Controversies in Sleep Apnea

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KEYWORDS

• OSA • obstructive sleep apnea • AHI • MMA • CPAP • PSG • MARPE • DOME

KEY POINTS

- Nocturnal Polysomnography (PSG) is considered the gold standard for diagnosing OSA.
- CPAP is the most commonly used treatment modality for OSA.
- OSA is the most prevalent sleep disorder, with incidence and prevalence on the rise.
- Increasing prevalence of OSA is due to rising obesity rates, aging populations, and increased awareness and detection rates.
- Face-to-face evaluation by a sleep medicine physician is essential for making OSA diagnosis.

INTRODUCTION

Sleep Apnea is a prevalent and multifaceted sleep disorder affecting millions worldwide. In fact, sleep apnea is the most common respiratory disorder of sleep (Faria and colleagues, 2021).[1] This condition is characterized by recurring episodes of partial or complete upper airway obstruction during sleep, resulting in a reduction in oxygen saturation, sleep fragmentation, and arousals. Morbidity frequently associated with OSA includes hypertension, coronary artery disease, obesity, and diabetes. Impacts of OSA on an individual's quality of life can have detrimental effects on their daily activities. Reported negative effects on daily life include sleepiness, impaired memory, attention, and cognitive function. In 2019, a study deduced that the prevalence of obstructive sleep apnea was estimated at 936 million for severe OSA and 425 million for moderate OSA globally.[2] Sleep apnea has been reported to have been the cause of 810,000 collisions and 1400 fatalities from car crashes in the United States.[1] Currently several nonsurgical and surgical therapeutic modalities exist. Conservative measures

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include oral mandibular advancement appliances, continuous positive airway pressure (CPAP) and diet modifications. Surgical treatment focus on modifying the soft tissue anatomy of the oropharynx, hypoglossal nerve stimulators or weight loss therapy such as bariatric surgery. Current treatment efforts often involve more than one provider and often providers have conflicting opinions on treatment strategies which may make treatment challenging and controversial. To muddy the water further, OSA is associated with a wide range of vague symptoms and objective parameters used for diagnosis (polysomnography) can be difficult to detect and analyze. It is important to focus on evidence-based treatment. The purpose of this paper is to provide a evidence based review of the current therapeutic treatment options for patients suffering from OSA. A particular focus will be placed on surgical options.

Apnea is defined as a complete pause or cessation of breathing, lasting for several seconds to over a minute, whereas hypopnea is defined as an overall partial reduction in airflow during sleep.[3] It is important to first define and distinguish between the two primary categories of sleep apnea: Obstructive Sleep Apnea (OSA) versus Central Sleep Apnea (CSA). Central Sleep Apnea is less common than OSA but is associated with the higher mortality rates. Per 100 people, in moderate and severe OSA, patients had a mortality rate of 9.36 and 13.11 respectively, compared to 11.47 and 15.59 in CSA.[4] In comparison, CSA can be characterized as a failure of ventilatory motor output via absence of nerve signals to thoracic muscles of inspiration, such as the diaphragm and the intercostal muscles, as well as the genioglossus muscle.[5,6] Central sleep apnea can result from damage to the respiratory centers such as from a stroke or heart failure. Certain medications such as opioids and benzodiazepines can have central apnea-like effects depressing the respiratory drive and suppressing the body's ability to respond to increased levels carbon dioxide.[7] Depending on the underlying cause and specific characteristics of the breathing disturbance, the pathophysiology of CSA can be further categorized as non-hypercapnic or hypercapnic. Non-hypercapnic CSA is marked by ventilatory instability due to high loop gain. In this context, "loop gain" refers to the relationship between the body's respiratory control system and its response to changes in oxygen and carbon dioxide levels. A high loop gain means that the body's response to these changes is exaggerated, leading to excessive fluctuations in breathing during sleep. Non-hypercapnic CSA is often seen in individuals with heart failure and other cardiovascular diseases. Hypercapnic CSA, on the other hand, is primarily a disorder of hypoventilation, meaning that the individual is not breathing enough to adequately remove carbon dioxide from the body. This can result in a buildup of carbon dioxide in the bloodstream, which can have serious health consequences. Hypercapnic CSA is often seen in individuals with chronic obstructive pulmonary disease (COPD) or other respiratory disorders that impair lung function.[8]

Obstructive Sleep Apnea is caused by an anatomic obstruction of the upper airway during sleep, typically due to relaxation of the parapharyngeal muscles and tongue. This obstruction leads to a cessation of breathing with resulting desaturation. In response to the decrease in oxygen saturation, there is a subsequent sympathetic response with catecholamine release triggering a microarousal facilitating a breath. OSA is increasingly prevalent in the population with recent estimates of as many as 1 billion adults between the ages of 30 to 69 worldwide. OSA is often associated with obesity, increasing age, and certain upper airway anatomic features such as enlarged neck circumference (>16 inches for women, >17 inches for men), macroglossia, tonsillar hypertrophy, an enlarged or elongated uvula (>35 mm), retrognathia, a high or arched palate, a Mallampati score of 3 or 4, nasal septum deviation or polyps, mandible to hyoid distance of 17 mm.[9,10]

Of note, it is also important to distinguish OSA from Upper Airway Resistance Syndrome (UARS). Since UARS was first diagnosed in the early 1990's, there has been debate over whether it is merely a part of the same spectrum as OSA and therefore not a distinct diagnosis. However, the current available evidence now supports the argument that suggests that UARS is, in fact, a distinct clinical phenomenon and should not be considered merely as a milder form of OSA.[11] UARS is characterized by repeated increases in the resistance of airflow in the upper airway, which causes a subsequent increase in respiratory effort, causing brief awakenings. These awakenings are known as respiratory effort-related arousals (RERAs) and are identified by a shift in alpha or fast theta frequency on the electroencephalogram (EEG), lasting from 3 to 10 seconds. RERAs differ from apneas or hypopneas, as they do not involve complete cessation of airflow or oxygen desaturation and are typically shorter in duration, comprising only one to three breaths. Additionally, patients with UARS have an apnea-hypopnea index (AHI) of less than five, which, would not meet the criteria for apneas or hypopneas.

Detection and treatment go hand-in-hand when diagnosing and treating OSA. Nocturnal Polysomnography (PSG) is considered the gold standard for diagnosis. It requires an overnight stay in a sleep lab and involves the use of various sensors to monitor brain activity, eye movement, heart rate, and breathing patterns. Essential to PSG studies are measurements via electrocardiograph (ECG), electroencephalogram (EEG), electro-oculogram (EOG), chin and limb electromyogram (EMG), and measurements of airflow signals, respiratory effort signals, oxygen saturation and body position. Though not required for essential PSG, some laboratories will also perform capnography studies to measure hypoventilation.[12] The second method is Home Sleep Apnea Testing (HSAT), which involves the use of a portable device to monitor breathing patterns and blood oxygen levels while the individual sleeps at home. The third method is the use of questionnaires and symptom assessments to identify potential sleep apnea symptoms such as snoring, daytime fatigue, and gasping for air during sleep. The fourth method is physical examination to identify anatomic abnormalities in the airway that may contribute to OSA. The fifth primary method is the use of smartphone apps and wearable devices that monitor sleep patterns and breathing during sleep. These methods can be used alone or in combination to detect OSA. These detection methods are important for identifying OSA and determining the appropriate treatment plan. A meta-analysis compared all currently available detection methods for OSA against PSG, finding PSG as a superior detection method to all, in its accuracy.[13]

With regards to treatment modalities, the most used treatment is Continuous Positive Airway Pressure (CPAP) therapy, achieving approximately 73% improvement in AHI, according the sleep foundation's analysis of available publications.[14,15] which involves wearing a mask over the nose and/or mouth during sleep, delivering a continuous flow of air to keep the airway open. Oral appliances are custom-made devices that position the jaw forward to help keep the airway open. The mechanics are thought to help with improving the diameter of the retroglossal space. Advancing the genial tubercule advances the tongue improving the posterior airway space. Surgery is another option for patients where CPAP and oral appliances are not effective or well-tolerated. Common surgical procedures include uvulopalatopharyngoplasty (UPPP), maxillomanibular advancement surgery, and genioglossus advancement. Additionally, surgical implantation of a nerve stimulation device, namely, the Inspire device, is also a less invasive surgical option. Weight loss is another option as obesity is a major risk factor for OSA, which has been shown to significantly improve AHI and symptoms in some patients. Longitudinal studies demonstrated that a weight gain of

10% over a period of 4 years is correlated with a 32% increase in AHI, and conversely, a reduction in weight of 10% is associated with a 26% decrease in AHI.[16] Lastly, positional therapy can help reduce symptoms of OSA, where sleeping in a different position, such as sleeping on one's side, may prevent the tongue and soft palate from collapsing into the airway.[17]

Despite the availability of several diagnostic and treatment modalities, there are still controversies regarding the optimal approach to diagnosing and treating OSA. A primary discussion surrounds the use of HSAT versus PSG. While HSAT is more convenient and cost-effective, some studies suggest that it may underestimate the severity of OSA compared to PSG. Another controversy surrounds the use of surgical versus non-surgical treatment options for OSA. While surgery may be effective in some patients, there is concern about the potential risks and complications associated with these procedures. Finally, there is controversy regarding the effectiveness of newer treatment modalities, such as hypoglossal nerve stimulation, in comparison to more established treatments like CPAP.[18] Overall, the controversies in diagnosing and treating OSA highlight the need for further research and individualized approaches to patient care and will be further discussed in this chapter.

EPIDEMIOLOGY OF OSA

It is widely posited that OSA poses significant health risks, specifically, linking it to increased risks of hypertension, stroke, myocardial infarction, diabetes, depression, anxiety, and cognitive impairment.[19] In addition, untreated OSA can lead to daytime fatigue, reduced productivity, and an increased risk of car accidents. However, despite the significant increase in the annual research publications attesting to the strong association between OSA and coronary artery disease, hypertension, heart failure and arrhythmias, whether or not OSA lies along the causal pathway to these conditions is not yet proven.[20,21]

Though OSA is already the most prevalent sleep disorder in the world, affecting millions of people worldwide, its incidence and prevalence continue to climb.[2] In North America, it is currently assumed that this is likely due to rising obesity rates, aging populations, and increased awareness and detection rates. Globally, it is estimated that 936 million people worldwide have mild to severe OSA, and 425 million people worldwide have moderate to severe OSA, between the ages of 30 and 69 years of age.[2] The condition is particularly prevalent in Western countries, where sedentary lifestyles and unhealthy diets are contributing to high rates of obesity and other metabolic disorders.[22]

Despite the high prevalence of sleep apnea, there is a general lack of awareness among the public about its serious health consequences. Many individuals who experience symptoms of sleep apnea, such as snoring, daytime fatigue, and gasping for air during sleep, may not recognize these as potential signs of a sleep disorder.[1] This perception is concerning as it may prevent individuals from seeking medical consultation, delaying diagnosis and treatment of OSA. As such, the timely and effective treatment of OSA is crucial for improving patients' health outcomes and quality of life, in addition to making a substantial socioeconomic impact.

CONTROVERSIES OF DIAGNOSIS

The World Sleep Society (WSS) and the American Academy of Sleep Medicine (AASM) provided recommendations and subsequent caveats to those recommendations for detecting OSA in clinical practice. In general, according to both organizations, clinical testing for OSA should be performed along with a thorough diagnostic test for OSA in adult patients who are suspicious for OSA based on clinical exam. The WSS advises that medical supervision of the diagnostic and treatment process are crucial, and clinicians must be aware of the advantages and limitations of HSATs and limited-channel sleep tests. The WSS also recommends that clinicians reassess the clinical assessment before further testing and prioritize PSG where available. However, if PSG is not an option, a higher-level limited channel test should be performed.[23] Testing may include or be limited to any or all the following: PSG (Type 1 testing), unattended HSAT (Type 2 testing), or cardiorespiratory polygraphy (Type 3 testing). The WSS recommends that medical professionals oversee the diagnostic and treatment process and have a clear understanding of the advantages and limitations of HSAT and limited channel sleep tests. They also advise caution when using limited, single-channel Type 4 tests (such as oximetry) as this requires a high level of clinical proficiency to determine the appropriate testing group and interpret the results (Table 1).

Due to the high prevalence of OSA, there is potential for substantial monetary strain on healthcare systems at large linked to conducting PSG for all patients suspicious for OSA. Additionally, in certain regions, in-laboratory testing may not be readily available. HSAT, despite its drawbacks, is a substitute method for diagnosing OSA in adults and may be less expensive and more practical in certain populations. However, HSAT may present certain drawbacks due to differences in which physiologic parameters are being measured and the availability of healthcare personnel to make sensor adjustments overnight as needed. The type and quantity of sensors utilized by HSAT devices can also vary significantly. Presently, sleep studies are classified as Type I, II, III, and IV, with unattended studies being categorized under Types II, III, and IV. Type II studies and PSGs utilized the same sensors, with the difference being that the patient is left unattended in type II studies (Table 2). In Type III studies, sensors will measure a restricted number of cardiopulmonary parameters, including at least two respiratory variables, such as effort to breathe and airflow, a cardiac variable, such as heart

Table 1
Primary detection methods of sleep apnea

Primary Detection Methods	Description
1. Nocturnal Polysomnography	Comprehensive sleep study that measures various physiologic variables during sleep, including airflow, respiratory effort, oxygen saturation, and brain wave activity. Considered gold standard for OSA Diagnosis.
2. Home Sleep Apnea Testing	Portable devices that monitor breathing patterns, oxygen levels, and heart rate during sleep. Less expensive and more convenient than PSG, but it may not be as accurate in detecting mild or positional OSA.
3. WatchPAT	Portable diagnostic device that measures peripheral arterial tone, heart rate, oxygen saturation, and body position to detect OSA. It is a simplified version of HSAT.
4. Clinical evaluation	Evaluate a patient's symptoms, medical history, and physical exam. However, clinical evaluation alone is not as reliable as NPSG or HSAT.
5. Questionnaires	Patients may be asked to fill out questionnaires, such as the Epworth Sleepiness Scale or the Berlin Questionnaire, to assess their risk for OSA. These questionnaires are not diagnostic tools but may be useful for identifying patients who need further evaluation.

Table 2
Sleep study types, excluding SCOPER classification system

Sleep Study Types	Monitoring Parameters	Advantages	Disadvantages
Type I	Full PSG monitoring sensors	High diagnostic accuracy	Costly, time-consuming, requires trained staff
Type II	Same monitoring sensors as Type I but unattended	Performed outside sleep laboratory, less expensive	Limited monitoring parameters, lack of real-time monitoring, inability to initiate CPAP
Type III	Limited cardiopulmonary parameters: 2 respiratory variables, O2 saturation, 1 cardiac variable	Easy to use, portable	No real-time monitoring, limited monitoring parameters, No CPAP
Type IV	Measures 1–2 parameters, typically oxygen saturation and heart rate, or in some cases, just airflow	Inexpensive, easy to use, portable	Limited monitoring parameters, lack of real-time monitoring, inability to initiate CPAP

rate, and oxygen saturation. Lastly, Type IV studies, which are the most restricted studies, are limited to measuring as few as 1 or 2 variables, such as heart rate and oxygen saturation, and in certain instances, merely a patient's airflow and nothing else.[23]

Compared to attended studies, the utilization of HSAT devices may heighten the risk of technical failures due to the absence of real-time monitoring by medical personnel and may also have intrinsic limitations stemming from the lack of capability of most devices to distinguish between the sleep state and waking states. Additionally, it is important to note that CPAP cannot be initiated with HSAT, in contrast to PSG, where CPAP can be administered if and when it is necessitated. Additionally, HSAT is associated with substantial measurement errors when compared to PSG since standard sleep staging channels, such as EEG, EOG, and EMG, are not typically monitored in HSAT. Due to this limitation, hypopneas that are only associated with cortical arousals cannot be detected. Also, from a logistical standpoint, measurement errors can arise due to sensor dislodgement and poor-quality signal during HSAT, which would not be noticed due to the lack of real-time personnel monitoring. These factors may lead to the underestimation of the actual Apnea-Hypopnea Index (AHI), an index used to indicate the severity of sleep apnea, and may necessitate repeat studies due to faulty data.[23]

Importantly, included in the battery of essential measurements of PSG, Electromyograms (EMGs) can be categorized into different types based on their purpose or technique. Needle EMG is a diagnostic test that involves inserting a needle electrode into a muscle to measure its electrical activity. Surface EMG is a non-invasive test that involves placing surface electrodes on the skin to measure the electrical activity of the muscles underneath. Single-fiber EMG is a diagnostic test that involves inserting a very fine needle electrode into a muscle to measure the electrical activity of individual muscle fibers. Repetitive nerve stimulation EMG is a diagnostic test that involves stimulating a nerve repeatedly and measuring the resulting muscle responses with surface electrodes. EMG can provide valuable information about muscle activity during different stages of sleep. During rapid eye movement (REM) sleep, muscle tone is typically relaxed, and the EMG activity is low, except for bursts of phasic activity during rapid eye movements. Alpha, beta, delta, and k-complex spindles can also be observed during sleep using EMG. Alpha activity is most observed during relaxed wakefulness and can also be seen during the transition to sleep. Beta activity is associated with wakefulness and is characterized by fast, low-voltage oscillations. Delta activity is associated with deep sleep and is characterized by slow, high-voltage oscillations. K-complexes are large, high-amplitude waves that are typically seen during non-rapid eye movement (NREM) sleep.[24,25] Sleep EEG characteristics associated with OSA include increased EEG power in certain frequency bands. These changes in EEG activity can indicate states of poor sleep quality in OSA patients. Ongoing studies are investigating EEG microstates that may serve as biomarkers to indicate OSA in patients.[26]

The AASM further conducted a review and analysis of all presently accepted, prominent OSA screening questionnaires and predictive models, including STOP-BANG and Epworth Sleepiness Scale (ESS). The STOP-BANG questionnaire is a widely-used screening tool used to assess the likelihood of a patient having obstructive sleep apnea (OSA). It consists of eight questions that ask about snoring, tiredness during the day, observed apneas, high blood pressure, body mass index (BMI), age, neck circumference, and gender. The ESS is a self-administered questionnaire that is also used to identify OSA, however, unlike STOP-BANG, ESS does not include metrics such as BMI, age, gender, and neck circumference. Compared to other screening tools for OSA, such as the ESS and the Berlin Questionnaire, the STOP-BANG questionnaire is more sensitive and specific. It has a higher positive predictive value for OSA and can accurately identify patients who are at a high risk of having OSA.[27]

The review then went on to compare STOP-BANG and ESS against PSG and HSAT regarding their diagnostic value. This review concluded that, by and large, clinical questionnaires, morphometric models, and clinical prediction rules paled in comparison in diagnostic power versus PSG or even HSAT. Although sensitivity levels were relatively high for these alternate predictive screening methods, they are not robust enough to effectively rule out OSA. Meanwhile, the low specificity led to the AASM's position that PSG or HSAT are required to make a definitive diagnosis of OSA, regardless of predictive screening tool results.[13]

Importantly, it is necessary to review the utility of radiological study of the airway to assist in diagnosis of OSA. 3D computed tomography (CT) imaging of the upper airway can help identify anatomic variations that may cause obstructions and can quantify anatomic dimensions of the airway that may be helpful in predicting at-risk patients for OSA. Presently, cone-beam computer tomography (CBCT), which is now routinely used in dental offices, has become a helpful tool in screening for patients who may be at risk for OSA. These radiographic tools can aid in the study of anatomic landmarks such as the mandibular plane to hyoid (MP-H) distance (15.4 ± 3 mm),[28] thickness of the soft palate, the diameter and area of the posterior airway space (PAS), as well as the volume of the tongue.[29,30]

Drug-induced sleep endoscopy (DISE) is another well-established diagnostic tool that has been increasingly utilized in clinical practice for evaluation of the upper airway. Specifically, DISE provides a dynamic assessment of the collapsibility of the upper airway and is performed under conscious sedation. The identification and characterization of specific sites of obstruction and the degree and pattern of collapse have important implications for the selection and planning of therapeutic interventions. This is particularly true in cases where CPAP or other conservative treatments have failed to provide adequate relief. The recorded findings of DISE are comprehensive and include documentation of the level, pattern, and degree of collapse observed, providing clinicians with valuable information to guide individualized treatment strategies for their patients. The precise characterization of airway obstruction through DISE may also aid in the development of new therapeutic modalities and further enhance the management of patients with sleep-disordered breathing.[31] Circumferential and anteroposterior (AP) collapse are two common types of airway collapse that occur in patients with sleep apnea. Circumferential collapse refers to the collapse of the upper airway in a circular or circumferential manner, typically involving the collapse of soft tissues such as the lateral walls of the pharynx, the tonsils, the base of the tongue, or the lateral pharyngeal walls. AP collapse refers to the collapse of the upper airway in an anteroposterior direction, often involving the posterior part of the tongue, the soft palate, or the base of the tongue. Treatment approaches for circumferential and AP collapse in sleep apnea aim to address the underlying causes of airway obstruction and may include CPAP therapy, oral appliances, weight loss, positional therapy, and surgical interventions. The specific treatment approach depends on the severity of the airway collapse and individual patient characteristics.

The Muller maneuver is an additional diagnostic technique commonly utilized to evaluate upper airway obstruction in patients with sleep apnea. This maneuver involves having the patient inhale to the maximum capacity and then exhale forcefully while the nose and mouth are closed. The resulting negative pressure in the upper airway can potentially aggravate any existing obstructions and cause a collapse of the airway, thereby reproducing the features of an apneic event. The Muller maneuver is a valuable tool for pinpointing the specific sites of airway obstruction and determining the extent of collapsibility, which can assist in determining the most appropriate treatment strategies for managing sleep apnea. However, when compared to DISE, there was a discrepancy between the incidence of severe retrolingual airway collapse in patients with OSA. Further research is needed to determine the source of this discrepancy (Soares and colleagues, 2013).[32]

It is important to define and delineate the role of Oral Surgeons and Dentist in diagnosis of OSA. Clarification has been provided via the publication of joint policy and practice guidelines by the AASM and the American Academy of Dental Sleep Medicine (AADSM), as well as a treatment protocol outlined by the AADSM. According to these guidelines and protocol, it is essential that patients receive a face-to-face evaluation by a sleep medicine physician to obtain a definitive diagnosis of OSA. While dentists certified by the American Board of Dental Sleep Medicine (ABDSM) may play a valuable role in the overall management of patients with OSA, they are not qualified to diagnose the condition themselves and must been evaluated by medical sleep specialists for definitive diagnosis.[33]

CONTROVERSIES OF MANAGEMENT

Several key issues lie at the center of ongoing debates regarding the management of OSA. These include uncertainty over the most appropriate initial therapy for mild to moderate OSA, with some advocating for CPAP as first-line treatment, and others suggesting alternative approaches such as oral appliances. Additionally, the role of surgery in managing severe OSA in patients who are intolerant or non-compliant with CPAP remains a topic of debate. Optimal follow-up protocols for patients undergoing OSA treatment, including the frequency and type of monitoring required, have yet to be agreed upon. Finally, it is increasingly recognized that individualized treatment plans that consider patient preferences, co-existing medical conditions, and other factors are important for achieving successful outcomes in OSA management[34] (**Table 3**).

Table 3
List of treatment modalities and subtypes

Treatment Modality	Types
Positive Air Pressure (PAP)	(1) Continuous PAP (2) Bi-level PAP (Bi-PAP)
Oral Appliance	(1) Tongue-retaining (2) Mandibular advancement
Surgery	(1) Phase I (nasal, palatal, tongue) (2) Phase II (maxillomandibular advancement)
Adjunctive	(1) Weight loss (medical, bariatric surgery) (2) Positional therapy (3) vNasal expiratory PAP (4) Noninvasive oral pressure therapy

FIRST-LINE MANAGEMENT

In contrast to other guidelines, according to the American Academy of Dental Sleep Medicine, it is reasonable to consider alternatives to CPAP therapy as a first-line treatment modality depending on the circumstances. For patients diagnosed with OSA, Oral Appliance Therapy (OAT) may be considered or recommended as a secondary option after other treatments, such as CPAP, have been unsuccessful. However, clinicians may even opt for referral for OAT as the first-line treatment. In a randomized crossover open label study, the efficacy of CPAP and MAD were compared over the course of 1 month of optimal treatment of OSA with CPAP, with optimal treatment being defined as achieving the greatest possible compliance and highest efficacy with each treatment under standard clinical conditions and practices. The study found that the two modalities were comparable in improving health outcomes for patients with OSA. In fact, the results showed that CPAP was more efficacious than MAD in reducing Apnea-Hypopnea Index (AHI) events (CPAP AHI, 4.5 $\pm$ 6.6/h; MAD AHI, 11.1 $\pm$ 12.1/h; $P < .01$), though compliance was greater with MAD (MAD, 6.50 $\pm$ 1.3 h per night vs CPAP, 5.20 $\pm$ 2 h per night; $P < .00001$).[35] OAT has been shown to have utility for patients with mild, moderate, and even severe OSA. Additionally, patients generally prefer OAT over CPAP therapy and are more likely to comply with treatment.[36] This also strongly suggests that patient preferences should be considered when recommending OSA therapy, given that patient compliance is instrumental in the treatment of OSA. However, it is worth noting that reported complaints are common for pain and/or discomfort in teeth, facial muscles, temporo-mandibular joint (TMJ), tongue, or other oral structures.[37]

At present, the use of CPAP therapy is widely accepted as the gold standard for treating Obstructive Sleep Apnea (OSA). However, the practicality of CPAP therapy and its impact on patient compliance must not be overlooked, as they can affect the success of OSA therapy. In a 2013 study by Vanderveken, it was found that OAT was as effective as CPAP therapy in reducing the AHI and improving subjective sleep quality.[36] They found that mean AHI (apnea-hypopnea index) decreased significantly from 18.4 $\pm$ 11.5 at baseline to 7.0 $\pm$ 6.5/h sleep with OA (oral appliance therapy), with a P-value of less than 0.001. The study also reported an OA efficacy of 56.0 $\pm$ 38.2% based on a sample size of 43 patients. This suggests that OA is an effective treatment for OSA, as it resulted in a significant reduction in AHI for most patients in the study. Subsequently, A previous study reported that patients with moderate OSA (defined as AHI between 15 and 30) who used CPAP (continuous positive airway pressure) for 4 hours per night saw a reduction in AHI ranging from 33.3% to 48.3%, with AHI scores ranging from 0 to 5. This suggests that CPAP is also an effective treatment for OSA, though it may be less effective than OA for some patients.[38,39]

Patients using OAT also reported fewer side effects than those using CPAP therapy. The study attributed these findings to differences in patient compliance, with patients using an oral appliance complying with the therapy 82% of the time, compared to considerably lower compliance rates for CPAP therapy. Over a period of 2 decades, from 1994 through 2015, CPAP compliance rates were found to be at a rate of 65.9%, with no trend of improvement in the compliance rate of CPAP over the course of that timeframe.[40] Furthermore, compliance appears not to be a static metric. In a 2015 paper by BaHammam et al., it was observed that adherence to CPAP sharply declined over the course of 10 months, with only one-third of OSA patients exhibiting good adherence even after receiving an educational intervention reinforcing compliance.[18] Long-term compliance with positive airway pressure therapy for OSA can vary widely, with rates ranging from 46% to 85%. According to a study published in the Journal of Sleep Medicine, in 2018, that measured CPAP compliance both with in-lab PSG and at home PSG monitoring, the mean CPAP use compliance was over 5 hours per night (5.8 ± 1.4 hours for at home PSG; 5.6 ± 1.3 hours for in-lab PSG), in more than 70% of days.[41] Patients often cite multiple impediments to complying with CPAP therapy, such as nasal discomfort, congestion, mask leaks, and claustrophobia, which can make therapy difficult to tolerate over extended periods.[42]

To complicate matters further, a randomized-controlled trial published in 2013 suggested that there was, in fact, no significant difference in compliance between CPAP and OAT.[35] However, the findings of this study did indicate that CPAP was more effective in reducing the AHI and resulted in higher levels of oxygen saturation in comparison to OAT. Additionally, CPAP was found to be more successful in treating patients with severe OSA. Nevertheless, oral appliance therapy remains a feasible alternative to CPAP, particularly when treating mild to moderate OSA. In patients with severe OSA who do not respond well to CPAP or have failed CPAP treatment attempts, oral appliances may be considered as a viable long-term option.

SURGICAL MANAGEMENT

In 2010, the American Academy of Sleep Medicine published its guidelines for how to treat OSA with surgical intervention. However, it failed to consider when and in what scenarios it is appropriate and beneficial to treat with various surgical interventions.[43] In 2021, The Journal of Sleep Medicine (JOSM) published a new proposed guideline to supplant the AASM's 2010 guideline by incorporating assertions for exactly when to opt for surgery and which surgical intervention is appropriate and why.[44]

As previously discussed, although CPAP is considered the most effective treatment for OSA when adhered to, some patients may have difficulties adhering to therapy or are unable to obtain optimal results with CPAP. As a result, although surgery may be considered a less effective treatment option, it could ultimately be a more effective solution in the long term due to its independence from compliance issues. The purpose of the JOSM's present guideline is to formulate a guideline that also incorporates patient-specific needs and preferences that evaluates the benefits, costs, risks, and potential adverse effects of different medical and surgical treatments. This guideline refers to existing evidence to endorse suggestions for considering surgical intervention based on the following 3 clinical situations: 1) Patients who are unable or unwilling to tolerate CPAP therapy; 2) Patients who exhibit ongoing inadequate CPAP adherence resulting from side effects associated with increased pressure; 3) Patients anatomic abnormalities of the upper airway that may be treatable with surgical intervention as a first-line approach to managing OSA.

Though many studies and reviews indicate the possible benefits of surgery for treatment of OSA in certain scenarios, controversy persists. The Annals of Internal Medicine offered a guideline in 2013 with regards to recommendations for surgical treatment of OSA. After their literature review of studies comparing control treatments to surgical interventions (UPPP, laser-assisted UPPP, radiofrequency ablation of inferior nasal turbinates, various combinations of pharyngoplasty, tonsillectomy, adenoidectomy, and genioglossal advancement septoplasty), there was insufficient data to support the superiority of surgical intervention as compared to control treatments.[45] As a follow-up to these guidelines, in 2019, Patel and colleagues published a review also in the Annals of Internal Medicine, expanding and commenting upon the Journal's previous recommendations. Their findings suggest that the role of surgical intervention in treating OSA is limited to certain patient populations with anatomic abnormalities that make it difficult to tolerate CPAP. In these cases, nasal procedures such as septoplasty or turbinate reduction can help increase tolerability in these patients. However, in the general OSA population, most surgeries to decrease upper airway collapsibility do not significantly reduce OSA severity or symptoms. For example, UPPP is a commonly known procedure for treating OSA, however, in the general OSA population it has been shown to have limited benefits, as fewer than half of patients experience a significant reduction in OSA severity over the long term. In contrast, there is some hope to be gleaned from the use of maxillomandibular advancement (MMA) in treating OSA. Though a highly invasive procedure with prolonged postoperative recovery, MMA has been shown to have a cure rate of over 90% for OSA, particularly in non-obese patients with retrognathia. Another emergent treatment modality is hypoglossal nerve stimulation, which has gained popularity due to its minimally invasive nature. However, though it does display high success rates in selected patients, it is recommended only for a patient with a body mass index (BMI) less than 32 kg/m2, in whom airway collapse in an anteroposterior direction can be seen under drug-induced sleep endoscopy (DISE).[10]

In a review published in 2009 by Powell of Stanford University, the data on the most performed surgical procedures for treating sleep apnea were reviewed. A protocol was developed for determining the appropriate surgical approach, which divided surgical procedures into 2 phases: Phase I, consisting of soft tissue procedures such as tonsillectomy, UPPP, and genioglossus advancement, and Phase II, consisting of the hard tissue procedure of Maxillomandibular Advancement (MMA). Phase I was further broken down by Dr. Fujita into 3 categories based on the level of upper airway obstruction: Type I, where the obstruction is at the retropalatal level, Fujita Type II, where the obstruction is at both the retropalatal and retrolingual levels, and Fujita Type III, where the obstruction is only at the retrolingual level. According to their findings, when Type I obstruction patients underwent UPPP soft tissue reconstruction surgery, a cure rate ranging from 80% to 90% was achieved. However, conversely, in patients with either Type II or Type III obstructions, that cure rate dropped to rates of only 5% to 30%. These data were compared to MMA surgery, which is a surgery of hard tissue. They found that Phase II MMA surgery achieved documented cure rates of 90% or greater. This is in comparison to the average cure rates of Phase I soft tissue surgeries in general of 42% to 75%.[46] Overall, surgical intervention should be tailored to specific patient-centric populations and should be carefully considered based on individual patient needs and characteristics.

A prominent multicenter randomized controlled trial studying Sleep Apnea Multilevel Surgery (SAMS) was conducted in 2019, with analysis and conclusions published in the Journal of the American Medical Association in 2020. In this initial investigation, adults suffering from moderate to severe OSA, who did not respond to traditional treatment such as CPAP or OAT, underwent a combination of palatal and tongue surgery. These patients exhibited a decrease in the occurrence of apnea and hypopnea events, as well as an improvement in self-reported sleepiness at the 6-month follow-up compared to those receiving conservative medical management. However, in a follow-up response to this publication by MacKay et al. in 2021, the 6-month follow-up was heavily criticized as being insufficient to monitor long-term success of surgical intervention. Additionally, this reply noted that long-term potential improvements in cardiovascular health and overall benefit to mortality in the long-term were not assessed. It goes on to note that the analysis of long-term follow-up of this clinical trial is still ongoing and will be complete in the near future. However, it does provide an encouraging update, stating that surrogate measures to cardiovascular health did improve over the long-term course of the study, such as AHI, 4% oxygen desaturation index, and sleep time with oxygen desaturation less than 90%.[47] The response concludes that given the present data, surgical procedures akin to those being studied in the trial may pose a very significant benefit to the estimated 50% of OSA patients who cannot tolerate conservative management, such as CPAP. All parties agree upon the assertion that further investigation is necessary to validate these outcomes across diverse patient populations and assess the clinical practicality, long-term effectiveness, and safety of multilevel upper airway surgery as a treatment option for OSA.

In a multicenter prospective cohort study published in 2019, the authors concurred with the findings for the SAMS study, primarily further specifically investigating the efficacy of MMA surgery. They attest to the safety and excellent success rate of MMA, concluding that it can lead to marked improvements in daytime sleepiness, quality of life (QOL), sleep-disordered breathing, and neurocognitive performance, as well as improvements in cardiovascular health, specifically blood pressure. With regards to daytime sleepiness, the authors compared results of patients' scores on the Epworth Sleepiness Scale (ESS), which is a self-reported questionnaire that measures daytime sleepiness. They found a significant reduction in patients' documented ESS score, from 13.3 to 4.9, with scores above 10 being classified as having excessive daytime sleepiness. 73% of these patients reported pathologic levels of daytime sleepiness prior to MMA, which sharply decreased to a mere 6.6% still reporting excessive levels of sleepiness. Similarly, when evaluating sleep-specific QOL metrics, 66.7% of patients reported normal QOL post-operatively, compared to only 10% pre-operatively. With regards to cardiovascular health as it pertains to blood pressure, the data suggests that there is a decrease in both mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP). Specifically, the mean SBP decreased by 3.7 mm Hg with a 95% confidence interval ranging from a decrease of 9.46 mm Hg to an increase of 2.06 mm Hg. Similarly, the mean DBP has decreased by 3.6 mm Hg with a 95% confidence interval ranging from a decrease of 6.50 mm Hg to a decrease of 0.70 mm Hg.[48]

An alternate and relatively new treatment modality is the Inspire implantable nerve stimulation device for treatment of OSA. It is a less invasive surgical option that may be recommended in situations where CPAP and/or OAT have failed.[49] The Inspire device works by sending electrical impulses to the hypoglossal nerve during sleep. The hypoglossal nerve controls the tongue's movement, and electrical stimulation of this nerve can prevent upper airway collapse during sleep. The Inspire system consists of three components: a small generator, a breathing sensor, and a stimulation lead. The generator is implanted in the chest wall, and the stimulation lead is placed near the hypoglossal nerve. The breathing sensor is placed under the skin between the ribs and monitors the patient's breathing during sleep.[50] In a 5-year retrospective analysis of patients who underwent surgical implantation of hypoglossal nerve stimulator devices, at patients' 5-year PSG exam, it was observed that 75% of participants achieved successful results, defined as a decrease in AHI of more than 50% and an AHI less than 20. Additionally, 44% and 78% of participants had AHIs less than 5 and 15, respectively at the 5-year mark. The proportion of participants with a normal ESS score of less than 10 rose from 33% at the start of the study to 78% after 5 years.[51] Furthermore, in the STAR study published in 2014 in the New England Journal of Medicine, the surgical outcomes were measured for patients who underwent implantation of hypoglossal nerve stimulation devices, such as the Inspire device. At the 12 month follow up interval, patients showed a decrease in AHI from 29.3 events/hr to a mere 9 events/hr, a 68% decrease.[52] The 5-year outcomes from the STAR study showed 75% of participants meeting the surgical definition of success, which was a reduction in AHI greater than 50% from baseline and an AHI of less than 20 events per hour, amounting to a 63% overall success rate at 5 years.[53]

An emerging and relatively new treatment modality for OSA is Distraction Osteogenesis Maxillary Expansion (DOME). This technique was developed by Drs. Stanley Liu and Audrey Yoon at Stanford University, specifically for the treatment of adult OSA patients with normal occlusion, narrow maxillae and high-arched palates. This phenotype is typically also associated with increased nasal resistance and posterior displacement of the tongue. DOME minimizes the need for extensive invasive surgery, while ensuring effective expansion of the adult maxilla. The procedure consists of the following steps: First, the maxillary expander with mini-implants is custom-fabricated to fit the narrow palatal vault. The implants and expander may be placed in an outpatient setting under local anesthesia. Next, a maxillary Lefort level I osteotomy is performed to separate the maxilla at the mid-palatal suture. Subsequent to the placement of the expander, patients themselves must turn the expander daily, achieving a gradual expansion of the nasal floor, at approximately 0.25 mm increments, with a final nasal floor expansion goal of 8 mm to 10 mm within 1 month. Finally, after completion of expansion, orthodontic treatment is initiated to close the diastema between the maxillary incisors. In their prospective cohort study, the authors observed significant improvements in measures such as the Epworth Sleepiness Scale (−36.59% change), Nose Obstruction Symptom Evaluation (−67.52% change), apnea-hypopnea index (−54.06% change), oxygen desaturation index (−62.17% change), and nasal airflow resistance (−28.57% change left nostril, and in −35.71% right nostril). Though these data are encouraging, the authors suggest that further long-term studies are needed to evaluate the sustained improvement in both objective and subjective indicators of OSA in this specific patient group.[54]

While CPAP therapy remains the most effective treatment for OSA, surgical interventions have emerged as a viable alternative for certain patient populations. The proposed 2021 guideline by the JOSM takes into consideration patient-specific needs and preferences and evaluates the benefits, costs, risks, and potential adverse effects of different medical and surgical treatments. However, despite the various surgical interventions available, controversy exists as to their effectiveness. While nasal procedures such as septoplasty or turbinate reduction have been shown to increase CPAP tolerability in certain patient populations, most surgeries to decrease upper airway collapsibility do not significantly reduce OSA severity or symptoms. Surgical interventions should be tailored to specific patient-centric populations and should be carefully considered based on individual patient needs and characteristics. Maxillomandibular advancement (MMA) and hypoglossal nerve stimulation have shown promising results but are highly invasive and recommended only for select patient populations. Ultimately, the decision to pursue surgical intervention should be made on a case-by-case basis with a comprehensive evaluation of the risks and benefits involved.[44]

ADJUNCTIVE THERAPY

Microimplant-assisted Maxillary Expansion (MARPE) is a procedure closely related to DOME, sharing similar principles and objectives. However, MARPE differs from DOME in that it is far less invasive, as it does not involve surgical osteotomy, and it is specifically appropriate for non-obese young adults with a maxillary transverse deficiency. MARPE aims to widen the mid-face and enhance the dimensions of the nasal and oral cavities. By doing so, it has the potential to alleviate airflow resistance and play a significant role in the treatment of obstructive sleep apnea (OSA) in certain patients. The MARPE procedure consists of inserting small screws, known as mini-implants, into the palate along with a customized expander appliance. These mini-implants serve as anchors and enable controlled expansion of the upper jaw by applying gradual outward pressure. This expansion widens the mid-face, nasal cavity, and oral cavity, thereby reducing airflow resistance and potentially enhancing breathing and sleep quality in individuals with OSA. As found in a multi-center prospective controlled trial, not only is the success rate of achieving palatal expansion very high, ranging from 87% to 100%, but positive and significant OSA results were also achieved. Participants who underwent MARPE experienced significant improvements in daytime sleepiness and quality of life related to obstructive sleep apnea (OSA), as measured by validated questionnaires. The intervention group also showed statistically significant enhancements in sleep test parameters, including a 65.3% reduction in AHI, improvements in mean oxygen saturation, snoring duration, and the bruxism to apnea index. Approximately 35.7% of the participants in the intervention group achieved an AHI of less than 5, indicating a positive outcome.[55,56]

Apart from the mainstay treatment modalities for OSA as already discussed, such as CPAP, OAT, and upper-airway-oriented surgical intervention, adjunctive therapies also exist, particularly as it pertains to a patient's weight and BMI. Obesity represents a significant risk factor for the development of OSA. In obese adults, the prevalence of OSA ranges from 42% to 48% in males and from 8% to 38% in females. It has been shown that weight loss significantly impacts treating OSA as it pertains to AHI metrics.[57] Observational studies have shown that significant weight loss, regardless of the weight-loss treatment, whether via bariatric surgery, lifestyle changes, or medical management, can substantially reduce OSA symptoms in approximately 60% to 80% of patients.[58] Important to note, that the study by Buchwald and colleagues assert that there was an indistinguishable difference between weight loss from bariatric surgery versus weight loss from lifestyle changes and medical management regarding the effect on OSA symptomatology. This, as well as future updates of this topic, bolster and corroborate the assertion that weight loss, regardless of the means to achieve this weight loss, is a primary treatment modality for the obese patient.[59]

According to Kent and colleagues in their paper published in the Journal of Clinical Sleep Medicine in 2021, they strongly recommend referring a patient for bariatric surgical consultation as a means for weight reduction in hopes to treat OSA. As part of a patient-centered discussion on alternative treatment options, the paper suggests that clinicians consider referring adults with OSA and obesity (BMI $\geq$35 kg/m2, Class II/III) who are intolerant or unwilling to use CPAP therapy. Given that weight loss has been proven to help treat OSA, and that bariatric surgery has been proven the most effective means for weight loss in patients of BMI ≥35 kg/m2, Class II/III, bariatric surgery is strongly recommended as a treatment option for patients of this category.[44]

DISCUSSION

Sleep apnea is a complex disorder that affects a significant portion of the population, and its management remains a controversial topic among clinicians. There are still many gaps in our understanding of its pathophysiology, long-term health consequences, optimal diagnostic modalities, and optimal treatment strategies. Management of the disorder remains a controversial topic among clinicians, with the use of CPAP therapy being one of the primary areas of contention. While CPAP is considered the gold standard treatment for moderate to severe OSA, its adherence rate is often low, and its efficacy in improving clinical outcomes beyond reducing symptoms and improving quality of life is not well-established.

Another contentious issue in OSA management is the use of OAT as an alternative to CPAP therapy. While OAT is less invasive than CPAP and may be more acceptable to some patients, the extent to which it is effective in reducing AHI and improving health outcomes is still debated. Furthermore, the optimal selection of patients for OAT and its long-term safety are not well-understood. The controversies in OSA management also extend to surgical interventions, positional therapy, and the management of comorbid conditions such as obesity and cardiovascular disease.

Given these controversies, personalized OSA management that considers patients' preferences, comorbidities, and disease severity is crucial. Clinicians should engage in shared decision-making with patients to select the most appropriate treatment modality. Regular monitoring of treatmeœnt adherence and clinical outcomes is necessary to ensure optimal management. Future research should focus on identifying biomarkers and phenotypes that can predict patients' response to different treatment modalities and developing innovative therapeutic approaches that target the underlying pathophysiology of the disorder.

Though CPAP is presently the first-line therapy for treating OSA, there remains definitive consensus regarding the superiority of CPAP versus OAT. Though, in theory, CPAP shows greater efficacy, its compliance has been show to be significantly less OAT. The American Academy of Sleep Medicine currently recommends CPAP as the first line and gold-standard therapy for treating OSA, but it bases its recommendations solely on a comparison between CPAP versus no treatment at all. Further reviews of all treatment modalities when compared to each other are certainly still needed to establish what the most efficacious first-line therapy is, considering compliance and adherence as integral to that determination.

While CPAP therapy remains the most effective treatment for OSA, surgical interventions have emerged as a viable alternative for certain patient populations. The proposed 2021 guideline by the JOSM takes into consideration patient-specific needs and preferences and evaluates the benefits, costs, risks, and potential adverse effects of different medical and surgical treatments. Surgical interventions should be tailored to specific patient-centric populations and should be carefully considered based on individual patient needs and characteristics.

OSA management and diagnosis remain complex and contentious issues with many unanswered questions. A personalized approach that emphasizes shared decision-making and regular monitoring of treatment outcomes is essential for optimal patient care. Collaboration between sleep specialists, primary care physicians, and patients is also necessary to improve sleep apnea awareness, diagnosis, and management. Further research is necessary to identify biomarkers and phenotypes that can predict patients' response to different treatment modalities and develop innovative therapeutic approaches. Ultimately, the decision to pursue a specific treatment modality should be made on a case-by-case basis, considering the individual patient's needs, preferences, and characteristics.

With regards to conservative treatment, there remains no clear consensus regarding CPAP versus OAT as a first-line therapy. By and large, this controversy stems from the issue of compliance and lack of adherence to therapies. Most studies show that compliance with OAT is greater than with CPAP. However, many reviews and guidelines are limited in their scope as they only base their recommendations on comparing the utilization of CPAP therapy to treat OSA compared to no treatment at all. This is presently the case for the American Academy of Sleep Medicine, which currently asserts CPAP to be the first-line and gold-standard therapy for treating OSA. This guideline explicitly stated that it did not base its recommendations on a comparison between CPAP versus OAT, rather, it is solely based on the comparison between CPAP versus no treatment at all. Further reviews of all treatment modalities when compared to each other are certainly still needed to establish what the most efficacious first-line therapy is, considering compliance and adherence as integral to that determination.

SUMMARY

The management of obstructive sleep apnea (OSA) presents a complex and evolving landscape of diagnostic and therapeutic options. This paper has provided an evidence-based review of current therapeutic treatments for patients suffering from OSA, with a particular focus on surgical interventions. Despite the challenges and controversies surrounding OSA diagnosis and treatment, surgery remains a valuable and promising avenue for patients who do not respond to or tolerate conservative measures. Surgical procedures such as uvulopalatopharyngoplasty (UPPP), maxillomandibular advancement surgery, genioglossus advancement, and the use of nerve stimulation devices offer viable alternatives for patients seeking long-term resolution of their sleep apnea symptoms. Moreover, weight loss interventions and positional therapy demonstrate their efficacy in improving OSA severity and associated symptoms. However, the selection of the most appropriate treatment approach should be guided by careful consideration of individual patient characteristics, preferences, and potential risks and benefits associated with each modality. The ongoing controversies and debates in the field underscore the need for continued research, collaborative efforts, and personalized care to optimize outcomes and enhance the quality of life for individuals affected by OSA. By advancing our understanding and refining our approaches, we can strive toward more effective and tailored interventions to alleviate the burden of sleep apnea on individuals and society as a whole.

DISCLOSURES

The authors have nothing to disclose.

CLINICS CARE POINTS

- Surgical intervention may be considered in patients who cannot tolerate CPAP therapy or have ongoing inadequate adherence.
- Obesity is a significant risk factor for OSA. Weight loss interventions, including lifestyle modifications and bariatric surgery, can improve OSA severity and associated symptoms.

- Regular monitoring of treatment adherence and clinical outcomes is essential to ensure optimal management of OSA
- A multidisciplinary approach between sleep specialists, primary care physicians, and patients is necessary to improve sleep apnea awareness, diagnosis, and management.
- Individual patient preferences, co-existing medical conditions, and other factors should be taken into account when determining the most suitable treatment plan for OSA

REFERENCES

1. Faria A, Allen AH, Fox N, et al. The public health burden of obstructive sleep apnea. Sleep Sci 2021;14(3):257–65.
2. Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 2019;7(8):687–98.
3. Yaggi HK, Strohl KP. Adult Obstructive Sleep Apnea/Hypopnea Syndrome: Definitions, Risk Factors, and Pathogenesis. Clin Chest Med 2010;31(2):179–86.
4. Oldenburg O, Wellmann B, Buchholz A, et al. Nocturnal hypoxaemia is associated with increased mortality in stable heart failure patients. Eur Heart J 2016;37(21):1695–703.
5. Fraigne JJ, Orem JM. Phasic motor activity of respiratory and non-respiratory muscles in REM sleep. Sleep 2011;34(4):425–34.
6. Javaheri S, Badr MS. Central sleep apnea: pathophysiologic classification. Sleep 2022;46(3).
7. Jullian-Desayes I, Revol B, Chareyre E, et al. Impact of concomitant medications on obstructive sleep apnoea. Br J Clin Pharmacol 2017;83(4):688–708.
8. Hernandez AB, Patil SP. Pathophysiology of central sleep apneas. Sleep Breath 2016;20(2):467–82.
9. Daghistani KJ. Conditions of the uvula: a 14 years experience. Auris Nasus Larynx 2000;27(3):261–4.
10. Patel SR. Obstructive Sleep Apnea. Ann Intern Med 2019;171(11):ITC81–96.
11. Tobias L, Won C. Upper Airway Resistance Syndrome Represents a Distinct Entity from Obstructive Sleep Apnea Syndrome. Journal of Dental Sleep Medicine 2016;3(1):21–4.
12. Rundo JV, Downey R. Polysomnography. Handb Clin Neurol 2019;160:381–92.
13. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med 2017;13(3):479–504.
14. Boyd SB, Upender R, Walters AS, et al. Effective Apnea-Hypopnea Index ("Effective AHI"): A New Measure of Effectiveness for Positive Airway Pressure Therapy. Sleep 2016;39(11):1961–72.
15. Pavwoski P, Shelgikar AV. Treatment options for obstructive sleep apnea. Neurol Clin Pract 2017;7(1):77–85.
16. St-Onge MP, Tasali E. Weight Loss Is Integral to Obstructive Sleep Apnea Management. Ten-Year Follow-up in Sleep AHEAD. Am J Respir Crit Care Med 2021;203(2):161–2.
17. Paidi G, Beesetty A, Jean M, et al. The Management of Obstructive Sleep Apnea in Primary Care. Cureus 2022;14(7):e26805.
18. BaHammam AS, Alassiri SS, Al-Adab AH, et al. Long-term compliance with continuous positive airway pressure in Saudi patients with obstructive sleep apnea. A prospective cohort study. Saudi Med J 2015;36(8):911–9.

19. Kendzerska T, Gershon AS, Hawker G, et al. Obstructive sleep apnea and risk of cardiovascular events and all-cause mortality: a decade-long historical cohort study. PLoS Med 2014;11(2):e1001599.
20. Tietjens JR, Claman D, Kezirian EJ, et al. Obstructive Sleep Apnea in Cardiovascular Disease: A Review of the Literature and Proposed Multidisciplinary Clinical Management Strategy. J Am Heart Assoc 2019;8(1):e010440.
21. Yeghiazarians Y, Jneid H, Tietjens JR, et al. Obstructive Sleep Apnea and Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation 2021;144(3):e56–67.
22. Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013;177(9):1006–14.
23. Hamilton GS, Gupta R, Vizcarra D, et al. Endorsement of: "clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American academy of sleep medicine clinical practice guideline" by the World Sleep Society. Sleep Med 2021;79:152–4.
24. Patel AK, Reddy V, Shumway KR, et al. Physiology, Sleep Stages. In: StatPearls. StatPearls publishing copyright © 2023, StatPearls Publishing LLC; 2023.
25. Stålberg E, van Dijk H, Falck B, et al. Standards for quantification of EMG and neurography. Clinical neurophysiology 2019;130(9):1688–729.
26. Xiong X, Ren Y, Gao S, et al. EEG microstate in obstructive sleep apnea patients. Sci Rep 2021;11(1):17178.
27. Vana KD, Silva GE, Goldberg R. Predictive abilities of the STOP-Bang and Epworth Sleepiness Scale in identifying sleep clinic patients at high risk for obstructive sleep apnea. Res Nurs Health 2013;36(1):84–94.
28. Kumari P, Roy SK, Roy ID, et al. Changes in posterior airway space and mandibular plane hyoid distance following mandibular advancement DO. Ann Maxillofac Surg 2016;6(2):182–9.
29. Barrera JE, Pau CY, Forest VI, et al. Anatomic measures of upper airway structures in obstructive sleep apnea. World J Otorhinolaryngol Head Neck Surg 2017;3(2):85–91.
30. Steffy DD, Tang CS. Radiographic Evaluation of Sleep-Disordered Breathing. Radiol Clin 2018;56(1):177–85.
31. Lan M-C, Liu SY-C, Lan M-Y, et al. Role of drug-induced sleep endoscopy in evaluation of positional vs non-positional OSA. J Otolaryngol 2020;49(1):83.
32. Soares D, Folbe AJ, Yoo G, et al. Drug-induced sleep endoscopy vs awake Müller's maneuver in the diagnosis of severe upper airway obstruction. Otolaryngol Head Neck Surg 2013;148(1):151–6.
33. Quan SF, Schmidt-Nowara W. The Role of Dentists in the Diagnosis and Treatment of Obstructive Sleep Apnea: Consensus and Controversy. J Clin Sleep Med 2017;13(10):1117–9.
34. Epstein LJ, Kristo D, Strollo PJ Jr, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009;5(3):263–76.
35. Phillips CL, Grunstein RR, Darendeliler MA, et al. Health Outcomes of Continuous Positive Airway Pressure versus Oral Appliance Treatment for Obstructive Sleep Apnea: A Randomized Controlled Trial. Am J Respir Crit Care Med 2013;187(8):879–87.
36. Vanderveken OM, Dieltjens M, Wouters K, et al. Objective measurement of compliance during oral appliance therapy for sleep-disordered breathing. Thorax 2013;68(1):91–6.

37. Sheats RD. Management of side effects of oral appliance therapy for sleep-disordered breathing: summary of American Academy of Dental Sleep Medicine recommendations. J Clin Sleep Med 2020;16(5):835.
38. de Almeida FR. Complexity and efficacy of mandibular advancement splints: understanding their mode of action. J Clin Sleep Med 2011;7(5):447–8.
39. Ravesloot MJ, de Vries N. Reliable calculation of the efficacy of non-surgical and surgical treatment of obstructive sleep apnea revisited. Sleep 2011;34(1):105–10.
40. Rotenberg BW, Murariu D, Pang KP. Trends in CPAP adherence over twenty years of data collection: a flattened curve. J Otolaryngol Head Neck Surg 2016;45(1):43.
41. Andrade L, Paiva T. Ambulatory Versus Laboratory Polysomnography in Obstructive Sleep Apnea: Comparative Assessment of Quality, Clinical Efficacy, Treatment Compliance, and Quality of Life. J Clin Sleep Med 2018;14(08):1323–31.
42. Donovan LM, Boeder S, Malhotra A, et al. New developments in the use of positive airway pressure for obstructive sleep apnea. J Thorac Dis 2015;7(8):1323–42.
43. Aurora RN, Casey KR, Kristo D, et al. Practice parameters for the surgical modifications of the upper airway for obstructive sleep apnea in adults. Sleep 2010;33(10):1408–13.
44. Kent D, Stanley J, Aurora RN, et al. Referral of adults with obstructive sleep apnea for surgical consultation: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med 2021;17(12):2499–505.
45. Qaseem A, Holty JE, Owens DK, et al. Management of obstructive sleep apnea in adults: A clinical practice guideline from the American College of Physicians. Ann Intern Med 2013;159(7):471–83.
46. Powell NB. Contemporary surgery for obstructive sleep apnea syndrome. Clin Exp Otorhinolaryngol 2009;2(3):107–14.
47. MacKay S, McEvoy RD, Weaver EM. The Effect of Surgical Treatment on Obstructive Sleep Apnea-Reply. JAMA 2021;325(8):789–90.
48. Boyd SB, Chigurupati R, Cillo JE Jr, et al. Maxillomandibular Advancement Improves Multiple Health-Related and Functional Outcomes in Patients With Obstructive Sleep Apnea: A Multicenter Study. J Oral Maxillofac Surg 2019;77(2):352–70.
49. Heiser C, Vries Nd. Upper Airway Stimulation in Obstructive Sleep Apnea: Best Practices in Evaluation and Surgical Management, 1st ed., 2022.
50. Heiser C, Knopf A, Bas M, et al. Selective upper airway stimulation for obstructive sleep apnea: a single center clinical experience. Eur Arch Oto-Rhino-Laryngol 2017;274(3):1727–34.
51. Woodson BT, Strohl KP, Soose RJ, et al. Upper airway stimulation for obstructive sleep apnea: 5-year outcomes. Otolaryngology-head and neck surgery 2018;159(1):194–202.
52. Strollo PJ Jr, Soose RJ, Maurer JT, et al. Upper-airway stimulation for obstructive sleep apnea. N Engl J Med 2014;370(2):139–49.
53. Mashaqi S, Patel SI, Combs D, et al. The Hypoglossal Nerve Stimulation as a Novel Therapy for Treating Obstructive Sleep Apnea-A Literature Review. Int J Environ Res Publ Health 2021;18(4).
54. Liu SY-C, Guilleminault C, Huon L-K, et al. Distraction Osteogenesis Maxillary Expansion (DOME) for Adult Obstructive Sleep Apnea Patients with High Arched Palate. Otolaryngology-head and neck surgery 2017;157(2):345–8.
55. Brunetto DP, Moschik CE, Dominguez-Mompell R, et al. Mini-implant assisted rapid palatal expansion (MARPE) effects on adult obstructive sleep apnea

(OSA) and quality of life: a multi-center prospective controlled trial. Prog Orthod 2022;23(1):3.
56. Ventura V, Botelho J, Machado V, et al. Miniscrew-Assisted Rapid Palatal Expansion (MARPE): An Umbrella Review. J Clin Med 2022;11(5).
57. Dixon JB, Schachter LM, O'Brien PE, et al. Surgical vs conventional therapy for weight loss treatment of obstructive sleep apnea: a randomized controlled trial. JAMA 2012;308(11):1142–9.
58. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA 2004;292(14):1724–37.
59. Chang SH, Stoll CR, Song J, et al. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003-2012. JAMA Surg 2014;149(3):275–87.