Obstructive Sleep Apnea/Obesity Hypoventilation Syndrome Overlap

Megan Acho, MD, MS

Clinical Assistant Professor

Division of Pulmonary and Critical Care Medicine

Conflicts of Interest

- None
- No funding

Goals and Objectives

- Review the diagnostic criteria and clinical sequelae of obstructive sleep apnea and obesity hypoventilation syndrome
- Describe the overlap between these two clinical conditions
- Discuss treatment options for patients with OSA/OHS overlap

Case

A 33-year-old female with a past medical history of pre-diabetes presents to clinic after her primary care doctor noted an elevated serum bicarbonate of 32 mEq/L on routine labs. Her vitals are notable for a body mass index (BMI) of 45. She reports daytime sleepiness (ESS 12/24) and frequent morning headaches. She snores and reports intermittent nocturnal choking and gasping. Her partner has shaken her awake during periods where she has ceased breathing.

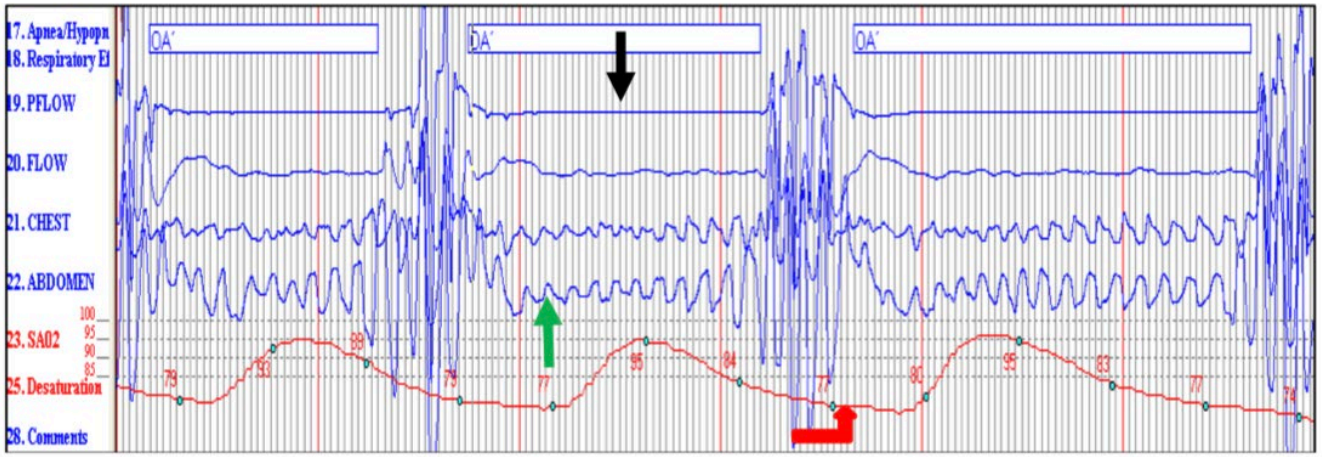
Pulmonary function testing reveals an FEV_1/FVC 80% and FVC 56%. Labs from the day of this visit demonstrate a $PaCO_2$ of 50 mmHg.

Case

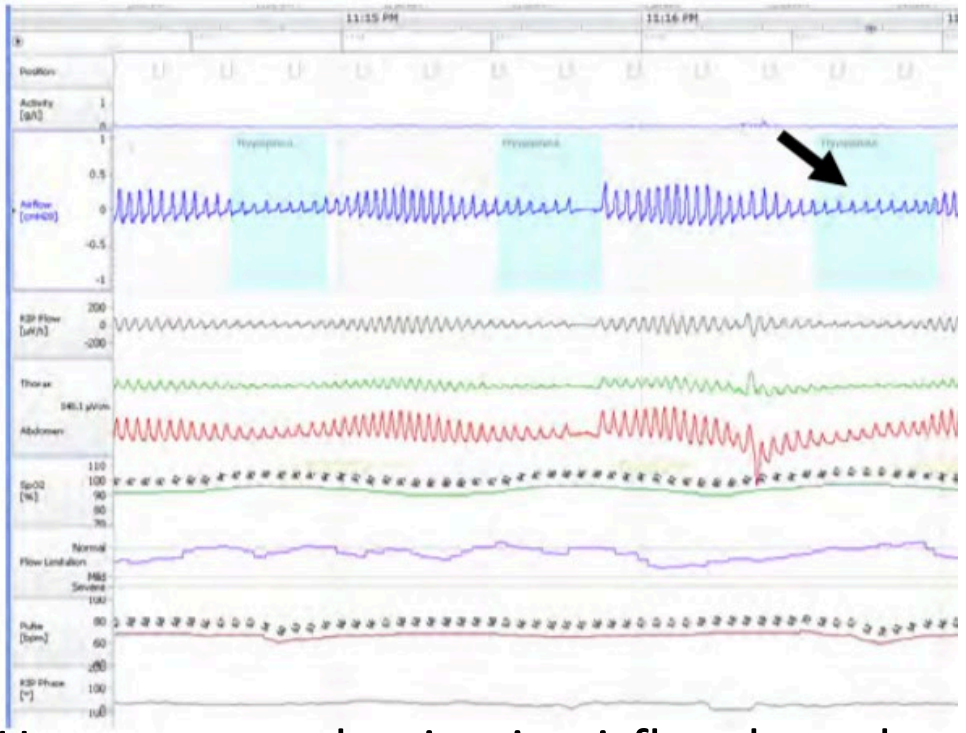
1. What pathology are you concerned about here?
2. What are the next steps in your work-up?
3. What types of treatment should you consider initiating?

What are you concerned about?: OSA

Characterized by repetitive episodes of nocturnal airway collapse



Apnea: Reduction in airflow by at least 90% for at least 10 seconds



Hypopnea: reduction in airflow by at least 30% for at least 10 seconds <u>with a desat</u>

Le et al. American Thoracic Society. 2015.

What are you concerned about?: OSA

- Apnea-Hypopnea Index (AHI) = $\frac{\text{\# apneas + \# hypopneas}}{\text{total sleep time}}$
  - AHI 5-14 events/hour = mild OSA
  - AHI 15-29 events/hour = moderate OSA
  - AHI 30+ events/hour = severe OSA

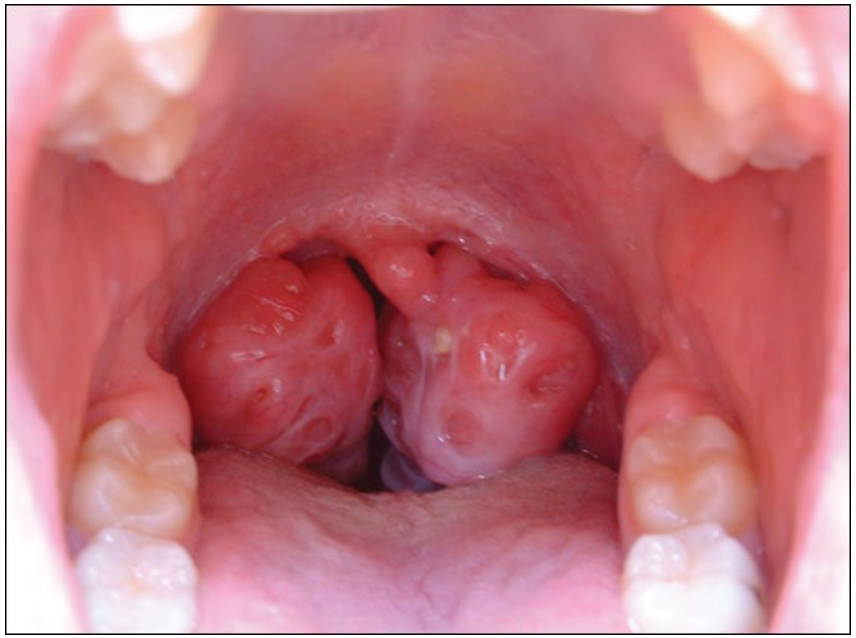
What are you concerned about?: OSA

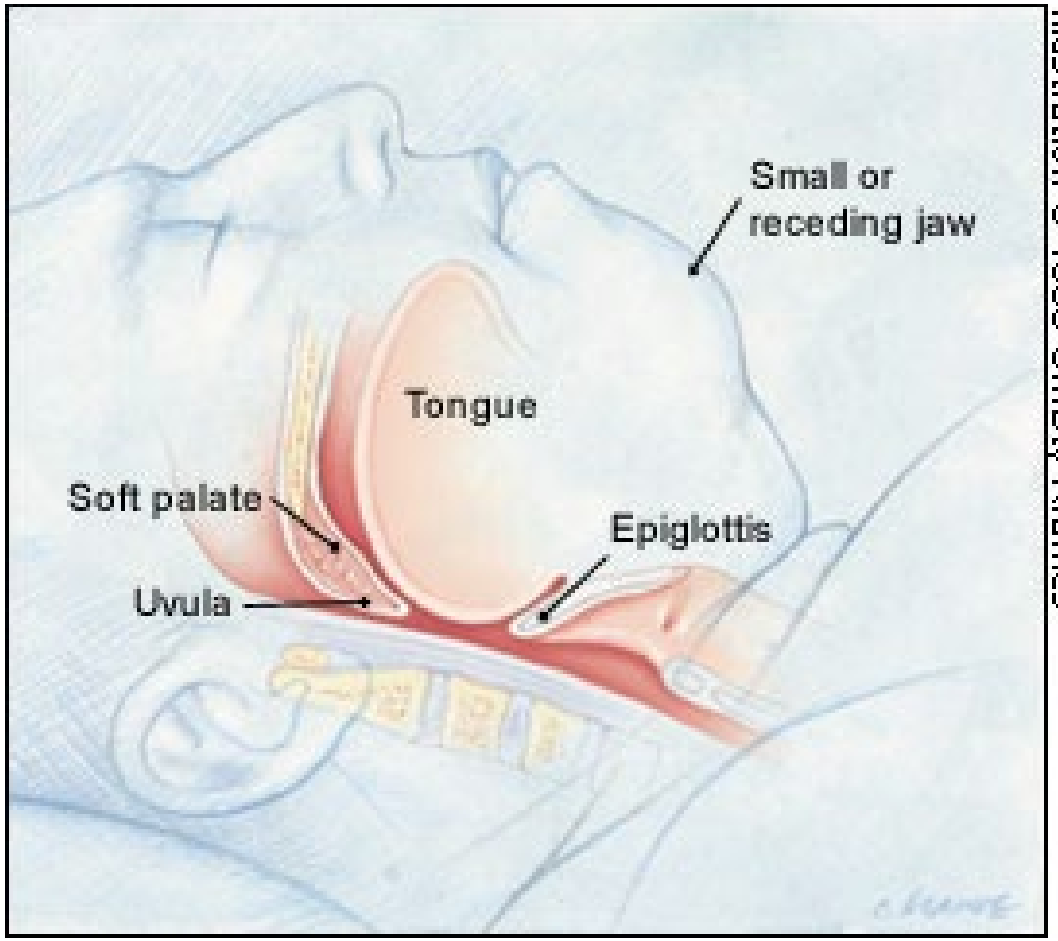
- Most common form of sleep-disordered breathing
- Prevalence: 15-30% of men, 10-15% of women in North America
- Risk factors:
  - Older age
  - Male gender
  - Smoking
  - Family history

Young et al. NEJM. 1993.
Young et al. JAMA. 2004.

What are you concerned about?: OSA

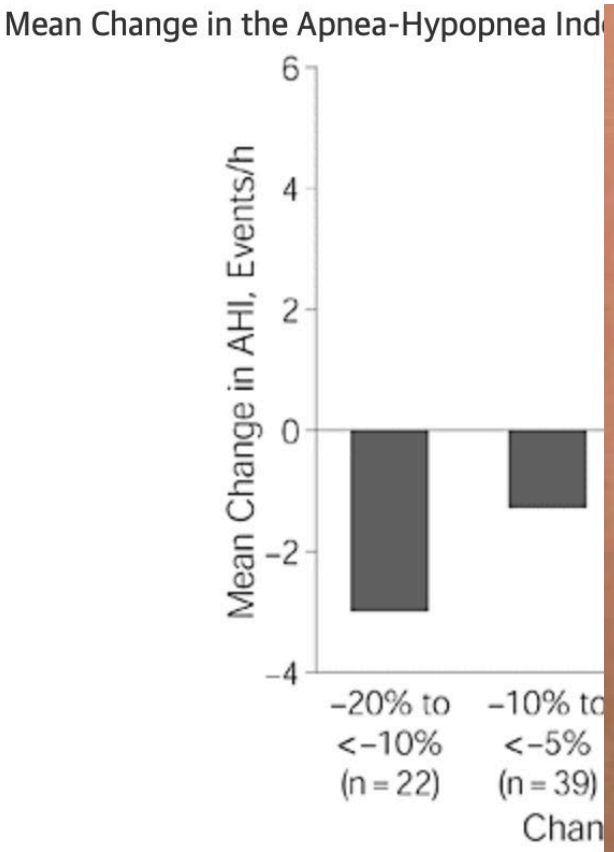
- Risk factors
  - Craniofacial abnormalities
  - Upper airway abnormalities





Victor et al. Am Fam Physician. 1999.
Peppard et al. JAMA. 2000.

What are you concerned about?: OSA



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nt*

Estimated Percent Change in AHI % Confidence Interval)†
−48 (−58 to −35)
−26 (−34 to −18)
−14 (−18 to −9)
+15 (+10 to +21)
+32 (+20 to +45)
+70 (+42 to +104)

onea index. Adjusted for sex,
s/wk, baseline body mass in-
age. All $P<.001$.
cted if weight remained stable.

Peppard et al. JAMA. 2000.

What are you concerned about?: OSA

- Clinical sequelae of untreated OSA
  - DM
  - HTN
  - Cardiovascular Disease
    - Coronary Artery Disease (CAD)
    - Atrial fibrillation, bradyarrhythmias, heart block
  - Pulmonary hypertension

Marshall et al. J Clin Sleep Med. 2009.

What are you concerned about?: OHS

- Obesity Hypoventilation Syndrome (OHS)
  - Definition: Obesity (BMI $\geq$ 30 kg/m^2), daytime awake hypercapnia ($PaCO_2 \geq$ 45 mmHg at sea level) not attributable to other causes of hypoventilation.
    - Other causes: central alveolar hypoventilation, chest wall deformity, neuromuscular disease, COPD, metabolic etiologies of hypoventilation

1909: "I have lost the tendency to sleepiness which made me think of the Fat Boy in Pickwick. My color is very much better and my ability to work is greater."

Mokhlesi et al. Respir Care. 2010.

What are you concerned about?: OHS

- Prevalence
  - 0.15-0.3% of US adults have OHS
    - 7.6% of the adult US population has BMI > 40
    - 15-30% of adult males have OSA
  - 90% will have concurrent OSA (nearly 70% have severe)
    - 10% have non-obstructive sleep apnea related hypoventilation
- Presentation
  - Symptomatically, very variable

Mokhlesi et al. Respir Care. 2010.
Masa et al. Am J Respir Crit Care Med. 2015.

What are you concerned about?: OHS

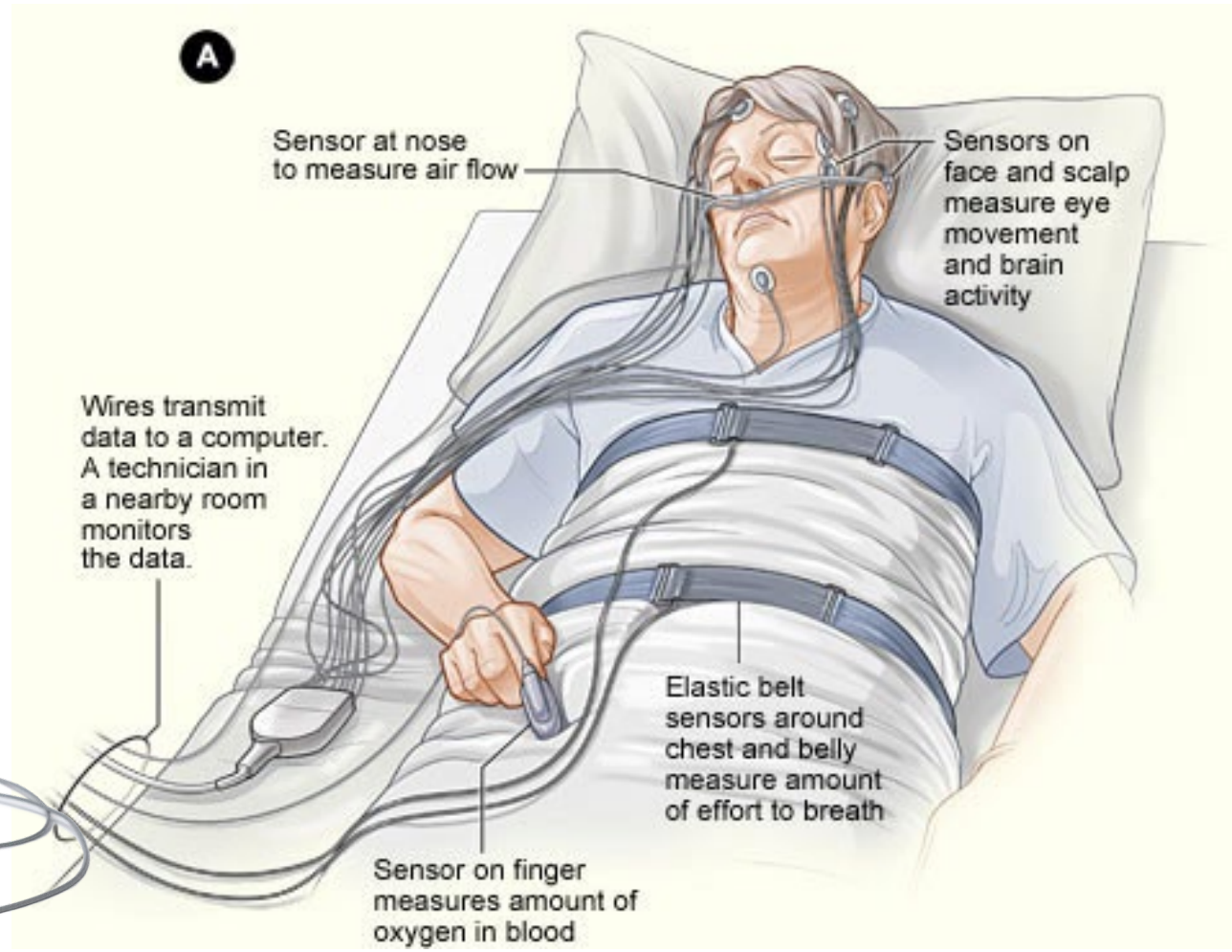
- Signs
  - Daytime awake hypercapnia (serum bicarbonate > 27)
  - Oftentimes, hypoxemia (PaO2 < 70)
    - Normal Aa gradient

$$P_AO2 = FiO2\ (Pb - PH20) - PCO2/R$$

- Clinical sequelae
  - Pulmonary hypertension, chronic right heart failure
  - Increased healthcare expenses 2/2 admissions for acute on chronic hypercapnic respiratory failure
  - **Increased mortality**

Mokhlesi. Sleep Breath. 2007.
Mokhlesi Am J Respir Crit Care Med. 2019.

What are the next steps in your work-up?



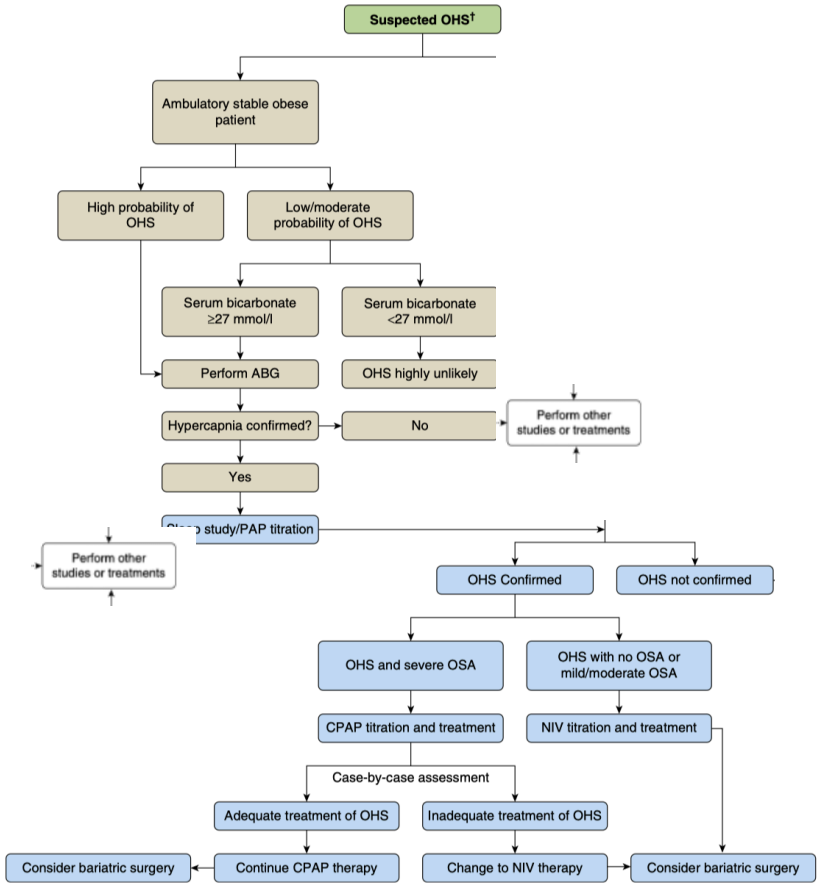
What types of treatment should you consider initiating?: PAP

American Thoracic Society (ATS) Clinical Practice Guidelines for patients with confirmed OHS

+ severe OSA: CPAP titration and treatment

  If inadequate treatment, change to NIV

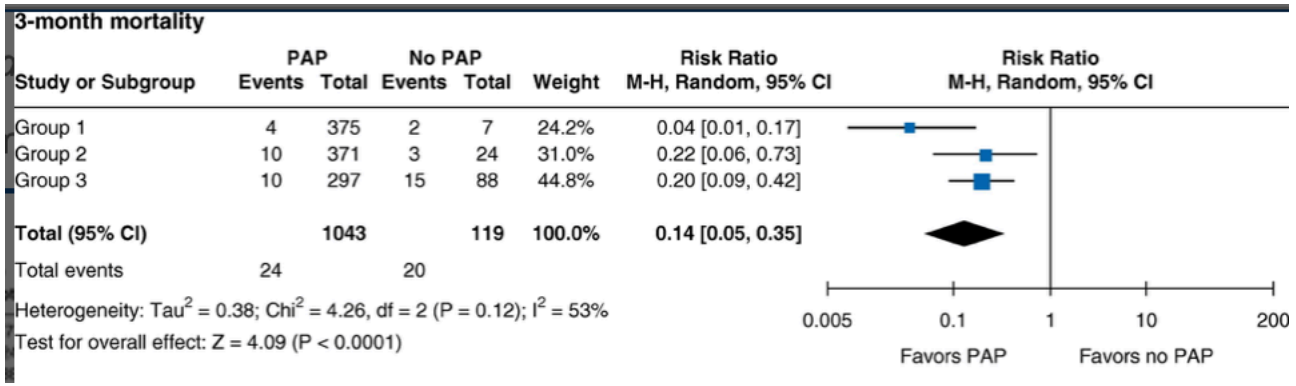
+ no OSA or mild/moderate OSA: NIV initiation and treatment with consideration of bariatric surgery

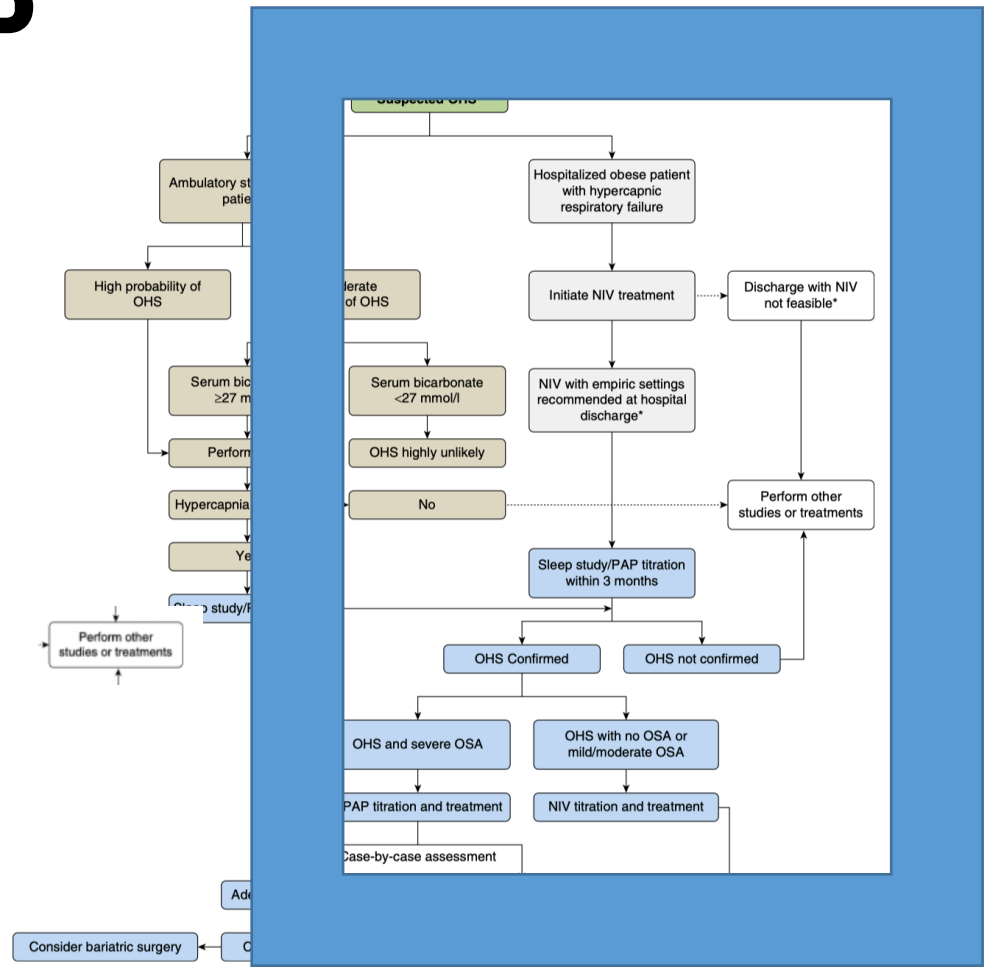


Mokhlesi Am J Respir Crit Care Med. 2019.

What types of treatment should you consider initiating?: PAP

Per the ATS, if admitted with acute on chronic hypercarbic respiratory failure in the setting of OHS, patients should be discharged with NIV





Mokhlesi Am J Respir Crit Care Med. 2019.
Mokhlesi. Ann Am Thoracic Soc. 2020.

NIV in Chronic OHS

[Sleep Original Research]

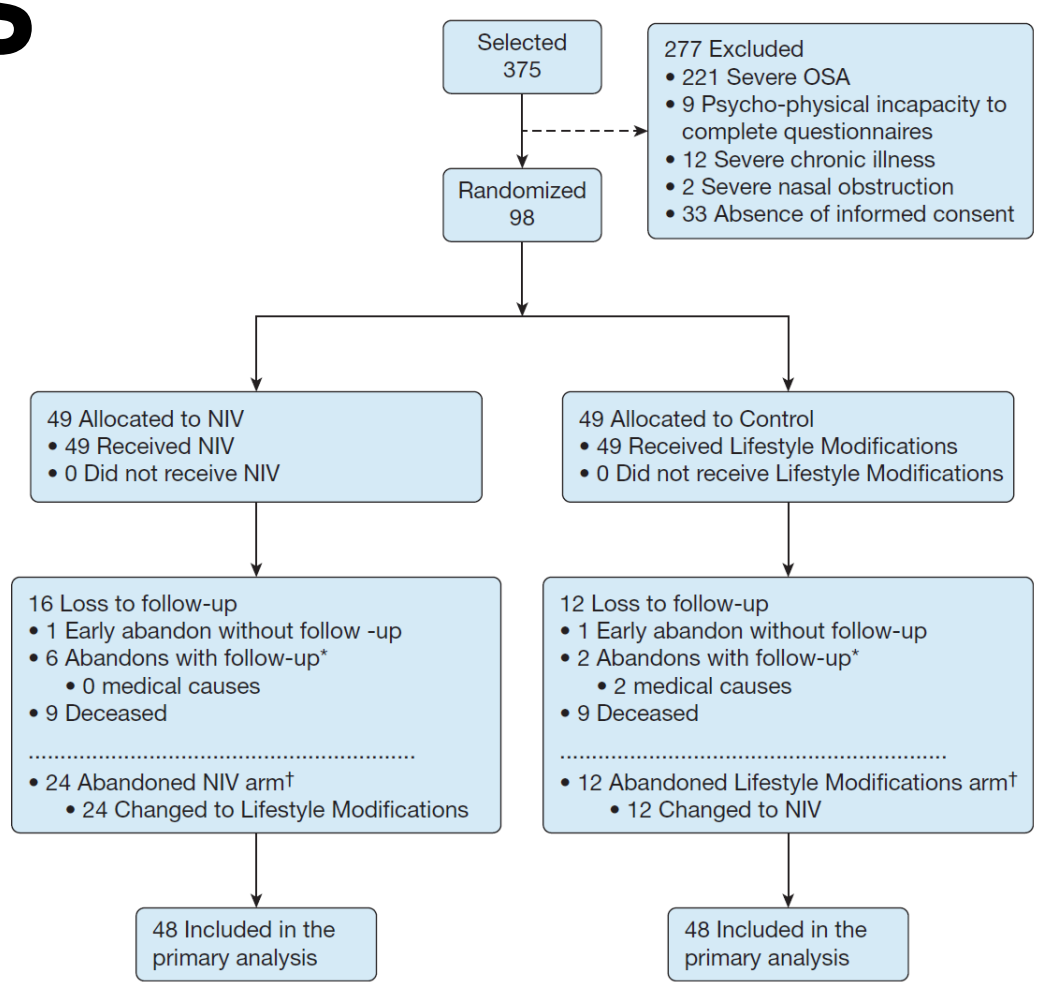
CHEST

Long-term Noninvasive Ventilation in Obesity Hypoventilation Syndrome Without Severe OSA

The Pickwick Randomized Controlled Trial

Check for updates

- VAPS vs lifestyle modification
- Inclusion: untreated OHS, mild-to-moderate OSA
- Exclusion: severe OSA, other sleep conditions, chronic nasal obstruction
- Primary endpoint: hospitalization days per year
- Secondary endpoint: hospital resource utilization, CV events, mortality, ABG data

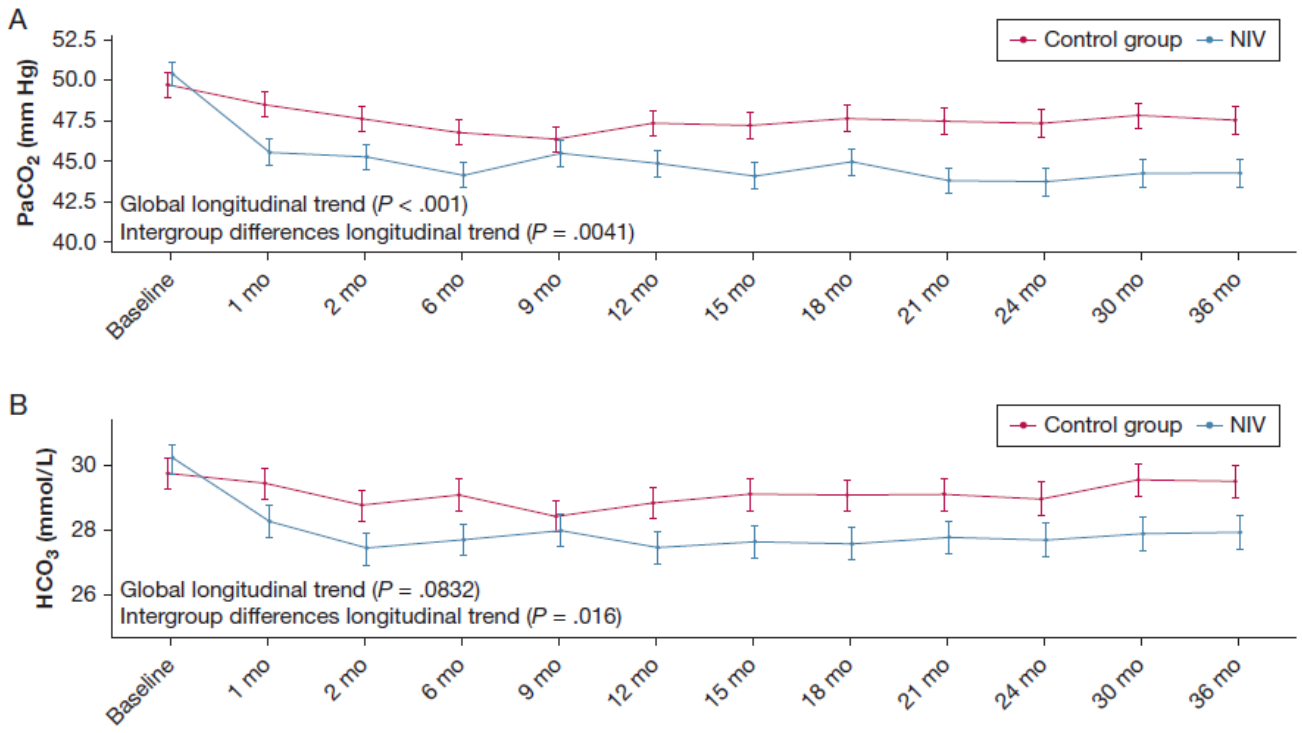


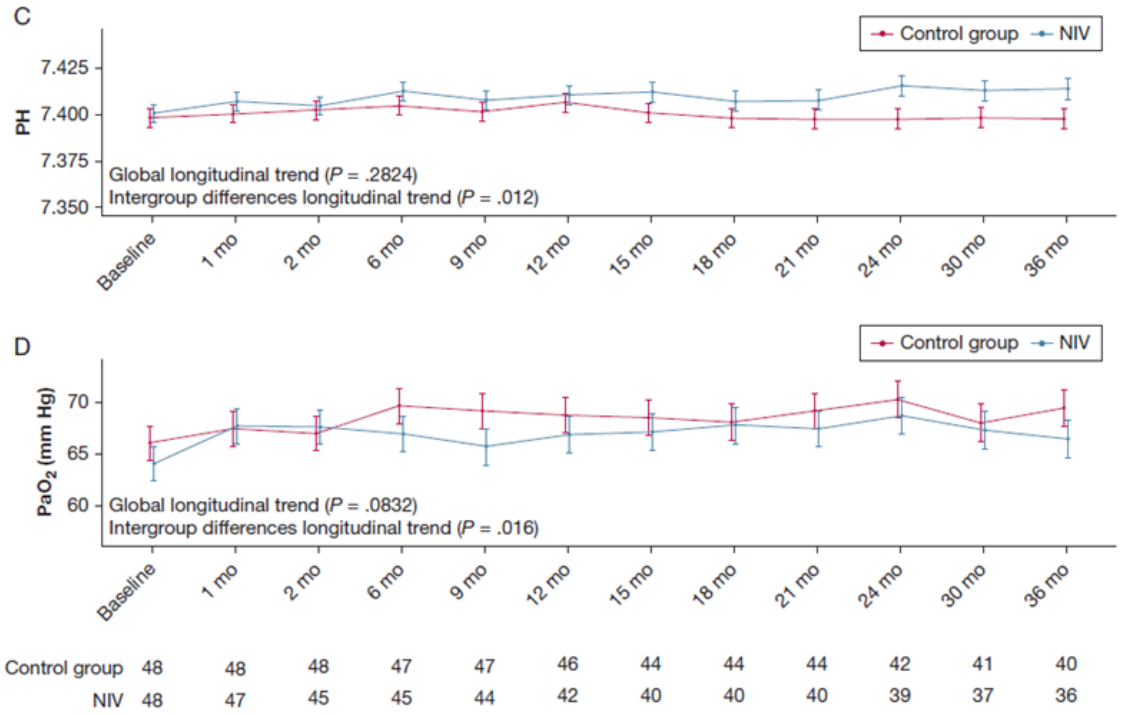
Masa et al. Chest. 2020.

NIV in Chronic OHS

- Primary outcome: Hospitalization days per year
  - Lifestyle modification group: 2.6 +/- 5.31d vs NIV: 2.71 +/- 4.52d (ns)
- Secondary outcomes:
  - Hospital resource utilization: dec in hospital admissions, ER visits among NIV
  - CV events: ns
  - Mortality: ns
    - Cause of mortality in the NIV group: CV events (67%)
    - Cause of mortality in the lifestyle modification group: respiratory failure (44%)

Masa et al. Chest. 2020.





Control group	48	48	48	47	47	46	44	44	44	42	41	40
NIV	48	47	45	45	44	42	40	40	40	39	37	36

Figure 2 – *A-D, Adjusted longitudinal changes of arterial blood gases during follow-up (mean and 95% CI). P values correspond to longitudinal changes for treatments and for intergroup control and NIV comparison from linear mixed-effects regression model: (A) $Paco_2$ changes, (B) HCO_3^- changes, (C) pH changes, and (D) Pao_2 changes. HCO_3^- = bicarbonate. See Figure 1 legend for expansion of other abbreviation.*

Masa et al. Chest. 2020.

VAPS in Chronic OHS

- Potential utility of VAPS
  - In obese patients, movement from sitting to supine increases respiratory muscle exertion with an associated fall in TV
  - Fixed PS may not maintain adequate ventilation due to variable pulmonary mechanics throughout sleep; autotitrating device may be more effective

Murphy et al. Thorax. 2012.

VAPS in Chronic OHS

- Murphy et al (2011)
  - Investigated whether the addition of VAPS to standard fixed bilevel PS improves physiologic and clinical outcomes in the treatment of OHS
  - Looked at stable OHS patients as well as those admitted for acute on chronic decompensated respiratory failure.
    - Patients received AVAPS (goal VT 8-10cc/kg) vs BPAP fixed PS (IPAP 18-22, EPAP 8-10), titrated via protocol
    - Primary outcome: PaCO2

Murphy et al. Thorax. 2012.

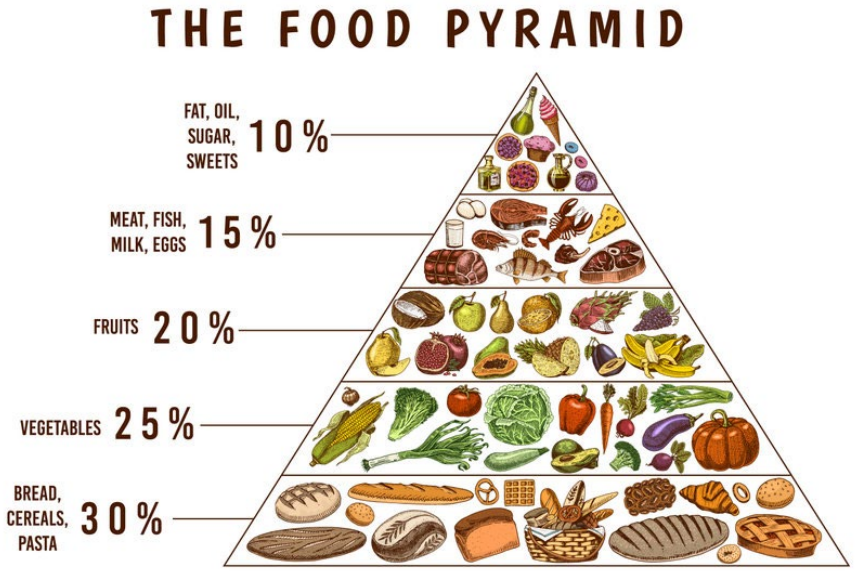
VAPS in Chronic OHS

	AVAPS	Fixed-level PS	Mean difference between treatments (95% CI)	p Value
$\Delta PaCO_2$ (kPa)	−0.6±1.0	−0.6±1.1	0 (−0.7 to 0.6)	0.867
ΔPaO_2 (kPa)	0.2±1.7	0.5±1.6	0 (−1 to 1)	0.519
ΔHCO_3 (mmol/litre)	−3±3	−3±4	0 (−2 to 2)	0.825
ΔBMI (kg/m^2)	−1±2	−2±4	1 (−1 to 2)	0.497
ΔFat free mass (kg)	−1±6	0±8	−1 (−4 to 3)	0.805
ΔWaist circumference (cm)	−3±5	−2±7	−1 (−3 to 4)	0.676
ΔFEV_1 (% predicted)	6±13	4±14	2 (−6 to 10)	0.588
ΔFVC (% predicted)	6±12	5±17	1 (−7 to 10)	0.777
ΔESS (/24)	−5±6	−6±6	1 (−2 to 5)	0.428
ΔSRI-SS (/100)	11±12	7±13	5 (−2 to 12)	0.212

Murphy et al. Thorax. 2012.

What types of treatment should you consider initiating?: Weight Loss

- Referral to a dietician for comprehensive lifestyle intervention
  - Goal is to establish a sustainable lifestyle
- Bariatric surgery



Summary

- Reviewed the diagnostic criteria and clinical sequelae of obstructive sleep apnea and obesity hypoventilation syndrome
- Described the overlap between these two clinical conditions
- Discussed treatment options for patients with OSA/OHS overlap

Happy to take any questions!

Works Consulted

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