

Policy Document

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Consensus & Evidence-based INOSA Guidelines 2014 (First edition)

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Obstructive sleep apnoea (OSA) and obstructive sleep apnoea syndrome (OSAS) are subsets of sleep-disordered breathing. Awareness about OSA and its consequences amongst the general public as well as the majority of primary care physicians across India is poor. This necessitated the development of the INdian initiative on Obstructive Sleep Apnoea (INOSA) guidelines under the auspices of Department of Health Research, Ministry of Health & Family Welfare, Government of India. OSA is the occurrence of an average five or more episodes of obstructive respiratory events per hour of sleep with either sleep related symptoms or co-morbidities or ≥ 15 such episodes without any sleep related symptoms or co-morbidities. OSAS is defined as OSA associated with daytime symptoms, most often excessive sleepiness. Patients undergoing routine health check-up with snoring, daytime sleepiness, obesity, hypertension, motor vehicular accidents and high risk cases should undergo a comprehensive sleep evaluation. Medical examiners evaluating drivers, air pilots, railway drivers and heavy machinery workers should be educated about OSA and should comprehensively evaluate applicants for OSA. Those suspected to have OSA on comprehensive sleep evaluation should be referred for a sleep study. Supervised overnight polysomnography (PSG) is the “gold standard” for evaluation of OSA. Positive airway pressure (PAP) therapy is the mainstay of treatment of OSA. Oral appliances are indicated for use in patients with mild to moderate OSA who prefer oral appliances to PAP, or who do not respond to PAP or who fail treatment attempts with PAP or behavioural measures. Surgical treatment is recommended in patients who have failed or are intolerant to PAP therapy.

Key words Bariatric surgery - CPAP - Indian guidelines - OSA - OSAS - polysomnography - sleep apnoea - sleep study - Syndrome Z

Introduction

In obstructive sleep apnoea (OSA), repetitive collapse of the upper airway occurs, that leads to snoring, frequent episodes of sleep interruption, hypoxemia, hypercapnia, swings in intrathoracic pressure and increased sympathetic activity. Management of OSA needs a long-term multi-disciplinary approach. Once diagnosed, patients should be properly counselled to manage their illness including co-morbidities through their active participation.

OSA is being increasingly recognized as an emerging important public health problem worldwide, including India. Awareness among lay public and even among primary care physicians is dismally low in India. This disorder is common among obese individuals, children and post-menopausal women. It is usually associated with several co-morbidities such as insulin resistance, metabolic syndrome, diabetes mellitus, hypertension, stroke, coronary artery disease, increased risk of vehicular accidents and various psychiatric disorders. Though there are guidelines regarding the diagnosis and management of this condition by various bodies in the western world, these recommendations may not be entirely applicable to the developing countries like India. There was a need to develop comprehensive guidelines on OSA in the Indian context. Thus, the consensus and evidence-based INdian initiative on Obstructive Sleep Apnoea Guidelines (INOSA Guidelines) were developed

under the auspices of Department of Health Research, Ministry of Health & Family Welfare, Government of India following a series of meetings and discussions under the convenership of the Department of Medicine, All India Institute of Medical Sciences (AIIMS), New Delhi, with the support of Indian Council of Medical Research (ICMR). During this first Indian initiative, in light of the available evidence, consensus statements were developed and finalized by the various national experts in the field of sleep medicine including internists, pulmonologists, neurologists, otorhinolaryngologists, endocrinologists, bariatric surgeons and dental surgeons.

In order to make the guidelines evidence based, the expert group reviewed the available evidence and graded the recommendations according to the quality of evidence as mentioned in Fig. 1¹.

1 Epidemiology and risk factors of OSA

1.1 Epidemiology

Obstructive sleep apnoea is a major public health problem. The International Classification of Sleep Disorders, Third Edition classifies sleep-disordered breathing into three basic categories: central sleep apnoea syndrome, obstructive sleep apnoea syndrome, and sleep-related hypoventilation/hypoxia syndrome^{2,3}. Community-based epidemiological studies from several parts of India have estimated that the prevalence of OSAS is 2.4 to 4.96 per cent in men and 1 to 2 per cent

Evidence Quality	Preponderance of Benefit or Harm	Balance of Benefit and Harm
A. Well designed RCTs or diagnostic studies on relevant population	Strong Recommendation	Option
B. RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies	Recommendation	
C. Observational studies (case-control and cohort design)		
D. Expert opinion, case reports, reasoning from first principles	Option	No Rec
X. Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit or harm	Recommendation	

Fig. 1. Evidence quality. Reproduced with permission from: American Academy of Pediatrics Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. *Pediatrics* 2004; 114 : 874-71.

in women⁴. Table I summarizes some of the important definitions⁵.

1.2 Pathogenesis

Multiple factors (Table II)^{6,7} are responsible for pathogenesis of OSA with inter-individual variation. OSA patients have repeated narrowing or obstruction of pharyngeal airway during sleep. It has been suggested that pathophysiological mechanisms, such as anatomic compromise, pharyngeal dilator muscle dysfunction, lowered arousal threshold, ventilatory control instability, and/or reduced lung volume tethering are the pathophysiological mechanisms leading to OSA⁸.

2 Consequences of OSA

2.1 OSA and Mortality

It has been demonstrated that OSA is associated with increased mortality. Severe sleep disordered breathing (SDB) has a 3.8 fold greater risk for all-cause mortality and 5.2-fold greater risk for cardiovascular mortality than those without SDB (Evidence Quality B)⁹. The consequences of OSA are described in Table III^{4,10-26}.

3 Diagnosis of OSA

3.1 History and Physical Examination

The diagnosis of OSA requires a high index of suspicion. OSA may be suspected during routine health check-up or while evaluating high-risk patients²⁷. The

chances of underdiagnosis are minimized if individuals with risk factors are subjected to a comprehensive sleep evaluation during routine health check-up. Similarly, high-risk patients like those with congestive heart failure, extreme obesity, diabetes mellitus, coronary artery disease, stroke, nocturnal dysrhythmias including atrial fibrillation, pulmonary hypertension, preoperative patients should have comprehensive sleep evaluation (Boxes 1 and 2)²⁷. Additionally, medical examiners evaluating drivers, pilots, railway drivers and heavy machinery workers should be educated about OSA and should refer them for evaluation if snoring, daytime sleepiness or obesity is noted (Evidence Quality B, Strong Recommendation).

In a patient suspected to have OSA, secondary causes such as hypothyroidism, facial abnormality, tonsil/adenoid hypertrophy and musculoskeletal abnormalities should be ruled out and the patient should be evaluated for consequences of OSA like metabolic syndrome, diabetes mellitus, hypertension, CAD, stroke and gastroesophageal reflux^{27,28}. Patient should also be investigated for associated co-morbid illnesses like allergic rhinosinuitis, nasal polyps, asthma, chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome and kyphoscoliosis^{27,28}. The clinical examination should include detailed anthropometry including measurement of neck circumference, BMI, modified Mallampati score and a comprehensive upper airway assessment²⁷.

Table I. Definitions⁵

Apnoea	Apnoea is defined as cessation of breathing or airflow for 10 seconds or longer in a polysomnography ⁵ .
<ul style="list-style-type: none"> • Obstructive apnoea • Central apnoea • Mixed apnoea 	<p>There is no airflow at nose or mouth but there are persistent respiratory efforts.</p> <p>There is no airflow at nose or mouth as well as no respiratory effort.</p> <p>It is a mixture of central and obstructive apnoea features.</p>
Apnoea-hypopnoea index (AHI)	AHI is calculated as number of apnoeas and hypopnoeas per hour of sleep.
Respiratory disturbance index (RDI)	RDI is the number of apnoeas, hypopneas and respiratory effort related arousals (RERAs) per hour of sleep, confirmed by EEG.
Hypopnoea	<p>A hypopnoea⁵ is defined by the presence of a clear decrease in the amplitude of airflow (quantitative or semi-quantitative) of >30% from baseline during sleep</p> <ul style="list-style-type: none"> • Or <p>A clear amplitude reduction of a valid measure of breathing during sleep that does not reach the above criterion, but is associated with either an oxygen desaturation of >3 per cent or an arousal</p> <ul style="list-style-type: none"> • And <p>The event lasts 10 seconds or longer.</p>
Overlap syndrome	The co-occurrence of both chronic obstructive pulmonary disease and OSA in the same individual is termed as overlap syndrome. Both are common diseases affecting adult population over 40 years of age.
Polysomnography (PSG)	PSG is a comprehensive in-laboratory overnight recording of different bio-physiological changes that occur during sleep.
Respiratory effort related arousal (RERA)	A RERA is defined as an arousal from sleep that follows a 10 second or longer sequence of breaths that are characterized by increasing respiratory effort, but which does not meet criteria for an apnoea or hypopnoea ⁵ . Snoring is usually but not always associated with this condition. Oesophageal pressure monitoring is used to measure respiratory effort; the pattern is of increasing negative pressure, terminated by a sudden change to a less negative pressure and a cortical arousal. Nasal pressure signal is a useful alternative to oesophageal pressure monitoring which allows RERAs to be detected non-invasively.
Upper airway resistance syndrome (UARS)	UARS is a condition in which patients have symptoms suggestive of OSA and frequent RERAs but AHI <5 events/h.

3.2 Other Diagnostic Investigations

Anthropometric measurements, nasal and upper airway examination, orthodontic assessments and radiological measurements have low sensitivity and specificity when used alone for diagnosis of OSA²⁸. Patients suspected to have OSA should be referred for an appropriate type of sleep study after detailed history, examination and basic investigations. Various questionnaires for the prediction of OSA are available and can be used prior to sleep study, but the same is not mandatory.

3.3 Epworth Sleepiness Scale (ESS)

Epworth Sleepiness Scale is a simple, self-administered measurement of sleep propensity during

daytime in adults that requires the subject to rate the probability of dozing off in eight different situations that are met in day-to-day life on a scale of 0-3. Thus, the sum of the score can vary from 0 to 24. ESS score >10 is defined as excessive daytime sleepiness and has a sensitivity of 49 per cent and specificity of 80 per cent for predicting OSA²⁹. (Evidence Quality C, Recommended).

3.4 Clinical prediction rules for OSA

Various algorithms have been devised for screening and risk stratification of patients suspected to have OSA. The utility of these tools to estimate the clinical severity of OSA and to suggest the likelihood of OSA related consequences have not been studied systematically³⁰.

Table II. Risk factors for obstructive sleep apnoea^{6,7}

<i>Demographic characteristics</i>
Older age
Male gender
Pregnancy
<i>Risk factors linked to OSA by strong published evidence</i>
Obesity
Central body fat distribution
Neck circumference
Anatomical abnormalities of the craniofacial region and upper airway specific syndromes (<i>e.g.</i> , Treacher-Collins syndrome, Pierre Robbins syndrome)
Retroposed mandible/maxillae, hypertrophied tonsils, tongue
<i>Other suspected (potential) risk factors</i>
Genetic predisposition
Familial aggregation
Tobacco smoking
Menopause
Alcohol use
Night time nasal congestion
Endocrine abnormalities: hypothyroidism/acromegaly
Polycystic ovarian syndrome
Down's syndrome
Drugs <i>e.g.</i> , benzodiazepines, muscle relaxants, testosterone therapy

Berlin questionnaire has three categories of questions. Category 1 questions are about snoring with five questions and 2 to 5 multiple choice answers. Category 2 includes excessive daytime sleepiness with four or more multiple choice answers. Category 3 has body mass index (BMI) and blood pressure. With Berlin questionnaire, OSA was considered probable if two of the categories are positive. The Berlin questionnaire was modified at AIIMS, New Delhi, in 2006 for application in the setting of developing countries³¹. Both Berlin questionnaire and modified Berlin questionnaire are moderately accurate (sensitivity and specificity generally <90%) in screening for OSA^{30,31} (Evidence Quality C; Recommended). Although, these questionnaires have not been adequately studied, these can be used to screen the patients for OSA. The snoring, daytime tiredness, observed apnoea, high blood pressure, body mass index, age, neck circumference, and gender (STOP-BANG) questionnaire (Evidence

Quality C, Recommended) is the most appropriate questionnaire for the screening in preoperative cases.

Patients who have both symptoms and physical findings suggestive of OSA on comprehensive sleep evaluation along with Epworth's sleepiness score greater than or equal to 10 have a high risk of OSA and the diagnosis is confirmed and severity determined with objective testing in an expedited manner in order to initiate treatment. Patients who have neither are at low probability and the rest have moderate probability for OSA. Fig. 2 shows the algorithm for the diagnosis of OSA.

3.5 Types of Sleep Study

The diagnosis and severity of OSA must be ascertained before initiating the treatment of OSA. The standard diagnostic test for OSA is an attended in-laboratory polysomnography (PSG) or portable monitoring (PM)²⁷. PSG is supervised by a trained technician with at least seven channels whereas PM is performed without a technician and has fewer channels. Various types of sleep studies are described in Fig. 3. In laboratory PSG with electroencephalography (EEG) based sleep staging, the "gold standard" for the diagnosis of OSA is not necessary in all patients suspected to have OSA²⁸. Portable monitoring with type 3 and 4 devices in conjunction with comprehensive sleep evaluation is adequate for diagnosis of OSA in patients with high pre-test probability of moderate to severe OSA without co-morbid sleep or medical disorders such as neuromuscular disease, pulmonary disease, or congestive heart failure (Evidence Quality A, Strong Recommendation)³². PSG is mainly useful for patients with symptoms of excessive daytime sleepiness but no objective evidence of obstructive sleep apnoea on PM (Box 3).

3.5.1 Attended in-laboratory polysomnography - Type 1 Sleep Study: Type 1 study or in-laboratory, technician-attended, overnight PSG is the present reference or "gold" standard for evaluation of sleep and sleep-disordered breathing (Evidence Quality A, Strong Recommendation)³³. The recommended parameters to be evaluated in PSG include sleep state and stages, ventilatory parameters, cardiac function and limb movements³⁴ by recording EEG, electro-oculography (EOG), electrocardiography (ECG), chin and leg electromyography (EMG), nasal and oral airflow, chest and abdominal efforts and pulse oximetry³³. The study requires the constant presence of a trained individual with appropriate sleep-related

Table III. Consequences of OSA^{4,10-26}

Hypertension	OSA is an independent risk factor for systemic hypertension (Evidence Quality A) ¹⁰ . Several studies have shown an increased prevalence of hypertension in patients with OSA (Evidence Quality A) ¹¹ . Increase in one additional apnoeic event per hour of sleep enhances the odds of developing hypertension by about 1. The odds of developing hypertension increases by 13 per cent with 10 per cent decline in nocturnal oxygen saturation.
Resistant hypertension	OSA is a very important but often missed diagnosis in patients with resistant hypertension. All patients with resistant hypertension should be evaluated for OSA (Evidence Quality A, Recommended) ¹² .
Coronary artery disease	There is an increased prevalence of coronary artery disease in OSA patients (Evidence Quality B). Studies have shown a graded increase in the risk of acute myocardial infarction with increasing AHI ¹³ .
Congestive heart failure	There is a high prevalence of OSA among patients with symptomatic heart failure with reduced ejection fraction (HFrEF) (Evidence Quality B) ¹⁴ .
Arrhythmias	OSA is independently associated with a high frequency of nocturnal arrhythmias such as atrial fibrillation, complex ventricular ectopy, and non-sustained ventricular tachycardia. (Evidence Quality B) ¹⁵ .
Cerebrovascular disease	OSA is associated with increased risk of stroke. Patients with recurrent strokes had a higher percentage of OSA (AHI > 10) than initial strokes (74% compared to 57%) (Evidence Quality B) ¹⁶ .
Diabetes mellitus (DM)	The prevalence of OSA in diabetic and pre-diabetic obese patients is higher than those with normal glucose tolerance. Moreover, the risk of developing type 2 DM increases with the severity of OSA (Evidence Quality B) ¹⁷ .
Dyslipidaemia	OSA is independently associated with increased total cholesterol and LDL cholesterol levels, and carotid intima-media thickness irrespective of the cardiovascular co-morbidity. RCTs have shown that PAP therapy may produce a clinically relevant fall in total cholesterol level, potentially reducing cardiovascular risk (Evidence Quality A) ¹⁸ .
Metabolic syndrome	OSAS has been shown to be strongly and independently associated with metabolic syndrome ¹⁹ . The combination of OSA and metabolic syndrome is called Syndrome Z. The prevalence of metabolic syndrome varies from 74 to 85 per cent among patients with OSA as compared to 37 to 41 per cent among patients with no OSA. (Evidence Quality C) ⁴ .
OSA and neurocognitive function	Slow thought process, early forgetfulness, impaired concentration and decreased work related performance have been observed in OSA (Evidence Quality C) ²⁰ . Impairment in verbal episodic memory, visuo-spatial episodic memory, attention span, driving ability, vigilance, executive function, have been associated with OSA (Evidence Quality B) ²¹ .
OSA and excessive daytime sleepiness	Excessive daytime sleepiness in OSA has been associated with increased risk of motor vehicle accidents ²² (Evidence Quality B).
OSA & Psychiatric disorders	There is high prevalence of depression in patients with OSA, especially in females (Evidence Quality C) ²³ . All patients with erectile dysfunction ²⁴ (Evidence Quality B: Recommendation) should be screened for OSA.
OSA and quality of life	Studies have shown impaired quality of life in OSA with correlation of arousal index with physical function, general health and physical roles which improves with PAP therapy (Evidence Quality B) ²⁵ .
OSA and economic impact	Potential costs attributable to OSA include the costs of diagnosis and treatment, the decrement in quality of life, the medical consequences, motor vehicle accidents, and occupational losses (Evidence Quality B) ²⁶ .

Box 1. Symptoms of OSAS**Nocturnal**

- Snoring: Is it loud? Is it audible in the other room? Is it crescendo-decrescendo in nature? Does he/she wake up with one's own snoring?
- Witnessed apnoea: Has the partner witnessed apnoeas or sudden interruption in the loud snoring sound?
- Nocturnal choking: Does he/she wake up with a gasping or choking sensation?
- Nocturia: How many times does he/she wake up due to nocturia?
- Sleep quality: Is the sleep disturbed with tossing and turning? Is there frequent sleep fragmentation and difficulty in maintaining sleep leading to insomnia? What is the total amount of sleep? Is there a feeling of un-refreshing sleep or early morning headache or dryness of throat?

Daytime

- Excessive daytime sleepiness: Does the patient feel sleepy during quiet activities like reading, watching television or during activities that generally require alertness like school, work, driving.
- Lethargy: Does he/she have daytime fatigue/tiredness, decreased alertness?
- Cognitive deficits: History of memory loss, poor concentration and intellectual impairment.
- Psychiatric symptoms: Personality and mood changes, depression, anxiety, sexual dysfunction like impotence and decreased libido.
- Systemic complaints: Gastroesophageal reflux, hypertension, diabetes.

*In patients with nocturia, UTI and BPH (in males) should be ruled out

Box 2. Clinical examination finding suggestive of OSAS

- Neck circumference >16 inches (40.6 cm) in women and > 17 inches (43.2 cm) in men
- Body mass index ≥ 30 kg/m²
- Modified Mallampati score 3 or 4
- Upper airway evaluation showing retrognathia, high arched palate, macroglossia, tonsillar hypertrophy, enlarged uvula, nasal abnormality

training who can monitor patient compliance, technical adequacy and relevant patient behaviour (Evidence Quality B, Recommended)²⁷. It is advisable to take prior informed consent for PSG. Social acceptability of full-night PSG for women is an issue in the Indian context. Full-night PSG is recommended for the diagnosis of OSA (Evidence Quality A, Strong Recommendation).

3.5.2 Unattended polysomnography-Type 2 Sleep Study: Type 2 devices can record the same variables as type 1 study in absence of a technician. Thus, type 2 sleep monitoring can be practically used as portable monitors, but is not used frequently in the outpatient setting. Type 2 study may identify apnoea hypopnoea index (AHI) suggestive of OSA with high positive likelihood ratio and low negative likelihood ratio, though differences in AHI have been encountered between type 2 study and PSG^{30,35} (Evidence Quality B, Recommended).

3.5.3 Portable monitoring/Out-of-centre Sleep Testing (OCST)/Home Sleep Testing (HST)/Unattended Limited Channel Testing (ULCT) (Type 3 & 4 Sleep Study):

Portable monitoring or OCST as a diagnostic test for OSA has evolved as an alternative to PSG²⁷ due to convenience and lower cost. The disadvantage of PM or OCST, however, is that AHI may be falsely low^{30,36}. This is because in the absence of EEG recording in these tests, actual sleep time cannot be determined and the denominator is the total recording time instead of the total sleep time. Comprehensive sleep evaluation should always be done prior to PM studies²⁷.

The diagnosis and severity assessment should be performed using the same definitions as used for PSG. PM should be performed only in conjunction with comprehensive sleep evaluation and in the presence of a practitioner eligible for conducting sleep studies (Evidence Quality B, Recommended)³². Overall, PM (type 3 and 4) may be useful, cost-effective, convenient and speedy method of diagnosis if the patient is selected carefully. Hospital-based PSG is the investigation of choice for patients who cannot be investigated adequately at home or whose home study result does not match with the clinical suspicion of the investigating physician²⁸.

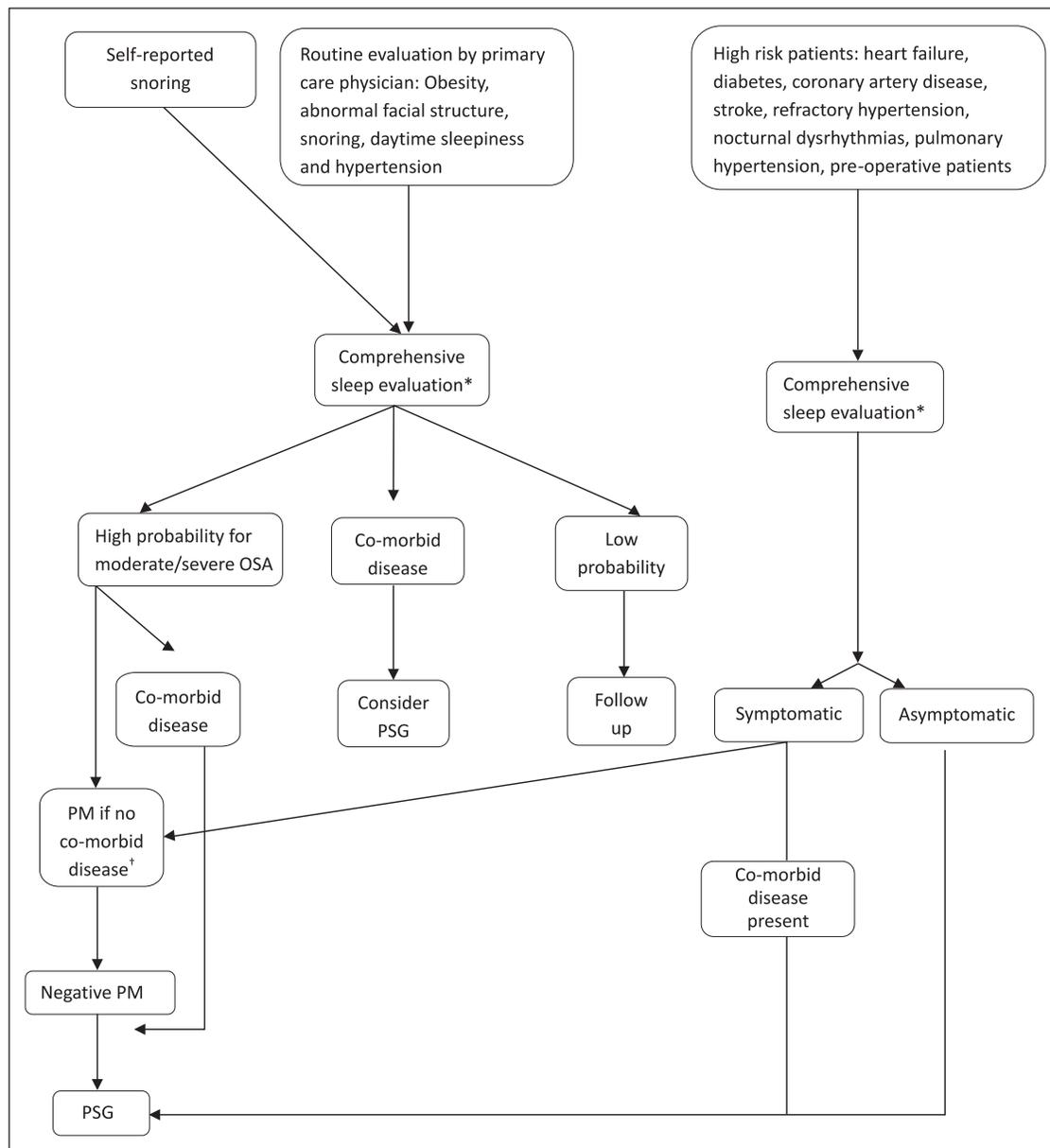


Fig. 2. Algorithm for diagnosis of OSA. *Boxes 1 and 2 †Pulmonary disease, neuromuscular disease, or congestive heart failure. PM, portable monitoring; PSG, polysomnography.

3.6 Preoperative Evaluation of OSA

The incidence of post-operative desaturation, respiratory failure, post-operative cardiac events and intensive care unit transfers is higher in patients with OSA (Evidence Quality A, Strong Recommendation)³⁷. Both PSG and portable monitoring are helpful in diagnosing and categorizing the severity of OSA, but portable monitoring reduces the likelihood of delay in the surgery, inconvenience and high cost of laboratory study. Alternatively, in a case at high risk of OSA, sleep

study may be deferred if it is not feasible or causes delay in surgery. Instead, a standby positive airway pressure device with a close monitoring may be advised³⁸. Patients who have previously been diagnosed to have OSA must be asked to use positive airway pressure (PAP) preoperatively and postoperatively.

3.7 Diagnostic criteria for OSA

The diagnostic criteria for OSA are summarized in Box 4.

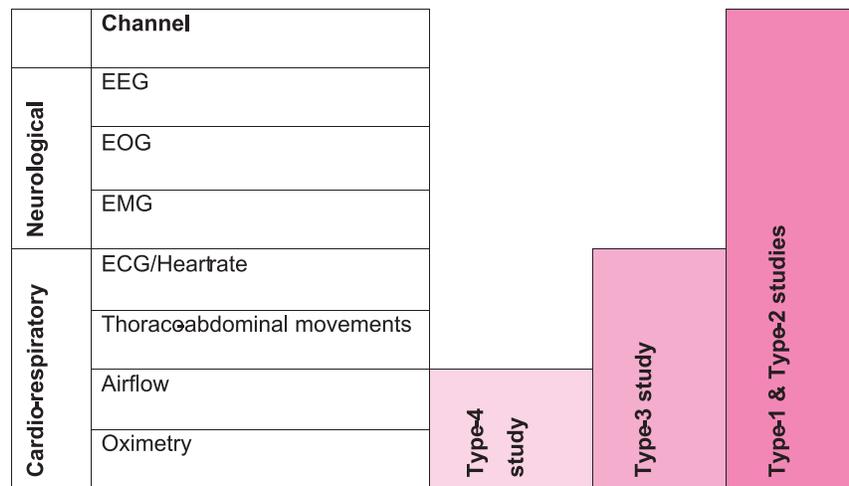


Fig. 3. Types of sleep studies. Type 1: Fully attended polysomnography (≥ 7 channels) in a laboratory setting, Type 2: Fully unattended polysomnography (≥ 7 channels), Type 3: Limited channel study (usually using 4-7 channels), Type 4: 1 or 2 channels usually using oximetry as one of the parameters, EEG, electroencephalography; EOG, electro-oculography; EMG, electromyography; ECG, electrocardiography.

3.8 Optimal continuous positive airway pressure (CPAP) titration

Optimal PAP to treat OSA is the effective pressure that eliminates sleep-disordered breathing events in all sleep positions and stages, particularly REM (rapid eye movement) sleep, improving sleep quality without creating any untoward pressure-related side effects for the patient.

Titration effectiveness has been described by a grading system, detailed below³⁹.

A. Optimal titration: AHI < 5 per hour and includes supine REM sleep.

B. Good titration: AHI < 10 per hour or reduced by 50 per cent if the baseline less than 15 per hour and includes supine REM.

C. Adequate titration: AHI cannot be reduced to less than 10 per hour, but is reduced by 75 per cent from baseline or criterion for optimal or good titration is attained, but without supine REM sleep.

D. Unacceptable titration: Any one of the above grades is not met, which requires a repeat titration.

3.9 Process of PAP Titration

CPAP titration is done by starting at a minimum pressure of 4 cm water (H_2O) which is then increased by 1 cm H_2O to a maximum of 20 cm H_2O every five minutes or more, with the target of eliminating all the events (Evidence Quality A, Strong Recommendation)⁴⁰. If this pressure does not allow adequate titration, bilevel positive airway pressure (BPAP) titration is recommended (Evidence Quality C, Recommended)⁴¹.

Box 3. Indications of portable monitoring (PM) and polysomnography (PSG)

Portable monitoring

- Patients with high pre-test probability of moderate to severe OSA.
- Patients for whom in-laboratory PSG is not possible by virtue of immobility, safety, or critical illness.
- To monitor response to non-PAP treatments for OSA including oral appliances, upper airway surgery, and weight loss.

Polysomnography

- Patients with significant co-morbid medical conditions (moderate to severe pulmonary disease, neuromuscular disease, congestive heart failure).
- Patients with EDS where PM is negative.
- Patients suspected to have other sleep disorders.
- Screening of asymptomatic high risk populations with heart failure, morbid obesity, diabetes, coronary artery disease, stroke, refractory hypertension, nocturnal dysrhythmias and atrial fibrillation.

OSA, Obstructive sleep apnoea; PAP, positive airway pressure; EDS, Excessive daytime sleepiness

Box 4. Criteria for diagnosis of OSA²

The diagnostic criteria for OSA as recommended in International Classification of Sleep Disorders, 3rd Edition, 2014 are the presence of (A and B) or C

A. Presence of one or more of the following:

- (a) Complains of sleepiness, nonrestorative sleep, fatigue, or symptoms of insomnia.
- (b) Waking up with breath holding, gasping, or choking.
- (c) Habitual snoring, interruptions in breathing, or both during sleep as reported by patient's bed partner or other observer.
- (d) Co-existing morbidities such as hypertension, type 2 diabetes mellitus, coronary artery disease, congestive heart failure, atrial fibrillation, stroke, mood disorder, or cognitive dysfunction.

B. PSG or OCST demonstrates

- (a) Five or more obstructive respiratory events (apnoeas, hypopnoeas, or RERAs) per hour of sleep during a PSG or per hour of monitoring with OCST.

OR

C. PSG or OCST demonstrates

- (a) Fifteen or more obstructive respiratory events (apnoeas, hypopnoeas, or RERAs) per hour of sleep during a PSG or per hour of monitoring with OCST, even in the absence of symptoms.

PSG, polysomnography; OCST, out-of-centre sleep testing; RERA, respiratory effort related arousal

Ideally, 15 min of supine REM sleep must be a part of the titration.

3.10 Split Night vs. Single Night Titration

Full-night PSG with attended manual PAP titration is regarded as the gold standard for prescription of PAP therapy (Evidence Quality A, Strong Recommendation). However, split-night study, *i.e.*, initial PSG followed by 3 h of PAP titration may be performed if AHI is >40 events/hour during the first two hours or between 20-40 events/hour with clinical judgment regarding definitiveness of prescribing PAP therapy (Evidence Quality A, Strong Recommendation). It is recommended that the arousals should be abolished with PAP; otherwise, a repeat study with PSG is indicated for PAP titration⁴². AutoPAP titration using autoPAP devices that monitor snoring, apnoea or hypopnoea by airflow, flow contour, and/or impedance by forced oscillation technique can be tried during attended titration with PSG (Evidence Quality B, Recommended) to determine a fixed PAP level in patients with moderate to severe OSA without significant co-morbid illness such as congestive heart failure (CHF), COPD, central sleep apnoea or hypoventilation syndromes (Evidence Quality B, Recommended).

4 Medical management of OSA**4.1 General measures, including pharmacotherapy⁴³⁻⁴⁷**

The general measures in the management of OSA are summarized in Box 5.

4.2 Pharmacotherapy in OSA

Several drugs have been tried in OSA in small trials and the data at present are insufficient to recommend primary drug treatment in OSA. Wake promoting agents - modafinil and armodafinil are the only agents approved for excessive daytime sleepiness (EDS) despite adequate PAP therapy in OSA patients^{48,49}. (Evidence Quality A, Strong Recommendation).

4.3 Positive airway pressure therapy

4.3.1 Introduction - The principle of positive airway pressure in OSA is based on providing air under positive pressure through an interface (nasal or face mask), thus creating a pneumatic splint in the upper airway which prevents collapse of the pharyngeal airway, acting at all potential levels of obstruction⁵⁰. PAP is the most effective and widely used treatment for OSA and is the first-line therapy for moderate to severe OSA. PAP improves quality of life, in terms of clear-cut reductions in daytime sleepiness and quality of life measures. Effective PAP therapy reduces snoring and nocturnal respiratory disturbances and improves nocturnal oxygenation and sleep architecture. Benefits of PAP therapy include reduced daytime sleepiness, improved driving performance, health status and improvement in neuro-cognitive performance. Positive effects on cardiovascular outcomes, such as hypertension, cardiac arrhythmias, nocturnal ischaemia, left ventricular function, and even overall mortality have been reported⁵¹⁻⁵³.

Box 5. General measures for treating OSA⁴³⁻⁴⁷

- Counselling regarding smoking cessation (Evidence Quality B, Strong Recommendation).
- Avoidance of alcohol, sedatives and nicotine (Evidence Quality D, Optional Recommendation).
- Treatment of nasal obstruction in consultation with otolaryngologist (Evidence Quality C, Optional Recommendation).
- Weight loss (Evidence Quality B, Strong Recommendation).
- Positional therapy (Evidence Quality C, Optional Recommendation).
- Counselling about sleep hygiene and avoidance of sleep deprivation.

4.3.2 Indications for CPAP and BPAP - CPAP is currently the 'gold standard' for treatment of moderate to severe OSA (AHI >15h), and an option for less severe OSA. Treatment of OSA is indicated with the following criteria on PSG: (Evidence Quality A, Strong Recommendation)^{10,54-56}.

1. AHI or (RDI) ≥ 15 events/h
2. AHI (or RDI) ≥ 5 but <15 events/h with any of the following symptoms:
 - (i) Excessive daytime sleepiness (confirmed by either a score of greater than 10 on ESS or inappropriate daytime napping (*e.g.* during driving, conversation, or eating) or sleepiness that interferes with daily activities on a regular basis.
 - (ii) Impaired cognition or mood disorders.
 - (iii) Hypertension.
 - (iv) Ischaemic heart disease.
 - (v) History of stroke.
 - (vi) Cardiac arrhythmias.
 - (vii) Pulmonary hypertension.

All these factors have to be taken into account while planning treatment of OSA.

Currently, three types of PAP devices are available for treatment of OSA: continuous PAP (CPAP), bi-level PAP (BPAP), and automatic self-adjusting PAP (APAP). CPAP devices generate a fixed continuous pressure during inspiration and expiration. In BPAP, the pressure alternates between a fixed inspiratory and lower expiratory level during the respiratory cycle, which allows differential titration of the inspiratory (IPAP) and expiratory positive airway pressures

(EPAP). In APAP, the pressure changes throughout the night in response to changes in airflow, respiratory events, and snoring. There is no evidence base to choose the modality of PAP.

4.3.3 Role of supplemental oxygen - Supplemental oxygen (O₂) is used after adequate CPAP/BPAP titration, for residual sleep-related hypoxemia. Specifically, O₂ supplementation is done during the PAP titration study, if the SpO₂ is less than 88 per cent for five or more minutes in the absence of sleep-disordered breathing events, and oxygen flow rate is increased at a rate of 1 l/min every 15 min to target SpO₂ ≥ 88 per cent. Patients on O₂ prior to PAP titration usually need a higher amount of O₂ with the PAP device due to flow related dilution of the supplied O₂. Supplemental O₂ is to be connected to the PAP device outlet and not to the mask. The possibility of a rise in CO₂ due to the supplemental O₂ is to be kept in mind, and should be monitored with an arterial blood gas next day after disconnecting the PAP device.

4.3.4 Recommendations for APAP⁵⁷⁻⁵⁸ - APAP is a concept based on continuously adjusting positive airway pressure to meet the patient's variable needs to maintain a patent airway, thereby reducing the overall mean airway pressure. This could be done in an unattended setting such as the patient's home, and potentially enhances tolerability and compliance. Figure 4 summarises PAP prescription.

1. Certain APAP devices may be useful for attended titration with PSG to identify a single pressure for use with standard CPAP [also called fixed CPAP (f-CPAP)] for management of moderate to severe OSA. (Evidence Quality B, Optional Recommendation)

2. Patients who are being treated with APAP itself, or f-CPAP calculated on the basis of APAP titration must have close clinical follow up to monitor treatment effectiveness. In the event of an inadequate symptomatic or objective response with APAP therapy, a standard attended CPAP titration should be done.

3. APAP devices are not recommended for split-night titration. (Evidence Quality A, Strong Recommendation)

4. Patients with CHF, COPD, CSA are not currently considered candidates for APAP titration or treatment. (Evidence Quality A, Not Recommended).

4.3.5 PAP compliance⁵⁹ - The treatment of sleep apnoea with PAP has inherent problems with initial acceptance and long-term adherence, together called

compliance due to discomfort from the mask interface, positive pressure itself, need for daily night use and long-term therapy. Compliance with PAP is a significant problem, and nasal congestion and mask intolerance are the most common complaints that reduce PAP compliance.

Some patients cannot tolerate PAP because of initial discomfort of sudden application of pressure, or discomfort perceived in exhaling against high pressure. Most PAP devices have a pressure “ramp”, where the pressure rise can be slow till it attains the target pressure, over as much as 45 min. An option for reducing expiratory pressure is BPAP, which allows independent adjustment of inspiratory and expiratory pressures, though the comfort benefits of BPAP have not been categorically demonstrated. Pressure-relief CPAP reduces the discomfort of breathing against high pressure during expiration by lowering the pressure at the onset of expiration. Recent Cochrane database review has concluded that pressure-relief CPAP did not improve compliance⁶⁰. Similarly, APAP, with a lower mean pressure through the night has a minimal impact on improving compliance.

4.3.6 Adverse effects of PAP therapy - Adverse effects of PAP therapy are summarized in Table IV.

4.4 Oral Appliances

4.4.1 Background and rationale - Oral appliances (OA) are an established treatment option for snoring and mild to moderate OSA in selected cases and not in severe OSA. OAs are less cumbersome than PAP therapy and should be considered for patients who have failed or refused PAP treatment, for those with snoring or mild to moderate OSA^{61,62}. Dental professionals trained in sleep medicine should prescribe and prepare appropriately fitting OA for the treatment of OSA.

4.4.2 Types of oral appliances

4.4.2.1 *Mandibular repositioning appliance*: Mandibular repositioning appliance (MRA) works by bringing the mandible forward, thereby increasing the airway volume. It can be either fixed (pre-determined advancement), titratable (adjustable) or either a one-piece or a two-piece appliance. The titratable MRA has an adjustable mechanism that allows progressive advancement of the mandible after initial construction until the optimal mandibular position is achieved. Single-piece or non-adjustable appliances often have to be made again if the initial jaw advancement is insufficient^{62,63}.

4.4.2.2 *Tongue retaining appliances*: Tongue retaining appliances (TRA) are indicated for patients with large tongue and when use of MRA is limited due to edentulous ridges. Once the patient is using the appliance routinely, overnight PSG is required to assess the clinical response objectively^{62,63}.

4.4.3 Effects of OA therapy - Effects of OA therapy are summarized in Table V^{61,63-70}.

4.4.4 Contraindications to OA therapy^{62,71,72} - Contraindications to OA therapy are summarized in Box 6.

4.4.5 Predictors of response to oral appliances^{73,74} - Predictors of response to oral appliances are summarized in Box 7.

4.4.6 Adverse effects of OAs⁷⁵⁻⁷⁷ - Adverse effects of OAs are summarised in Box 8.

4.4.7 Compliance with OAs - The compliance depends on benefits and discomfort. Various studies reported different level of compliance for different types of OAs in OSA; it ranges from 51 to 88 per cent. Among the various types of oral appliances, compliance

Table IV. Adverse effects of PAP therapy

Problem	Solution
Nasal congestion, rhinorrhoea, nasal dryness, sinus pain	Nasal steroids, heated humidification
Mask discomfort, leakage	Using suitable mask interface, good mask fitting
Skin breakdown, abrasions	Gel and air-cushion interface masks
Mask claustrophobia	Other types of masks, nasal pillows
Pressure intolerance, difficulty in exhalation	Use “ramp”, pressure-relief, BPAP, auto-PAP
Mouth breathing	Chin strap, full face or oro-nasal mask
Bed partner intolerance	Teaching adaptation skills to the patient and bed partner

Table V. Effects of oral appliances (OAs)

Effects on snoring	OAs are beneficial in decreasing snoring in the majority of OSA patients on both subjective and objective assessment ^{63,64} . (Evidence Quality A)
Effects on OSA	OAs are effective in the treatment of mild to moderate OSA ⁶¹ with improvement in the AHI and oxygen saturation following OA therapy ^{61,64-67} . (Evidence Quality B)
Effects on daytime functions	Improvement in daytime sleepiness assessed by Epworth Sleepiness Scale is seen with usage of oral appliances ^{64,66,68} . The assessment of neuropsychological function showed significant improvement in measures of self-reported sleepiness, fatigue and energy levels and simulated driving performance ^{68,69} . (Evidence Quality B)
Effects on vascular diseases	There is a modest favourable effect of OAs on systolic and diastolic blood pressure and on mean arterial pressure ⁷⁰ . (Evidence Quality A)

is better with mandibular advancement devices (MAD) than any other appliance^{74,77,78}.

(Evidence Quality C)

4.4.8 Other recent advances in the treatment of OSA - Nasal EPAP device is a single-use device applied over the nostrils that functions like an inspiratory valve allowing unimpeded inspiration but offers resistance to expiration, creating an EPAP. This resultant EPAP cannot be titrated. In a large randomized controlled trial (RCT), the nasal EPAP device significantly improved AHI (43 vs. 10%) and ESS at three months as compared to a sham device. However, some patients do not show any improvement in AHI with nasal EPAP, and among the responders not all would achieve an AHI < 10 events/h. The clear-cut indication for nasal EPAP devices is still not well defined⁷⁹.

5 Surgical treatment of OSA

PAP therapy has been considered to be the first-line of management for patients with OSAS⁸⁰. However, some patients may prefer alternative treatment options because they are unable to tolerate, and are non-compliant⁸¹ or do not benefit from PAP therapy. The lack of randomized controlled trials comparing PAP therapy and surgical treatment make it very difficult to attain a consensus in selecting the appropriate management

Box 6. Contraindications to oral appliance (OA) therapy^{62,71,72}

- Inadequate number of healthy teeth in upper and lower dental arch (At least 6-10 teeth in each arch desirable).
- Periodontal diseases.
- Patients with full dentures.
- Limitation in forward protrusion of mandible and jaw opening.
- Temporomandibular joint diseases.

Box 7. Predictors of response to oral appliances^{73,74}

Better response is seen with:(Evidence Quality C)

- Female sex
- Younger age
- Lower BMI
- Smaller neck circumference
- Cephalometric parameters:
 - Short palate
 - Large retro-palatal airway space
 - Narrow anterior posterior position of mandible (small SNB angle)
 - Higher anterior posterior position of the maxilla (large SNA angle)

BMI, body mass index; SNA, sella nasion A; SNB, sella nasion B

Box 8. Adverse Effects of oral appliances (OAs)⁷⁵⁻⁷⁷

Adverse effects of OAs (Evidence Quality C)

- Excessive salivation
- Temporary discomfort after awakening
- Mucosal dryness
- Transient discomfort in teeth, gum and Temporomandibular joint
- Headache
- Mesial migration of lower dentition
- Distal migration of upper dentition

option⁸². The decision for surgical management should be strictly individualized after careful assessment of patient with due importance given to the sites of obstruction. The following description provides an insight into the procedures that are currently available and their potential role in routine management.

5.1 Evaluation of level of obstruction: The most significant concern in the assessment of airway is that it can only be performed in an awake patient and the scenario hardly simulates the exact status during sleep. Apart from drug-induced sleep nasoendoscopy

(DISE)⁸³⁻⁸⁵ in patients who are planned for surgery and fiberoptic nasopharyngoscopy with Mueller manoeuvre (FNMM)⁸⁶, other methods like cephalometry, acoustic analysis, somnofluoroscopy, CT and sleep MRI are not recommended for routine use to assess the level of obstruction.

5.2 Surgeries in OSA: Surgical options in OSA are site directed surgeries and bariatric surgery.

5.2.1 Nasal and nasopharyngeal surgery - Patients with OSAS frequently have nasal obstruction which results in snoring and mild sleep apnoea, but nasal blockage *per se* does not lead to severe OSA.

1. Nasal surgery (correction of anatomical defects) alone is not a useful method of treatment of moderate

to severe sleep apnoea⁸⁷. (Evidence Quality B, Not recommended).

2. It also improves the compliance with PAP and also improves its effectiveness^{87,88}. (Evidence Quality B, Recommended).

5.2.2 Maxillo-mandibular surgeries - Malpositioning of maxilla and mandible contribute to OSAS by reducing the posterior hypopharyngeal space. Role of surgery in the correction of such anatomical abnormalities is summarized in Table VI⁸⁹⁻⁹⁸.

5.2.3 Role of bariatric surgery for treatment of OSAS - Bariatric surgery (BS) is a surgery done in order to create caloric restriction and/or malabsorption for weight loss. The commonly performed bariatric

Table VI. Maxillo-mandibular surgeries

Genioglossus advancement (Evidence Quality C, Optional Recommendation) ⁸⁹	Genioglossus advancement is found to be helpful in patients with hypopharyngeal soft tissue and tongue base abnormalities. The short- and long-term effects of genioglossus advancement are improvement of Epworth scale, AHI score and oxygen saturation.
Maxillo-mandibular advancement surgery ⁹⁰ (Evidence Quality C, Optional Recommendation)	Maxillo-mandibular advancement surgery is an option for severe OSA patients with maxillary and mandibular retrusion, unable to tolerate PAP therapy and in whom oral appliances have failed. It can also be considered in patients who have failed to improve after other surgical procedures.
Distraction osteogenesis (Evidence Quality C, Optional Recommendation) ⁹¹	Distraction osteogenesis can be employed in patients with severe OSA due to maxillofacial skeletal disharmony, particularly mandibular and maxillary retrusion where more than 10-12mm advancement is required.
Uvulopalatopharyngoplasty (UPPP) (Evidence Quality C, Recommended in patients with retropalatal obstruction) ^{92,93}	UPPP is the standard mode of management in patients with retropalatal obstruction.
Laryngeal surgery (Evidence Quality C, Recommended only for patients with laryngeal pathology) ⁹⁴	Laryngeal surgery is limited to patients with laryngeal obstruction requiring surgical excision for its management. PAP therapy is the primary mode of management in patients with laryngeal pathology. Surgery is usually preferred for intractable cases or patients with poor compliance to PAP.
Tonsillectomy (Evidence Quality C, Recommended in adults with tonsillar hypertrophy) ⁹⁵	Tonsillectomy is indicated in adults with tonsillar hypertrophy which is non-responsive to medical management.
Multilevel surgery (MLS) in OSAS ^{96,97} (Evidence Quality C, Recommended for cases with documented multiple level obstruction)	Multilevel surgery refers to surgical procedures performed at two or more sites in the upper airway. The three main levels of obstruction identified are nasal, retropalatal and retroglossal/hypopharyngeal. MLS is a viable option for patients who failed PAP or other conservative methods. The suitable candidates include those with mild-moderate OSA, BMI <30kg/m ² , age <60 years, retroglossal obstruction and without any co-morbidity.
Tracheostomy for OSAS ⁹⁸ (Evidence Quality C, Optional Recommendation)	Tracheostomy is poorly accepted in the present scenario. Patients with significant OSA who have failed all medical and surgical procedures might require permanent tracheostomy. It significantly decreases apnoea index, desaturation index, sleepiness and mortality in OSA subjects but does not correct central apnoea.

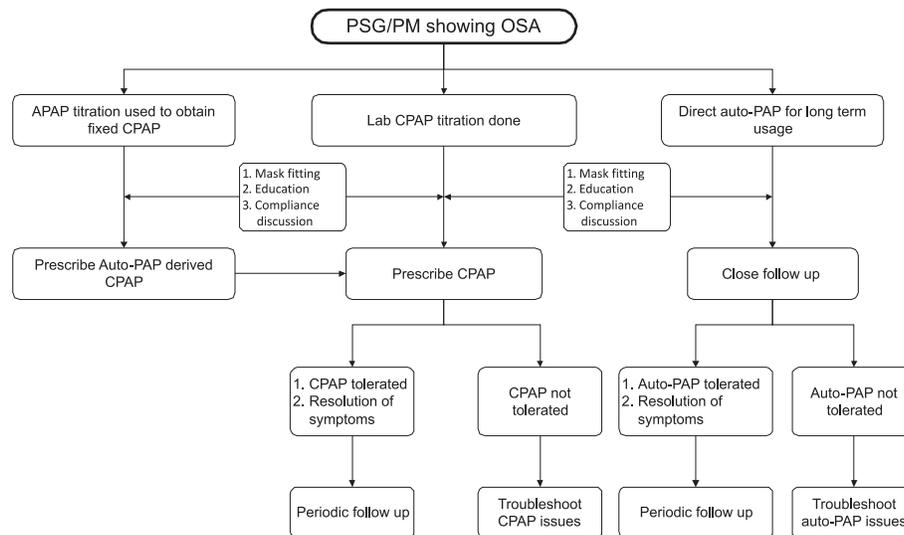


Fig. 4. Comprehensive approach to PAP prescription. PAP, positive airway pressure; PSG/PM, polysomnography/portable monitoring; APAP, auto-titrating positive airway pressure; CPAP, continuous positive airway pressure.

procedures are adjustable gastric banding (AGB), Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG) and bilio-pancreatic diversion (BPD).

5.2.3.1 Impact of BS on OSA: Following BS, there is improvement of post-operative sleep quality, reduction in day time sleepiness, improvement in quality of life, decrease in use of PAP and decrease in use of high PAP pressure requirement. Gastric bypass was the most successful procedure in improving or resolving OSA followed by gastroplasty, BPD and gastric banding being the least effective procedure⁹⁹. However, in the majority of the patients (62%), the mean residual AHI after surgery was more than 15 events per hour. This indicates that there is a persistent residual disease, even though there has been considerable improvement. As such, all patients should undergo repeat PSG after surgical weight loss and those patients who have residual disease consistent with moderately severe OSA need continued treatment with PAP. The available evidence suggests that the patients cured of OSA were less obese and younger than those who had residual OSA after bariatric surgery¹⁰⁰.

In a recent meta-analysis of 13,900 patients who underwent bariatric surgery, 79 per cent of patients experienced either resolution or improvement of their sleep apnoea. Bariatric surgery is strongly recommended¹⁰¹ for obese OSA patients with BMI $\geq 35\text{kg/m}^2$ (Evidence Quality B).

Conflicts of interest: None

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