# Obesity Hypoventilation Syndrome: A Review for Primary Care

**Jeffrey Thomas Budd, MD**

**ABSTRACT:** Obesity hypoventilation syndrome (OHS) is a potentially unrecognized complication of obesity that carries a significant health care burden and worrisome morbidity and mortality rates. OHS appears to be a result of an increased respiratory load from obesity and a lack of a fully compensatory increase in respiratory drive. Cardiovascular and metabolic comorbidities associated with OHS increase health care consumption and worsen patient outcomes. The diagnosis is made in a patient with a body mass index of 30 kg/m$^2$ or greater with documented daytime hypercapnia and sleep-disordered breathing. The diagnosis should be considered for any patient with obesity who has hypersomnolence, changes in cognitive function, headache, peripheral edema, or cor pulmonale, and for any patient with obesity who is hospitalized for acute on chronic hypercapnic respiratory failure. Treatment includes positive airway pressure and weight loss.

**KEYWORDS:** Obesity, obesity hypoventilation syndrome, hypercapnia, obstructive sleep apnea, sleep-disordered breathing, positive airway pressure, weight loss

Obesity hypoventilation syndrome (OHS) is the finding of reduced alveolar gas exchange during the daytime in a person with obesity and coexisting sleep-disordered breathing (SDB). It is a carryover of impaired nocturnal respiration into waking hours. **Figure 1** summarizes the definition of OHS. In most patients (90%) with OHS, the sleep component is obstructive sleep apnea (OSA), with the remainder having nonobstructive sleep hypoventilation.[1] Nearly 70% of patients with OHS have severe OSA at more than 30 apneic events per hour.[2]

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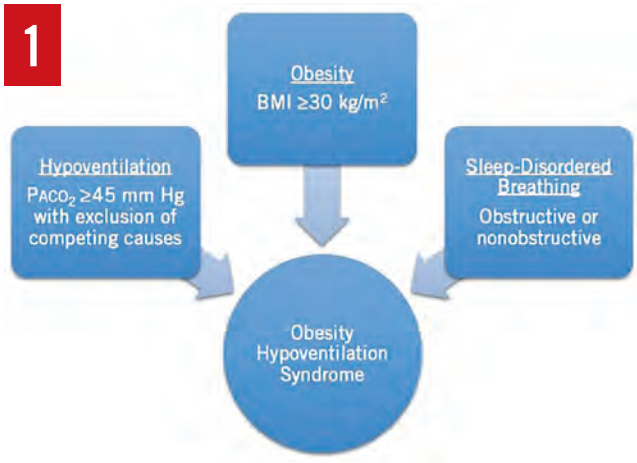
OHS is an often underrecognized complication of obesity that undoubtedly will increase in prominence as the prevalence of obesity increases.

Obesity has become a worldwide pandemic, nearly tripling in prevalence in the past 4 decades.[3] Almost 40% of the global population is overweight (body mass index [BMI] ≥25 kg/m$^2$), and 13% of the global population is obese (BMI ≥30 kg/m$^2$). Obesity is now responsible for greater mortality globally than malnutrition and being underweight.[3] In the United States, the prevalence is considerably worse than this global average, with 70.2% of the US population overweight, 37.7% obese, and 7.7% extremely obese (BMI ≥40 kg/m$^2$).[4]

OHS often appears to be misdiagnosed, not identified when present, or not properly treated when found. Surprisingly, an estimated 75% of patients in intensive care units (ICUs) with hypercapnic respiratory failure from OHS may be misdiagnosed and treated as having chronic obstructive pulmonary disease (COPD) or asthma.[5] And, 43% of all hospitalized patients with OHS exacerbations may be misdiagnosed as having COPD.[6] Only 13% of discharged patients meeting the diagnostic criteria for OHS are recognized and discharged with a treatment plan.[7] Unfortunately, most patients with OHS are undiagnosed or are diagnosed late in the course of disease, with delayed initiation of effective treatment.[2,8]




Definition of OHS

## EPIDEMIOLOGY AND COMORBIDITIES

The prevalence of OHS in the United States is estimated to be 0.15% to 0.3% of the general population,[9] but the prevalence is nearly 20% in patients with OSA[10] and is 8% to 20% among patients with obesity referred to sleep centers.[2] As would be expected, the prevalence of OHS correlates with BMI and severity of obesity. In non-Asian patients, the prevalence is approximately 10% in those with a BMI between 30 and 35 kg/m$^2$, doubles or even triples to 18% to 31% in those with a BMI of 40 kg/m$^2$ or greater, and may represent half of those with a BMI of 50 kg/m$^2$ or greater.[10]

The average age at diagnosis is from 50 to 60 years.[1] Interestingly, despite the male predominance in patients with OSA, no gender predominance is seen with OHS.[11] OHS may appear at a lower BMI in Asian persons than in White persons; otherwise, there is no clear racial or ethnic variation in prevalence.[1]

Comorbidities in patients with OHS are associated with increased health care consumption and negative outcomes.[11] Cardiovascular and metabolic diseases appear to be the most influential.[11,12] Endothelial dysfunction[13] and increased sympathetic activity from sustained hypoxia and hypercapnia[14] may be responsible for the increased cardiovascular risk. And, insulin resistance seen in patients with OHS may be largely responsible for increased metabolic disease.[13] The estimated prevalence of hypertension in patients with OHS ranges from 55% to 88%.[11] Pulmonary hypertension is likely a direct consequence of chronic hypoventilation and is present in 50% of patients with OHS.[11]

## IMPACT AND PROGNOSIS

Because obesity is associated with numerous serious medical conditions requiring hospital admission, the prevalence in OHS in hospitalized patients is likely greater than in the general population.[6] In fact, 30% of hospitalized patients with a BMI greater than 35 kg/m$^2$ on internal medicine services,[7] and nearly 8% of all admissions to an intensive care service,[5] may have OHS.

Quality of life scores for patients with OHS are worse than those for patients with obesity and pure OSA (OSA without OHS).[15] OHS also consumes health care resources. Patients with OHS have nearly twice the number of medical office visits per year and more hospital admissions than patients with obesity without OHS.[16] The 5-year mortality rate is 16%, which is 3 times that of patients with pure OSA.[17] Mortality rates for hospitalized patients after discharge may be nearly 23% at 18 months[7] and 31% at three years.[6] Cardiovascular comorbidities appear to be key factors in mortality.[8] Patients with OHS have twice the risk of a cardiovascular event than those with pure OSA.[17]

## PATHOPHYSIOLOGY

The underlying pathophysiology of OHS is incompletely understood, but it appears to result from an obesity-mediated increase in the mechanical load of breathing coupled with an impaired compensatory respiratory response.[13] Obesity increases airway resistance and hinders respiratory compliance through fat accumulation around the ribs, diaphragm, and abdomen.[18] Furthermore, respiratory muscles are weakened by overstretching.[18]

Although these mechanical changes are present in all patients with obesity, not all obese patients develop OHS as a result of a compensatory increase in respiratory drive. For unclear reasons, patients with OHS appear to have an impaired central respiratory response to hypercapnia.[1] Leptin produced in adipose tissue appears to stimulate respiratory drive and to be a component in a typical compensation seen in obesity,[1] and resistance to leptin may play a role in the development of OHS.[19-21] Patients with OHS are capable of voluntarily hyperventilating to eucapnia.[22] Treatment with nocturnal positive airway pressure (PAP) appears to correct the deficient respiratory drive.[23]

## CLINICAL PRESENTATION

The clinical presentation of OHS can be indolent with gradual development of hypersomnolence, changes in cognitive function, headache, hypertension, peripheral edema, and heart failure.[24] Patients with OHS are more likely to report dyspnea and to have cor pulmonale than those with pure OSA.[10] Sometimes the presentation can be nonspecific, and the diagnosis should be considered for patients with obesity and with worsening dyspnea or somnolence, normal chest radiography findings, and no history of tobacco smoking.[24] A common presentation at time of diagnosis is an admission to an ICU for acute-on-chronic exacerbation with respiratory acidosis.[1]

## DIAGNOSIS

Early recognition and treatment of OHS is critical to improve outcomes.[2] **Figure 2** summarizes the diagnostic pathway for OHS.

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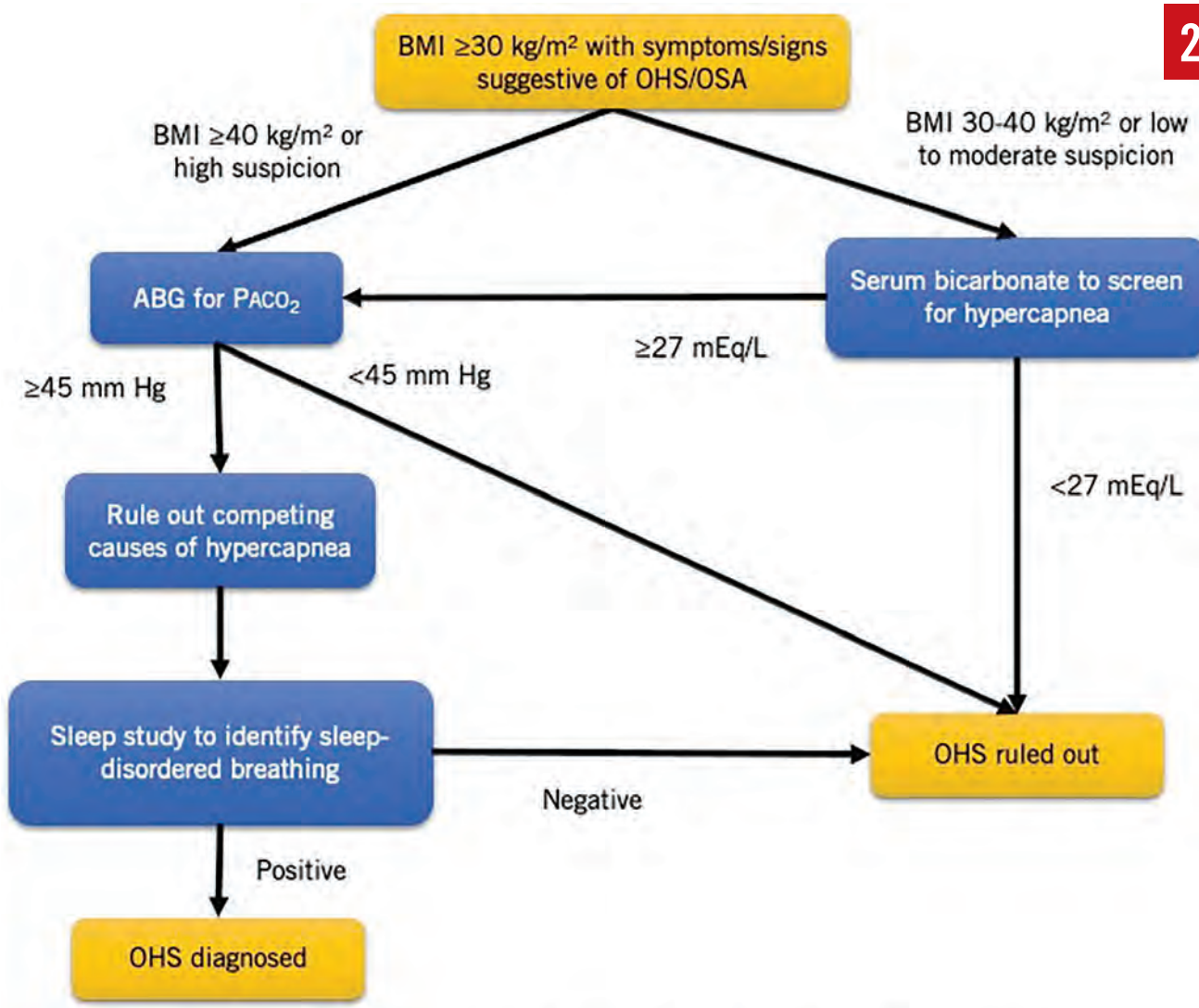


Diagnosis of OHS

The first step after recognition of potential signs and symptoms in a patient with obesity is to assess for hypercapnia. In patients at high risk (BMI ≥40 kg/m$^2$ with symptoms of SDB) measurement of $P_{ACO_2}$ by arterial blood gas (ABG) is recommended as this first step.[2] Because obtaining an ABG is not common practice in an ambulatory clinic setting and can be difficult to coordinate, the serum bicarbonate level can be used for screening low- to moderate-risk patients (BMI <40 kg/m$^2$).[2] When the serum bicarbonate level is less than 27 mEq/L, OHS is unlikely, and coordinating an ABG is not necessary.[2] However, an ABG should be considered for patients with a serum bicarbonate level of 27 mEq/L or greater.[2]

After confirming hypercapnia, the next step is to rule out any other potential causes of hypercapnia, including severe COPD, interstitial lung disease, chest wall disorders such as kyphoscoliosis, and severe hypothyroidism.[1,11] After obtaining a history and conducting a physical examination, the workup may include pulmonary function testing, chest radiography, and assessment of thyrotropin levels. The final step in the diagnosis of OHS is a sleep study to evaluate for SDB.

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## TREATMENT

The timing of OHS recognition and treatment initiation is important. Early treatment initiation may avoid hospital readmissions, ICU admissions for acute-on-chronic respiratory failure, and even death.[1] PAP is the cornerstone of treatment, because it improves responsiveness to hypercapnia,[25,26] hypoxia,[27,28] daytime sleepiness and dyspnea,[29,30] and survival.[31] PAP also reduces the number of hospitalizations[16,32] and the occurrence of pulmonary hypertension.[33] Approximately 40% of patients with combined OSA and OHS require supplemental oxygen with PAP to maintain oxygen saturations greater than 90% despite relief of obstruction.[34]

PAP needs to be initiated immediately, preferably even within an hour of presentation to an emergency department, for patients with acute exacerbations of OHS.[11] Thereafter, PAP should be continued as much as tolerated during the first 24 hours following admission. Then the patient can be weaned from it during daytime hours as respiratory acidosis resolves but continued on PAP nocturnally.[11] Coordination of discharge with PAP is critical, because the 3-month mortality rate is nearly 17% in patients discharged without PAP compared with 2% for patients discharged with PAP.[2] Patients can be discharged with hospital PAP settings until further outpatient workup and titration can be completed.[2]

Weight loss is also an important component of OHS treatment, because obesity is the crucial modifiable determinant for the development and severity of OHS.[2] Losses of 25% to 30% of body weight have potential for clinically meaningful reduction or even resolution of hypoventilation.[2] Cardiovascular morbidity and mortality persist in patients with OHS despite adequate treatment with PAP but can improve with weight loss.[2] Physical rehabilitation and weight loss can also lead to improved exercise capacity and improved quality of life.[35] Bariatric surgery appears to be more effective than nonsurgical therapy for sustained weight reduction and improvement of obesity comorbidities in general,[36] including OHS.[2]

Some common avoidable mistakes in the management of OHS include the misdiagnosis and treatment of hypercapnia associated with OHS as COPD; excessive oxygen supplementation leading to worsening hypercapnia; over-diuresis for peripheral edema that worsens metabolic alkalosis, leading to worsening hypoventilation; and overuse of sedating or psychiatric medications that exacerbate SDB and worsen hypercapnia.[37]

## SUMMARY

Primary care providers need to be aware of several key points about OHS. First, OHS is increasing in prevalence along with the global increase in obesity. Patients with severe obesity are at highest risk. Second, OHS is responsible for considerable health care costs, morbidity, and mortality. Third, the presentation may be indolent at first and difficult to identify. OHS is often unrecognized or diagnosed late in its course. A patient who is obese, especially one with a BMI of 40 kg/m$^2$ or greater, with hypersomnolence, headache, worsening cognitive status, dyspnea on exertion, excessive snoring, or suggestion of cor pulmonale should be worked up for OHS. A common initial presentation is hospitalization of a patient with obesity for hypercapnic respiratory failure. Unfortunately, this is often misdiagnosed as a COPD exacerbation. Fourth, after hypercapnia is demonstrated in a patient with a BMI of 30 kg/m$^2$ or greater, a patient should be referred to a sleep clinic to demonstrate SDB, complete the diagnosis, and start treatment. Lastly, prompt treatment with PAP is decisive in improving outcomes. When diagnosed during a hospitalization, discharge planning to complete the workup and continue PAP is essential. Weight loss and lifestyle changes are important to mitigate cardiovascular comorbidity. ■

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