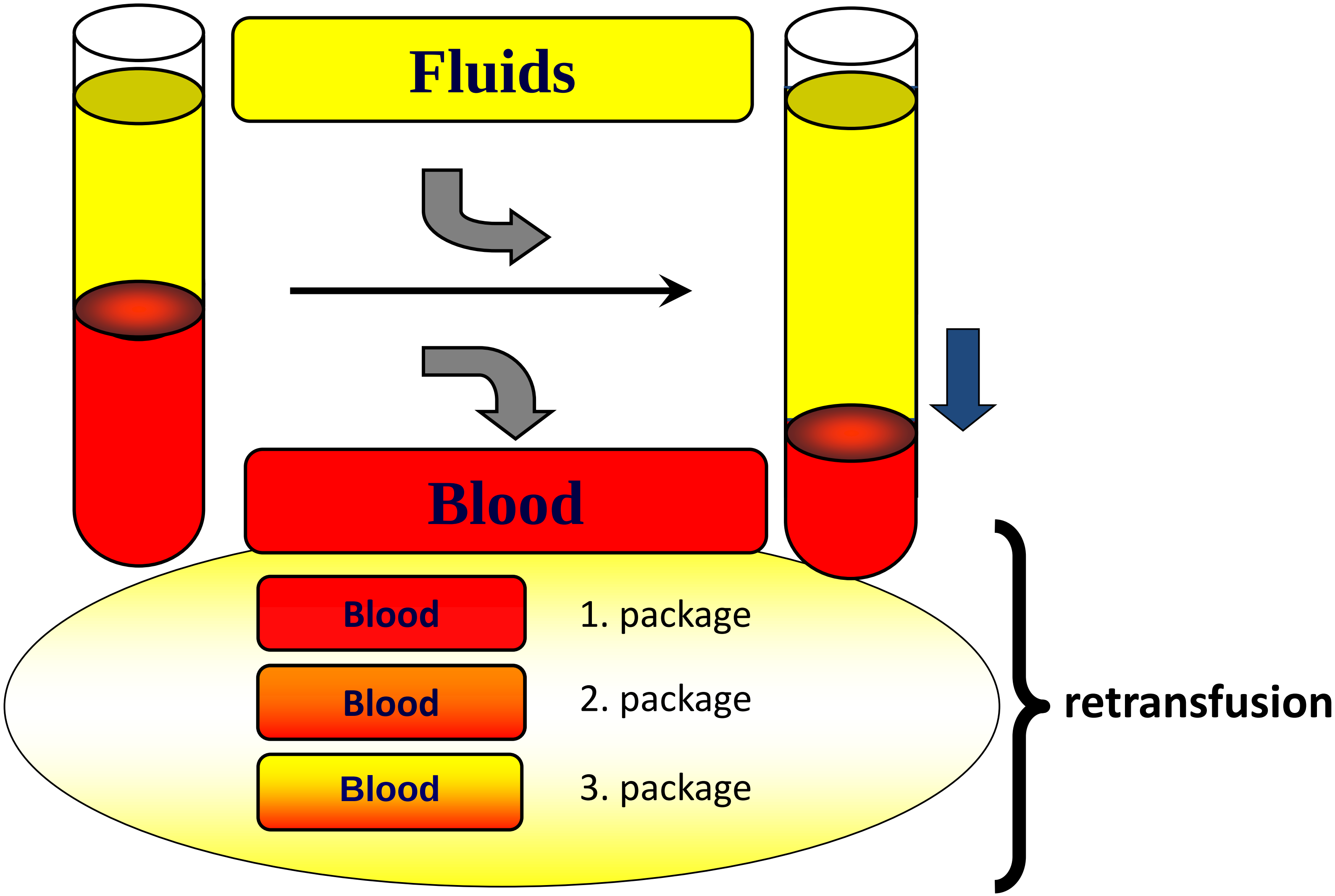
Acute Normovolemic Hemodilution



Acute Normovolemic Hemodilution

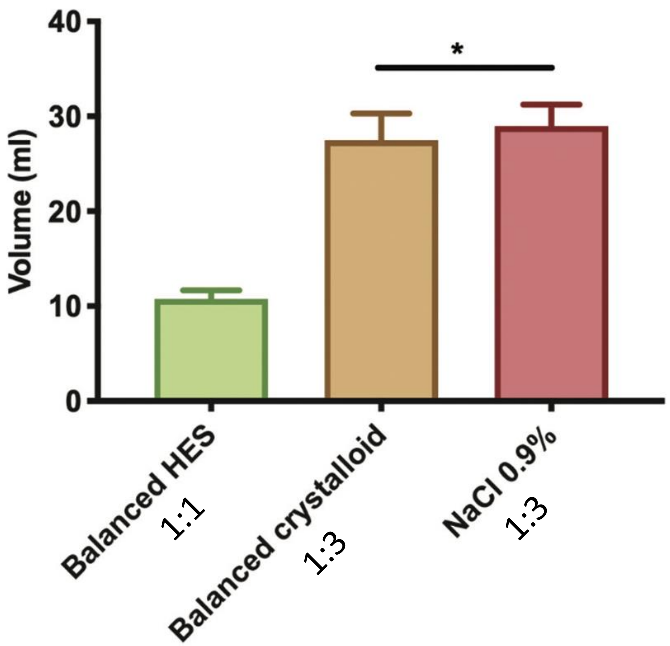


Acute Normovolemic Hemodilution

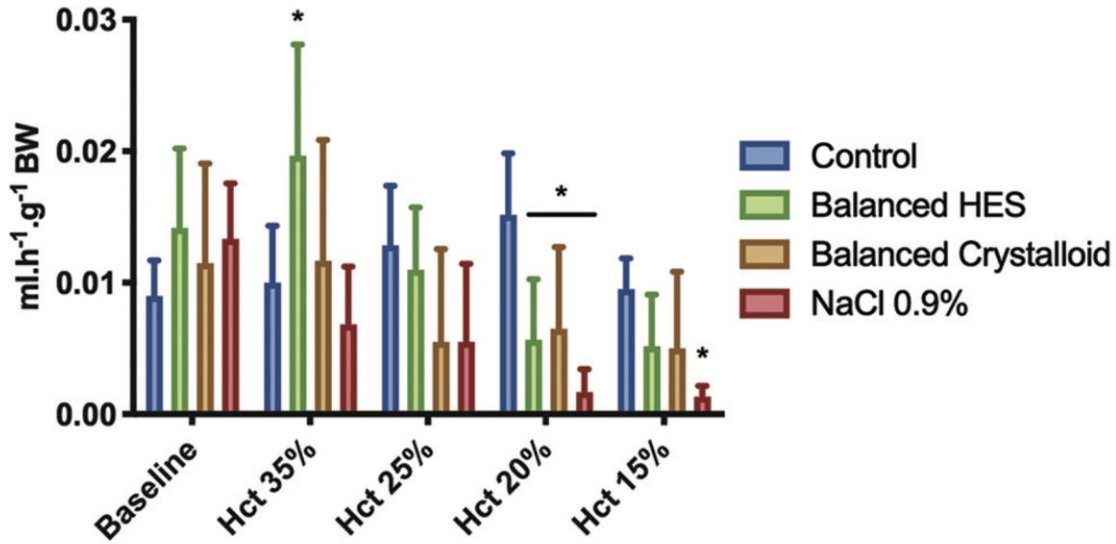


Which solution should be used?

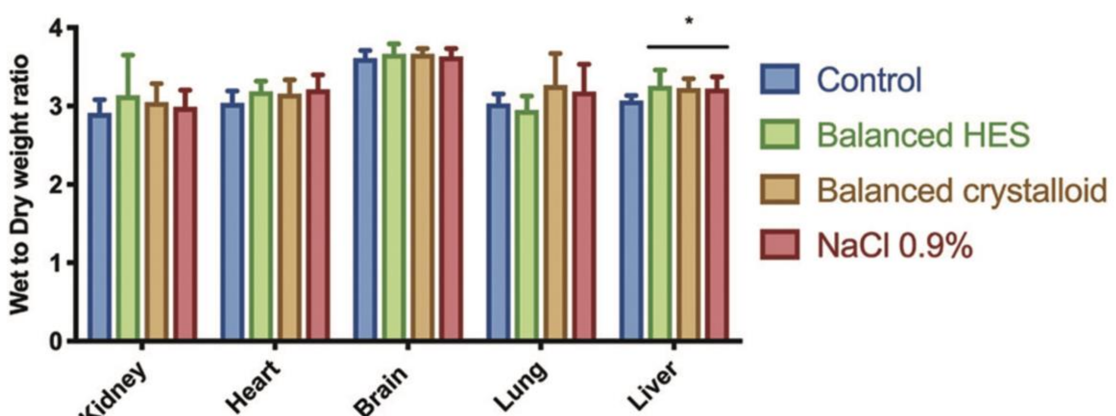
Exchange volume



Urine output

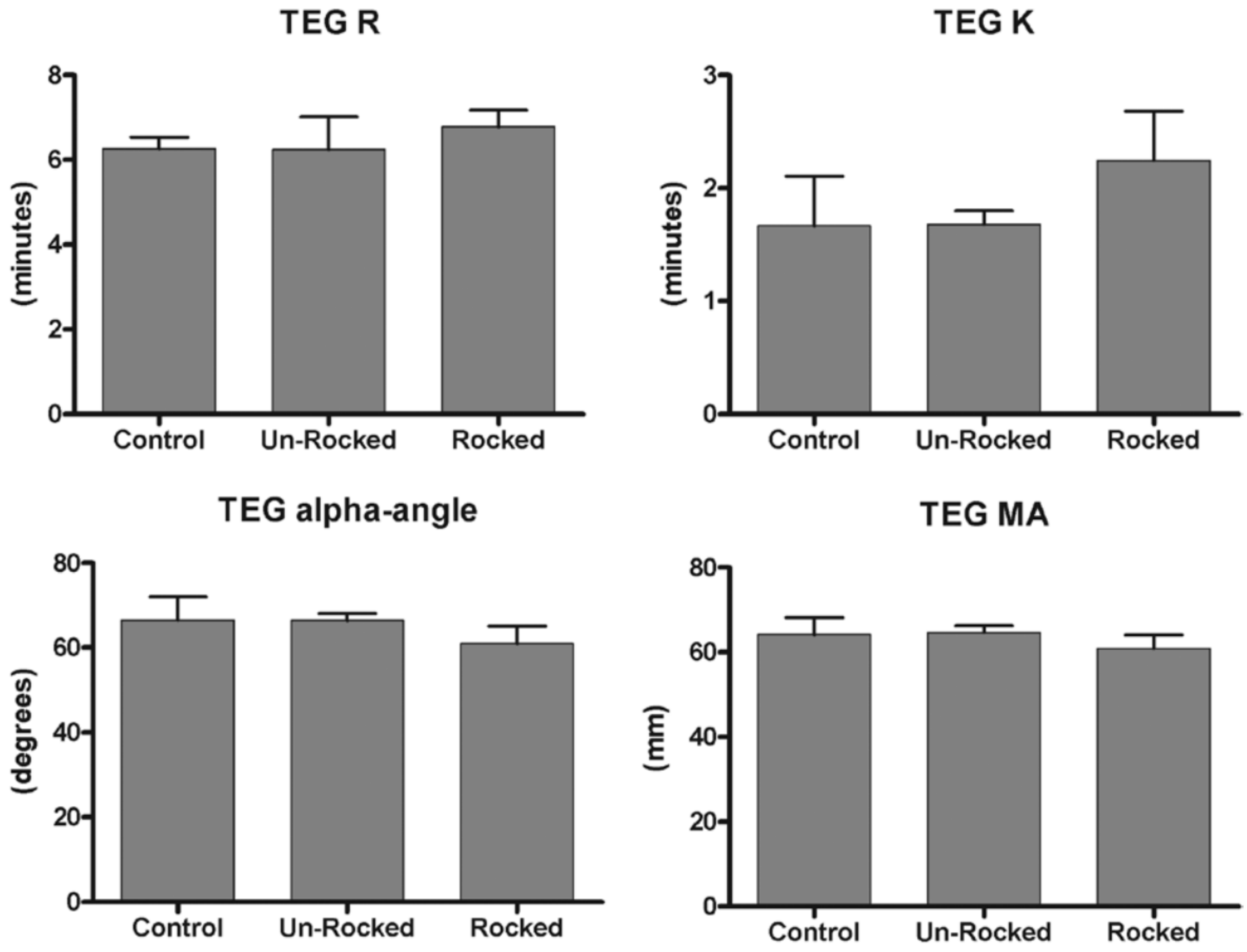


Tissue edema



Ergin, J Clin Transl Res, 2020

Shaking needed for 8 hour storage?



Goldberg, Ann Thorac Surg, 2015

And the benefit?

	no ANH
Hkt	45 %
Hb	15 g/dl
bleeding	1000 ml
loss of hemoglobin	150 g
pRBCs	

And the benefit?

JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

	no ANH	moderate ANH
Hkt	45 %	21 %
Hb	15 g/dl	7 g/dl
bleeding	1000 ml	1000 ml
loss of hemoglobin	150 g	70 g
pRBCs		

And the benefit?

	no ANH	moderate ANH	extreme ANH
Hkt	45 %	21 %	9 %
Hb	15 g/dl	7 g/dl	3 g/dl
bleeding	1000 ml	1000 ml	1000 ml
loss of hemoglobin	150 g	70 g	30 g
pRBCs			

The more exchangeable blood volume in cardiac surgery – the better

Table 3. Adjusted Postoperative Outcomes by Use and Volume of Acute Normovolemic Hemodilution (ANH)

Variables	No ANH	ANH	ANH Volume <400 mL	ANH Volume 400–799 mL	ANH Volume ≥800 mL	p Value[a]	p Value[b]
Observations	11,197	2,337	308	958	1,071		
Reoperation for bleeding (%)	2.3%	1.9%	2.5%	2.0%	1.0%	0.30	0.09
Stroke (%)	1.8%	1.3%	1.8%	1.4%	1.0%	0.22	0.14
Acute kidney injury (%)	28.2%	24.1%	28.3%	25.6%	20.9%	<0.001	<0.001
Renal failure (%)	2.9%	1.3%	2.8%	1.4%	1.1%	<0.001	<0.001
Intraaortic balloon pump (%)	8.2%	4.9%	7.5%	5.3%	3.3%	<0.001	<0.001
Red blood cells (%)							
None	59.7%	66.5%	66.1%	63.1%	70.7%	<0.001	<0.001
Intraoperative only	8.5%	7.7%	3.5%	9.4%	7.1%	0.78	0.81
Postoperative only	21.9%	16.1%	25.9%	18.7%	6.6%	<0.001	<0.001
Intraoperative + postoperative	10.4%	4.9%	5.9%	6.6%	2.7%	<0.001	<0.001
Plasma (%)	8.5%	4.9%	7.3%	5.8%	3.3%	<0.001	<0.001
Platelets (%)	8.5%	5.2%	7.8%	6.1%	3.4%	<0.001	<0.001
Prolonged length of stay (%)	15.9%	12.4%	18.2%	13.0%	10.5%	<0.001	<0.001
30-day mortality	2.8%	1.5%	2.0%	0.01%	2.0%	<0.001	0.01
Readmission (%)	12.1%	11.4%	9.5%	12.5%	10.5%	0.61	0.66

[a] For the comparison of ANH use. [b] For the comparison across ANH volume categories.

Goldberg, Ann Thorac Surg, 2015

Which Hb will be reached?

JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

Mathematical and computer modeling of acute normovolemic hemodilution

M.E. Brecher and M. Rosenfeld

Background: Advocates of acute normovolemic hemodilution (ANH) frequently neglect to consider the decreasing hematocrit of the patient during both hemodilution and the subsequent operative procedure and the need to begin transfusion at some minimal hematocrit.

Table 1. *Units of RBCs saved in typical examples of ANH* and the number of units of blood collected during ANH*

Number of ANH units collected	Minimum Hct 0.25† EBV (mL)					Minimum Hct 0.18† EBV (mL)				
	1000	1500	2000	2250	2500	1000	1500	2000	2250	2500
1	0.14	0.20	0.25	0.25	0.24	0.14	0.20	0.25	0.27	0.30
2	0.26	0.38	0.43	0.42	0.40	0.26	0.38	0.48	0.53	0.57
3	0.38	0.50	0.53	0.52	0.50	0.38	0.54	0.69	0.75	0.82
4	0.45	0.55	0.58	0.56	0.54	0.48	0.69	0.88	0.96	1.03
5	0.45	0.55	0.57	0.56	0.54	0.58	0.83	1.04	1.11	1.17

Number of units saved

* Estimated EBV, 5000 mL; pre-ANH Hct, 0.40, for various EBLs.

† Hct at which

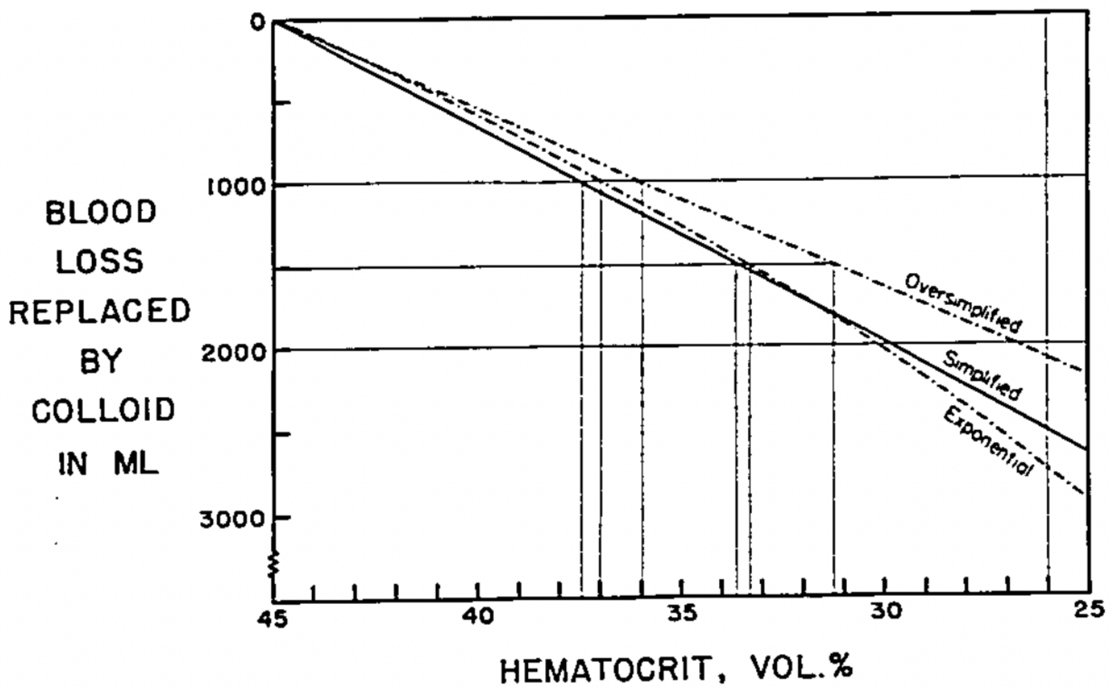
may apply to the use of ANH. If, as our modeling predicts, there is little advantage to the use of ANH, we must seriously question whether we are unnecessarily placing patients at risk by decreasing their Hct in the period immediately before operation and by allowing further lowering of Hct during the surgical procedure.

Brecher, Transfusion, 1994

Which Hb will be reached?

Anesthesiology
V 41, No 6, Dec 1974

CLINICAL REPORTS



$$EBV = BV \times \ln\left(\frac{hb_0}{hb_t}\right)$$

Blood loss = estimated volume × the natural logarithm of the ratio of initial to final hematocrit.

Bourke, Anesthesiology, 1974

Are these calculations correct?

JOHANNES KEPLER UNIVERSITÄT LINZ

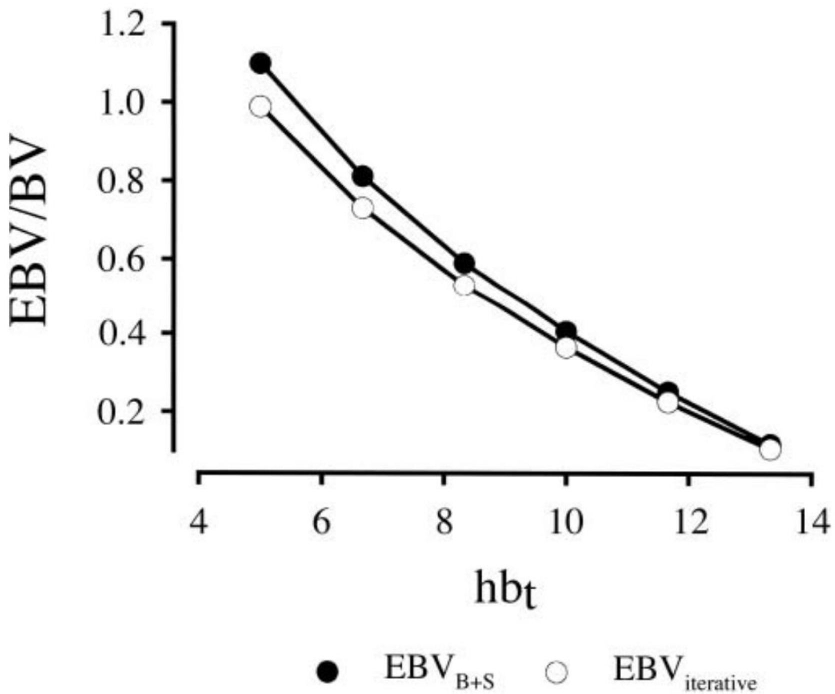
Kepler Universitäts Klinikum

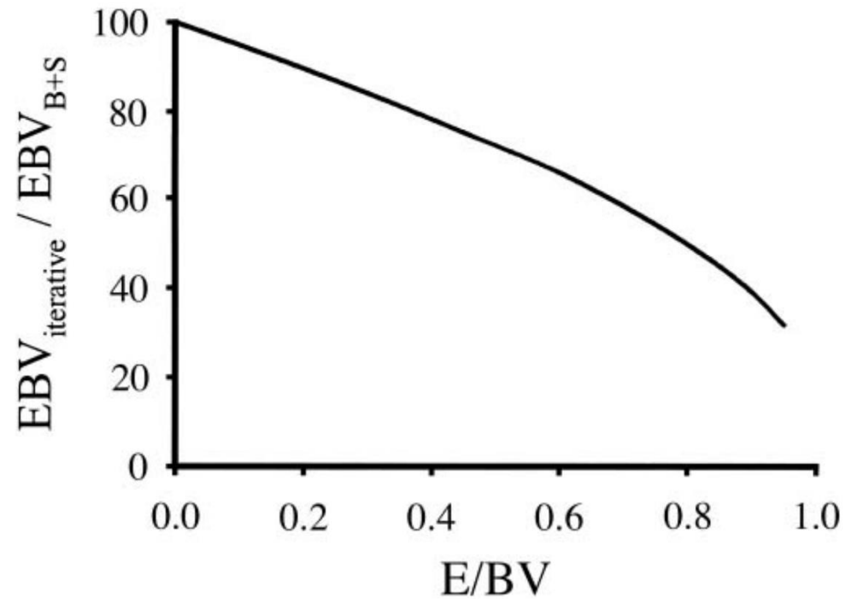
Acta Anaesthesiol Scand 2003; **47:** 37–45
Printed in Denmark.

ACTA ANAESTHESIOLOGICA SCANDINAVICA
0001-6349

New mathematical model for the correct prediction of the exchangeable blood volume during acute normovolemic hemodilution

J. Meier[1], M. Kleen[2], O. Habler[2], G. Kemming[1,2] and K. Messmer[1]
[1]Institute for Surgical Research, [2]Clinic of Anesthesiology, Klinikum Großhadern, Ludwig-Maximilians-University Munich, Germany



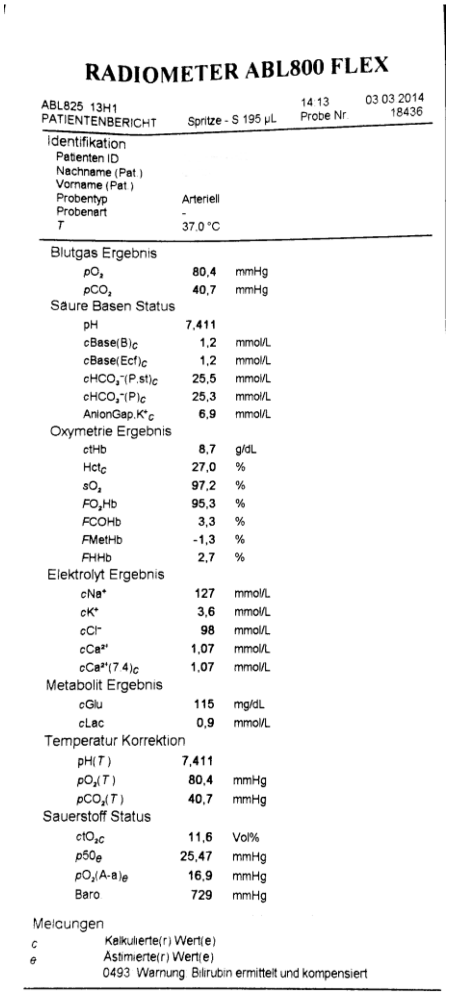


Meier, Acta Anaesth Scand, 2003

What makes ANH effective?

JOHANNES KEPLER UNIVERSITÄT LINZ
Kepler Universitäts Klinikum

1. High starting Hb
2. Low target Hb
3. Huge blood volume
4. Significant perioperative blood loss



RADIOMETER ABL800 FLEX

ABL825 13H1 PATIENTENBERICHT — Spritze - S 195 µL — 14 13 Probe Nr. — 03 03 2014 18436

Identifikation

Patienten ID		
Nachname (Pat.)		
Vorname (Pat.)		
Probentyp	Arteriell	
Probenart	-	
T	37,0 °C	
Blutgas Ergebnis		
pO_2	80,4	mmHg
pCO_2	40,7	mmHg
Säure Basen Status		
pH	7,411	
$cBase(B)_c$	1,2	mmol/L
$cBase(Ecf)_c$	1,2	mmol/L
$cHCO_3^-(P.st)_c$	25,5	mmol/L
$cHCO_3^-(P)_c$	25,3	mmol/L
$AnionGap.K^+_c$	6,9	mmol/L
Oxymetrie Ergebnis		
ctHb	8,7	g/dL
Hct_c	27,0	%
sO_2	97,2	%
FO_2Hb	95,3	%
FCOHb	3,3	%
FMetHb	-1,3	%
FHHb	2,7	%
Elektrolyt Ergebnis		
cNa^+	127	mmol/L
cK^+	3,6	mmol/L
cCl^-	98	mmol/L
cCa^{2+}	1,07	mmol/L
$cCa^{2+}(7.4)_c$	1,07	mmol/L
Metabolit Ergebnis		
cGlu	115	mg/dL
cLac	0,9	mmol/L
Temperatur Korrektion		
pH(T)	7,411	
$pO_2(T)$	80,4	mmHg
$pCO_2(T)$	40,7	mmHg
Sauerstoff Status		
ctO_{2c}	11,6	Vol%
$p50_e$	25,47	mmHg
$pO_2(A-a)_e$	16,9	mmHg
Baro	729	mmHg

Meldungen

c Kalkulierte(r) Wert(e)
e Astimierte(r) Wert(e)
0493 Warnung Bilirubin ermittelt und kompensiert

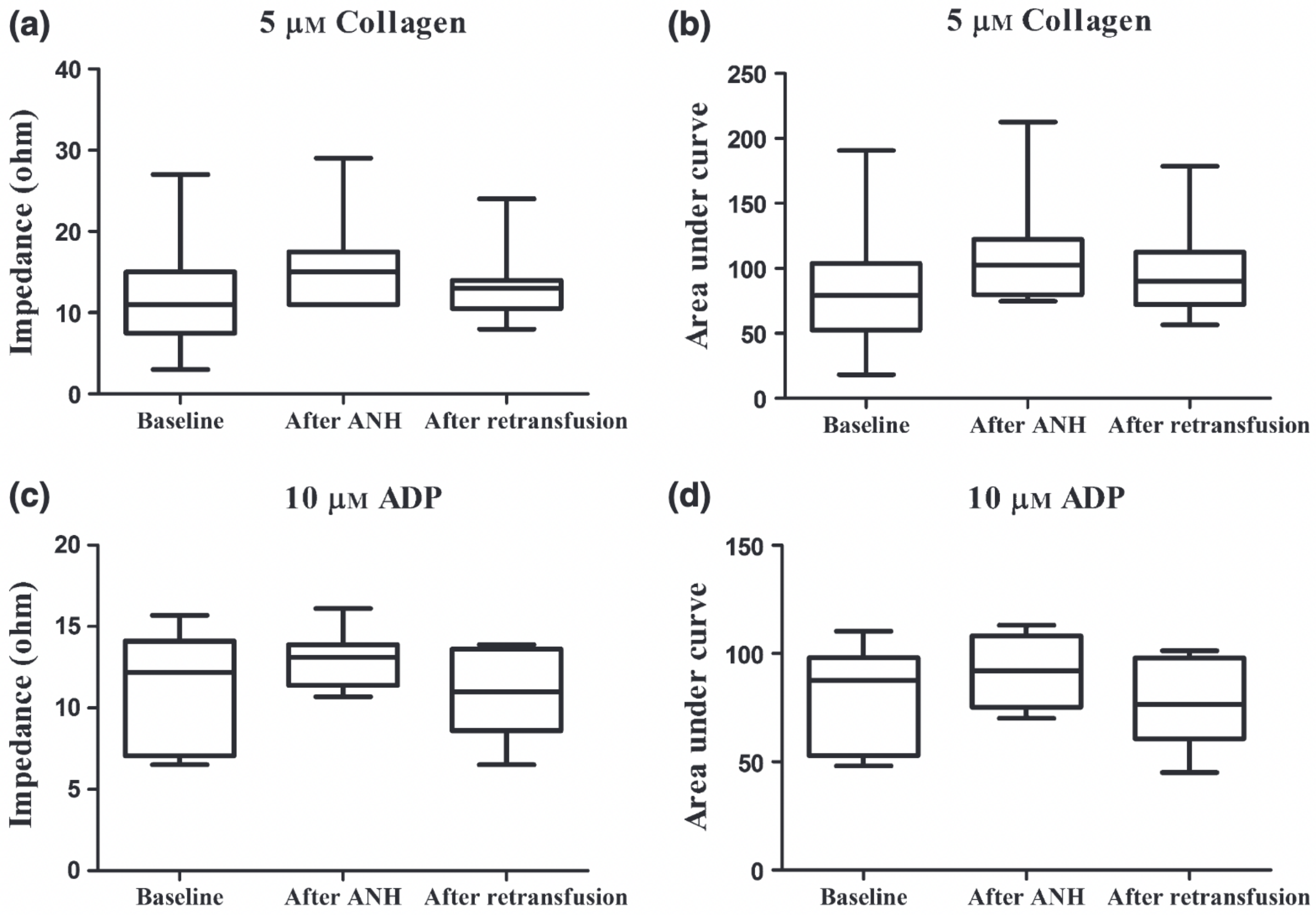
Effect of ANH on patients' coagulation

Johannes Kepler Universität Linz
Kepler Universitäts Klinikum

	Reference values	Baseline	After ANH
INTEM			
CT; s	100–240	169.0 (148.5–198.5 [114–212])	118.0 (103.5–122.5 [87.0–146.0])*
CFT; s	30–110	78.0 (64.5–86.5 [57.0–99.0])	92.0 (82.0–119.0 [73.0–159.0])*
α; °	70–83	74.0 (72.0–77.0 [65.0–79.0])	71.0 (64.0–73.5 [49.0–75.0])*
MCF; mm	50–72	60.0 (56.5–62.5 [33.0–63.0])	58.0 (51.0–59.0 [41.0–61.0])
EXTEM			
CT; s	38–79	40.0 (31.5–44.0 [22.0–48.0])	49.0 (44.5–58.5 [38.0–61.0])
CFT; s	34–159	80.0 (71.5–110.5 [69.0–397.0])	107.0 (96.5–137.0 [83.0–441.0])*
α; °	63–83	74.0 (70.0–76.0 [68.0–80.0])	69.0 (63.0–70.5 [37.0–73.0])*
MCF; mm	50–72	63.0 (56.0–66.0 [35.0–87.0])	57.0 (50.5–59.5 [38.0–62.0])*
FIBTEM			
MCF; mm	9–25	15.0 (10.0–18.0 [8.0–19.0])	9.0 (6.5–11.0 [5.0–11.0])*

Shin, Anaesthesia, 2015

Effect of ANH on patients‘ platelet function



Shin, Anaesthesia, 2015

Coagulation in the ANH blood

JKU JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

EXTEM	Reference range [11]	0	4 h	8 h	12 h	24 h
CT, s	42–74	67 ± 6	55 ± 5	61 ± 7	60 ± 3	64 ± 6
CFT, s	46–148	111 ± 5	121 ± 11	133 ± 9	120 ± 9	141 ± 7**
MCF, mm	49–71	62 ± 1	61 ± 1	58 ± 1***	56 ± 2*	55 ± 1***
MCE, (G dynes/cm^2)/50	105–235	167 ± 6	155 ± 4	139 ± 6***	131 ± 10*	121 ± 5***

Mean ± SEM

CT clotting time *CFT* clot formation time, *MCF* maximum clot firmness, *MCE* maximal clot elasticity;

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ vs. 0

FIBTEM	Reference range [11]	0	4 h	8 h	12 h	24 h
CT, s	43–69	59 ± 3	56 ± 5	61 ± 4	47 ± 4	52 ± 3
MCF, mm	9–25	15 ± 2	15 ± 2	13 ± 1	14 ± 1	14 ± 1
MCE, (G dynes/cm^2)/50	13–27	18 ± 2	19 ± 4	15 ± 2	17 ± 2	16 ± 1

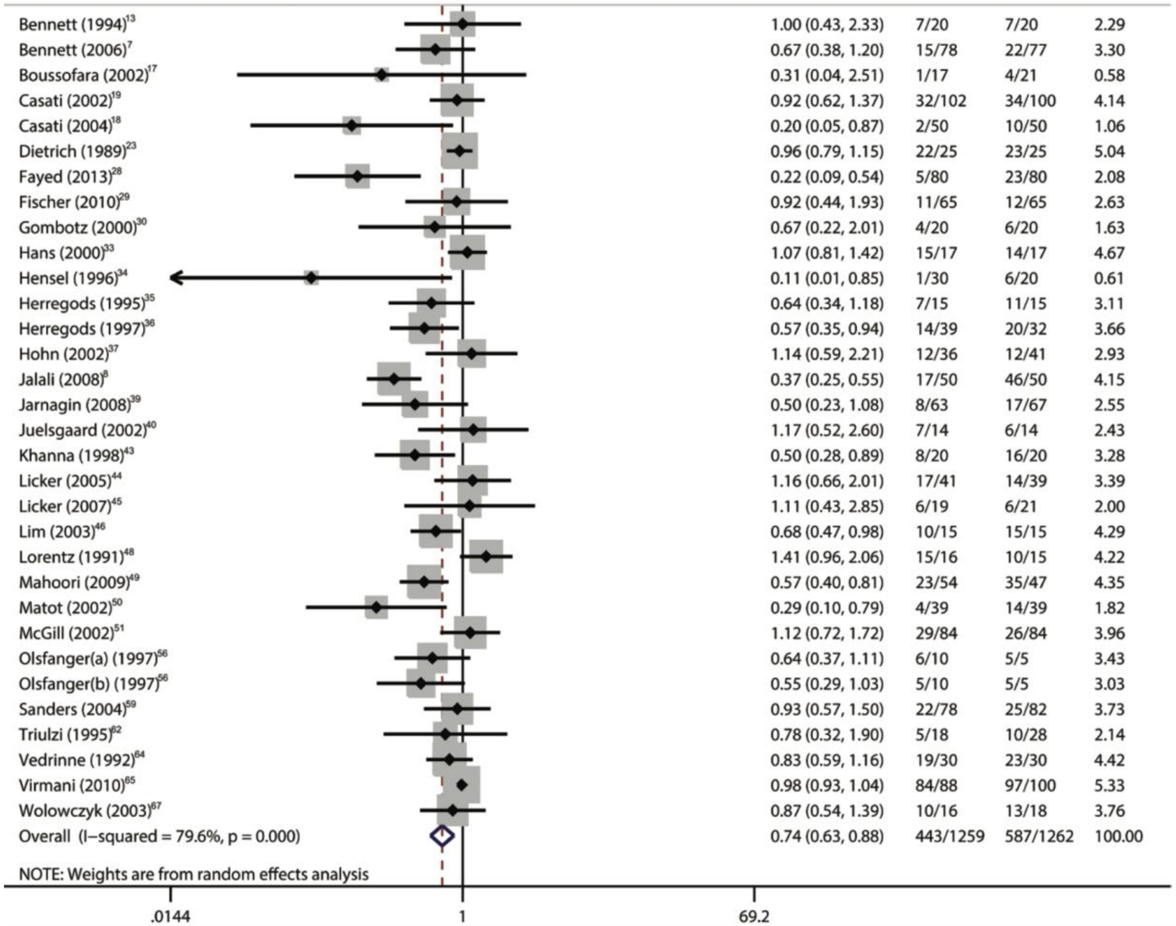
Mean ± SEM

CT clotting time, *CFT* clot formation time, *MCF* maximum clot firmness, *MCE* maximal clot elasticity

Kinoshita, J Anesth, 2021

Efficacy in non-cardiac + cardiac surgery

- RBC transfusion -

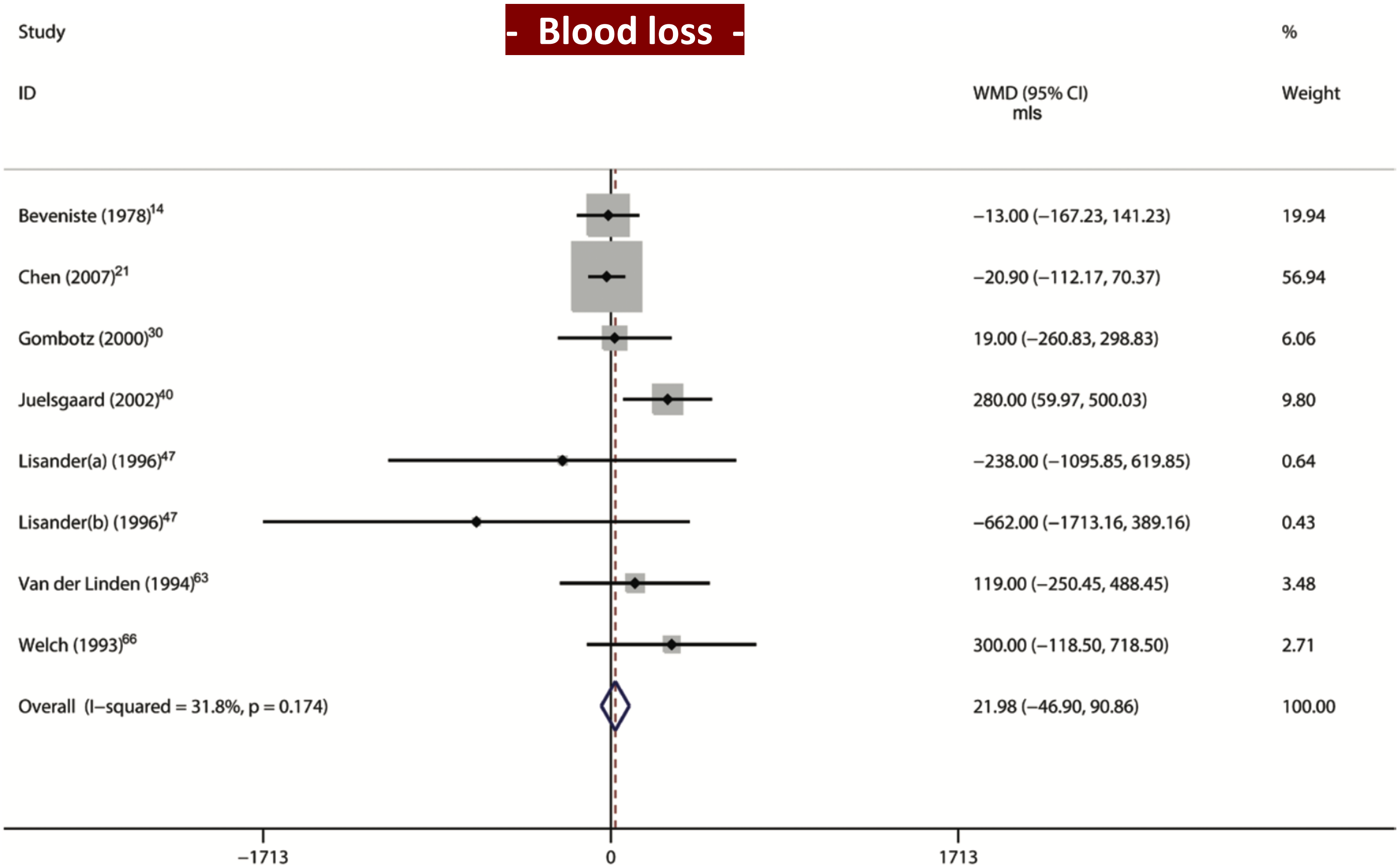


Study ID	RR (95% CI)	Events, PANH	Events, PANH	% Weight
Bennett (1994)[13]	1.00 (0.43, 2.33)	7/20	7/20	2.29
Bennett (2006)[7]	0.67 (0.38, 1.20)	15/78	22/77	3.30
Boussofara (2002)[17]	0.31 (0.04, 2.51)	1/17	4/21	0.58
Casati (2002)[19]	0.92 (0.62, 1.37)	32/102	34/100	4.14
Casati (2004)[18]	0.20 (0.05, 0.87)	2/50	10/50	1.06
Dietrich (1989)[23]	0.96 (0.79, 1.15)	22/25	23/25	5.04
Fayed (2013)[28]	0.22 (0.09, 0.54)	5/80	23/80	2.08
Fischer (2010)[29]	0.92 (0.44, 1.93)	11/65	12/65	2.63
Gombotz (2000)[30]	0.67 (0.22, 2.01)	4/20	6/20	1.63
Hans (2000)[33]	1.07 (0.81, 1.42)	15/17	14/17	4.67
Hensel (1996)[34]	0.11 (0.01, 0.85)	1/30	6/20	0.61
Herregods (1995)[35]	0.64 (0.34, 1.18)	7/15	11/15	3.11
Herregods (1997)[36]	0.57 (0.35, 0.94)	14/39	20/32	3.66
Hohn (2002)[37]	1.14 (0.59, 2.21)	12/36	12/41	2.93
Jalali (2008)[8]	0.37 (0.25, 0.55)	17/50	46/50	4.15
Jarnagin (2008)[39]	0.50 (0.23, 1.08)	8/63	17/67	2.55
Juelsgaard (2002)[40]	1.17 (0.52, 2.60)	7/14	6/14	2.43
Khanna (1998)[43]	0.50 (0.28, 0.89)	8/20	16/20	3.28
Licker (2005)[44]	1.16 (0.66, 2.01)	17/41	14/39	3.39
Licker (2007)[45]	1.11 (0.43, 2.85)	6/19	6/21	2.00
Lim (2003)[46]	0.68 (0.47, 0.98)	10/15	15/15	4.29
Lorentz (1991)[48]	1.41 (0.96, 2.06)	15/16	10/15	4.22
Mahoori (2009)[49]	0.57 (0.40, 0.81)	23/54	35/47	4.35
Matot (2002)[50]	0.29 (0.10, 0.79)	4/39	14/39	1.82
McGill (2002)[51]	1.12 (0.72, 1.72)	29/84	26/84	3.96
Olsfanger(a) (1997)[56]	0.64 (0.37, 1.11)	6/10	5/5	3.43
Olsfanger(b) (1997)[56]	0.55 (0.29, 1.03)	5/10	5/5	3.03
Sanders (2004)[59]	0.93 (0.57, 1.50)	22/78	25/82	3.73
Triulzi (1995)[62]	0.78 (0.32, 1.90)	5/18	10/28	2.14
Vedrinne (1992)[64]	0.83 (0.59, 1.16)	19/30	23/30	4.42
Virmani (2010)[65]	0.98 (0.93, 1.04)	84/88	97/100	5.33
Wolowczyk (2003)[67]	0.87 (0.54, 1.39)	10/16	13/18	3.76
Overall (I–squared = 79.6%, p = 0.000)	0.74 (0.63, 0.88)	443/1259	587/1262	100.00

NOTE: Weights are from random effects analysis

Zhou, Anesth Analg, 2015

Efficacy in non-cardiac + cardiac surgery



Zhou, Anesth Analg, 2015

Complications in non-cardiac + cardiac surgery

Table 2. Adverse Events and Other Outcomes

Events	Number of studies	PANH *n*+	PANH Total	Control *n*+	Control Total	M-H pooled RR/I-V pooled WMD: RR/WMD (95% CI)	*z*	*P*	Heterogeneity χ^2	Heterogeneity I^2 (%)	Heterogeneity *P*
Mortality	22[7,18,19,29,35–41,44,45,49,50,55,58,63–65]	9	968	11	960	0.82 (0.37, 1.84)	0.48	0.634	3.04	0.0	0.80
Reoperation for bleeding	18[7,9,18,20,28,35,36,39,41,44,45,49,50,63,64,68]	15	798	16	764	0.93 (0.49, 1.79)	0.21	0.836	4.93	0.0	0.90
Any infection	10[7,14,17,20,34,38,39,49,50,64]	31	527	49	543	0.64 (0.42, 0.97)	2.08	0.037	7.66	21.6	0.26
Deep vein thrombosis	7[7,20,29,46,58,62,63]	9	286	5	289	1.82 (0.63, 5.32)	1.10	0.271	0.51	0.0	0.92
Pulmonary embolus	9[7,19,20,29,46,47,62,63]	4	333	2	331	1.56 (0.42, 5.75)	0.67	0.504	1.29	0.0	0.73
Stroke	11[19,20,29,40,44–47,50,63]	7	405	4	402	1.59 (0.53, 4.76)	0.83	0.408	0.78	0.0	0.94
Myocardial ischemia/ infarction	18[18–20,29,36,37,39–41,44,45,47,50,63,64,67]	9	646	10	634	0.90 (0.39, 2.04)	0.26	0.794	1.66	0.0	0.95
Renal dysfunction	9[18,19,40,44,45,47,50,65]	15	353	24	351	0.61 (0.34, 1.11)	1.62	0.105	3.57	0.0	0.61
Length of hospital stay	7[17,30,37,41,61,62]	129		134		−0.15 (−0.89, 0.58)	0.41	0.679	2.65	0.0	0.85

n+ = The number of patient with adverse event; Total = the number of the total patients; RR = relative risk; WMD = weighted mean difference; M-H = Mantel-Haenszel; I-V = inverse-variance.

Zhou, Anesth Analg, 2015

Efficacy in cardiac surgery

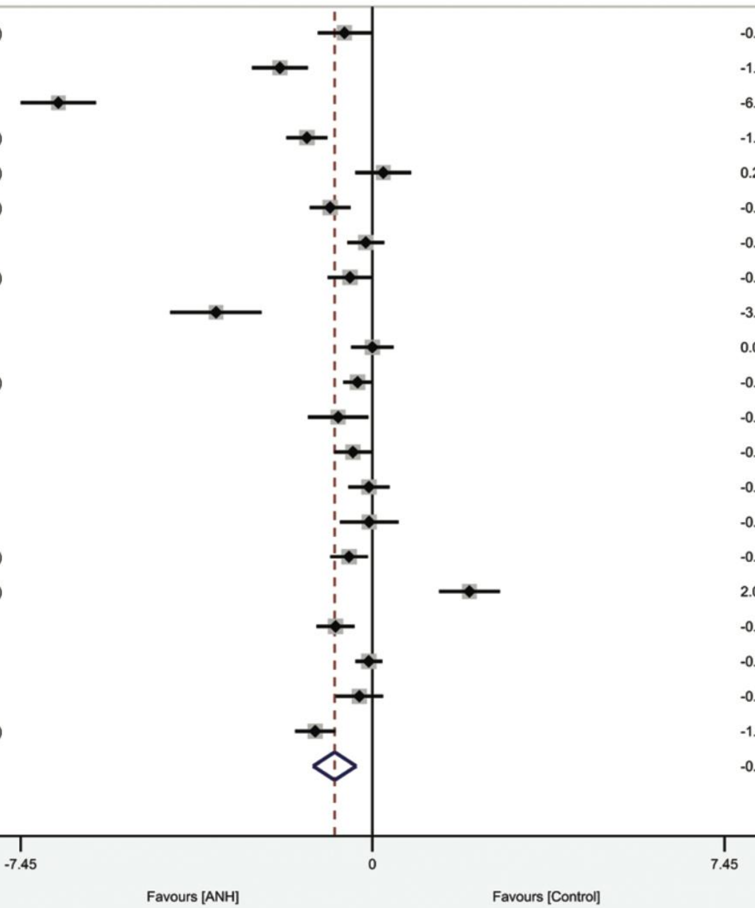
JKU JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

- RBC transfusion -

STUDY	YEAR	SAMPLE SIZE	ANH, mean (SD)	CONTROL, mean (SD)	SMD (95% CI)	% Weight
Hallowell P [27]	1972	50	2.64 (2.55)	3.96 (1.86)	-0.59 (-1.16, -0.02)	4.72
Kaplan JA [28]	1977	80	7.82 (0.87)	9.49 (0.8)	-1.96 (-2.55, -1.36)	4.69
Hurpe JM [29]	1987	160	3.7 (0.2)	5.4 (0.3)	-6.65 (-7.45, -5.86)	4.40
Dietrich W [30]	1989	100	2.07 (1.99)	5.77 (3.21)	-1.39 (-1.82, -0.95)	4.86
Triulzi DJ [34]	1995	46	0.94 (1.76)	0.64 (0.91)	0.23 (-0.36, 0.82)	4.68
Helm RE [35]	1996	90	0.28 (0.66)	1.14 (1.19)	-0.89 (-1.33, -0.46)	4.87
Kochamba GS [36]	1996	100	0.96 (1.87)	1.2 (1.54)	-0.14 (-0.53, 0.25)	4.90
Herregods L [38]	1997	71	0.56 (0.97)	1.09 (1.28)	-0.47 (-0.95, 0.00)	4.82
Kahraman S [39]	1997	42	2.2 (0.3)	3.1 (0.2)	-3.31 (-4.28, -2.35)	4.13
Ho¨hn L [43]	2002	77	2 (2.96)	2 (1.48)	0.00 (-0.45, 0.45)	4.85
McGill N [44]	2002	168	0.63 (1.22)	1.07 (1.56)	-0.31 (-0.62, -0.01)	4.98
Durmus M [45]	2003	40	1.7 (1.78)	2.8 (1.2)	-0.72 (-1.37, -0.08)	4.62
Casati V [46]	2004	100	0.1 (0.51)	0.48 (1.2)	-0.41 (-0.81, -0.02)	4.90
Licker M [47]	2005	80	0.9 (1.3)	1 (1.4)	-0.07 (-0.51, 0.36)	4.86
Licker M [48]	2007	40	1.1 (1.4)	1.2 (1.5)	-0.07 (-0.69, 0.55)	4.65
Jalali A [49]	2008	100	1.04 (0.39)	1.27 (0.53)	-0.49 (-0.89, -0.10)	4.90
Ela Y [50]	2009	57	1.64 (0.52)	0.53 (0.56)	2.05 (1.41, 2.70)	4.62
Mahoori A [51]	2009	101	1.39 (1)	2.55 (1.9)	-0.78 (-1.19, -0.37)	4.89
Virmani S [53]	2010	188	1.4 (1.2)	1.5 (1.4)	-0.08 (-0.36, 0.21)	4.99
Momeni M [54]	2012	62	0.3 (0.8)	0.6 (1.3)	-0.28 (-0.78, 0.23)	4.79
Soltanzadeh M [55]	2012	100	0.4 (0.67)	1.48 (1.07)	-1.21 (-1.64, -0.78)	4.87
Overall (I-squared = 95.1%, p = 0.000)					-0.80 (-1.25, -0.34)	100.00

NOTE: Weights are from random effects analysis



Barile, Anesth Analg, 2017

Efficacy in cardiac surgery

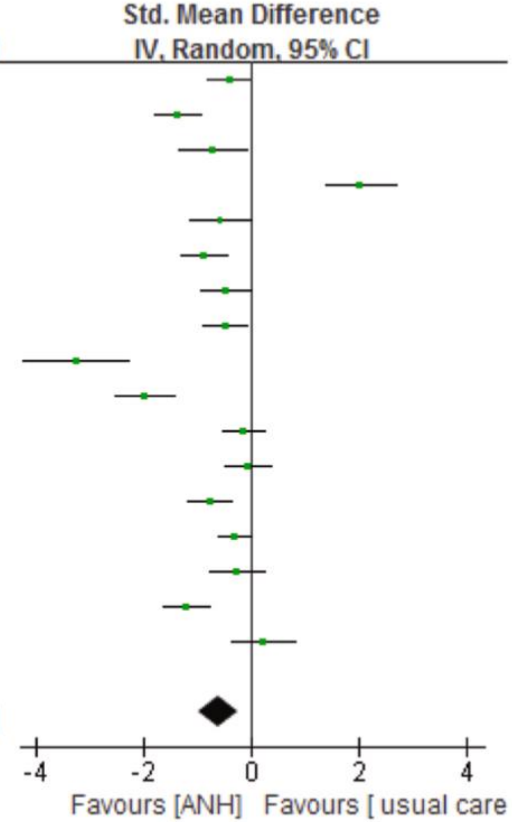
Kepler Universitäts Klinikum

- RBC transfusion -

Study or Subgroup	ANH Mean	ANH SD	ANH Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Random, 95% CI
Casati V et al.2004	0.1	0.51	50	0.48	1.2	50	6.2%	-0.41 [-0.81, -0.01]
Dietrich W et al.1989	2.07	1.99	50	5.77	3.21	50	6.1%	-1.37 [-1.81, -0.94]
Durmus M et al.2003	1.7	1.78	20	2.8	1.2	20	5.5%	-0.71 [-1.35, -0.07]
Ela Y et al.2009	1.64	0.52	28	0.53	0.56	29	5.5%	2.02 [1.38, 2.67]
Hallowell P et al.1972	2.64	2.55	25	3.96	1.86	25	5.7%	-0.58 [-1.15, -0.02]
Helm RE et al.1996	0.28	0.66	45	1.14	1.19	45	6.1%	-0.89 [-1.32, -0.45]
Herregods L et al.1997	0.56	0.97	39	1.09	1.28	32	6.0%	-0.47 [-0.94, 0.01]
Jalali A et al.2008	1.04	0.39	50	1.27	0.53	50	6.2%	-0.49 [-0.89, -0.09]
Kahraman S et al.1997	2.2	0.3	28	3.1	0.2	14	4.5%	-3.25 [-4.22, -2.28]
Kaplan JA et al.1977	7.82	0.87	40	9.49	0.8	40	5.8%	-1.98 [-2.52, -1.44]
Kochamba GS et al.1996	0.96	1.87	50	1.2	1.54	50	6.2%	-0.14 [-0.53, 0.25]
Licker M et al.2005	0.9	1.3	43	1	1.4	41	6.1%	-0.07 [-0.50, 0.35]
Mahoori A et al.2009	1.39	1	54	2.55	1.9	47	6.2%	-0.77 [-1.18, -0.37]
McGill N et al.2002	0.63	1.22	84	1.07	1.56	84	6.4%	-0.31 [-0.62, -0.01]
Momeni M et al.2012	0.3	0.8	31	0.6	1.3	31	5.9%	-0.27 [-0.77, 0.23]
Soltanzadeh M et al.2012	0.4	0.67	50	1.48	1.07	50	6.1%	-1.20 [-1.63, -0.77]
Triulzi DJ et al.1995	0.94	1.76	18	0.64	0.91	28	5.7%	0.23 [-0.37, 0.82]
Total (95% CI)			**705**			**686**	**100.0%**	**-0.60 [-0.96, -0.24]**

Heterogeneity: Tau² = 0.51; Chi² = 163.53, df = 16 (P < 0.00001); I² = 90%

Test for overall effect: Z = 3.26 (P = 0.001)



Li, Int J Surg, 2020

Efficacy in cardiac surgery

JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

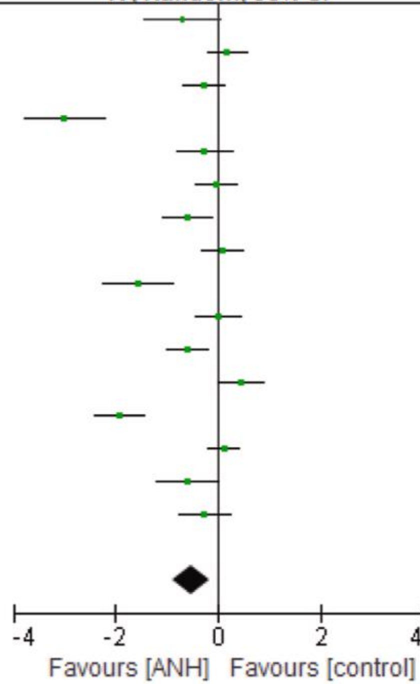
- Estimated blood loss -

Study or Subgroup	ANH Mean	ANH SD	ANH Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Boldt J et al.1991	840	350	15	1,080	320	15	5.5%	-0.70 [-1.44, 0.04]
Casati V et al.2004	375	168	50	350	106	50	6.6%	0.18 [-0.22, 0.57]
Dietrich W et al.1989	1,858	241	50	1,929	249	50	6.6%	-0.29 [-0.68, 0.11]
Ela Y et al.2009	259	38	28	388	46	29	5.4%	-3.01 [-3.78, -2.24]
Hallowell P et al.1972	961	489	25	1,110	602	25	6.1%	-0.27 [-0.82, 0.29]
Helm RE et al.1996	855	321	45	868	321	45	6.5%	-0.04 [-0.45, 0.37]
Herregods L et al.1997	965	470	39	1,295	600	32	6.3%	-0.61 [-1.09, -0.13]
Jalali A et al.2008	561	300	50	536	339	50	6.6%	0.08 [-0.31, 0.47]
Kahraman S et al.1997	592	70	21	712	79	21	5.6%	-1.58 [-2.28, -0.88]
Kaplan JA et al.1977	825	84	40	825	84	40	6.5%	0.00 [-0.44, 0.44]
Kochamba GS et al.1996	696	311	50	916	410	50	6.6%	-0.60 [-1.00, -0.20]
Licker M et al.2005	623	108	41	567	137	39	6.4%	0.45 [0.01, 0.90]
Mahoori A et al.2009	871	48	54	975	59	47	6.3%	-1.93 [-2.41, -1.46]
McGill N et al.2002	852	526	84	796	443	84	6.8%	0.11 [-0.19, 0.42]
Triulzi DJ et al.1995	475	192	18	735	519	28	5.9%	-0.60 [-1.21, 0.00]
Zisman E et al.2009	732	205	27	820	413	35	6.3%	-0.26 [-0.76, 0.25]
Total (95% CI)			**637**			**640**	**100.0%**	**-0.53 [-0.88, -0.17]**

Heterogeneity: $Tau^2 = 0.46$; $Chi^2 = 141.60$, df = 15 ($P < 0.00001$); $I^2 = 89\%$

Test for overall effect: Z = 2.88 (P = 0.004)

Std. Mean Difference IV, Random, 95% CI



Li, Int J Surg, 2020

ANH – when should it be used in cardiac surgery?

JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

ANH acceptable with these conditions

Pre-autologous donation
Left main stenosis in a stable compensated cardiac surgery patient
Previous cardiac surgery
Anticipated prolonged cardiopulmonary bypass (e.g., >2.5 hours)

SOCIETY FOR THE ADVANCEMENT OF BLOOD MANAGEMENT®

No ANH

Hemodynamically significant arrhythmia
Presence of acute infection (i.e., bacteremia or sepsis)

SABM standards and best practice for acute normovolemic hemodilution

Use clinical judgment

Unstable angina
Symptomatic LV dysfunction
Presence of symptomatic CV disease
Severe AS
Combination of CAD and severe AS
Emergency surgery
Severe COPD
Hypoxemia (e.g., O_2sat <90% on room air)
Severe pulmonary HTN
History of CVA
Presence of carotid stenosis (>70% stenosis)
Presence of renal insufficiency (GFR <60)
Presence of hemoglobinopathy
Presence of significant coagulopathy (history of spontaneous or challenged bleeding and/or high risk of bleeding

Shander, J Cardioth and Vasc Surg, 2020

Conclusion

- ANH results in an anemic patient that looses less HB during bleeding
- Harvested blood can be given back at the end of surgery
- ANH is effective if Hb_0 is high, Hb_{target} is low, BV is high and bleeding is substantial
- Today ANH is often used in cardiac surgery
- ANH is effective in cardiac surgery
- ANH is safe in cardiac surgery
- In case of diminished anemia tolerance ANH is not advised.

ANH – ancient or modern?

JOHANNES KEPLER UNIVERSITÄT LINZ

Kepler Universitäts Klinikum

Europ. Surg. Res. 4: 55–70 (1972)

Acute Normovolemic Hemodilution

Changes of Central Hemodynamics and Microcirculatory Flow in Skeletal Muscle[1]

K. Messmer, D. H. Lewis, L. Sunder-Plassmann, W. P. Klövekorn, N. Mendler and K. Holper

Institute for Surgical Research, Surgical University Clinic, Munich, and Department of Surgery I, University of Gothenburg, Gothenburg

Key Words
Oxygen transport capacity
Oncotic properties of dextran-60
In vivo viscosity
Capillary transport
^{51}Cr-EDTA clearance
Limited hemodilution

Abstract. Isovolemic hemodilution down to hematocrit values of 10% has been performed in splenectomized dogs during pentobarbital anaesthesia. Circulatory changes were followed in the systemic circulation; for the estimation of capillary flow and capillary transport in skeletal muscle a double isotope technic has been applied. Progressive hemodilution resulted in a significant increase of cardiac output and skeletal muscle flow; peripheral resistance decreased clearly parallel with the whole blood viscosity as measured at different shear rates. The transport capacity (PS) in skeletal muscle was not significantly changed. From this finding and from the lack of changes in the local effluent blood it is concluded that hypoxia does not occur when limited hemodilution is performed normovolemically. These data, therefore, add further support to the concept of limited hemodilution as a therapeutic tool in microcirculatory disorders.

The interest in the relationship of hematocrit and blood viscosity *in vivo* has been greatly stimulated by viscometric findings of recent years. By different groups it has been demonstrated that acute changes in hematocrit are followed by an increase in cardiac output [19, 21, 24]

[1] Paper presented at the 6th Congres of the European Society for Experimental Surgery, Hälsingborg, April 1971.

Received: September 10, 1971; accepted: September 28, 1971.

International Journal of Surgery 83 (2020) 131–139

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu

ELSEVIER

Review

Effect of acute normovolemic hemodilution on coronary artery bypass grafting: A systematic review and meta-analysis of 22 randomized trials

Shengping Li[a], Yulin Liu[b,*], Ying Zhu[b]

[a] Department of Anesthesiology, Jingzhou Central Hospital, Jingzhou, 434020, China
[b] Department of Anesthesia, Chongqing Emergency Medical Center (Chongqing University Central Hospital), Chongqing, 400014, China

ARTICLE INFO

Keywords:
Acute normovolemic hemodilution
Coronary artery bypass grafting
Blood loss
Transfusion

ABSTRACT

Background: Efficacy of minimal acute normovolemic hemodilution (ANH) in avoiding homologous blood transfusion during cardiovascular surgery remains controversial. Postoperative bleeding and transfusion remain a source of morbidity and cost after open heart operations. To better understand the role of acute normovolemic hemodilution (ANH) in coronary artery bypass grafting (CABG), we compared ANH with standard intraoperative care in a systematic review including a standard pairwise meta-analysis of randomized controlled trials (RCTs).
Methods: We searched the Cochrane Library, PubMed, EMBASE, Web of Science and Chinese National Knowledge Infrastructure (CNKI) up to April 1, 2020. The primary outcome was to assess the incidence of ANH-related number of allogeneic red blood cell units (ARBCu) transfused. Secondary outcomes included the rate of allogeneic blood transfusion and estimated total blood loss.
Results: A total of 22 RCTs including 1688 patients were identified for the present meta-analysis. Of these studies, 19 were about CABG with on-pump and three with off-pump. Our pooled result indicated that patients received ANH experienced fewer ARBCu transfusions, with a standardized mean difference (SMD) of −0.60 (95%CI −0.96 to −0.24; $P = 0.001$). The rate of allogeneic blood transfusion in ANH group was significant reduced when compared with controls, with a relative risk (RR) of 0.65 (95%CI 0.52 to 0.82; $P = 0.0002$). In addition, less postoperative estimated total blood loss was present, with a SMD of −0.53 (95%CI −0.88 to −0.17; $P = 0.004$).
Conclusions: The present meta-analysis indicated that ANH could reduce the number of ARBCu transfused in the CABG surgery setting. In addition, ANH could also reduce the rate of ARBCu transfusion and estimated total blood loss for CABG patients.

1. Introduction

In cardiac surgery, postoperative bleeding accounts for 15%–20% of total transfusion request, within a national blood supply range [1]. Allogeneic red blood cell units (ARBCu) transfusions as a safeguard for surgical bleeding, however, are associated with a worse short- and long-term outcome [1,2]. However, there is an additive risk of mortality and cardiac adverse events for each unit transfused [3–6]. Satisfactory control of major bleeding in operation and management of blood losses can reduce the proportion of transfused patients and post-operative re-interventions rate [7,8]. Although there were guideline indications and numerous approaches to reduce bleeding and to lower hemoglobin transfusion threshold at present, it was estimated that approximately more than 50% of the patients undergoing coronary artery bypass grafting (CABG) experienced transfusions [9,10]. Thus, additional different approaches, acute normovolemic hemodilution (ANH), could be a valid alternative. However, it is still controversial as to whether ANH is capable of reducing the need for allogeneic blood and for exerting a positive effect on morbidity and mortality.

ANH is performed by drawing a specific amount of blood volume from the patient, hydrating the patient to maintain isovolemia, storing patient's blood in storing bags at room temperature with anticoagulants, and re-administering it during surgery, usually after cardiopulmonary bypass (CPB) or according to the patient's need. ANH may be beneficial to a reduction of risk of adverse reactions related to transfusion of allogeneic blood products, preservation of erythrocytes from CPB damage, enhancing coagulation with the possibility of re-administering the patient's whole blood containing clotting factors and platelets, and

* Corresponding author. Department of Anesthesia, Chongqing Emergency Medical Center (Chongqing University Central Hospital), No., Jiankang Road, Chongqing, 400014, China.