Chapter

50 SLEEP MEDICINE AND ANESTHESIA

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INTRODUCTION

The neurophysiologic mechanisms governing sleep and wakefulness have been identified during recent years. These mechanisms have provided new insights into mechanisms of different arousal states and the impact of different anesthetic drugs on modulation of key components of the sleep-wake neuronal circuits. The similarities and differences between sleep and anesthesia states need to be understood in order to examine a patient's vulnerability to anesthesia and different anesthetic drugs. These differences are also likely to determine the likelihood of complications in one state compared to the other, such as upper airway collapse, hypoventilation, and other respiratory problems.

Human Sleep

Sleep is defined as a state of decreased arousal that is actively generated by nuclei in the hypothalamus, brainstem, and basal forebrain and is crucial for the maintenance of health.[1,2] Humans spend approximately one third of their lives sleeping. Sleep is described as being under the control of two processes: (1) a circadian clock (the circadian drive) that regulates the appropriate timing of sleep and wakefulness across the 24-hour day and (2) a homeostatic process (the homoeostatic drive) that regulates sleep need and intensity according to the time spent awake or asleep.[3] The daily drive to sleep is modulated by the hypothalamic suprachiasmatic nuclei that coordinate circadian (24-hour) rhythm. The perceived sensation of sleepiness is likely the result of a circadian drive, process C (people tend to get sleepy according to their accustomed sleep times during a 24-hour cycle), along with a homeostatic drive, process S (sleep deprivation leads to increasing sleepiness).[4] These two sleep drives are additive. Also, a temporal organization must be preserved to obtain a subjective experience of being refreshed and

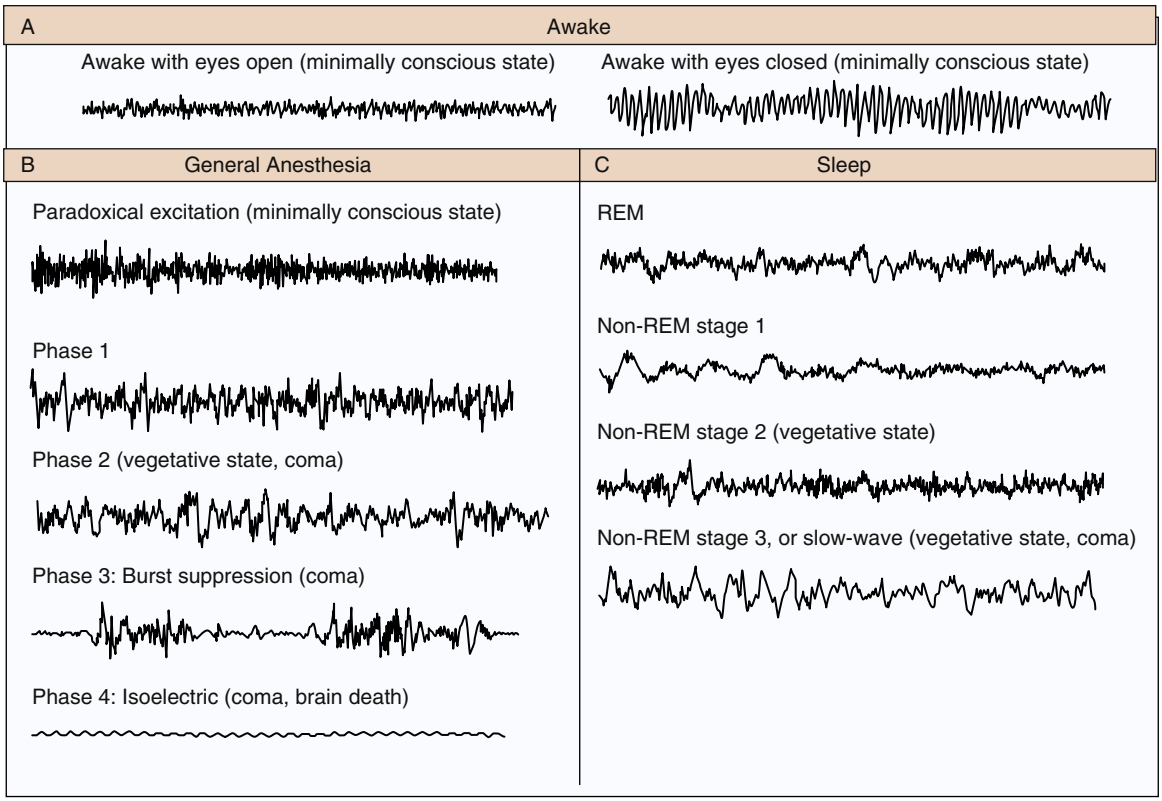

Fig. 50.1 Electroencephalographic changes seen with different states of consciousness and arousal (awake state, general anesthesia, and sleep stages). *NREM,* Non–rapid eye movement; *REM,* rapid eye movement. (From Brown EN, Lydic R, Schiff ND. General anesthesia, sleep, and coma. *N Engl J Med.* 2010;363(27):2638-2650, used with permission.)

restful.[5,6] For example, patients with chronic insomnia often have difficulties because the two sleep drives are not aligned with each other; in such patients, afternoon naps taken to compensate for sleep deprivation would likely delay sleep onset later in the night).

Normal sleep exhibits a dynamic architecture and is a nonhomogeneous state that can be divided into non–rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. These two states cycle at an ultradian (less than 24 hour) rhythm of approximately 90- to 120-minute intervals, consolidated in bouts of 6 to 8 hours.[2,5,6]

The American Academy of Sleep Medicine (AASM) has classified wakefulness and sleep into various stages based on characteristic electroencephalogram (EEG) patterns.[7,8] *Wakefulness*, or *stage W*, is characterized by beta activity with eyes open (low amplitude, 12 to 40 Hz) and alpha activity with eyes closed (low amplitude, 8 to 13 Hz). NREM sleep has three distinct EEG stages, based on characteristic patterns on the EEG (Fig. 50.1). *Stage N1 sleep* is characterized by attenuation of alpha activity during wakefulness, to a low amplitude, mixed frequency signal (4 to 7 Hz), and vertex sharp waves (prominent sharp waves lasting <0.5 second and maximal over the central EEG region). *Stage N2 sleep* is characterized by the presence of K-complexes (well-delineated, negative, sharp waves followed by a positive deflection, lasting 0.5 second) and sleep spindles (high-frequency bursts of 11 to 16 Hz, with tapering ends, distinct from the background rhythm and last ≥0.5 second). *Stage N3 sleep* is characterized by the presence of higher-amplitude (75 μV), lower-frequency (0.5 to 2 Hz) rhythms, also known as *delta waves*, accompanied by waxing and waning muscle tone, decreased body temperature, and decreased heart rate.[2] *Stage R*, or *REM sleep*, is characterized by rapid eye movements, dreaming, irregular breathing and heart rate, and skeletal muscle hypotonia.[1] In REM sleep, the EEG shows active high-frequency, low-amplitude rhythms (see Fig. 50.1). This activated EEG pattern has given rise to descriptions of REM sleep as "active" or "paradoxical" sleep and to the NREM phase of sleep as "quiet" sleep.[9,10] Cognitive changes and vivid dreaming are well known to occur during REM sleep.[11]

General Anesthesia

General anesthesia could be described as a reversible drug-induced coma. Nevertheless, anesthesia providers often refer to the unconsciousness induced by anesthetic drugs as *sleep* because of the negative connotation of the term

coma. The EEG patterns of general anesthesia-induced consciousness are described in three periods (see Fig. 50.1).

Before *induction of anesthesia*, the patient has a normal, active EEG, with prominent alpha activity (10 Hz) when the eyes are closed. Small doses of hypnotic drugs acting on the γ-aminobutyric acid type A ($GABA_A$) receptors induce a state of sedation in which the patient is calm and easily arousable, with the eyes generally closed. This state is followed by a brief period of paradoxical excitation, characterized by an increase in beta activity on the EEG (13 to 25 Hz).

During the *maintenance* period, four distinct phases have been described.[12] Phase 1, a light state of general anesthesia, is characterized by a decrease in EEG beta activity (13 to 30 Hz) and an increase in EEG alpha activity (8 to 12 Hz) and delta activity (0 to 4 Hz). During phase 2, the intermediate state, beta activity decreases and alpha and delta activity increases, with so-called anteriorization, that is, an increase in alpha and delta activity in the anterior EEG leads relative to the posterior leads. The EEG in phase 2 resembles that seen in stage 3, NREM (or slow-wave) sleep. Phase 3 is a deeper state, in which the EEG is characterized by flat periods interspersed with periods of alpha and beta activity (burst suppression). As this state of general anesthesia becomes more intense, the time between the periods of alpha activity lengthens, and the amplitudes of the alpha and beta activity decrease. Surgery is usually performed during phases 2 and 3. In phase 4, the most profound state of general anesthesia, the EEG is isoelectric (completely flat), indicated in conditions such as induced coma or neuroprotection during neurosurgery (also see Chapter 30).[12]

During *emergence* from general anesthesia, the EEG patterns proceed in approximately reverse order from phase 2 or 3 of the maintenance period to an active EEG that is consistent with a fully awake state. Anesthetic drugs induce unconsciousness by altering neurotransmission at multiple sites in the cerebral cortex, brainstem, and thalamus. Recent advances in spectral EEG analysis have allowed spatiotemporal characterization of the effects of various intravenous and inhaled anesthetics.[13]

Other Arousal States

Coma is characterized by a state of profound unresponsiveness, which could be drug-induced or a result of brain injury. EEG activity in comatose patients is variable and resembles the high-amplitude, low-frequency activity seen in patients under general anesthesia. The EEG patterns are also dependent on the severity and extent of brain suppression or injury (see Fig. 50.1).[2]

Sleep and Anesthesia: How Different Are They?

The similarities and differences between sleep and anesthesia states should be understood.[14] Sleep is a natural state of decreased arousal, controlled by circadian and homeostatic drives. Anesthesia, on the other hand, is a drug-induced state that is independent of these intrinsic rhythms. Sleep states are amenable to disruptive influences such as psychological and environmental factors. Anesthesia, on the other hand, is immune to such influences. Sleep is characteristically a nonhomogeneous state with distinct stages, periodic arousals, and variable body postures, occurring in a cyclic pattern. Anesthesia is a relatively homogeneous state, the depth and duration of which are directly dependent on drug pharmacokinetics and pharmacodynamics. In the presence of significant sensory stimulation, the sleep state gets disrupted and the subject arouses. Yet, a basic tenet of anesthesia is suppression of arousals, rendering the subject insensate to bodily injury during surgery. Sleep state reversal occurs spontaneously after putative restorative functions are completed. However, anesthesia state reversal requires voluntary stoppage of drug administration as well as effective drug elimination.

FUNCTIONAL NEUROANATOMY OF SLEEP AND AROUSAL PATHWAYS

Common neurophysiologic mechanisms and neural pathways during sleep are also activated by anesthetic drugs.[12,15] Sedative drug requirements decrease with both sleep deprivation and circadian rhythm disruption. Anesthesia on its own, in the absence of surgical stimulation, also has sleep-like restorative properties.[16,17]

Anesthesia-induced loss of consciousness results from interactions of anesthetics with the neural circuits regulating sleep and wakefulness states. Ascending activation of the cerebral cortex by subcortical center activity is important in the maintenance of wakefulness. Deactivation of the thalamus occurs in imaging studies for both the sleep and anesthesia states, indicating that thalamic and extrathalamic pathways are involved in sleep state modulation.[18]

Sleep state modulation is regulated by two groups of neural centers. The wakefulness promoting centers are the locus ceruleus (LC), dorsal raphe (DR), and tuberomammillary nucleus (TMN); and the sleep promoting center is primarily the hypothalamic ventrolateral preoptic nucleus (VLPO).[19,20] One exception is the median preoptic area that contains both wake-active and sleep-active neurons.[19,20] Discrete neurochemical mediators are involved in sleep stage transition during which the cholinergic (in brainstem and forebrain), noradrenergic (in the LC), and serotonergic (in the DR) activity are noted to be less active in NREM sleep; yet, the cholinergic activity increases in REM sleep.[19] The GABAergic/galanin activity from the VLPO is increased in NREM sleep as it inhibits the histaminergic TMN.[19] Orexinergic pathways from the perifornical nucleus are also inactive during NREM sleep and may be the cause of characteristic daytime hypersomnolence and disrupted nocturnal sleep, as noted in narcolepsy.[19]

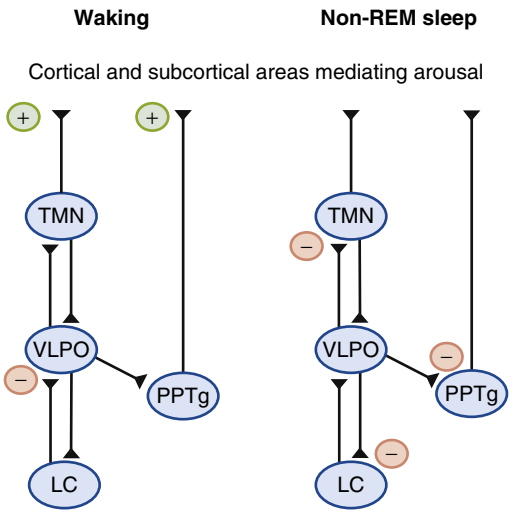

Fig. 50.2 A simplified diagram showing some of the major arousal pathways and their connections with the tuberomammillary nucleus (TMN). *LC,* Locus ceruleus; *PPTg,* pedunculopontine tegmental nuclei; *VLPO,* ventrolateral preoptic nucleus. (From Harrison NL. General anesthesia research: aroused from a deep sleep? *Nat Neurosci.* 2002;5(10):928-929, used with permission.)

During wakefulness, the LC is active and exerts an inhibitory influence on the hypothalamic VLPO. When sleep starts, the LC activity decreases, disinhibiting the VLPO, which now exerts an inhibitory influence on key brainstem and thalamic centers and restrains the ascent of arousal promoting pathways to the cortex through them (Fig. 50.2).[14,20] VLPO projects back onto the LC causing feedback inhibition. Widespread inhibition of ascending arousal promoting pathways occurs, as well as reinforcement of LC output inhibition, resulting in sleep onset. The mutual inhibition between VLPO and LC acts to produce a switch-like, *bistable states* of wakefulness and sleep at a certain threshold.[20] This effect is also caused by anesthetic drugs such as propofol and benzodiazepines, acting on the same target receptors and neural pathways that are integral to sleep and wakefulness.

SLEEP-DISORDERED BREATHING OR SLEEP-RELATED BREATHING DISORDERS

Sleep-disordered breathing (SDB) is characterized by abnormalities of respiration patterns during sleep. The abnormal patterns of breathing are broadly grouped into obstructive sleep apnea (OSA) disorders, central sleep apnea (CSA) disorders, sleep-related hypoventilation disorders, and sleep-related hypoxemia disorders.[21] OSA disorders are characterized by complete or incomplete upper airway closure during sleep. CSA disorders are characterized by reduction (hypopnea) or cessation (apnea) of airflow due to absent or reduced respiratory effort. Central apnea or hypopnea may occur in a cyclic, intermittent, or irregular (ataxic) fashion. We will primarily focus on OSA, as this is the most common entity encountered perioperatively.

OBSTRUCTIVE SLEEP APNEA (OSA)

OSA is characterized by episodes of apnea or hypopnea during sleep, resulting in varying severity of hypoxemia and hypercapnia. The obstructive apnea or hypopnea is caused by repeated episodes of complete or partial closure of the pharynx, accompanied with hypoventilation and desaturation, and terminated by EEG arousal.[22-25]

Pathophysiology of Upper Airway Collapse in OSA

Upper airway collapsibility and patency are dependent on a continuous balance between collapsing and expanding forces influenced by sleep-wake arousal. Polysomnographic data of important physiologic variables can be used to study characteristic features of an obstructive apnea[26] (Fig. 50.3). During wakefulness, the upper airway stability and patency are achieved by increased genioglossus muscle tone, which pulls the tongue forward.[27] During sleep, upper airway collapse in OSA patients occurs owing to a complex interaction of multiple factors such as loss of upper airway dilating muscle tone, impaired response to mechanoreceptors sensing intrapharyngeal pressures, ventilator overshoot (high loop gain of the respiratory control system), and an increased arousal threshold.[27] Moreover, patients with OSA have an upper airway that is predisposed to collapse, which occurs in the presence of smaller upper airway cross-sectional areas and increased critical closure pressures than those seen in patients without OSA.[28] During NREM sleep and anesthesia, reduction of wakeful cortical influences, reflex gain, and ventilatory drive predispose to upper airway collapse and hypoventilation.[14] These effects are more intense during general anesthesia as the decrease in tonic and phasic muscle activity is profound and abolition of protective arousal response predisposes to prolonged obstruction and more severe oxygen desaturation.

Clinical Diagnostic Criteria

Classically, the gold standard for the definitive diagnosis of OSA requires an overnight polysomnography (PSG) or sleep study. Based on the AASM recommendations, apneas and hypopneas are defined as a reduction in the rate of airflow from intranasal pressure of at least 90%, or between 50% and 90%, respectively, for at least 10 seconds accompanied by either a 3% to 4% decrease in oxygen saturation or an EEG arousal.[8] Hypopneas are classified as obstructive if thoracoabdominal motion is out of phase or if airflow limitation is observed on the nasal pressure signal, whereas central hypopneas are

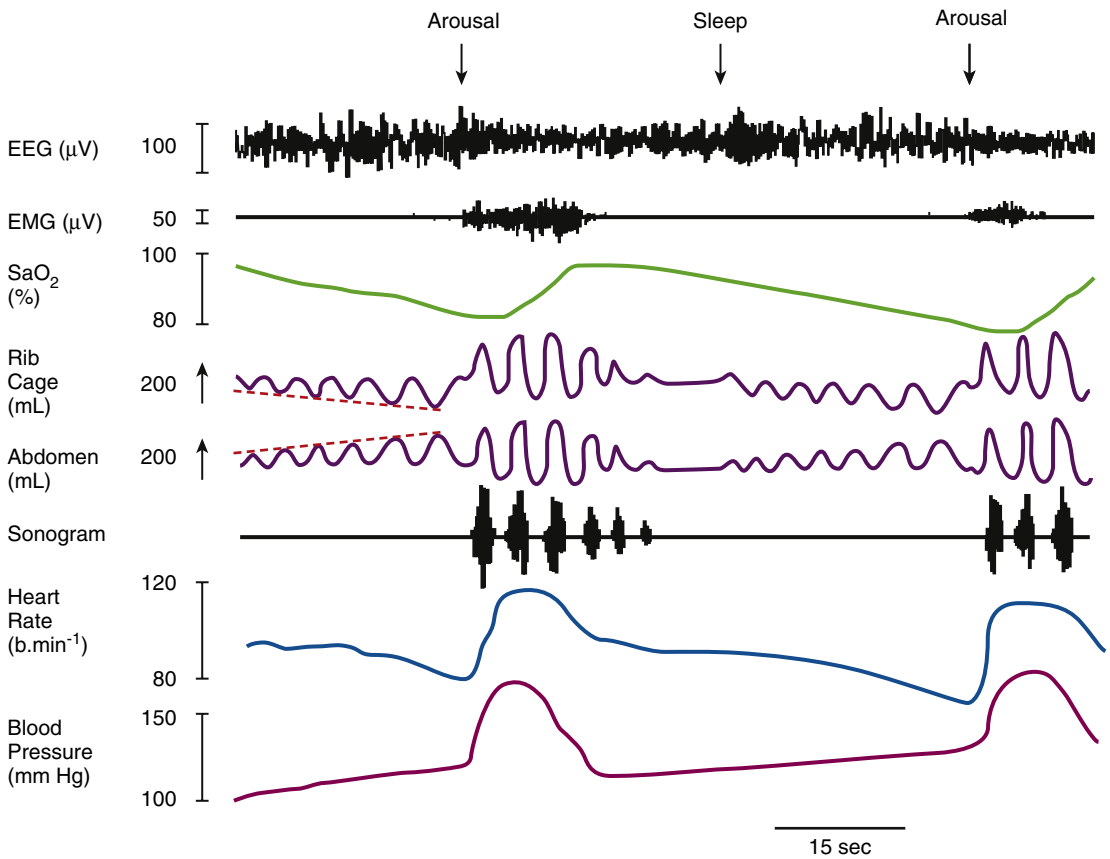

Fig. 50.3 Polysomnographic recordings of obstructive apnea in a patient with obstructive sleep apnea. Note that during the hypopnea, rib cage and abdominal motion are out of phase (i.e., moving in opposite directions indicating upper airway obstruction). Upper airway obstruction leads to drop in O_2 saturation. The ineffective breathing attempts continue until the patient awakes, as seen by the EEG arousal, and pharyngeal obstruction is relieved. The resuscitative breath now leads to normalization of the oxygen saturation until the next obstructive event ensues. The surge in heart rate and arterial blood pressure occurs along with the arousal, highlighting the activation of sympathetic stimulation in these patients, and placing them at higher risk of long-term cardiovascular complications. The arrows indicate arousals from sleep and sleep onset as determined from the EEG and EMG traces. The sonogram indicates breathing sounds due to snoring. *EEG*, Electroencephalogram; *EMG*, submental electromyogram; *Sao_2*, arterial oxygen saturation. (From Thompson SR, Ackermann U, Horner RL. Sleep as a teaching tool for integrating respiratory physiology and motor control. *Adv Physiol Educ.* 2001;25:101-116, used with permission.)

classified when thoracoabdominal motion is in-phase and there is no evidence of airflow limitation on the nasal pressure signal.[29] Mixed apneas are classified for events that begin as central for at least 10 seconds and end as obstructive, with a minimum of three obstructive efforts. Wherever applicable, ataxic breathing or Cheyne-Stokes type of respiration is also described.[29,30]

The apnea-hypopnea index (AHI) is defined as the average number of abnormal breathing events per hour of sleep. OSA severity is determined by the AHI as follows: mild, 5 to 15 events per hour; moderate, more than 15 to 30 events per hour; and severe, more than 30 events per hour.[8,31] The clinical diagnosis of OSA requires either an AHI of 15 or more, or an AHI more than or equal to 5 events, with symptoms such as excessive daytime sleepiness, unintentional sleep during wakefulness, unrefreshing sleep, loud snoring reported by a partner, or observed obstruction during sleep.[21,32]

Polysomnography and Portable Devices

A laboratory-based sleep study is set up and analyzed by a registered sleep technologist using standard criteria.[8] All studies are performed using a uniform montage of electrograms including central, occipital, and frontal EEGs; right and left electrooculogram (EOG); chin electromyogram (EMG); electrocardiogram (ECG); and anterior tibialis muscle EMG bilaterally. Thoracoabdominal motion is usually

Box 50.1 Symptoms and Clinical Features of Obstructive Sleep Apnea (OSA)

Symptoms and Behaviors	Comorbid Conditions
Daytime sleepiness	Obesity
Loud snoring	Large neck circumference
Nonrestorative sleep	Craniofacial deformities (retrognathia, midfacial hypoplasia)
Witnessed apneas by bed partner	Crowded pharynx
Awakening with choking	Systemic hypertension
Insomnia with frequent brief nocturnal awakenings	Hypercapnia or high serum bicarbonate
Lack of concentration	Cardiovascular disease
Cognitive deficits	Cerebrovascular disease
Changes in mood	Cardiac dysrhythmia
Morning headaches	Metabolic syndrome
Sleep walking, confusional arousals (arousals from NREM sleep)	Pulmonary hypertension
Vivid, strange, or threatening dreams (arousals from REM sleep)	Obesity hypoventilation syndrome
Gastroesophageal reflux	Cor pulmonale
Nocturia	Polycythemia
Drowsy driving, and motor vehicle accidents	Floppy eyelid syndrome

NREM, Non-rapid eye movement; *REM,* rapid eye movement.
Modified from Olson E, Chung F, Seet E. Surgical risk and the preoperative evaluation and management of adults with obstructive sleep apnea. In Post TW, ed. *UpToDate.* Waltham, MA: UpToDate; 2015.

monitored by respiratory inductance plethysmography (RIP), and airflow is monitored using either a nasal pressure transducer or nasal thermistor. Arterial oxygen saturation (Sao_2) is monitored by pulse oximetry. Body position and snoring are recorded manually.

Home sleep testing may be a viable alternative to standard PSG for the diagnosis of OSA in certain subsets of patients.[33,34] The Portable Monitoring Task Force of the AASM has classified level 2 (full unattended PSG with seven or more recording channels), level 3 (devices limited to four to seven recording channels), and level 4 (monitors with one to two channels including nocturnal oximetry) devices.[33] In particular, the level 2 portable PSG device has a diagnostic accuracy similar to that of standard PSG,[35] whereas nocturnal oximetry is both sensitive and specific for detecting OSA in high-risk surgical patients.[36] Preoperative overnight oximetry may be a useful screening test (when mean preoperative overnight saturation is less than 93%, oxygen desaturation index more than 29 events per hour, overnight duration of oxygen saturation less than 90% for more than 7% of total sleep time) and predicts postoperative adverse events.[37] Portable devices may be considered when there is high pretest likelihood for moderate to severe OSA without other substantial comorbid conditions[33] and proper standards for conducting the test and interpretation of results are met.[32]

Prevalence of OSA in the General and Surgical Population

The prevalence of moderate to severe OSA (AHI ≥ 15 events per hour) is 13% among men and 6% among women, respectively, in the general population.[38] The estimates were more frequent with increasing age and body mass index.[39] The difference could be explained by the underdiagnosis of OSA, as 80% of patients with moderate to severe OSA remain undiagnosed.[38,40] In the general population, OSA diagnosis is an independent risk factor for cardiovascular morbidity and mortality.[41-44]

The prevalence of undiagnosed moderate to severe OSA (AHI > 15 events per hour) among surgical patients is difficult to assess[39] but appears to be higher than that in the general population.[45,46] Sixty percent of patients with moderate to severe OSA (AHI ≥15 events per hour) were not diagnosed by the anesthesia provider preoperatively (also see Chapter 13).[47]

OSA and Comorbid Conditions

OSA is associated with long-term cardiovascular morbidity including myocardial ischemia, heart failure, hypertension, arrhythmias, cerebrovascular disease, metabolic syndrome, insulin resistance, gastroesophageal reflux, and obesity (Box 50.1).[48] Craniofacial deformities (e.g., macroglossia, retrognathia, midfacial hypoplasia), endocrine disorders (e.g., hypothyroidism, Cushing disease), and demographic (male, age older than 50 years) and lifestyle (e.g., smoking, alcohol consumption) are factors closely associated with OSA.[48] Perioperative physicians (also see Chapter 13) should be aware of the possible coexistence of these medical conditions, which can possibly be improved preoperatively, and risk stratification may be instituted at the time of surgery.

Surgery and OSA Severity

Factors contributing to the postoperative worsening of OSA have been defined.[49,50] Compared to the preoperative baseline, the AHI significantly increased on the first night, with peak increase occurring on the third night.[49,50]

Preoperative AHI, age, and opioid dosage were significant predictors of postoperative AHI.[50] These findings are clinically significant for surgical patients who may not be monitored as closely during the second and third postoperative nights.

Postoperative complications such as myocardial infarction, congestive heart failure, and pulmonary embolus can be more likely to occur during the second or third postoperative day. According to a 2015 analysis of the American Society of Anesthesiologists (ASA) Closed Claims Project database, 88% of opioid-induced respiratory depression incidents occurred within the first 24 hours of surgery, of which 97% were deemed as preventable.[51] Multiple prescribers (33%), concurrent administration of nonopioid sedating medications (34%), and inadequate nursing assessments or response (31%) were identified as contributory factors.[51] Life-threatening critical respiratory events with opioids occur mostly during the first 24 hours after surgery for all patients[52] and within the first 72 hours for OSA patients.[53] Factors such as OSA, intense levels of sedation, nighttime events, and postoperative acute renal failure are associated with fatality following these events.[54] Increased postoperative complications on the second or third postoperative day may be associated with increased AHI and decreased oxygen saturation.

OSA and Postoperative Complications

A systematic review of 61 studies[55] and a meta-analysis of 13 studies demonstrated that patients with OSA versus non-OSA were associated with a significantly higher risk of postoperative events, such as acute respiratory failure, desaturation, and intensive care transfer.[56] Large population-based studies have shown that patients with a diagnosis of OSA have an increased risk of perioperative complications, such as the need for emergent endotracheal intubation,[57-59] noninvasive or mechanical ventilation,[57-59] aspiration of gastric contents–induced pneumonia,[58] pulmonary embolism,[58] and atrial fibrillation.[57,59]

Recently, in 2015, a large perioperative database (26,000 patients in 50 U.S. hospitals) was analyzed to determine complications in patients with OSA.[60] Compared with treated OSA, untreated OSA was independently associated with more cardiopulmonary complications, including unplanned reintubation of the trachea and myocardial infarction.[60]

OSA patients who remain undiagnosed at the time of surgery are at increased risk of postoperative complications.[61] Mutter and associates conducted a matched cohort analysis of polysomnography (PSG) data and health administrative data. Patients with undiagnosed OSA were found to have a threefold higher risk of cardiovascular complications, primarily cardiac arrest and shock, compared to diagnosed OSA patients with prescription of continuous positive airway pressure (CPAP) therapy.[61] Severity of OSA may play an important factor. Patients with severe OSA (AHI >30) had a 2.7-fold increase in postoperative respiratory complications.[61] If available, information on the diagnosis and severity of OSA in the anesthetic assessment may be helpful.

Clinical Pathways and Principles of Perioperative Management

The perioperative management of OSA patients is challenging, and a sound understanding of the condition is required of anesthesia providers involved in the care of such patients. The 2016 Society of Anesthesia and Sleep Medicine (SASM) guidelines for preoperative screening and assessment of adult patients with OSA recommend that screening for OSA may be useful to provide heightened awareness and potential risk reduction by implementing appropriate interventions[62] (Table 50.1). In addition, the American Society of Anesthesiologists (ASA) updated report on "Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea" offers guidance on perioperative management of OSA patients.[63,64] The Society for Ambulatory Anesthesia (SAMBA) consensus statement has provided guidelines addressing the selection of suitable OSA patients for ambulatory surgery.[65] Different clinical pathways and algorithms have been constructed to simplify the approach to OSA patients in the perioperative setting.[63,64,66-68]

Preoperative Assessment (Also See Chapter 13)

Patients With Diagnosed OSA

A thorough history and physical examination are essential. Focused questions regarding nature and severity of OSA symptoms should be asked. Previous consultation with a specialized sleep physician and sleep reports should be reviewed, if possible. (Fig. 50.4).

Patients with long-standing OSA may present with signs and symptoms of significant comorbid conditions including morbid obesity, metabolic syndrome, uncontrolled or resistant hypertension, arrhythmias, cerebrovascular disease, and heart failure.[69] Preoperative assessment should also rule out the presence of significant nocturnal hypoxemia, hypercarbia, polycythemia, and cor pulmonale. Obesity hypoventilation syndrome (OHS) and pulmonary hypertension should be ruled out in OSA patients.[70,71] The likelihood of developing respiratory failure following noncardiac surgery was more than 10-fold in OHS patients with OSA, compared to patients with OSA alone.[72] A serum bicarbonate level of 28 mmol/L or more indicates metabolic compensation for chronic hypercapnia and is a useful screening tool for OHS (Fig. 50.5).[73] A preoperative transthoracic echocardiogram (TTE) may be considered in patients suspected of having severe pulmonary hypertension and if intraoperative acute increases in pulmonary arterial pressures (high-risk or long-duration surgery) are anticipated.[66]

Table 50.1 Executive Summary of the Society of Anesthesia and Sleep Medicine (SASM) guidelines

Recommendations: Executive Summary

- **Patients with obstructive sleep apnea (OSA) undergoing procedures under anesthesia are at increased risk for perioperative complications compared with patients without the disease diagnosis.** Identifying patients at high risk for OSA before surgery for targeted perioperative precautions and interventions may help to reduce perioperative patient complications.
- **Screening tools help to risk stratify patients with suspected OSA with reasonable accuracy.** Practice groups should consider making OSA screening part of standard preanesthetic evaluation.
- **There is insufficient evidence in the current literature to support canceling or delaying surgery for a formal diagnosis (laboratory or home polysomnography) in patients with suspected OSA,** unless there is evidence of an associated significant or uncontrolled systemic disease or additional problems with ventilation or gas exchange.

- The patient and the health care team should be aware that both diagnosed OSA (whether treated, partially treated, or untreated) and suspected OSA may be associated with increased postoperative morbidity.
- If available, consideration should be given to obtaining results of the sleep study and, where applicable, the patient's recommended positive airway pressure (PAP) setting before surgery.
- If resources allow, facilities should consider having PAP equipment for perioperative use or have patients bring their own PAP equipment with them to the surgical facility.

- **Additional evaluation to allow preoperative cardiopulmonary optimization should be considered in patients with diagnosed, partially treated/untreated, and suspected OSA where there is indication of an associated significant or uncontrolled systemic disease or additional problems with ventilation or gas exchange such as: (i) hypoventilation syndromes, (ii) severe pulmonary hypertension, and (iii) resting hypoxemia in the absence of other cardiopulmonary disease.**
- **Where management of comorbid conditions has been optimized, patients with diagnosed, partially treated/untreated OSA, or suspected OSA may proceed to surgery provided strategies for mitigation of postoperative complications are implemented.**
- The risks and benefits of the decision to proceed with or delay surgery include consultation and discussion with the surgeon and the patient.
- **The use of PAP therapy in previously undiagnosed but suspected OSA patients should be considered case by case.** Because of the lack of evidence from randomized controlled trials, we cannot recommend its routine use.
- **Continued use of PAP therapy at previously prescribed settings is recommended during periods of sleep while hospitalized, both preoperatively and postoperatively.** Adjustments may need to be made to the settings to account for perioperative changes such as facial swelling, upper airway edema, fluid shifts, pharmacotherapy, and respiratory function.

From: Chung F, Memtsoudis SG, Ramachandran SK, et al. Society of Anesthesia and Sleep Medicine Guidelines on Preoperative Screening and Assessment of Adult Patients With Obstructive Sleep Apnea. Anesthesia and Analgesia. 2016;123(2):452-473.

OSA patients may be using positive airway pressure (PAP) devices for treatment, such as CPAP, bilevel positive airway pressure (BiPAP), and auto-titrating positive airway pressure (APAP) devices. APAP devices provide upper airway stability during sleep by using airflow measurements, fluctuations in pressure, or airway resistance based on internal algorithms. This approach has the potential to account for night-to-night variability of OSA severity.[74] The SASM guidelines recommend review of sleep study and compliance data from the PAP devices to evaluate information on the current PAP setting, and AHI indicating successful treatment of respiratory events.[62] Per the SASM guidelines, additional evaluation for preoperative cardiopulmonary optimization should be considered in patients who have a known diagnosis of OSA and are nonadherent or poorly adherent to PAP therapy and where there is indication of uncontrolled systemic conditions or additional problems with ventilation or gas exchange. These conditions include, but may not be limited to (1) hypoventilation syndromes, (2) severe pulmonary hypertension, and (3) resting hypoxemia not attributable to other cardiopulmonary disease.[62]

A 2015 meta-analysis of six studies and 904 patients evaluated the use of perioperative CPAP on postoperative outcomes in OSA patients.[75] Perioperative CPAP significantly reduced the postoperative AHI from baseline preoperative AHI, in association with a modest reduction of hospital length of stay.[75]

Patients who are noncompliant to PAP therapy should be counseled to resume therapy preoperatively.[76] Moreover, patients with significant comorbid conditions, a high serum bicarbonate (indicating chronic hypercapnia), and preoperative hypoxemia in the absence of respiratory disease are candidates for preoperative evaluation and initiation of PAP therapy.[76] Current guidelines recommend that surgical patients with moderate or severe OSA who are compliant with PAP therapy should bring the device to the hospital and continue its use.[64] In the general population, mild OSA was not an independent risk factor for higher mortality rate.[42] Patients with mild OSA may not be at a higher risk of undergoing surgery and anesthesia, and preoperative PAP use may not be indicated in these patients.

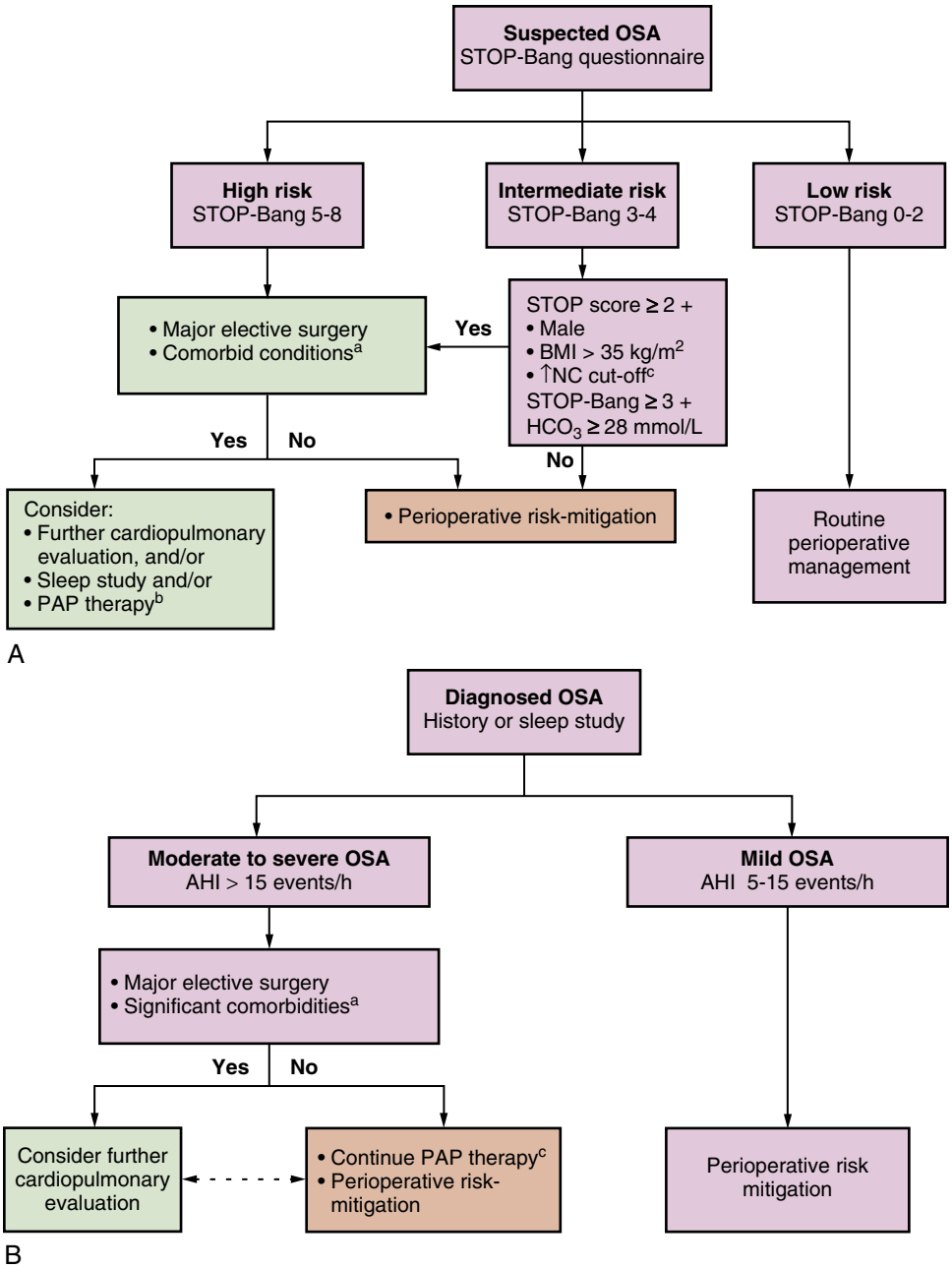

Fig. 50.4 Preoperative evaluation of a patient with known or suspected obstructive sleep apnea in the pre-admission clinic. (A) Suspected OSA and (B) Diagnosed OSA. A, Per the 2016 SASM guidelines, further cardiopulmonary evaluation may be indicated in patients with uncontrolled systemic disease or additional problems with ventilation or gas exchange, such as hypoventilation syndromes, severe pulmonary hypertension, and resting hypoxemia in the absence of other cardiopulmonary disease.[62] [a]Significant comorbidities: heart failure, arrhythmias, uncontrolled hypertension, cerebrovascular disease, metabolic syndrome, obesity (body mass index >35 kg/m^2), obesity hypoventilation syndrome, pulmonary hypertension. [b]Positive airway pressure (PAP) therapy: includes continuous PAP, bilevel PAP, and autotitrating PAP. [c]Neck circumference (NC) cut-offs 17 inches/43 cm in male, 16 inches/41 cm in female.[84] *STOP-Bang*, STOP-Bang questionnaire cut-off values.

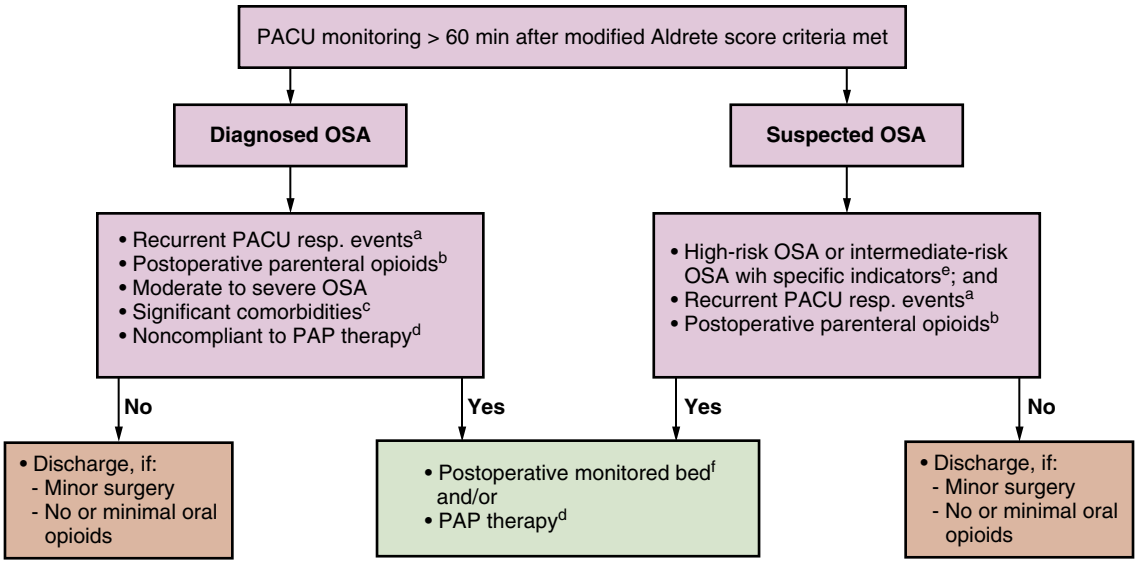

Fig. 50.5 Postoperative management of the patient with known or suspected obstructive sleep apnea after general anesthesia. [a]Recurrent postanesthesia care unit (PACU) respiratory event: repeated occurrence of oxygen saturation less than 90%, or bradypnea less than 8 breaths/min, or apnea 10 seconds and longer, or pain-sedation mismatch (high pain and sedation scores concurrently).[88] [b]Postoperative parenteral opioid requirement more than the usual standard of care such as multiple routes, long-acting preparations, or high dose infusions. [c]Per the 2016 SASM guidelines, uncontrolled systemic disease or additional problems with ventilation or gas exchange such as: hypoventilation syndromes, severe pulmonary hypertension, and resting hypoxemia in the absence of other cardiopulmonary disease.[62] [d]Positive airway pressure (PAP) therapy: includes continuous PAP, bilevel PAP, or autotitrating PAP. [e]Intermediate-risk and specific indicators include: STOP score ≥ 2 + male or BMI > 35 kg/m^2 or ↑NC cutoff (where, NC: neck circumference cut-offs 17 inches/43 cm in male, 16 inches/41 cm in female[82]) and STOP-Bang ≥ 3 + HCO3 ≥ 28 mmol/L. [f]Monitored bed: environment with continuous oximetry and the possibility of early medical intervention (e.g., intensive care unit, step-down unit, or remote pulse oximetry with telemetry in surgical ward).

Methods for Perioperative Screening for OSA

An overnight PSG is the gold standard diagnostic test for OSA. However, routine screening with PSG can be costly and resource intensive. As a result, simple, economical, and sensitive screening tests have been developed to detect patients with suspected OSA.

Preoperatively, the use of sensitive clinical criteria to identify and risk-stratify potential OSA patients is advocated. An updated 2014 ASA Practice Guideline for the perioperative management of patients with obstructive sleep apnea recommends a comprehensive preoperative evaluation including a medical records review, patient/family interview and screening protocol, and physical examination.[63,64] Perioperative risk is predicted by a scoring system based on OSA severity, invasiveness of procedure, and expected postoperative opioid requirement.[64] Other screening tools that have been validated in surgical patients are the STOP-Bang questionnaire,[77] the Berlin Questionnaire,[78] and the Perioperative Sleep Apnea Prediction (P-SAP) score.[79]

The STOP-Bang questionnaire is a concise and easy-to-use screening tool for OSA consisting of eight easily administered questions with the acronym STOP-Bang (Box 50.2).[77,80] It is a self-administered screening tool and includes four "yes/no" questions (*s*noring, *t*iredness, *o*bserved that you stopped breathing, high blood *p*ressure) and questions concerning the demographic data of *b*ody mass index (BMI) (>35 kg/m^2), *a*ge (>50 years), *n*eck circumference (>40 cm), and *g*ender (male). Patients are deemed to be at lower risk with scores of 0 to 2, intermediate risk with 3 to 4, and higher risk of OSA with scores of 5 to 8.[77,80-82] The STOP-Bang questionnaire has a high sensitivity and a high negative predictive value for patients with moderate to severe OSA.[77] The sensitivity of a STOP-Bang score of 3 or more to detect moderate to severe OSA (AHI > 15) and severe OSA (AHI > 30) is 93% and 100%, respectively. The corresponding negative predictive values are 90% and 100%. As the STOP-Bang score increases from low risk (0 to 2) to high risk (7 to 8), the probability of moderate to severe OSA increases from 18% to 60%, and the probability of severe OSA increases from 4% to 38%.[81] In patients whose STOP-Bang scores are the mid-range (3 or 4), further criteria are required for classification. For example, a STOP-Bang score of ≥ 2 +

Box 50.2 Updated STOP-Bang Questionnaire

Snoring?	Do you **Snore Loudly** (loud enough to be heard through closed doors or your bed partner elbows you for snoring at night)?
Tired?	Do you often feel **Tired, Fatigued, or Sleepy** during the daytime (such as falling asleep during driving)?
Observed?	Has anyone **Observed** you **Stop Breathing** or **Choking/Gasping** during your sleep?
Pressure?	Do you have or are you being treated for **High Blood Pressure**?

Body Mass Index more than 35 kg/m^2?
Age older than 50 years old?
Neck size large? (Measured around Adams apple)
For male, is your shirt collar 17 inches/43 cm or larger?
For female, is your shirt collar 16 inches/41 cm or larger?
Gender: Male?
Scoring Criteria:
For general population
Low risk of OSA: Yes to 0-2 questions
Intermediate risk of OSA: Yes to 3-4 questions
High risk of OSA: Yes to 5-8 questions
or Yes to 2 or more of 4 STOP questions + male gender
or Yes to 2 or more of 4 STOP questions + BMI > 35 kg/m^2
or Yes to 2 or more of 4 STOP questions + neck circumference large (17 inches/43 cm in male, 16 inches/41 cm in female)

BMI, Body mass index; *OSA*, obstructive sleep apnea.
Modified from Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology.* 2008;108(5):812-821; Chung F, Subramanyam R, Liao P, et al. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth.* 2012;108:768-775; Chung F, Yang Y, Brown R, et al. Alternative scoring models of STOP-Bang questionnaire improve specificity to detect undiagnosed obstructive sleep apnea. *J Clin Sleep Med.* 2014;10:951-958. Proprietary to University Health Network. www.stopbang.ca.

(BMI > 35 kg/m^2 or male or neck circumference > 43 cm in males, and > 41 cm in females) or a STOP-Bang score ≥ 3 + serum HCO_3 ≥ 28 mmol/L would classify that patient as having a high risk for moderate to severe OSA (Box 50.2 and Fig. 50.4).[81] In addition, patients identified as high risk with a STOP-Bang score of 5-8 have an increased severity of OSA and are at a higher risk of postoperative complications.[83,84]

Patients With Suspected OSA

In patients suspected of OSA, a focused clinical examination should be performed with emphasis on pertinent symptoms and signs of OSA (Box 50.1). History from the bed partner in the preoperative clinic is useful in the assessment of loud snoring and observed apneic episodes while asleep. In emergency situations, the patient should proceed for surgery, preventing delay of life- or limb-saving surgery. Perioperative risk-mitigation strategies should be implemented based on the clinical suspicion of OSA (Fig. 50.4).[67,85]

For elective non-urgent surgery, the 2016 SASM guidelines state that insufficient evidence exists to support canceling or delaying surgery to formally diagnose OSA in those patients identified as being at intense risk of OSA preoperatively, unless there is evidence of uncontrolled systemic disease or additional problems with ventilation or gas exchange, such as hypoventilation syndromes, severe pulmonary hypertension, and resting hypoxemia, in the absence of other cardiopulmonary disease.[62] (Table 50.1, Fig. 50.4). In these patients, additional cardiopulmonary evaluation is recommended to allow for optimization of the medical conditions and planning of the intraoperative and postoperative management.[63,64] Once the comorbid conditions have been made as optimal as possible, patients with diagnosed, partially treated or untreated OSA, or with suspected OSA may proceed to surgery provided strategies for mitigation of postoperative complications are implemented. The risks and benefits of the decision to proceed with or delay surgery include consultation and discussion with the surgeon and the patient[62] (Table 50.1). If the subsequent intraoperative and postoperative course suggests an increased likelihood of OSA, such as difficult airway,[87] or recurrent postoperative respiratory events, such as desaturation, hypoventilation, or apnea,[88] postoperative referral to a sleep physician may be useful for long term follow-up.

Perioperative Risk-Mitigation Strategies

Preoperative sedative premedication in an unmonitored setting should be avoided. Intraoperatively, the anesthesia provider should be prepared for difficulties with ventilation via a mask, laryngoscopy, and endotracheal intubation.[89,90] Guidance from the ASA practice guidelines for the management of a difficult airway is useful, and the presence of skilled personnel and advanced airway equipment should be ensured at the time of airway management.[91] Adequate preinduction of anesthesia oxygenation, head-elevated body position, and measures to decrease the risk of aspiration of gastric acid, such as preoperative proton-pump inhibitors, antacids, and rapid sequence induction with cricoid pressure, should be considered.

The use of long-acting anesthetics should be minimized and short-acting drugs such as propofol, remifentanil, and desflurane should be used. Pulmonary hypertension can occur and patients with evidence of right-sided heart failure, and reduced effort tolerance may need additional tests for evaluation. Care should be taken to prevent increased pulmonary artery pressures by avoiding hypercarbia, hypoxemia, hypothermia, and acidosis.

Alveolar hypoventilation in conjunction with central respiratory depression, decreased consciousness, and upper airway obstruction are results of opioid administration

and can lead to opioid-induced respiratory depression.[92] Important components of OSA like sleep fragmentation and intermittent hypoxia modulate pain behavior and increase sensitivity to opioid analgesics.[92] Nonopioid analgesics should be used, such as acetaminophen or nonsteroidal antiinflammatory drugs (NSAIDs, celecoxib); partial opioid analgesics (tramadol); anticonvulsants (pregabalin or gabapentin); corticosteroids (dexamethasone); *N*-methyl-D-aspartate (NMDA); receptor antagonist, ketamine[93]; and the α_2-adrenergic agonists, clonidine and dexmedetomidine.[94] Extubation of the trachea should be performed with no residual neuromuscular blockade in an awake, fully conscious patient who is able to obey commands and maintain a patent airway. After extubation of the trachea, patients should be recovered in a nonsupine (semiupright or lateral) position (also see Chapter 13).[64]

Local or regional anesthesia techniques reduce opioid requirements postoperatively and may be of benefit as they avoid manipulation of the airway and reduce the need for postoperative sedating analgesic medications. Patients previously receiving PAP therapy at home may continue using their PAP devices during procedures under mild to moderate sedation.[95] A secured airway is preferred to an unprotected one for procedures requiring deep sedation.[64]

Postoperative Disposition of OSA Patients (Also See Chapter 39)

The postoperative disposition of the OSA patient depends on the nature of surgery, OSA severity, and the requirement for postoperative parenteral opioids (see Fig. 50.5). A patient with severe OSA who underwent a major surgery and is receiving large-dose intravenous opioids is more likely to require continuous monitoring than another patient with suspected OSA undergoing a superficial cataract surgery via a local anesthetic with minimal opioid analgesic requirements. The attending anesthesia provider is responsible for the final decision, taking into account all patient-related, logistic, and circumstantial factors.

Fig. 50.5 presents a simplified algorithm on the postoperative management of patients with OSA based on recommendations of the 2016 SASM guidelines and expert opinion.[62,67,86] All patients with known or suspected OSA who have received general anesthesia should have extended monitoring in the postanesthesia care unit (PACU) with continuous oximetry. There are currently no evidence-based guidelines addressing the optimal length of monitoring required in the PACU, and some recommendations are difficult to follow, especially in the context of cost and resource management.[95] It is reasonable to observe a suspected or documented OSA patient in the PACU for an additional 60 minutes in a quiet environment after the modified Aldrete criteria for discharge have been met.[67]

The existence of recurrent respiratory events in the PACU is another indication for continuous postoperative monitoring.[88] Recurrent PACU respiratory events are defined as (1) episodes of apnea for 10 seconds or more, (2) bradypnea fewer than 8 breaths per minute, (3) pain-sedation mismatch, and (4) repeated oxygen desaturation to less than 90%. Patients with suspected OSA (i.e., scored as high risk on screening questionnaires) who develop recurrent PACU respiratory events postoperatively are at increased risk of postoperative respiratory complications.[88] Monitoring in surgical wards equipped with continuous oximetry is indicated for these patients. Postoperative PAP therapy may be initiated at an empiric basis to abolish recurrent obstructive events associated with significant hypoxemia.[95] Patients with previously diagnosed OSA already receiving PAP should continue PAP therapy postoperatively.[76]

CONCLUSION

Understanding the similarities and differences between sleep and anesthesia has enhanced our learning of the neural pathways modulating arousal and the interaction with medications. Common sleep disorders impact this relationship further, and knowledge of timely diagnosis, treatment, and perioperative precautions is necessary for an anesthesiology trainee. Ongoing research and new diagnostic and monitoring technologies will define the change in the diagnosis and management with an impact on health care costs and resource management.

QUESTIONS OF THE DAY

1. What are the characteristic electroencephalographic (EEG) patterns associated with general anesthesia?
2. What factors contribute to upper airway collapse in a patient with obstructive sleep apnea (OSA)?
3. What is the definition of the Apnea-Hypopnea Index (AHI) during a sleep study? What are the criteria for a clinical diagnosis of OSA based on symptoms and AHI?
4. What are the most common medical conditions associated with OSA?
5. What postoperative events are more likely to occur in a patient with OSA compared to a patient without OSA?
6. What are the components of the STOP-Bang questionnaire for OSA screening? What is the sensitivity of the STOP-Bang score to detect moderate to severe OSA?
7. What strategies can be used to decrease the risk of an adverse outcome during the perioperative period in a patient with OSA?

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