Literature Review

Obesity Hypoventilation Syndrome (Pickwickian Syndrome): A Literature Review

Alfin Ridha Ramadhan[1*], Betcy[2], Ruth Grace Aurora[1], Prasenohadi[3], Mohamad Fahmi Alatas[3]

[1]Department of Cardiovascular Medicine, Faculty of Medicine, Universitas Indonesia, Depok
[2]Division of Clinical Cardiology, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Indonesia, National Cardiovascular Center Harapan Kita, Jakarta
[3]Department of Pulmonology and Respiratory Medicine, Persahabatan General Hospital, Jakarta

Corresponding Author:
Alfin Ridha Ramadhan | Department of Cardiovascular Medicine, Faculty of Medicine, Universitas Indonesia, Depok | alfinrr@yahoo.com

Submitted: August 20th, 2024
Accepted: November 7th, 2024
Published: November 29th, 2024

Respir Sci. 2024; 5(1): 48-61
https://doi.org/10.36497/respirsci.v5i1.155

Abstract

Obesity hypoventilation syndrome (OHS), also known as Pickwickian syndrome, is a respiratory disorder characterized by reduced alveolar ventilation and elevated daytime carbon dioxide levels, primarily associated with obesity. If untreated, OHS can progress to pulmonary hypertension (PH) and ultimately heart failure. The exact prevalence of OHS in the general population remains unclear, but studies estimate it to range from 8% to 12.3%, increasing with obesity prevalence. This review discusses the diagnostic criteria for OHS, the utility of the STOP-Bang questionnaire in screening, and advances in understanding the pathophysiology and management of OHS, focusing on heart failure with preserved ejection fraction (HFpEF). Accurate diagnosis of OHS is critical and requires a thorough approach involving an extensive patient medical history and physical examination to differentiate OHS from obstructive sleep apnea (OSA). Key diagnostic tests include serum bicarbonate levels and arterial blood gas (ABG) analysis, to confirm the hypercapnia and identify the severity of hypoventilation. Given the rising prevalence of obesity worldwide and the serious complications associated with untreated OHS, early and accurate identification of OHS is essential, as it can prevent the progression to severe pulmonary hypertension (PH) and the subsequent development of heart failure (HF).

Keywords: HFpEF, obesity hypoventilation syndrome, Pickwickian syndrome

INTRODUCTION

Obesity hypoventilation syndrome (OHS), also known as Pickwickian syndrome, is characterized by obesity (BMI ≥30 kg/m²) and chronic daytime hypoventilation with hypercapnia ($PaCO_2$ >45 mmHg), in the absence of significant underlying pulmonary, metabolic, or neuromuscular disorders.[1]

In patients with OHS, OSA frequently coexists as a concurrent condition. As a result, the majority of prevalence studies have concentrated on individuals referred to sleep centers for the assessment of sleep-related breathing disorders, leading

to a reasonable estimate of OHS prevalence among OSA patients.[2] Numerous studies have found that the prevalence of OHS ranges between 8-12.3%.[3,4] OHS is strongly associated with cardiometabolic comorbidities, including pulmonary hypertension (PH), heart failure (HF), and coronary artery disease.[1]

The five-year mortality rate was 15.5% in the OHS group, compared to 4.5% in the OSA group. It has been reported that patients with OHS experienced a two-fold increased risk of mortality and are 1.86 times greater risk of experiencing a cardiovascular event.[5]

Given these outcomes, it is crucial for clinicians to properly identify and manage OHS, however, the condition is often neglected.[2] Therefore, This review examines the pathophysiology, diagnostic criteria, screening methods, and management strategies for OHS, with a particular focus on its role in heart failure with preserved ejection fraction (HFpEF).

RESPIRATORY PHYSIOLOGY

Normally, gas moves from high-pressure to low-pressure areas based on Boyle's principle. During respiration, inspiration and expiration involve the coordinated action of the diaphragm and rib muscles, working together to contract and relax, changing the volume of the lungs and creating a pressure gradient that allows airflow into and out of the lungs.[6]

The lungs are elastic structures that rely on the proper stretching of elastic fibers to function. Lung collapse is prevented by the pleura, comprising the parietal and visceral layers, which maintain lung integrity through cohesive forces.[7]

Intrapleural pressure at rest is approximately -4 mmHg relative to atmospheric pressure and decreases to around -18 mmHg during maximal inspiration, ensuring lung expansion.[7] Additionally, the pleural liquid acts as a lubricant during ventilation, providing cohesive force between the pleural layers. These mechanisms maintain the elasticity of the lungs.[8]

RESPIRATORY FAILURE

Respiratory failure occurs when the pulmonary system fails to adequately exchange gases, defined by a partial pressure of oxygen (PaO_2) <60 mmHg and/or partial pressure of carbon dioxide ($PaCO_2$) >50 mmHg.[9]

Respiratory failure can result from central or peripheral nervous system dysfunction, airway obstruction, or alveolar disorders. It is categorized by onset (acute, chronic, or acute-on-chronic) and by arterial blood gas (ABG) abnormalities as type 1 (hypoxemic) or type 2 (hypercapnic).[9]

Type 1 respiratory failure, or hypoxemia, is characterized by a PaO_2 <60mmHg with or without changes in $PaCO_2$. Alveolar disorders, including pulmonary edema and pneumonia, commonly cause this condition. Type 2 respiratory failure, or hypercapnia, is characterized by an increase in $PaCO_2$ >50mmHg, which is often accompanied by

hypoxemia. This condition is typically caused by airway obstruction or neuromuscular disorders.[9]

Acute respiratory distress syndrome (ARDS) results in respiratory failure and occurs in individuals with pneumonia, sepsis, gastric acid aspiration, or trauma. ARDS is marked by hypoxemia, lung edema, and the requirement for a ventilator. It causes damage to the alveolar epithelium and lung tissue.[10]

Conditions that cause type 1 respiratory failure include decreased inspiratory PaO_2, alveolar hypoventilation, ventilation/perfusion (V/Q) inconsistency, diffusion defect, and shunt from right to left. Decreased inspiratory PaO_2 occurs when the fraction of inhaled oxygen (FiO_2) is reduced, which occurs at high altitudes where barometric pressure is lower.[11]

Diffusion disorders occur when gas exchange is disrupted due to damage to the alveolar or blood vessel walls, as seen in pulmonary edema, pulmonary fibrosis, and ARDS. V/Q mismatches occur when ventilation decreases in areas with normal perfusion or when ventilation is normal in areas with decreased perfusion, such as pulmonary embolism, airway obstruction, and pneumonia. Right-to-left shunt occurs when oxygenated blood mixes with deoxygenated blood.[11]

Type 2 respiratory failure can be triggered by factors such as reduced alveolar ventilation due to airway obstruction, decreased respiratory function in neuromuscular diseases, and damage to the brain and spinal cord, decreasing the respiratory drive. Additionally, increased CO_2 production can occur in conditions that boost metabolism, such as sepsis, fever, or burns.[11]

OBESITY HYPOVENTILATION SYNDROME

Definition

OHS is defined as the coexistence of obesity, persistent alveolar hypoventilation ($PaCO_2$ ≥45 mmHg), and daytime hypoxemia (PaO_2 <70 mmHg), often accompanied by sleep-related respiratory disorders.[12]

Pathophysiology

The mechanisms underlying obesity-induced hypoventilation are complex and not fully understood. Hypothesized mechanisms include altered respiratory mechanics due to excess weight, impaired central responses to hypercapnia and hypoxemia, the presence of sleep-disordered breathing, and leptin resistance.[13]

Obesity results in significant mechanical stresses, reducing total respiratory compliance, increasing pulmonary resistance, and weakening the respiratory muscles, which encourages impaired respiratory function.[13]

Obese patients often enhance their respiratory function to keep CO_2 levels normal. Nevertheless, changes in their breathing effort can cause hypoventilation, particularly during paradoxical sleep. In this phase, muscle relaxation occurs, and the ventilation is controlled by the diaphragm and central nervous system. This leads to a suppression of respiratory

centers, causing daytime hypercapnia. This may explain the high occurrence of central hypoventilation in the OHS.[12]

A pathophysiological model of OHS has been suggested that integrates sleep-related respiratory disorders, central respiratory drive, and renal compensation. In OSA patients, there is stable minute ventilation during sleep due to a marked rise in minute ventilation between episodes of obstructive apnea. Nevertheless, OSA can result in acute hypercapnia if the periods of hyperventilation between apneic events are insufficient to clear the built-up CO_2.[12,14]

The present condition results in a modest elevation in serum bicarbonate levels that remain uncorrected before the subsequent sleep period, as the CO_2 excretion time is shorter than bicarbonate. An increase in serum bicarbonate concentration diminishes the baseline ventilatory response to CO_2 by decreasing the shift in hydrogen ion concentration for a specific increase in CO_2. Consequently, this leads to elevated CO_2 levels during wakefulness. [12,14]

Risk Factors

Key risk factors for OHS include severe obesity (BMI >40 kg/m²), OSA with an apnea-hypopnea index (AHI) >50 events/hour, oxygen saturation below 60% during polysomnography, moderate-to-severe lung function limitations, and large neck, waist, and hip circumferences.[15]

Clinical Manifestations and Diagnosis

Most cases are diagnosed when the patient seeks medical attention in an acute condition, such as severe acute exacerbations characterized by acute respiratory acidosis or sleep disorders. The onset of OHS can vary, but it typically appears in the age range from 50 to 60. Its presentation is often diverse, with a wide range of clinical severity.[16]

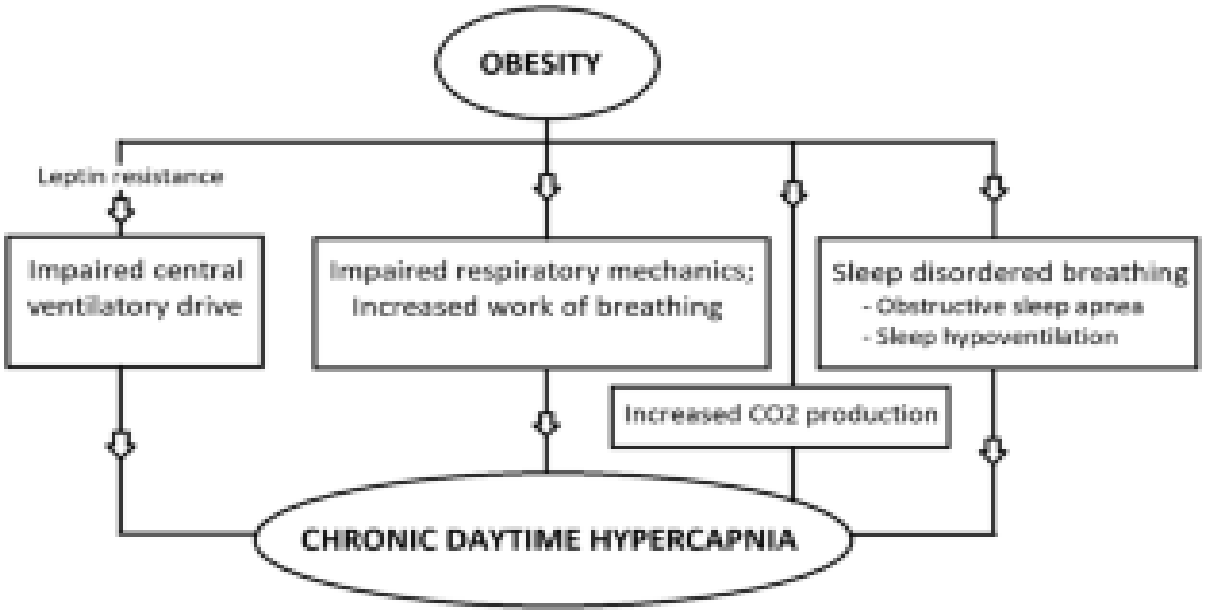

Figure 1. OHS Pathophysiology[14]

Symptoms arise from obesity and disrupted sleep, including fatigue, persistent daytime sleepiness, morning headaches, mood disturbances, difficulty concentrating, and memory impairment.[16]

The signs and symptoms in patients with OSA are heavy snoring with a crescendo-decrescendo pattern, nighttime choking, and gagging, as well as apneas observed by the bedmate.[16] Physical exam shows a typical obese person, who has a short and broad neck, a congested oropharynx, and a low-hanging uvula. They often showed signs of right HF due to PH, such as elevated JVP, an accentuated pulmonic component of the second heart sound, hepatomegaly, and lower extremity edema.[17]

Hematological examination reveals polycythemia with a hematocrit of over 50% and erythrocytosis. A room air ABG analysis remained the gold standard for diagnosing hypoventilation, which shows a reduction in PaO_2 and a rise in $PaCO_2$ during sleep and awake hours. Chronic hypercapnia in OHS patients will show elevated serum bicarbonate levels (>27 mEq/L) resulting from metabolic adjustment to chronic respiratory acidosis.[16]

A new noninvasive method for monitoring hypercapnia during the night and day is end-tidal or transcutaneous CO_2 monitoring. Lung function assessment including lung volume and capacity measurements, and spirometry where applicable, along with flow-volume loops and indices to check any obstruction in the upper airway.[16]

Additionally, hypercapnia should be considered if hypoxemia is detected on pulse oximetry in a conscious patient, as hypoxemia during wakefulness is uncommon in OSA. Performing lung function tests and chest X-rays should be done to exclude other causes of hypercapnia.[1]

STOP-Bang Scoring Model	
1. Snoring Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?	Yes/No
2. Tired Do you often feel tired, fatigued, or sleepy during daytime?	Yes/No
3. Observed Has anyone observed you stop breathing during your sleep?	Yes/No
4. Blood pressure Do you have or are you being treated for high blood pressure?	Yes/No
5. BMI BMI more than 35 kg/m^2?	Yes/No
6. Age Age over 50 years old?	Yes/No
7. Neck circumference Neck circumference greater than 40 cm?	Yes/No
8. Gender Gender male?	Yes/No
High risk of OSA: answering yes to three or more items Low risk of OSA: answering yes to less than three items	

Figure 2. STOP-Bang Questionnaire[18]

Nocturnal polysomnography (PSG) is used to diagnose OSA or OHS. However, the diagnosis can often be overlooked if only nocturnal pulse oximetry is used to assess sleep disorder breathing.[16]

The STOP-Bang questionnaire, commonly used for OSA, can serve as an early screening tool for OHS. It comprises 8 queries related to snoring, daytime drowsiness, noted episodes of apnea, history of hypertension, BMI, age >50, neck circumference, and gender.[18]

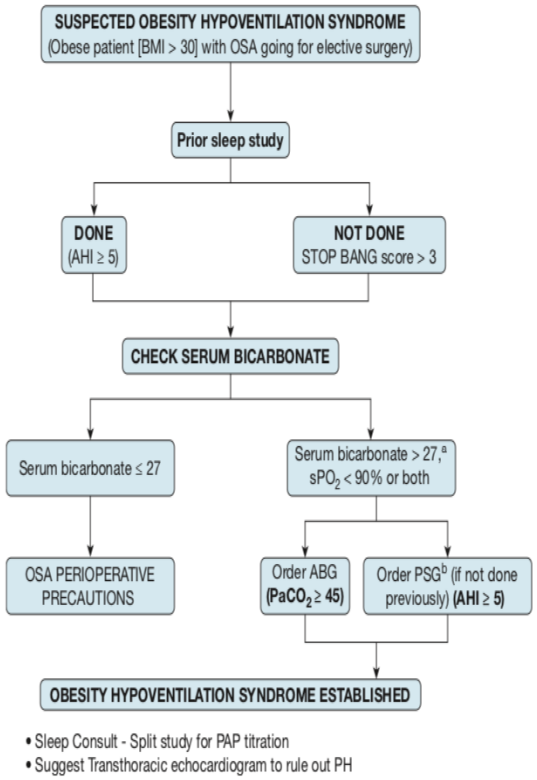

Figure 3. OHS Screening and Diagnosis Algorithm[19]

Early screening for OHS can be performed using the STOP-Bang questionnaire, assessment of oxygen saturation with a pulse oximeter, and serum bicarbonate. If the STOP-Bang score is ≥3, the SpO_2 value is <90% and the serum bicarbonate level is elevated, these findings indicate a high risk of OHS, and ABG analysis should be performed to assess for hypercapnia.[19]

HFpEF

HF is a complex medical condition characterized by the reduced structural and functional capability of the ventricles to fill with and pump blood. This condition presents with various symptoms such as difficulty breathing, fatigue, and increased jugular venous pressure (JVP) on physical examination. HF can be classified based on left ventricular function, using ejection fraction (EF) as a parameter. EF indicates the proportion of blood ejected from the heart with each heartbeat, with a normal value of 50% or greater.[20]

HF with a normal EF is known as HFpEF, also called diastolic heart failure. If the EF is less than 40%, the condition is termed heart failure with reduced ejection fraction (HFrEF), or systolic heart failure. Others with an EF between 40-49% may be classified as having heart failure with mid-range ejection fraction (HFmrEF).[20]

For patients with HF who are not in an emergency setting, a natriuretic peptide test can help determine the need for echocardiography. In acute cases, an immediate diagnosis of HF is necessary to identify any cause of symptoms. Patient's previous medical records, potential triggers, clinical evaluation, and additional tests such as electrocardiograms, chest X-rays, laboratory tests, and echocardiography should be noted to diagnose.[20]

The diagnosis of HFpEF can be confirmed by elevated natriuretic peptides (B-type natriuretic peptide [BNP] >35 pg/ml and/or NT-proBNP >125 pg/ml), and cardiac structural or functional abnormalities indicating HF. If the diagnosis remains uncertain, a stress test or invasive approach of left ventricular filling pressures can be performed.[20]

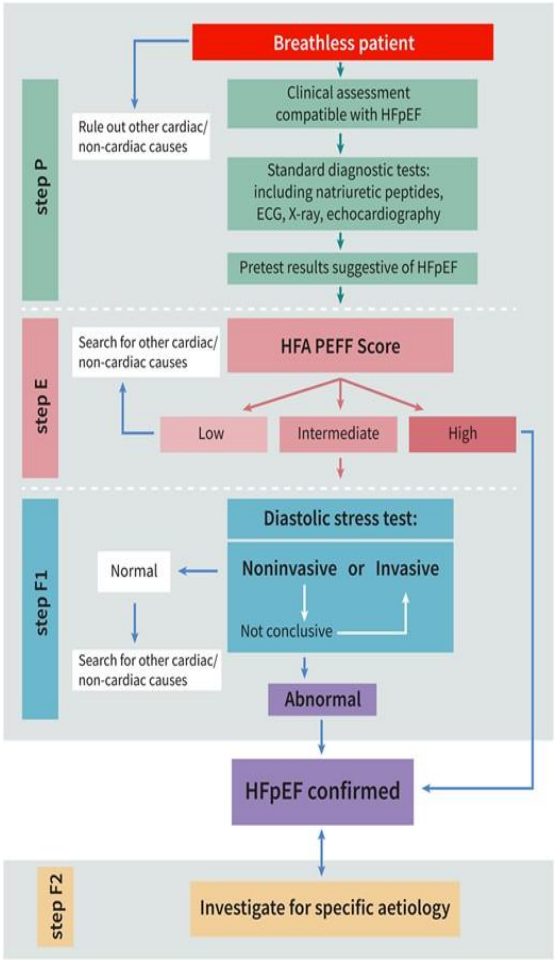

Figure 4. Flowchart of the HFA-PEFF diagnostic algorithm[21]

In 2021, the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) developed a scoring system to diagnose HFpEF. This score includes functional, morphological, and biomarker domains, with each domain containing major and minor criteria. A major criterion scores 2 points, while a minor criterion scores 1 point. Each domain can contribute a maximum of 2 points if major criteria are met, or 1 point if only minor criteria are met.[21]

OHS in HFpEF

OHS is a condition that can cause shortness of breath, right HF, and severe PH, yet it remains underdiagnosed. Warricker, et al reported a case of a young woman experiencing severe PH and right HF who recovered after being diagnosed with OHS and receiving appropriate treatment.[22]

Similarly, another case reported by Terla et al was about a 53-year-old male experiencing right ventricular dysfunction, PH, and BNP levels of 160 pg/ml, without a history of smoking, and his lung function tests did not indicate any obstructive or restrictive lung disease. A pulmonary CT angiography was conducted, but no abnormalities were found. Therefore, chronic obstructive pulmonary disease, pulmonary embolism, or interstitial lung disease were ruled out. However, transthoracic echocardiography revealed moderate pulmonary hypertension, suggesting OHS as the underlying cause.[22]

OHS is associated with Grade 3 PH.[24] Recent studies reported about 52-68.8%[25,26] of OHS cases with PH. Right heart catheterization is considered the gold standard for diagnosing PH. However, transthoracic echocardiography is frequently used for assessment and observation because it is non-invasive,

affordable, accessible, and reliable to diagnose.[27]

The underlying causes of PH and right HF (with normal EF) in OHS patients are believed to be long-term daytime and nighttime hypoxia, hypercapnia, and acidosis. Additional conditions contributing to PH in these patients include restrictive pulmonary disease resulting from severe obesity and significant fluctuations in pressure within the thoracic cavity during the respiratory cycle owing to increased resistance in the upper airway. Obstruction in the upper airway leads to intense negative pressure within the thoracic cavity during inspiration, which boosts venous return and right ventricular filling, causing the intraventricular septum to shift leftward. As a result, left ventricular (LV) filling is reduced, leading to a lower stroke volume.[25]

MANAGEMENT

Positive Airway Pressure Ventilation

Positive airway pressure (PAP) works to keep the airway from collapsing, acting as a pneumatic splint, and has been the primary treatment for OHS. PAP can be delivered consistently throughout the breathing cycle, known as continuous PAP (CPAP), or varying pressures during inspiration and expiration referred to as bilevel PAP (BiPAP) or non-invasive ventilation (NIV).[16]

BiPAP aids in reducing the effort required for breathing, relieving the pulmonary muscles, and improving gas exchange, which results in higher O_2 levels and lower CO_2 levels.[16] Held et al reported patients with severe PH due to alveolar hypoventilation, who showed significant improvement after 3 months of NIV.[28]

CPAP provides a steady pressure throughout the breathing cycle to prevent obstructive apneas and hypopneas, without extra ventilatory support like NIV does. However, CPAP can still help to clear CO_2 that has built up during prolonged complete or partial obstructive events during sleep.[1]

Recent research has shown a substantial improvement of PAP therapy in fewer lengths of stay in hospital, management of sleep disorder breathing, and in the measures of the quality of life. The pulmonary function metrics, performance on the 6-minute walk distance test, and echocardiographic outcomes also showed a significant improvement.[26,29,30]

There is no definitive evidence showing one mode of PAP therapy is superior to the other. The choice typically relies on various factors, including the type of obstructive events of hypoventilation during sleep, the complexity of adjustments, and the cost.[1]

According to American Thoracic Society guidelines, patients diagnosed with OHS who are in stable condition should receive PAP therapy during sleep. For patients diagnosed with both OHS and severe OSA (AHI >30), CPAP is preferred as the primary treatment over NIV.[31]

If CPAP is not tolerated due to air leakage or discomfort, or if hypoventilation and desaturation episodes do not improve, it can be replaced with BiPAP. The target

SaO_2 for patients is >90%. If this target is not reached despite eliminating obstruction and hypoventilation, oxygen supplementation can be added.[31]

For hospitalized OHS patients with respiratory failure, NIV should be initiated before discharge, with PAP therapy titrated slowly over the first three months after discharge.[31]

A multicenter randomized controlled trial (RCT) in Spain involving stable patients with OHS and severe OSA, found that NIV and CPAP have comparable long-term effectiveness. Since CPAP is less complex and more cost-effective, it may be the preferred first-line PAP treatment option until further research is conducted.[32]

In addition, a recent systematic review and meta-analysis comparing the effectiveness of PAP treatments on OHS revealed that BiPAP provided the greatest improvement in hypercapnia and objective sleep patterns, including an increase in the percentage of paradoxical and deep sleep.[33]

Weight Loss Strategies

American Thoracic Society guidelines advised to reduce body weight by 25-30% through lifestyle modifications or bariatric surgery to improve hypoventilation.[31] Weight loss improves sleep-disordered breathing, OHS, and cardiometabolic health. Bariatric surgery is more effective than lifestyle modifications for achieving significant weight loss.[34]

A recent systematic review of weight loss interventions for patients with OHS showed that a comprehensive weight loss program successfully lowers body weight but shows no marked benefits compared to standard care (such as diet and exercise advice provided during ambulatory visits). Contrary, the bariatric approach is linked to more efficient weight loss, subsidence of OHS, lower OSA severity, and improvements in pulmonary artery pressure, gas exchange, and daytime drowsiness.[34]

OHS with HF

The Pickwick project showed that PAP therapy improves PH and LV diastolic function. Both NIV and CPAP treatments significantly lowered systolic pulmonary artery pressure, though right ventricular function remained unchanged in either PAP group. No notable changes were observed in left ventricular hypertrophy or systolic function; however diastolic function showed substantial improvement with PAP therapy.[35]

The principles for treating patients with HF and OHS are similar to those for patients without OHS, focusing on reducing congestive symptoms with diuretics.[36] However, it is crucial to address acute HF episodes in OHS patients carefully.[36]

Loop diuretics can increase serum bicarbonate levels, reducing the respiratory response and worsening hypercapnia in OHS patients. Studies have shown that carbonic anhydrase inhibitors, such as acetazolamide, are safe for OHS patients because they can prevent alkalosis by lowering bicarbonate concentration and enhancing respiratory responses.[36]

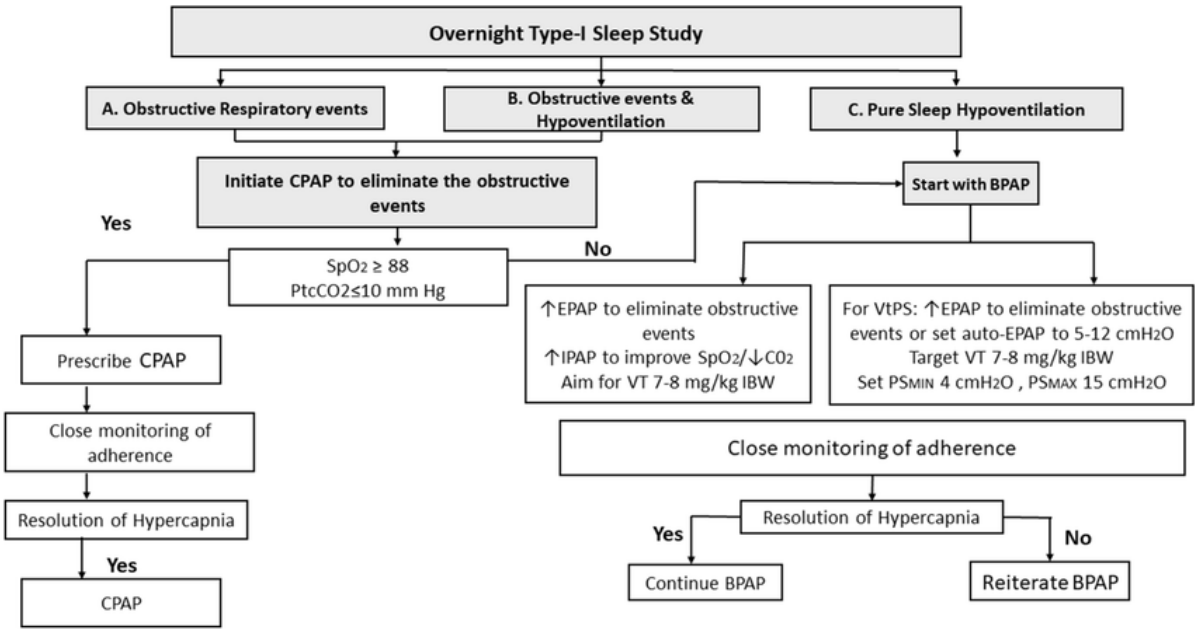

Figure 5. A Proposed Algorithm to Applying PAP in OHS Patients[37]

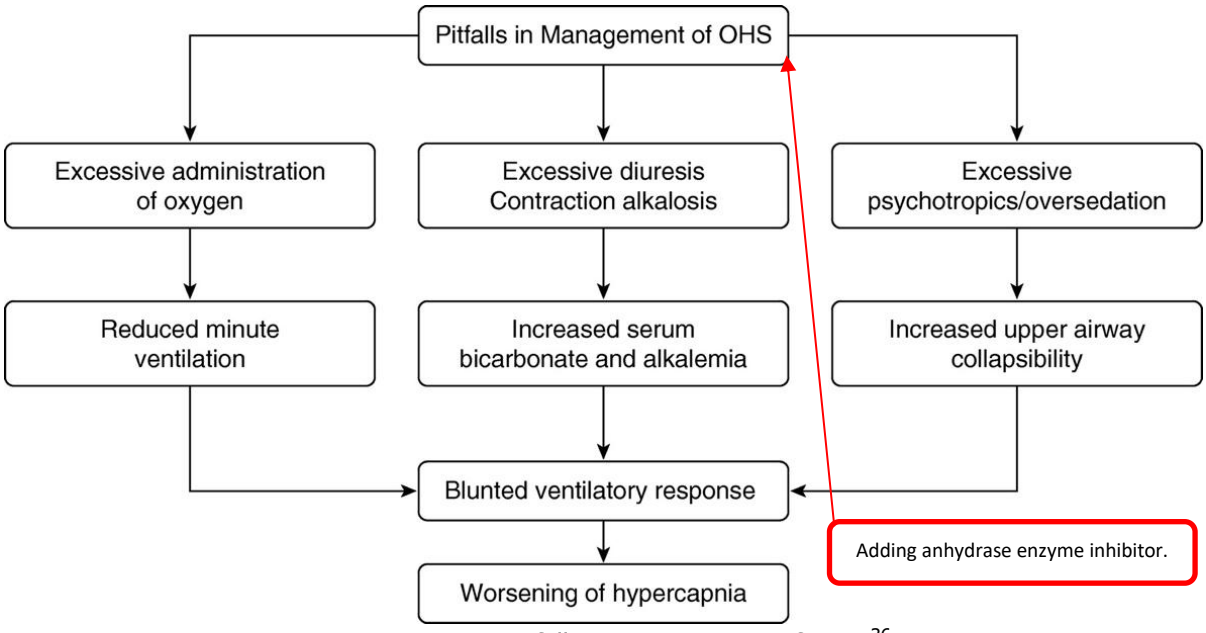

Figure 6. Pitfalls in Management of OHS.[36]

PROGNOSIS

Mortality rates in OHS were substantially higher than in OSA. The 5-year mortality rates were 15.5% in OHS and 4.5% in OSA. OHS patients had a twofold increase in mortality risk and a 1.86 times risk of having a cardiovascular event.[5]

Another study showed the 5- and 10-year survival rates were lower in the OHS patients compared to OSA patients, with rates of 83% versus 96% at 5 years and 74% versus 91% at 10 years. Moreover, ventilation therapy by CPAP and BiPAP has significantly lowered mortality in all patients.[38]

CONCLUSION

OHS is a frequently underrecognized cause of HFpEF. Its pathophysiology includes increased mechanical loads on the respiratory system, elevated airway resistance, and reduced pulmonary compliance, culminating in pulmonary artery remodeling, PH, and right heart failure.

Early diagnosis and timely intervention are crucial to preventing deaths from heart failure. Preliminary screening for OHS can be performed by utilizing basic tests like pulse oximetry and serum bicarbonate levels, followed by ABG analysis to rule out OSA.

PAP ventilation remains the cornerstone of treatment for OHS, particularly in HFpEF. Long-term management strategies, including significant weight loss, improve vital capacity and reduce chronic hypercapnia.

REFERENCES

1. Masa JF, Pépin JL, Borel JC, Mokhlesi B, Murphy PB, Sánchez-Quiroga MÁ. Obesity hypoventilation syndrome. European Respiratory Review. 2019 Mar 31;28(151).
2. Balachandran JS, Masa JF, Mokhlesi B. Obesity Hypoventilation Syndrome Epidemiology and Diagnosis. Sleep medicine clinics. 2014;9(3):341.
3. Bahammam AS. Prevalence, clinical characteristics, and predictors of obesity hypoventilation syndrome in a large sample of Saudi patients with obstructive sleep apnea. Saudi medical journal. 2015;36(2):181–9.
4. Harada Y, Chihara Y, Azuma M, Murase K, Toyama Y, Yoshimura C, et al. Obesity hypoventilation syndrome in Japan and independent determinants of arterial carbon dioxide levels. Respirology. 2014 Nov 1;19(8):1233–40.
5. Castro-Ãón O, De Llano LAP, De La Fuente Sánchez S, Golpe R, Marote LM, Castro-Castro J, et al. Obesity-Hypoventilation Syndrome: Increased Risk of Death over Sleep Apnea Syndrome. PLoS ONE. 2015 Feb 11;10(2):e0117808.
6. Sowho M, Amatoury J, Kirkness JP, Patil SP. Sleep and respiratory physiology in adults. Clinics in chest medicine. 2014;35(3):469–81.
7. Pulmonary Compliance - StatPearls - NCBI Bookshelf [Internet]. [cited 2024 Jul 20]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538324/
8. Casha AR, Caruana-Gauci R, Manche A, Gauci M, Chetcuti S, Bertolaccini L, et al. Pleural pressure theory revisited: a role for capillary equilibrium. Journal of Thoracic Disease. 2017 Apr 1;9(4):979.
9. Respiratory Failure in Adults - StatPearls - NCBI Bookshelf [Internet]. [cited 2024 Jul 20]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526127/
10. Matthay MA, Zemans RL, Zimmerman GA, Arabi YM, Beitler JR, Mercat A, et

al. Acute respiratory distress syndrome. Nature Reviews Disease Primers 2019 5:1. 2019 Mar 14;5(1):1–22.

11. Lamba TS, Sharara RS, Singh AC, Balaan M. Pathophysiology and Classification of Respiratory Failure. Critical care nursing quarterly. 2016;39(2):85–93.
12. González BNO, Plascencia NR, Zapata JAP, Domínguez AEL, González JSR, Diaz JM, et al. Obesity hypoventilation syndrome, literature review. SLEEP Advances. 2024 Jan 1;5(1).
13. de Athayde RAB, Filho JRB de O, Filho GL, Genta PR. Obesity hypoventilation syndrome: A current review. Jornal Brasileiro de Pneumologia. 2018;44(6):510–8.
14. Sunwoo BY. Obesity Hypoventilation: Pathophysiology, Diagnosis, and Treatment. Current Pulmonology Reports 8. 2019 Apr 11;8(2):31–9.
15. Bingol Z, Pıhtılı A, Cagatay P, Okumus G, Kıyan E. Clinical predictors of obesity hypoventilation syndrome in obese subjects with obstructive sleep apnea. Respiratory care. 2015 May 1;60(5):666–72.
16. Utpat K, Desai U, Joshi JM, Bharmal RN. Obesity Hypoventilation Syndrome: New Insights in Diagnosis and Management. Indian Journal of Sleep Medicine. 2020;
17. Rubin R, Fields AM. Pickwickian Syndrome. Essence of Anesthesia Practice E-Book. 2024 Feb 3;291.
18. Neves JAS, Fernandes APA, Tardelli MA, Yamashita AM, Moura SMPGT, Tufik S, et al. Cutoff points in STOP-Bang questionnaire for obstructive sleep apnea. Arquivos de neuro-psiquiatria. 2020 Sep 1;78(9):561–9.
19. Kaw R, Bhateja P, Mar HP, Hernandez A V., Ramaswamy A, Deshpande A, et al. Postoperative Complications in Patients With Unrecognized Obesity Hypoventilation Syndrome Undergoing Elective Noncardiac Surgery. Chest. 2016 Jan 1;149(1):84–91.
20. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European Heart Journal. 2016 Jul 14;37(27):2129–200.
21. Pieske B, Tschöpe C, De Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). European heart journal. 2019 Oct 21;40(40):3297–317.
22. Terla V, Rajbhandari GL, Kurian D, Pesola GR. A Case of Right Ventricular Dysfunction with Right Ventricular Failure Secondary to Obesity

Hypoventilation Syndrome. The American Journal of Case Reports. 2019;20:1487.

23. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European Respiratory Journal. 2015 Oct 1;46(4):903–75.
24. Almeneessier AS, Nashwan SZ, Al-Shamiri MQ, Pandi-Perumal SR, BaHammam AS. The prevalence of pulmonary hypertension in patients with obesity hypoventilation syndrome: a prospective observational study. Journal of Thoracic Disease. 2017 Mar 1;9(3):779.
25. Alawami M, Mustafa A, Whyte K, Alkhater M, Bhikoo Z, Pemberton J. Echocardiographic and electrocardiographic findings in patients with obesity hypoventilation syndrome. Internal medicine journal. 2015 Jan 1;45(1):68–73.
26. Oldroyd SH, Manek G, Bhardwaj A. Pulmonary Hypertension. StatPearls. 2024 May 1;
27. Held M, Walthelm J, Baron S, Roth C, Jany B. Functional impact of pulmonary hypertension due to hypoventilation and changes under noninvasive ventilation. The European respiratory journal. 2014 Jan 1;43(1):156–65.
28. Ojeda Castillejo E, de Lucas Ramos P, López Martin S, Resano Barrios P, Rodríguez Rodríguez P, Morán Caicedo L, et al. Noninvasive mechanical ventilation in patients with obesity hypoventilation syndrome. Long-term outcome and prognostic factors. Archivos de bronconeumologia. 2015 Feb;51(2):61–8.
29. Masa JF, Corral J, Alonso ML, Ordax E, Troncoso MF, Gonzalez M, et al. Efficacy of Different Treatment Alternatives for Obesity Hypoventilation Syndrome. Pickwick Study. American journal of respiratory and critical care medicine. 2015 Jul 1;192(1):86–95.
30. Mokhlesi B, Masa JF, Afshar M, Balachandran JS, Brozek JL, Dweik RA, et al. Evaluation and Management of Obesity Hypoventilation Syndrome. An Official American Thoracic Society Clinical Practice Guideline. https://doi.org/101164/rccm201905-1071ST. 2019 Aug 1;200(3):E6–24.
31. Masa JF, Mokhlesi B, Benítez I, Gomez de Terreros FJ, Sánchez-Quiroga MÁ, Romero A, et al. Long-term clinical effectiveness of continuous positive airway pressure therapy versus non-invasive ventilation therapy in patients with obesity hypoventilation syndrome: a multicentre, open-label, randomised controlled trial. The Lancet. 2019 Apr 27;393(10182):1721–32.
32. Xu J, Wei Z, Li W, Wang W. Effect of different modes of positive airway pressure treatment on obesity hypoventilation syndrome: a systematic review and network meta-

analysis. Sleep Medicine. 2022 Mar 1;91:51–8.

33. Kakazu MT, Soghier I, Afshar M, Brozek JL, Wilson KC, Masa JF, et al. Weight loss interventions as treatment of obesity hypoventilation syndrome: A systematic review. Annals of the American Thoracic Society. 2020 Apr 1;17(4):492–502.
34. Masa JF, Mokhlesi B, Benítez I, Mogollon MV, De Terreros FJG, Sánchez-Quiroga MÁ, et al. Echocardiographic Changes with Positive Airway Pressure Therapy in Obesity Hypoventilation Syndrome. Long-Term Pickwick Randomized Controlled Clinical Trial. American journal of respiratory and critical care medicine. 2020 Mar 1;201(5):586–97.
35. Manthous CA, Mokhlesi B. Avoiding management errors in patients with obesity hypoventilation syndrome. Annals of the American Thoracic Society. 2016 Jan 1;13(1):109–14.
36. Al-Abri MA, BaHammam AS. Noninvasive Ventilation in Obesity Hypoventilation Syndrome: What Practitioners Need to Know? Sleep and Vigilance. 2023 Dec 1;7(2):219–30.
37. Kreivi HR, Itäluoma T, Bachour A. Effect of ventilation therapy on mortality rate among obesity hypoventilation syndrome and obstructive sleep apnoea patients. ERJ Open Research. 2020 Apr 1;6(2).