A Systemic Review of Obstructive Sleep Apnea and Its Implications for Anesthesiologists

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BACKGROUND: Obstructive sleep apnea (OSA) is present in a significant proportion of the population, but the majority of patients remain undiagnosed. It is crucial that anesthesiologists and surgeons recognize the increased perioperative risks associated with undiagnosed OSA. We present a systematic review of the literature on the perioperative management of surgical patients with OSA.

METHODS: The scope of this review is restricted to publications in all surgical specialties and in the adult patient population. The main search key words were: “perioperative care,” “sleep apnea,” “obstructive sleep apnea,” “perioperative risk,” and “perioperative care.” The databases Medline, Embase, Biological Abstract, Science Citation Index, and Healthstar were searched for relevant English language articles from 1966 to March 2007.

RESULTS: The literature supports an increased perioperative risk in OSA patients. The American Society of Anesthesiologists guidelines support the routine screening for OSA during preoperative assessment, and methods of OSA screening are discussed in this review. This review suggests a number of perioperative management strategies to reduce surgical risk in patients with OSA. However, apart from the consensus-based American Society of Anesthesiologists guidelines, it is important to note that evidence-based recommendations are lacking in the literature.

CONCLUSIONS: This review suggests ways to screen for OSA in the preoperative setting and proposes perioperative management strategies. The ultimate goal is to reduce the perioperative risk of OSA patients but, to realize that goal, research will be needed to determine whether screening for OSA and/or adapting specific perioperative management approaches translates into a lessening of adverse events in surgical patients with undiagnosed OSA.

Obstructive sleep apnea (OSA) is a common sleep disorder caused by repetitive partial or complete obstruction of the upper airway and is characterized by episodes of cessation of breathing during sleep lasting for more than 10 s. Population-based epidemiologic studies have shown a frequent prevalence of undiagnosed OSA, and even mild OSA is associated with significant morbidity1 and mortality.2 The American Society of Anesthesiologists (ASA) recently issued practice guidelines for the perioperative management of OSA patients.3 The purpose of the guidelines was to reduce the risk of adverse outcomes in patients with OSA and to improve perioperative care.

The development of the guidelines was built on the scientific evidence derived from the research literature and opinion-based evidence obtained from the ASA task force and consultants. The guidelines indicate that the literature lacked sufficient evidence-based findings to enable clinicians to formulate strategies for preoperative evaluation and postoperative management of OSA. Relevant recommendations were primarily based on the consensus of consultants’ opinions. Identification of shortfalls in the research literature is warranted to promote future research. The purpose of this review is to examine the current evidence on the perioperative risk of sleep apnea, its implication for perioperative management, and to identify the gaps in knowledge regarding this important issue in anesthesia care. The objectives of this review are to discuss the following issues: 1) Does evidence from pathophysiologic studies, pharmacodynamic models, and methodologically sound cohort studies point towards OSA, posing a special challenge to anesthesiologists? 2) Are surgical patients with OSA especially vulnerable with sedation, anesthesia and analgesia? 3) Can episodic sleep-related oxygen desaturations, incidences of unexplained cardiorespiratory events or sudden, unexpected death in a number of perioperative patients be attributed to undiagnosed OSA? 4) Is it possible to...
screen for OSA preoperatively? 5) What considerations (e.g., identification of contributors to increased perioperative risk, choice of sedatives, anesthetics and analgesics) are needed to develop a perioperative management plan for OSA patients?

METHODS

The scope of this review is restricted to studies in all surgical specialties and in the adult patient population with an emphasis on outcome in patients who were previously or subsequently diagnosed with sleep apnea. The following key words were used for literature search: “perioperative care,” “sleep apnea,” “obstructive sleep apnea,” and “perioperative risk.” The medical subject heading index terms on Medline were “Perioperative Care,” “Sleep apnea,” and “Perioperative Care and Obstructive Sleep apnea.” We also used “perioperative risk” and “sleep apnea” as index terms to capture data relating to themes of “sleep apnea,” “risk,” and “perioperative care.” Other search areas included “sleep apnea” combined with “etiology” or “prevalence,” “screening instruments,” “sedation,” “anesthesia,” and “analgesia.” The databases Medline, Embase, Biological Abstract, Science Citation Index and Healthstar, as listed below, were thoroughly searched for relevant articles. Studies focusing on central sleep apnea were excluded by including “NOT central sleep apnea” in the search string.

1. Ovid MEDLINE(R) 1966 to March 2007
2. Ovid CINAHL—Cumulative Index to Nursing & Allied Health Literature (1982–March 2007)
4. Cochrane Database of Systematic Reviews (1st Quarter 2007)
6. Database of Abstracts of Reviews of Effects (1st Quarter 2007)

The databases of the Cochrane Library were used to verify the completeness of the search. The time period searched was from 1966 to 2007. Classification of relevant articles was judged according to whether they contributed primary empirical evidence to the review topics. Critical appraisal of each paper was conducted by the authors. All the papers were classified according to the Oxford Centre for Evidence-based Medicine Levels of Evidence.4 The appraisal process focused on the strength of the study design. The classification was as follows: Level I: blinded, randomized controlled trial with narrow confidence intervals; Level II: nonblinded randomized controlled trial; Level III: nonrandomized controlled or cohort, case-control studies; and Level IV: nonrandomized case-series report.

RESULTS

The search strategy resulted in 8897 articles. Whenever possible, Level I and II papers were preferentially used, however, Level III and IV papers were used whenever Level I and II papers were unavailable. Information from reviews and abstracts was also included in cases where reports of a higher evidence level were unavailable. Limiting those articles to English Language and Adult population (19+ yr) reduced the number to 3974. Further limitation of search results to evidence level I and II articles (clinical trials, meta-analyses, practice guidelines and randomized controlled trials) netted 411 available articles. Nine of these articles were excluded as they were not available at the University of Toronto, the University Health Network or through the Consortium of Toronto Area Hospitals. Of those remaining, 198 studies were selected based on content and suitability for this review.

The lack of adequate blinding, a control group or randomization, 18 articles of evidence level III and IV had to be included in this review due to a lack of studies at a higher evidence level.

DISCUSSION

What Is the Prevalence of OSA?

For OSA to represent a problem in the perioperative setting, there would have to be a substantial number of surgical patients with OSA. The prevalence of OSA varies widely depending on the demographics of the population studied, the definitions of the disorder and the methods of diagnosis. The accepted minimal clinical diagnostic criteria for OSA is an apnea hypopnea index (AHI) of 10 plus symptoms of excessive daytime sleepiness.5 AHI is the number of episodes of apnea or hypopnea per hour during sleep.

Many epidemiological studies6–9 estimated the OSA prevalence using polysomnography (PSG) as the “gold standard” for diagnosis (Table 1). In primary care practice, about 38% of men and 28% of women are at high risk of having sleep apnea,10 Other patient populations at greater risk for or having a higher prevalence of OSA include patients who smoke (OR 6.7 for heavy smokers)11 and those with medical conditions such as diabetes (prevalence of 36%),12 treatment-resistant hypertension (63%),13 overweight men and older women with congestive heart failure (men: OR for a Body Mass Index [BMI] >35 kg/m², 6.10; 95% CI 2.86–13.00; women: OR for age >60 yr, 6.04; 95% CI 1.75–20.00),14 during the acute phase of first-ever stroke (prevalence of 71%),15 primary open angle glaucoma (prevalence of 20%),16 hypothyroidism (prevalence of 45%),17 alcoholism (prevalence of 17% in subjects aged 40–59 yr),18 and head and neck cancer (prevalence of 76%).19 These medical disorders are of particular importance to tertiary care centers that typically provide care for a sicker patient population.

In the general population, moderately severe OSA (AHI >15) is present in 11.4% and 4.7% of men and women, respectively.7,8,20 Apart from a significant male gender predominance, an elevated AHI is significantly associated with age (Odds Ratio, per 10-yr
Table 1. Prevalence of Obstructive Sleep Apnea (OSA) in the General Population

<table>
<thead>
<tr>
<th>Study location and population</th>
<th>Numbers (n)</th>
<th>Age range (yr)</th>
<th>Estimated prevalence (%) of mild OSA (AHI &gt; 5) (95% CI)</th>
<th>Estimated prevalence (%) of moderate OSA (AHI &gt; 15) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wisconsin (state employees)⁶</td>
<td>602 M = 352 F = 250</td>
<td>30–60</td>
<td>24 (19–28)</td>
<td>9 (6–12)</td>
</tr>
<tr>
<td>Pennsylvania (hospital population)⁷</td>
<td>1741 M = 741 F = 1000</td>
<td>20–100</td>
<td>17 (15–20)</td>
<td>—</td>
</tr>
<tr>
<td>Spain (general population)⁹</td>
<td>2148 M = 1050 F = 1098</td>
<td>30–70</td>
<td>26 (20–32)</td>
<td>28 (20–35)</td>
</tr>
</tbody>
</table>

The above table is based on four studies with similar design and methodology that evaluated AHI (apnea-hypopnea index–number of episodes of apnea or hypopnea per hour during sleep) among various adult populations.⁶–⁹

M = male; F = female.

Table 2. Frequency of OSA in Specific Surgical Populations

<table>
<thead>
<tr>
<th>Surgical patient population</th>
<th>Age and gender</th>
<th>Methods used to diagnose OSA</th>
<th>No. of patients with OSA (percentage in brackets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General surgery (excluding cardiac and OSA surgery)²⁷</td>
<td>44 ± 17 yr 212 F, 221 M</td>
<td>Symptoms &amp; PSG</td>
<td>41/433 (9.5%) patients with 2 or more symptoms of OSA AHI &gt; 5: 14/433 (3.2%)</td>
</tr>
<tr>
<td>Surgery for intracranial tumor²⁶</td>
<td>54 ± 18 yr 8 M, 3 F</td>
<td>PSG</td>
<td>AHI &gt; 5: 7/11 (64%) AHI &gt; 20: 6/11 (55%)</td>
</tr>
<tr>
<td>Bariatric surgery²⁴</td>
<td>7 M, 34 F, F: 43 yr (25–60 yr) M: 50 yr (19–58 yr)</td>
<td>PSG</td>
<td>AHI &gt; 5: 29/41 (71%)</td>
</tr>
<tr>
<td>Epilepsy patients undergoing surgical treatment²⁵</td>
<td>With OSA: 40 ± 9 yr 9 M, 4 F without OSA: 33 ± 10 yr 9 M, 17 F</td>
<td>PSG</td>
<td>AHI &gt; 5: 13/39 (33%) AHI &gt; 20: 5/39 (13%)</td>
</tr>
</tbody>
</table>

M = male; F = female; PSG = polysomnography; AHI = apnea-hypopnea index; OSA = obstructive sleep apnea.

increase, 1.79 (95% CI: 1.41–2.27).²¹ OSA is also more prevalent in obese individuals.²² In a follow-up to the Wisconsin Sleep Cohort Study,²³ the percentage of obese subjects (BMI > 40 kg/m²) with an AHI ≥ 15 is 42%–55% of men and 16%–24% of women.²³ Further, in older adults, logistic regression points to BMI as the strongest, independently significant predictor of having OSA (dependent variable AHI ≥ 10, BMI factor, logistic regression coefficient 0.0869, P = 0.0067).²⁰

No epidemiologic studies have been conducted to determine the prevalence of OSA in the general surgical population. However, a few studies²⁴–²⁷ have used PSG to determine the frequency of OSA in the surgical population (Table 2). In most instances, the frequency of OSA in these surgical populations is substantially higher than the incidence in the general population (Table 1), and it varies with the surgical population. In particular, about 7 of every 10 patients undergoing bariatric surgery were found to have OSA,²⁴ presumably due to the high level of obesity in this surgical population. Of even greater concern, despite OSA being present in the majority of patients presenting for bariatric surgery,²⁴,²⁹ most cases were not diagnosed unless careful screening was implemented before surgery.²⁸ Further studies of OSA prevalence in general surgical patients are needed. One problem with undertaking such a study is that it is difficult to recruit surgical patients to undergo PSG studies. As illustrated in the study by Fidan et al.,²⁷ less than half (18 of 41, 44%) of the patients identified as being at risk for OSA agreed to undergo a sleep study. More importantly, of the patients agreeing to a PSG, the majority (78%) were found to have AHI > 5.

Consistent with the above figures, in a nationwide survey of Canadian anesthesiologists, 67% of respondents reported that they provided care for 1 to 5 patients with OSA each month.²⁹ Another study of patients undergoing total joint arthroplasty reported that, by asking patients to complete a few screening questionnaires on OSA, they were able to identify 10 cases of undiagnosed OSA out of 254 patients.³⁰ Recently, we have studied patients undergoing elective surgery and 24% were identified preoperatively at high risk for OSA using the Berlin questionnaire (BQ).³¹ In North America, OSA affects millions of middle-aged men and women,⁶ and it has been estimated that, of these, more than 80% of men and 90% of women are not clinically diagnosed and, hence, remain untreated.³² In short, the magnitude of the problem may have profound implications for anesthesiologists in the perioperative care of patients with previously unrecognized OSA.

What Are the Effects of Sedatives, Anesthetics and Analgesics on Respiratory Function?

Impact of Sedatives and Anesthesia on Respiration

The dose-dependent depression of muscle activity of the upper airway by general anesthesia has been well established.³³–³⁶ An increasing depth of propofol
anesthesia is associated with the increased collapsibility of the upper airway.36 This dose-related inhibition is likely to be the combined result of the depression of central respiratory output to the upper airway dilator muscles and the upper airway reflexes.36 In addition, most anesthetics or opioids used for analgesia can alter the control of breathing by affecting the chemical, metabolic or behavioral control of breathing. For example, halothane depresses ventilation by abolishing peripheral drive from the chemoreceptors at the carotid bodies and by general depression of respiratory centers in the central nervous system. Halothane also depresses ventilation by suppression of the function of intercostal muscles and the diaphragm.34,37–39 Other sedative and anesthetics also affect the upper airway. Thiopental administration has been shown to result in the loss of tonic activity in the sternothyroid and sternohyoid muscles in surgical patients.40 In normal subjects, propofol anesthesia was shown to produce a dose-dependent inhibition of genioglossus muscle activity resulting in greater collapsibility of the upper airway.36 Midzolam is commonly used in combination with other sedative and anesthetic drugs,41–43 so it is difficult to ascertain from the literature if obstructive events, when they occur, are a direct consequence of midozolam, the other sedatives or anesthetic drugs, or the combination of drugs. However, there is evidence from one study suggesting that midozolam, when administered at sedative doses, can increase supraglottic airway resistance leading to obstructive episodes.44

A few papers have documented the benefits of using dexmedetomidine as a sedative and anesthetic in OSA patients because of the lack of respiratory depression associated with dexmedetomidine use.45,46 Further, dexmedetomidine’s analgesic properties allow for reduced administration or avoidance of opioid drugs in the perioperative period.45,46 Of note, one case report has cautioned that dexmedetomidine can enhance respiratory depression when co-administered with opioids.47 Further investigations on the utility of using dexmedetomidine in surgical patients with OSA are needed.

Impact of Opioids on Respiration

Opioids can impair respiratory function. In the animal model, morphine has been shown to have a direct action on the respiratory motor activity of the hypoglossal and phrenic nerve.48 Weil et al. first reported a decreased ventilatory response to hypoxia and hypercapnia after morphine in healthy subjects in 1975.49

Factors such as ethnicity and gender can also influence the ventilatory response to morphine. In contrast to Caucasians, North American Aboriginal Indians have been observed to have an 18% greater reduction in the ventilatory response to morphine administration.50 Morphine has an effect on the apneic threshold in men, but not women; however, morphine decreases the hypoxic sensitivity in females, but not in males.51 Opioids may profoundly impair respiration in the postoperative period leading to obstructive apneas and drastic oxygen desaturation.52,53 There are clinical trials52,53 comparing the respiratory effects of IV morphine versus extradural bupivacaine in patients undergoing hip and abdominal surgery. Compared to those in the regional anesthesia group, patients receiving morphine experienced postoperative obstructive apneas, ventilation disturbances, acute oxygen desaturation and elevated end-tidal CO2.52,53 A greater frequency of tachyarrhythmia and ventricular ectopic beats were also noted in the morphine group.53 The obstructive apneas and oxygen desaturation were found to occur only when the patients were asleep, and the vast majority of the hypoxic episodes occurred within 6 to 8 h after surgery.52 Depression of the tonic activity of the upper airway muscles is well documented in sleep.54,55 It was proposed that the deleterious respiratory effect of morphine may be enhanced in sleep because of the diminution in airway function.52 Further studies are necessary to assess the effect of long-term opioid treatment on respiration during sleep, the interaction of opioids with other medications and the risk factors predisposing patients to sleep breathing disorders with opioid use.44

Is There a Greater Impact on Ventilation of Sedation, Anesthesia and Analgesia in OSA Patients?

Impact of Upper Airway Dynamics

Although the etiology of OSA remains uncertain, the general consensus is that upper airway obstruction occurs when the negative pressure generated by the inspiratory muscles exceeds the capacity of the upper airway dilator muscles to maintain airway patency.57 In general, the negative pressure generated by inspiration is counterbalanced by the contraction of the pharyngeal muscles. However, medications or conditions (such as fat deposits in obesity) that reduce lumen diameter or impair the ability of the upper airway muscles to overcome the negative forces of inspiration will result in greater upper airway resistance during breathing, thus predisposing the patient to obstructive events. These factors are of particular importance in OSA patients since, during both wake and sleep, they seem to have a reduced upper airway diameter, especially in the retropalatal region.58–60 To complicate matters, research also suggests that OSA patients may also have a primary myopathy of their genioglossus muscles.61,62 Thus, OSA patients may have a lowered threshold in their ability to overcome factors that predispose them to increased negative pharyngeal pressures during inspiration or that reduce upper airway muscle tone.

There is evidence that a compromised upper airway can be exacerbated by opioids. In a paper describing two case reports of patients with upper airway narrowing due to enlarged tonsils or tumor,63 both patients died after morphine use. In both cases, death
was due to the effects of severe upper airway narrowing coupled with the respiratory depressant action of morphine. The authors highlighted the dangers of using morphine in individuals with a compromised upper airway. The evidence suggests that OSA patients are in this category since they have a narrowed airway and perhaps a primary pharyngeal myopathy. In addition, sleep can be a dangerous time for OSA patients. The decline in electromyographic activity in the pharyngeal dilator muscles at sleep onset is much greater in OSA patients than in controls. There is enhanced neuromuscular activity during wakefulness in OSA patients that offsets deficiencies in their airway anatomy or functioning. However, in sleep, this neuromuscular compensation is lacking. This finding indicates that upper airway patency during sleep is particularly compromised in OSA patients.

OSA patients also seem more vulnerable to respiratory depressants. Alcohol ingestion in patients with mild OSA results in an increased number and duration of hypoxic events and almost triple the number of episodes of oxygen desaturation. Furthermore, the hypoxic episodes occur earlier in the sleep period and SaO2 levels may not return to normal after the long hypoxic episodes. A greater number of apneic episodes at night but levels above 90% were maintained. An important study by Brown et al. showed that the total analgesic opiate dose in children with OSA and recurrent hypoxemia was one-half of that required in children without such a history. Previous recurrent hypoxemia in OSA children is associated with a greater analgesic sensitivity to morphine administration. There are no studies investigating whether adult OSA patients require less opioids.

There are only case reports of the effects of opioids in adult patients with OSA. A compilation of case reports of patients with OSA receiving sustained-release opioids treatment for chronic pain has demonstrated that these patients have longer apnea duration, more severe hypoxia, irregular respiratory pauses and gasping, and periods of obstructive hypoventilation lasting for 5 min or longer. Postoperative epidural morphine in a patient with a history suggestive of OSA was documented to result in apneas, respiratory depression and cyanosis. As outlined above, sedatives, anesthetics and analgesics seem to selectively compromise respiratory function in OSA patients. Although there remains a lack of good evidence in the literature of the effect of opioids administration on respiration in OSA patients, the general recommendation is that opioids and other drugs with central respiratory and sedating effects should be avoided, if possible. The compromised airway in OSA patients may exacerbate the respiratory-depressive effects of these drugs. However, preoperative screening for OSA is not routinely performed, and use of analgesics is common in the postoperative period. At the very least, use of any sedative and analgesic in OSA patients should be done with extreme caution.

**Postoperative Implications**

After sedation, anesthesia or analgesia, the resulting hypoventilation or hypoxia may produce central instability in respiratory control resulting in low levels of oxygen saturation. However, there is evidence that airway obstruction is a major contributor to oxygen desaturation in the perioperative period. In surgical patients without a diagnosis of OSA, decreases in SaO2 <80% were observed to be primarily associated with obstructive apnea and paradoxical breathing, and no correlation was found between the duration of anesthesia and postoperative SaO2 levels after postoperative morphine. In support of that hypothesis, administration of oxygen in surgical patients who did not have a prior OSA diagnosis was found to improve the oxygen saturation, but not to alter the number and severity of obstructive apneic or hypopneic events. Moreover, increased numbers and duration of apneic events is observed in healthy volunteers and asymptomatic nonsurgical patients after sedation with healthy, nonobese ASA class I-II females without a history of OSA did not result in apnea. In this study, SaO2 was decreased during the first postoperative night but levels above 90% were maintained.

**Effects of Opioids**

A differential effect of opioid administration in individuals with and without OSA is evident from the literature. Oral hydromorphone administration in healthy adults without a history of OSA does not significantly alter the number of apneic or hypopnea episodes. A greater number of apneic episodes at higher doses of hydromorphone (4 mg) predominantly occurred in patients with a larger baseline number of obstructive events. Similarly, in the postoperative setting, analgesia with oxycodone in...
various sedative medications such as midazolam, fentanyl, and flurazepam. A careful study of sedative medications in OSA patients has not been conducted, but the aforementioned suggestion of a compromised upper airway (reduced diameter and myopathy of pharyngeal muscles) would likely more greatly predispose OSA patients to the deleterious effects of sedatives. The respiratory-depressant effects of sedatives, anesthetics and analgesics have direct clinical relevance for the perioperative management of a patient with OSA, but our knowledge at present is inadequate to propose evidence-based anesthetic procedures that can minimize the impact of the anesthesia or sedation on OSA.

Can OSA Affect Perioperative Outcome and Are Patients with OSA at an Increased Risk for Perioperative Complications?

OSA-Associated Morbidity

It is well-established that untreated OSA results in greater morbidity and an increased mortality rate. Untreated OSA patients are at a greater risk of developing cardiovascular disease (OR 3.1, 95% CI 1.2–8.3), including heart failure, arrhythmias (2–4 fold increase), hypertension (10-fold increase), and stroke (OR 4.33, 95% CI 1.32–14.24, P < 0.02). Furthermore, OSA is independently linked (OR 9.1, 95% CI 2.6–31.2, P < 0.0001) to the development of metabolic syndrome characterized by insulin resistance, impaired glucose tolerance and dyslipidemia. The impact of OSA is also seen on Paco2 levels and the coagulation systems. In a large observational cohort study, untreated OSA significantly and independently increased the risk (HR 1.97, CI 95%, 1.12–3.48, P = 0.01) of stroke or death from any cause.

In determining whether OSA patients are at greater risk perioperatively, one needs to determine if the presence of OSA directly or indirectly translates to greater incidences of adverse events in the perioperative setting. That is, are untreated OSA patients at a greater risk of having respiratory adverse events in the perioperative period? Further, the underlying morbidity associated with longstanding untreated OSA, particularly those of a cardiovascular nature, may predispose OSA patients to severe perioperative adverse events or may reduce the patients’ ability to cope should adverse events occur. However, it is possible that even patients with treated OSA are at a greater perioperative risk compared to normal patients due to the etiology of the disease including upper airway pathology or upper body obesity.

OSA-Postoperative Outcome

The presence of sleep apnea in the postoperative period as indicated by frequent episodes of oxygen desaturation has been reported. Ten of 16 surgical non-OSA patients receiving morphine infusion had a total of 456 episodes of pronounced oxygen desaturation (SaO2 <80%) when they were monitored for 16 h after surgery. These occurred only while the patients were asleep and were associated with disturbances in ventilatory pattern such as obstructive apnea (144 episodes), paradoxical breathing and periods of slow ventilatory rate. In patients with OSA-associated severe postoperative respiratory events, the need for postoperative reintubation has been documented. However, since OSA is a risk factor for increased difficulty with tracheal intubation, problems with postoperative reintubation could seriously impact patient morbidity.

It seems that the preoperative values of the apnea index and minimal level of oxygen saturation can be used to help predict the postoperative occurrence of obstructive apneas and adverse respiratory events. In OSA patients undergoing uvulopalatopharyngoplasty (UPPP), predisposing factors for respiratory complications included a higher preoperative AHI (AHI 69 vs 43, P < 0.008) and lower minimal levels of oxygen saturation (minimal O2 Sat 71.9% vs 77.8%, P < 0.01). Esclamado et al. retrospectively reviewed 135 patients with OSA after UPPP and associated procedures. They compared 18 patients with complications with 117 patients without complications. Preoperative AHI more than 70 or minimal oxygen saturation <80 was considered a risk factor for the development of complications. Pang et al. in a retrospective review of 118 OSA patients for upper airway surgery, concluded that patients with severe OSA AHI >60 and minimal oxygen saturation <80% were at high risk of postoperative oxygen desaturation (Table 3). Two studies, however, found no significant difference between those with and without complications regarding the severity of AHI in patients undergoing tonsillectomy or UPPP (Table 3).

For 24,157 surgical patients given general anesthesia, but not specifically diagnosed with OSA, the risk of a critical respiratory event in the postanesthesia care unit (PACU) was 1.3% (hypoxemia 0.9%, hypoventilation 0.2%, airway obstruction 0.2%). Significant risk factors for adverse respiratory events postoperatively were older age, male gender, diabetes, and obesity. The choice of anesthetic drug was also an important contributing factor. Use of opioids, fentanyl, atracurium or thiopental, either alone or in combination, were associated with greater anesthetic risk with odds ratios ranging from 1.6 to 2.5. However, the risk factor of an OSA diagnosis was not studied in this population.

Apart from respiratory complications, sustained arrhythmias and hypertension are commonly reported in association with OSA and may have implications for postoperative outcome in OSA patients. Arrhythmias and conduction abnormalities resulting from sleep apnea-associated hypoxemia have been reported in OSA patients undergoing gastric bypass surgery. The hemodynamic instability associated with arrhythmias can significantly affect perioperative morbidity. Morphine infusion in asymptomatic surgical patients has been shown to increase the...
<table>
<thead>
<tr>
<th>Study design and evidence level</th>
<th>Study subjects</th>
<th>Patient history</th>
<th>Finding and perioperative/postoperative outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case report; Level IV&lt;sup&gt;75&lt;/sup&gt;</td>
<td>Male (65 yr) with prostatic carcinoma aborted radical prostatectomy.</td>
<td>History suggestive of OSA. No formal diagnosis.</td>
<td>Morphine 5 mg, epidural for analgesia. 8 h later, patient found unresponsive, with apneic spells and cyanosis. Patient made a complete recovery.</td>
</tr>
<tr>
<td>Case report; Level IV&lt;sup&gt;109&lt;/sup&gt;</td>
<td>Male( 38 yr) emergency mastoidectomy.</td>
<td>History of loud snoring and subsequently diagnosed with OSA.</td>
<td>Patient developed severe upper airway obstruction upon extubation. Reintubated but airway obstruction reoccurred.</td>
</tr>
<tr>
<td>Case report; Level IV&lt;sup&gt;111&lt;/sup&gt;</td>
<td>3 cases. Ages 41–66. 2 orthopedic surgery, 1 ventral hernia repair.</td>
<td>All 3 diagnosed with OSA before surgery.</td>
<td>Epidural opioids for analgesia. On postop days 2 and or 3, patients found unresponsive with irregular or no respiratory pattern. These cardiac and respiratory arrests led to death.</td>
</tr>
<tr>
<td>Case report; Level IV&lt;sup&gt;112&lt;/sup&gt;</td>
<td>Male (74 yr) aortic reconstructive surgery.</td>
<td>Preoperative oximetry suggested severe, previously undiagnosed OSA.</td>
<td>IV morphine for analgesia. Severe respiratory obstruction and large fluctuations in systolic and diastolic blood pressure 4 h after extubation.</td>
</tr>
<tr>
<td>Observational study; Level IV&lt;sup&gt;121&lt;/sup&gt;</td>
<td>80 patients major surgery.</td>
<td>All patients had a history suggestive of OSA confirmed by preop oximetry.</td>
<td>Postop the frequency of the nocturnal hypoxemic episodes, as measured by oxygen desaturation index (ODI), did not change. Severity of the hypoxemic events was increased with more time spent below 90% O2.</td>
</tr>
<tr>
<td>Retrospective review; Level IV&lt;sup&gt;102&lt;/sup&gt;</td>
<td>347 patients, uvulopalatopharyngoplasty (UPPP) and associated procedures for OSA treatment.</td>
<td>All study patients had PSG-confirmed OSA diagnosis.</td>
<td>5 of the patients had postop airway complications. Preop AHI and SaO2 levels were worse in the patients who developed complications but this trend was not significant. Complications were found to be related to number of surgical procedures conducted.</td>
</tr>
<tr>
<td>Retrospective review; Level IV&lt;sup&gt;112&lt;/sup&gt;</td>
<td>109 patients upper airway surgery for OSA treatment.</td>
<td>All patients had a preexisting diagnosis of OSA.</td>
<td>23 patients (21%) used CPAP postoperatively. Hypertension was the most common adverse event occurring in 13 (12%) of patients with 6 of these requiring pharmacologic management.</td>
</tr>
<tr>
<td>Case report; Level IV&lt;sup&gt;113&lt;/sup&gt;</td>
<td>A subset of three patients, laparoscopic weight reduction surgery.</td>
<td>All patients were diagnosed with OSA.</td>
<td>Patients developed postop prolonged heart block during sleep.</td>
</tr>
<tr>
<td>Case report; Level IV&lt;sup&gt;108&lt;/sup&gt;</td>
<td>Obese male (42 yr) ear surgery.</td>
<td>Previous diagnosis of OSA.</td>
<td>Cardiac arrest noted 3 h after IM morphine. Severe hypoxic encephalopathy and brain death.</td>
</tr>
<tr>
<td>Retrospective; Level IV&lt;sup&gt;95&lt;/sup&gt;</td>
<td>101 OSA patients and 101 matched controls hip and knee surgery.</td>
<td>PSG OSA diagnosis before or after surgery. Controls did not undergo PSG.</td>
<td>Postop complications greater in OSA patients versus controls. Hospital stay significantly longer and requirement for ICU transfer greater in OSA patients.</td>
</tr>
<tr>
<td>Newsletter report; Level IV&lt;sup&gt;110&lt;/sup&gt;</td>
<td>Composite cases based on 8 cases reviewed.</td>
<td>All patients eventually diagnosed with OSA.</td>
<td>Cardiopulmonary arrest following opioid administration (6 IV/IM, 1 spinal, 1 epidural). Time course of events not given. One patient died and another had anoxic brain damage.</td>
</tr>
<tr>
<td>Observational; Level IV&lt;sup&gt;119&lt;/sup&gt;</td>
<td>10 patients UPPP and septroplasty for OSA treatment.</td>
<td>All patients had an established OSA diagnosis. AHI range 2–30.</td>
<td>Night following surgery: increased AHI and decreased SaO2. Within 24 h postop, significant increase in systolic and diastolic blood pressure (BP) and heart rate and increased urinary catecholamines during 1st postop night.</td>
</tr>
<tr>
<td>Retrospective; Level IV&lt;sup&gt;101&lt;/sup&gt;</td>
<td>130 patients tonsillectomy with UPPP.</td>
<td>All patients had an established OSA diagnosis.</td>
<td>Patients spent an average of 18 h in the step down unit. Postoperative desaturation below 90% was observed in 8 patients (6.2%).</td>
</tr>
<tr>
<td>Retrospective; Level IV&lt;sup&gt;117&lt;/sup&gt;</td>
<td>234 patients with OSA Outpatient surgical procedures and equal number of matched controls.</td>
<td>All study patients had PSG-confirmed OSA diagnosis. Control patients did not undergo PSG to exclude OSA diagnosis.</td>
<td>No significant difference in rate of unplanned hospital admissions or other adverse postop events between OSA and non-OSA patients. The majority of the patients (62%) were using CPAP treatment, and almost all of them (95%) reported nightly use.</td>
</tr>
</tbody>
</table>

(Continued)
incidence of conduction abnormalities.\textsuperscript{53} Furthermore, a preoperative diagnosis of OSA has been shown to be an independent predictor of atrial fibrillation after coronary bypass surgery.\textsuperscript{107}

There are numerous case reports (Table 3) indicating that adverse perioperative outcomes have been reported in OSA patients, including respiratory and cardiac arrest leading to death.\textsuperscript{75,108-113} These patients all received opioids. There was no preoperative screening for OSA, although, in most cases, the patient had a history suggestive of OSA or there was an established diagnosis of OSA before surgery. Unfortunately, the postoperative management plan did not include frequent monitoring of vital signs and oximetry. In these case reports, the use of perioperative opioids in these OSA patients might have contributed to the compromised respiration, however, this has not been clearly established. A retrospective review of OSA patients undergoing cardiac surgery also noted more postoperative adverse events and a longer intensive care unit (ICU) stay.\textsuperscript{114} Two reviews on anesthesia in OSA patients emphasize that these patients are at greater risk of perioperative adverse events.\textsuperscript{115,116} A major limitation of the aforementioned studies that provide information on the relationship between OSA and postoperative outcome (Table 3) is that, in general, they have a poor level of evidence.

Not all studies have endorsed a greater perioperative risk in OSA patients. A retrospective study of 234 OSA patients versus control group\textsuperscript{117} concluded that a preoperative diagnosis of OSA was not a risk factor for unanticipated admissions (23.9% vs 18.8%, odds ratio 1.4 95% CI 0.8–2.5). However, this study had a number of serious limitations that bring their findings into question. The study patients were scheduled for outpatient surgery implying that these OSA patients may have had less preexisting morbidity. Other limitations included a lack of information on the screening process and whether the anesthesia and surgical team altered their perioperative management based on the OSA diagnosis. A further confound was that the majority of OSA patients were using continuous positive airway pressure (CPAP) treatment. In addition, the incidence of unanticipated admission was an exceptionally high 19%–24% in both OSA and control groups, whereas the rate of unanticipated admission in ambulatory surgery is normally around 1%–2%.\textsuperscript{118}

In contrast to the above findings, a retrospective matched case-controlled study of OSA patients undergoing hip or knee replacement surgery,\textsuperscript{95} reported longer hospital stays (OSA vs control 6.8 days vs 5.1 days, $P < 0.007$) and 2.5 times the number of serious postoperative complications (OSA vs control 24% vs 9%, $P < 0.04$). These serious complications included the need for urgent respiratory support and more ICU transfer. Despite the different findings, this study,\textsuperscript{95} suffers from many of the same limitations as the above study\textsuperscript{117} given the retrospective nature and the inability to exclude a diagnosis of OSA in their control groups.

There are also a number of reports of OSA patients undergoing upper airway surgery, including UPPP, for surgical management of their sleep apnea.\textsuperscript{98,100-102,119-122} Postoperatively, there are reports of increased obstructions and desaturations\textsuperscript{98,119,121} and changes in systolic and diastolic blood pressure.\textsuperscript{119} It was further documented that postoperative complications were more frequent in OSA patients that had an

### Table 3. Continued

<table>
<thead>
<tr>
<th>Study design and evidence level</th>
<th>Study subjects</th>
<th>Patient history</th>
<th>Finding and perioperative/postoperative outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective review; Level IV\textsuperscript{98}</td>
<td>90 patients UPPP and associated procedures for OSA treatment.</td>
<td>All 90 had a PSG confirmed diagnosis of OSA.</td>
<td>Postop complications in 19 (21%) of patients &amp; respiration complication in 12 (13%). Airway-related complications in 5 (6%), SaO\textsubscript{2} &lt;90 in 8 (9%), bleeding in 7 (8%), ECG change in 1 (1%).</td>
</tr>
<tr>
<td>Retrospective review; Level IV\textsuperscript{120}</td>
<td>110 OSA UPPP and associated procedures as outpatient surgical treatment of OSA.</td>
<td>All patients had a PSG confirmed diagnosis of OSA.</td>
<td>90 (82%) of patients discharged on same day. 20 (18%) kept for observation. Of the 25 patients with AHI &gt;50: 5 (20%) admitted; 2 patients with AHI &gt;90 admitted due to oxygen desaturation. Desaturation requiring admission in 3% of patients. 10 (10%) patients had minor postop complications. No major complications.</td>
</tr>
<tr>
<td>Retrospective review; Level IV\textsuperscript{100}</td>
<td>118 patients upper airway surgery for OSA treatment.</td>
<td>All patients had a preexisting diagnosis of OSA.</td>
<td>Combined perioperative complication rate of 14%, including oxygen desaturation, hypertension and upper airway compromise.</td>
</tr>
<tr>
<td>Retrospective review; Level IV\textsuperscript{114}</td>
<td>37 OSA patients undergoing cardiac surgery.</td>
<td>All patients had a diagnosis of OSA.</td>
<td>Significantly greater occurrences of postoperative encephalopathy and infection and longer ICU stay.</td>
</tr>
</tbody>
</table>

OSA = obstructive sleep apnea; AHI = apnea-hypopnea index; postop = postoperative; preop = preoperative; UPPP = uvulopalatopharyngoplasty; CPAP = continuous positive airway pressure; ICU = intensive care unit; ECG = electrocardiogram.
increased AHl and higher levels of desaturation preoperatively (Table 3).98,102,121

Most studies are case reports, retrospective reviews or noncontrolled observational studies. This may contribute to the varied findings, i.e., why some studies, but not others, report more perioperative adverse events. Thus, although multiple case reports support increased perioperative risk of patients with OSA, there remains insufficient level 1 or 2 evidence to clarify if treated or untreated OSA patients are at increased risk during the perioperative period for either respiratory or cardiovascular adverse events. As level 1 studies may be difficult to perform, we may have to accept that these case reports or retrospective studies are sufficient evidence that OSA patients are at greater risk for perioperative adverse outcomes and greater emphasis should be placed on diagnosing patients with OSA and determining best practices during the perioperative period to reduce the risk for adverse outcomes.

**Perioperative OSA-Associated Complications**

**Relationship Between Acute Hypoxemia and Cardiovascular Events**

Apart from respiratory complications, sustained arrhythmias, and hypertension104 are commonly reported in association with OSA and may have implications for postoperative outcome in OSA patients. Arrhythmias and conduction abnormalities resulting from sleep apnea-associated hypoxemia105 have been reported in OSA patients undergoing gastric bypass surgery.106 The hemodynamic instability associated with arrhythmias can significantly impact postoperative morbidity. Morphine infusion in asymptomatic surgical patients has been shown to increase the incidence of conduction abnormalities.53 Further, a preoperative diagnosis of OSA has been shown to be an independent predictor of atrial fibrillation after coronary bypass surgery.107

Apneas and hypopneas have been shown to produce acute changes in systolic and diastolic arterial blood pressure123 in patients not undergoing surgery. In a population of middle-aged adults with subclinical sleep-disordered breathing, large fluctuations in systolic blood pressure (23 ± 10 mm Hg) and diastolic pressure (15 ± 6 mm Hg) were observed during and after apneic events. Transient changes in heart rate mirror the acute arterial blood pressure responses to apneas; bradycardia develops during the obstructive event and is followed by abrupt tachycardia and decreases in left ventricular stroke volume immediately after apnea termination.124,125

As a consequence of the OSA-related increases in systolic blood pressure, high levels of myocardial blood flow are required to maintain the oxygen balance in heart muscles.126 In an animal model of limited coronary flow reserve, oxygen desaturation can result in myocardial ischemia, thus subsequently impairing left ventricular function.127 Preoperative hypoxemia, especially in OSA patients has been found to be a predictor of severe postoperative hypoxemia98,119,121 while decreases in arterial oxygen saturation (SpO₂) have been found to be significantly higher on postoperative nights than preoperatively128,129 (Table 3). Thus patients with moderate to severe OSA may be at increased risk for myocardial infarction or congestive cardiac failure in the postoperative period.

There are numerous reports that support the link between OSA and cardiac arrhythmias and conduction disturbances.130–135 In a retrospective analysis of 400 nonsurgical OSA patients, sinus bradycardia was seen in 7%, second degree atrioventricular conduction block in 8%, and sinus arrest in 11% of these patients.104,133 Another study130 confirms 7% frequency of heart block (sinus arrest, II and III atrioventricular block) in nonsurgical OSA patients. Earlier studies suggested that heart block occurred exclusively with arterial oxygen desaturation below 72%,104 however, heart block with oxygen desaturation exceeding 4% has been noted.133 In 121 coronary artery bypass surgery patients, atrial fibrillation was more common in OSA patients and preoperative OSA with nocturnal hypoxemia was an independent predictor of postoperative atrial fibrillation.107

Pulmonary hemodynamics are also acutely altered during apneas resulting in oscillations in pulmonary artery pressure with each apnea.136 Prolonged severe hypoxemia results in greater changes in intrathoracic pressure and larger swings in pulmonary artery pressure. Greater inspiratory effort during the apnea in OSA patients promotes an increase in pulmonary capillary wedge pressure resulting in decreased right ventricular stroke volume. This reduction in ventricular stroke volume, in turn, leads to a diminished cardiac output at apnea resolution which occurs regardless of the postapneic tachycardia. In the animal model, pulmonary edema and deterioration of gas exchange has been shown to occur after 8 h of recurrent obstructive apneas.137 Incidences of fatal pulmonary edema have been reported in the postoperative setting138,139 and particularly in patients with OSA.140 With the increased risk of prolonged hypoxia in OSA patients, there is the distinct possibility of pulmonary edema occurring in the perioperative period.

**Increased Risk of Difficulty with Tracheal Intubation**

Difficult tracheal intubation is a significant concern for anesthesiologists. Difficult tracheal intubation and OSA seem to share similar etiological pathways of predisposing upper airway abnormalities. A retrospective case-controlled study of 253 patients was conducted to determine the occurrence of difficult intubation in OSA patients.96 The OSA patients were matched with controls of the same age, gender, and type of surgery. Difficult intubation was assessed by laryngoscopy using the Cormack and Lehane classification.141 Difficult intubation was found to occur 8 times as often in OSA patients versus controls (21.9%
In OSA patients undergoing ear, nose, and throat surgery, a 44% prevalence of difficult intubation had similarly been reported. Furthermore, patients with severe OSA (AHI >40) were found to have a much higher prevalence of difficult intubation. A study of more than 1500 nonobese and obese patients concluded that increased age, male gender, pharyngo-oral pathology, and the presence of OSA are all associated with a more frequent occurrence of difficult intubation. The corollary of the relationship is also true, that is, patients with difficult tracheal intubation have also been shown to have a greater risk of having OSA. In a small retrospective study of 15 patients with difficult intubation, 53% (8 of 15) of patients were diagnosed with OSA. In a prospective study of 15 patients with difficult intubation, 66% of patients with difficult intubation were subsequently found to have AH1 >5. These reports suggest that anesthesiologists should refer patients with difficult intubation for PSG sleep investigation of OSA.

Apart from the above-mentioned studies, there is no research investigating the causal and anatomical relationship between OSA and difficult tracheal intubation and the implications for perioperative management. It can be assumed, but has yet to be proven, that a combination of the two conditions would increase the perioperative risk of patients. Despite the higher prevalence of OSA in patients with difficult intubation, it needs to be determined whether it is cost effective for all patients with difficult intubation to undergo a diagnostic sleep study and if preoperative CPAP treatment could ameliorate the difficulty with tracheal intubation.

What Is the Evidence Suggesting That Perioperative CPAP Treatment May Decrease the Risk of Perioperative Complications in OSA Patients?

Nasal application of CPAP is the most widely used treatment for OSA because of its efficacy and low level of invasiveness. CPAP acts as a pneumatic splint to prevent occlusion of the airway during sleep, thereby significantly reducing apneas and hypopneas and the associated hypoxic and hypercapnic events. CPAP has been shown unequivocally to alleviate the symptoms of OSA including: amelioration of excessive daytime sleepiness, restoration of quality of life, improvement in vigilance, concentration and memory, lessening of fatigue, reduction in health care usage, and a decrease in traffic accidents.

The efficacy of CPAP has not been established in the perioperative setting. There is insufficient evidence from the literature to evaluate whether the perioperative use of CPAP may reduce adverse events in OSA patients undergoing surgery. It is not known whether CPAP can reduce the risk of perioperative cardiorespiratory events in OSA patients when the upper airway is further compromised by sedation, anesthesia or analgesia. There are no randomized controlled studies that specifically address this issue. The following is a summary of the possible potential beneficial effects of CPAP in OSA patients undergoing surgery.

Acute Effect of CPAP on Hemodynamics

In general, acute elevation in arterial blood pressure is a common adverse event in the perioperative setting that accounts for more than 10% of the complications in the PACU. There are a number of reports of serious postoperative hypertensive events in OSA patients. The efficacy of long-term CPAP treatment in reducing arterial blood pressure in OSA patients not undergoing surgery has been demonstrated. Acute CPAP use for 1–3 days in nonsurgical OSA patients with hypertension can lead to a reduction of arterial blood pressure (systolic blood pressure from 125 ± 15 mm Hg to 120 ± 10 mm Hg, diastolic pressure from 86 ± 16 mm Hg to 83 ± 12 mm Hg). However, the literature is not without controversy as others have reported that acute CPAP does not alter blood pressure. Apart from one case report documenting the beneficial effects of CPAP in treating hypertension in the postoperative period, there is no available evidence from randomized controlled studies. Evidence that acute CPAP treatment can reduce blood pressure perioperatively is required before the use of CPAP in the perioperative setting can be considered.

With regards to cardiac rhythm abnormalities, CPAP treatment reduces the number of apnea-associated cardiac arrhythmias and the beneficial effects of CPAP on sinus arrest and episodes of heart block during sleep have been reported. In a study of 17 patients, CPAP treatment reduced the number of arrhythmias from 1575 to 165 episodes per night (P < 0.01). These studies provide preliminary support for the use of CPAP for perioperative cardiac rhythm abnormalities among OSA surgical patients.

Cardiovascular adverse events with OSA patients in the perioperative setting are a growing concern. CPAP has been shown to improve cardiac function with long-term use but evidence of a beneficial cardiovascular effect with short-term CPAP use is required. A single night of CPAP was documented to reduce the variability in systolic and diastolic blood pressure and pulse interval during sleep. Also, a 10-min application of CPAP in patients with congestive heart failure was found to improve oxygen saturation, significantly decrease left ventricular stroke volume, reduce myocardial oxygen consumption, and reduce cardiac output. A favorable hemodynamic effect within a few minutes of application suggests a potential role for postoperative CPAP.

Research Studies Using Postoperative CPAP: What Is the Strength of Evidence?

The level of evidence is poor regarding the benefits of postoperative CPAP. There are only three studies...
on the benefits of postoperative CPAP in OSA patients: a small prospective study, one case report and one retrospective study. The findings of these studies suggest that CPAP can alleviate postoperative airway obstruction, decrease major postoperative complications, and reduce the length of hospital stay in OSA patients undergoing surgery. However, all three studies have low evidence levels and suffer from methodological problems, including small sample sizes and the lack of an appropriate prospective, randomized, controlled design, thus, limiting the ability to generalize the results of these studies.

A randomized, controlled and nonblinded study was conducted in abdominal surgery patients without a diagnosis of OSA. Either routine oxygen or a trial of CPAP plus oxygen was administered to these non-OSA patients who developed severe postoperative hypoxemia. Patients using CPAP were found to have decreased need of reintubation to treat respiratory failure and less postoperative complications. Conversely, two studies, one in nonsurgical non-OSA patients admitted to intensive care and another in abdominal surgery patients without a history of OSA, found no benefit of postoperative CPAP use.

Well-designed research studies on the postoperative effect of CPAP in OSA surgical patients are lacking. Such studies would need to be geared towards evidence-based medicine and would have to address the following questions: how long should CPAP be applied, preoperatively and/or postoperatively, for optimum efficacy, what type of surgery would benefit most from CPAP treatment, should OSA severity influence the decision to use CPAP postoperatively, would use of preoperative prophylactic CPAP confer a reduced postoperative risk, and would CPAP allow for safer administration of analgesics?

Perioperative Risk Management—a Significant Challenge in OSA Patients

The evidence of the potential deleterious effect of sedatives, anesthesia and analgesics in OSA patients and the increased risk of perioperative adverse events implies that clinical management strategies need to be specifically tailored. It is important for anesthesiologists to meet the challenge of maintaining upper airway patency and preventing perioperative complications in these patients. The recently developed ASA guidelines emphasize the importance of evaluation, detection and preparation in the preoperative workup and the necessity of using forethought and vigilance when developing perioperative management for OSA patients undergoing surgery. The following questions arise: is it feasible for anesthesiologists to identify patients with undiagnosed OSA in the preoperative clinic, can we identify factors that may increase the perioperative risk in OSA patients, is it possible to modify anesthetic techniques to reduce perioperative risk in OSA patients, are there safer alternatives to opioid analgesics for postoperative pain control, and finally, what are the optimal postoperative management strategies for OSA patients?

Is It Feasible to Identify OSA in the Preoperative Clinic?

The current “gold standard” in the clinical diagnosis of OSA is an overnight sleep laboratory study with PSG. PSG is a highly reliable diagnostic tool but screening of every surgical patient is not feasible due to the time-commitment, expense and burden on the health care system. Moreover, PSG is not practical for rapid screening in a fast-paced preoperative clinic. A number of questionnaire-based screenings are available in the literature. In general, the problem is that these questionnaires ask a variety of questions about sleep that are not specifically geared towards identifying which patients have OSA. To complicate matters, 2 of the questionnaires contain 100 or more items, thereby reducing their practicality.

The BQ is a self-report instrument specifically designed to identify undiagnosed OSA. It has been shown to perform well in a large population of 744 primary care patients with a sensitivity of 0.89 and specificity of 0.71. The BQ has also been validated in atrial fibrillation patients and shown to perform with a similar sensitivity (0.86) and specificity (0.89). The 10-item BQ is comprised of 5 questions on snoring, 3 on excessive daytime sleepiness, 1 on sleepiness while driving, and 1 inquiring about a history of hypertension. Details of age, gender, weight, height, and neck circumference are also recorded. The BQ stratifies patients into high or low risk of having OSA based on their endorsement of symptom severity.

The BQ has been shown to be a valuable tool for OSA screening in primary care and atrial fibrillation patients, but its usefulness in determining which surgical patients are at greater risk of having OSA has yet to be established. Recently, we screened 318 patients using BQ at our hospital and 24% (n = 76, 95% CI 19%–29%) were found to be at high risk of having OSA.

The number of questions and the complicated scoring procedure of BQ may be too cumbersome for anesthesiologists and their patients. To facilitate the widespread usage of an OSA screening tool, we developed a shorter 4-item OSA screening questionnaire (STOP). The STOP questionnaire contains four questions: S: “Do you snore loudly, loud enough to be heard through closed door,” T: “Do you feel tired or fatigued during the daytime almost every day,” O: “Has anyone observed that you stop breathing during sleep,” and P: “Do you have a history of high blood pressure with or without treatment”? Patients answering “yes” to two or more questions were assigned as being at high risk of having OSA. The sensitivity of the STOP questionnaire at AHI >5, >15, and >30 cutoff levels was 65.6%, 74.3%, and 79.3%, respectively. When incorporating BMI more than 35 kg/m² (B),
age over 50 yr (A), neck circumference larger than 40 cm (N) and male gender (G) into the STOP questionnaire, STOP-BANG, the sensitivity was increased to 83.6%, 92.9%, and 100% for the same AHI cutoffs above.\(^{179}\)

The ASA taskforce on OSA\(^3\) also developed a 16-item checklist to assist anesthesiologists in identifying OSA. The checklist is comprised of three categories of predisposing physical characteristics, symptoms and complaints attributable to OSA. Patients endorsing symptoms or signs in two or more of the categories are to be considered at high risk of having OSA. The major drawback to this screening tool is time commitment because the checklist needs to be completed by the clinician.

With the development of the BQ, STOP, and ASA checklist, a necessary step before their use as an OSA screening tool in the preoperative clinic is the determination of their validity. We have conducted a study to compare the validity of the BQ, STOP, and ASA checklist in 177 surgical patients who were concurrently studied with PSG.\(^{180}\) The sensitivity of the BQ, the ASA checklist, and the STOP questionnaire was 68.9%, 72.1%, and 65.6% at AHI > 5; 78.6%, 78.6%, and 74.3% at AHI >15; 87.2%, 87.2%, and 79.5% at AHI >30, respectively. There is no significant difference in the predictive parameters of the three screening tools.\(^{180}\) The STOP questionnaire is a concise and easy to use screening tool for OSA. It has been validated in surgical patients at the preoperative clinic and is equivalent to the BQ and ASA checklist. Incorporating BMI, age, neck size, and gender with the STOP questionnaire, STOP-BANG, will give a higher sensitivity and negative predictive value for patients with moderate to severe OSA.\(^{180}\) A recent study found that the percentage of patients with oxygen desaturation index (the number of times per hour the oxygen saturation decreases by ≥4% from baseline) >10 was significantly higher in patients identified as being at high risk of having OSA and having recurrent PACU respiratory events.\(^{181}\) The anesthesiologist may be the first health professional to inquire about sleep, and therefore, will have an important role in identifying these patients and preventing both short and long-term complications. Use of a practical screening tool in the preoperative clinic is highly recommended.

Possible Factors Contributing to Increased Perioperative Risk in OSA Patients

Certainly, not all OSA patients undergoing surgery have serious adverse perioperative events and of those who do, the time course of the serious adverse events varies greatly (Table 3). A review of the findings points to possible multiple factors in surgical patients with OSA that could lead to perioperative adverse events. Further research in this area is needed, not only to identify these factors, but to elucidate their level of involvement by determining the varying odds ratios. The impact of anesthetics and analgesics in OSA patients is a definite consideration in determining risk. These will be discussed below.

Other factors related directly to the etiology of OSA or the associated morbidity also merit consideration. Studies of patients undergoing surgical treatment for their OSA\(^{98–100,119,121}\) or major surgery, excluding upper airway procedures, have documented that patients with a preoperative history of more severe OSA tend to have more perioperative complications (Table 3). These findings would imply that preoperative screening and identification of those patients with more severe OSA would allow for better preparation for perioperative complications. However, these studies are either retrospective or observational and are of too low evidence level (Level IV) to enable firm conclusions. Moreover, two other studies\(^{102,117}\) at the same evidence level found that higher AHI and lower \(\text{SaO}_2\) levels preoperatively were not correlated with postoperative complications (Table 3). Therefore, more research is needed to correlate AHI and preoperative oxygen level with perioperative complications.

Further information on this matter can be gleaned from studies of obese surgical patients with a high prevalence of OSA. While obesity is associated with a greater risk of perioperative complications,\(^{182,183}\) multivariate analyses do not implicate a history of OSA as a risk factor for increased surgical complications in patients undergoing gastric bypass surgery.\(^{184}\) Rather, it seems that preexisting pulmonary disorders are more predictive of the need for postoperative ICU monitoring and longer hospital stay.\(^{185}\) This suggests that it is not the obesity \textit{per se}, but the associated morbidity that increases perioperative risk. That OSA may not feature prominently as a cause of postoperative complications may also be explained by the fact that bariatric surgery candidates undergo extensive preoperative medical examination before being allowed to undergo surgery.\(^{186}\) Overnight PSG screening for OSA is also commonly included in the preoperative work-up so that OSA can be identified and treated before surgery. It remains to be determined whether preoperative treatment of OSA could significantly reduce the perioperative risk in these patients.

An alternative hypothesis is that long-standing untreated OSA is associated with greater morbidity and perioperative morbidity may be a more sensitive indicator of perioperative complications. A retrospective study of 311 patients undergoing bariatric surgery for weight reduction reported that OSA was associated with a longer length of hospital admissions (OR 5.5) but that stronger predictors of longer hospitalization included coronary artery disease (OR 8.7) and the presence of the metabolic syndrome (OR 6.7–10.2).\(^{187}\)

The change in sleep architecture with surgery could possibly contribute to a greater postoperative risk in OSA patients. Among patients undergoing abdominal surgery, anesthesia initially suppresses rapid eye movement (REM) sleep but there is intense REM rebound towards the middle of the first postoperative...
This alteration in sleep architecture can have a substantial impact on the respiratory variables in OSA patients. In REM sleep, upper airway muscle activity in the late apneic phase is reduced and, consequently, apneas are of larger duration and are associated with a greater degree of hypoxemia during REM sleep than non-REM sleep. Hemodynamic changes are also evident in REM sleep as REM-related incidences of desaturation were found to be linked to significantly higher postapnea increases in arterial blood pressure. Coincidently, numerous ventilatory disturbances, including apneas and hypopneas, have been observed on the second and third postoperative nights. There are no studies directly linking changes in sleep stage with ventilatory disturbances during the postoperative period.

There are also reports of numerous obstructive hypopnic and/or apneic events within the first 12 h postoperatively. Moreover, the respiratory disturbances in the early postoperative period have been reported to occur mainly in Stages 1 and 2 sleep since most patients did not have slow wave sleep or REM sleep in the early postoperative period. More recent studies have documented that the more serious complications occurred within the first 24 h after surgery in OSA patients. In a study of non-OSA surgical patients, more than 75% of postoperative patients had respiratory events within 13 to 24 h after surgery and significant risk factors included older age, having more than one comorbidity and whether hydromorphone was administered for analgesia. Similar studies in OSA patients undergoing surgery are needed to determine if the timing of respiratory events is similar and which risk factors are significant for this population. The time course of adverse postoperative events suggests the involvement of other factors than sleep architecture, but it may help to elucidate the period of greatest postoperative risk. That is, the REM-related impact on respiratory events would take place a number of days postoperatively and may represent a second period of greater risk of postoperative respiratory complications. However, the above studies suggest that postoperative complications are quite common within the first 24 h postoperatively.

Can Choice of Anesthetics or Anesthetic Technique Reduce Perioperative Risk in OSA Patients?

There are numerous reviews on the subject of anesthetic management of OSA patients that emphasize that the type of anesthesia may have differential impact on the respiration of patients. Despite these reviews, there are no randomized controlled trials of the safety of various anesthetics in the perioperative period. As mentioned previously, different analgescics have different margins of safety and result in varying levels of respiratory depression. A relatively recent study has documented the impact of propofol on upper airway collapsibility by investigating the relationship between varying concentrations and the critical airway closing pressure. The use of healthy individuals, and not patients with OSA, as subjects coupled with the lack of a randomized controlled design, are significant limitations of this study. Nevertheless, the findings highlight that a carefully chosen concentration of anesthetic may play an important role in the airway management of OSA patients.

An important consideration in the choice of inhaled anesthesia is the presence of any carryover anesthetic effects into the postoperative period that could impair respiration and/or enhance the deleterious respiratory effects of analgesics. In OSA patients undergoing UPPP, there was delayed recovery in those patients receiving isoflurane versus propofol. Propofol anesthesia was found to result in better oxygen saturation in the first postoperative hour and more rapid recovery of spontaneous breathing versus isoflurane. However, these studies were not done on OSA patients. Short-acting anesthetics, such as remifentanil, have also been shown to result in a rapid postoperative recovery, better oxygen saturation profile and shorter postoperative length of stay. Also, morbidly obese patients who underwent major abdominal surgery awoke significantly faster after desflurane than after sevoflurane anesthesia. The patients anesthetized with desflurane had higher oxygen saturation on entry to the PACU.

Premedication sedatives, especially benzodiazepines, such as flunitrazepam or midazolam, have been shown to cause postoperative airway obstruction. In this study, 12 patients did not have a premorbid history of OSA but were observed to snore loudly postoperatively. Conversely, some premedication drugs have been shown to be beneficial in OSA patients. In a case report of a morbidly obese woman with tracheal stenosis, dexmedetomidine, an α-2 adrenergic agonist, was used as a premedication due its anxiolytic and sedative properties. The benefit of dexmedetomidine is the lack of significant respiratory depression within the clinical dose range. Similarly, in a randomized controlled trial, orally administered clonidine was found to reduce the propofol dose required for induction of anesthesia. Unfortunately, there are no trials of the efficacy of varying premedication drugs in OSA patients undergoing surgery, but the above studies illustrate their importance.

Are There Safer Alternatives to Opioid Analgesics for Postoperative Pain Control?

Postoperative analgesia is another factor that can influence respiration in surgical patients with OSA. In a retrospective study of 1600 patients, not specifically OSA patients, who had received postoperative patient-controlled analgesia with IV opioids, 8 cases of serious respiratory depression were reported. Contributing factors were the concurrent use of a background...
infusion of opioids, advanced age, concomitant administration of sedative or hypnotic medications and a pre-existing history of sleep apnea. Two retrospective reviews of more than one-thousand surgical patients indicated that postoperative respiratory depression after morphine-based patient-controlled analgesia was observed to occur in about 1%–2% of patients.203,204 This respiratory depression occurred between 2 to 31 h after initiation of the IV patient-controlled analgesia205 indicating the need for long-term diligent patient monitoring.

A review conducted to identify the risk factors for respiratory depression subsequent to patient-controlled analgesia concluded that there is no single indicator for respiratory depression but that OSA, whether suspected or verified by patient history, is one of the risk factors for respiratory depression. Other factors include older age, hepatic, pulmonary or cardiac disease, concurrent use of central depressants, obesity, and higher bolus doses of patient-controlled analgesia.205 There are no prospective randomized studies examining the respiratory effect of patient-controlled analgesia in OSA patients.

In general, the consensus is that opioids are to be avoided in OSA patients, if possible, especially when they undergo upper airway surgical treatment for OSA.206 The ASA guidelines recommend regional anesthesia to reduce the possibility of adverse events associated with systemic opioids.3 A multimodal approach with combinations of analgesics from different classes and different sites of analgesic administration is a prudent strategy for perioperative pain management.207–209 The use of nonsteroidal anti-inflammatory analgesics210 is strongly recommended.3 Drugs such as acetaminophen, tramadol, and other nonopioid analgesics and their combination can be used to provide effective pain relief and reduce opioid consumption, thus alleviating the opioid-related adverse effect of respiratory depression. Other novel approaches, such as ketamine, clonidine, or gabapentin can be used.201,207–209 In a case report, the nonopioid sedative dexmedetomidine45 has been shown to reduce the need for postoperative opioids. Other techniques that avoid medication, such as transcranial magnetic stimulation,211 are also being investigated.

The opiate-sparing strategies geared towards OSA patients are summarized (Table 4). A major drawback of these studies is that they are predominantly case reports. Unfortunately, there are no studies comparing the safety and efficacy of different anesthetic techniques, general anesthesia, regional anesthesia or monitored anesthesia care in OSA patients undergoing surgery or studies on different analgesics or adjuvants.

### Table 4. Strategies for Reducing Use of Postoperative Opioids

<table>
<thead>
<tr>
<th>Agent/technique</th>
<th>Study level</th>
<th>Subject group</th>
<th>Study results</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV NSAIDS–ketoprofen (5 mg/kg/24)</td>
<td>Nonrandomized study; Level III210</td>
<td>22 tonsillectomy patients and 31 UPPP patients.</td>
<td>Over 90% of patients reported that ketoprofen was effective. Patient-controlled analgesia requirement on the first postop day was reduced by 1/3 compared to the second postop day. Postoperatively, pain scores and total analgesic consumption were reduced.</td>
</tr>
<tr>
<td>Dexmedetomidine premedication</td>
<td>Case report; Level IV45</td>
<td>Morbidly obese patient undergoing gastric bypass surgery.</td>
<td></td>
</tr>
<tr>
<td>Oral clonidine premedication</td>
<td>Randomized, double-blind prospective study; Level II201</td>
<td>30 OSA patients undergoing ENT surgery.</td>
<td></td>
</tr>
<tr>
<td>Transcranial magnetic stimulation (TMS)</td>
<td>Randomized, controlled study; Level II211</td>
<td>20 gastric bypass surgery patients and matched controls.</td>
<td>TMS allowed a 40% reduction in total morphine use.</td>
</tr>
</tbody>
</table>

IV = intravenous; OSA = obstructive sleep apnea; UPPP = uvulopalatopharyngoplasty; ENT = ear, nose and throat; NSAID = nonsteroidal antiinflammatory drugs.

### Postoperative Management Strategies for OSA Patients

Clearly, anesthesiologists need to develop effective management strategies to minimize perioperative risk for patients with OSA undergoing surgery. To that end, the ASA recently published guidelines,3 a Level IV evidence document based on expert consensus report, that propose strategies for overall perioperative care of OSA patients. The clinical practice review committee of the American Academy of Sleep Medicine also indicated that the scientific literature regarding the perioperative risk and best management techniques for OSA patients was scanty and of limited quantity. They used the available data to make a statement on the perioperative management of OSA patients instead of standards of practice recommendations.212 Due to the high risk of complications and morbidity associated with upper airway surgery for OSA treatment, suggestions for perioperative monitoring in OSA patients undergoing upper airway surgery were initially introduced 15 yr ago,216 however, no consensus-based guidelines for the perioperative management of OSA patients undergoing airway surgery were formulated. Moreover, the upper airway surgical literature is specifically oriented towards upper airway procedures thus lessening the applicability of these management strategies to other types of surgery. For example, steps to minimize upper airway edema with topical corticosteroids213 are crucial with...
upper airway surgery but have much less applicability to other types of surgery. Nonetheless, a closer examination of management strategies for upper airway surgery may help to provide information that is applicable to OSA patients undergoing surgery.

Pertinent information can also be gleaned from reports of patients undergoing bariatric surgery for obesity. A major confound with the bariatric surgery population is the presence of obesity and the added risk of the associated morbidity that render it difficult to extrapolate these findings to the general surgical population. Of positive note, it was shown that anesthesia need not be associated with postoperative complications in obese patients with OSA undergoing bariatric surgery. With careful postoperative monitoring in the PACU and the ward, surgery was reported to be safe in this high-risk group of patients.

Surgery in OSA patients is associated with significant perioperative risk. As mentioned earlier, cardiovascular morbidity is common in patients with longstanding untreated OSA thus further increasing the likelihood of adverse perioperative events. The incidence of perioperative complications associated with upper airway surgery for OSA is about 3.5% (range, 0.6–8.9), and a 0.4% to 1.6% incidence of mortality has been reported. Airway-related postoperative complications occur in about 6% of patients, oxygen desaturations in 9% and electrocardiogram changes in 1%. Others have documented that about one-third of the complications involve the airway. Cardiac complications, such as hypertension, have also been commonly reported. Alerting surgeons, anesthesiologists, and nurses to the potential perioperative complications associated with surgery in OSA patients is a first step to reducing the rate of morbidity and mortality.

The ASA guidelines recommend that the preoperative evaluation be conducted well in advance of the surgery in patients suspected of having OSA. This procedure would allow for the necessary preoperative evaluation and development of an appropriate perioperative management plan. However, patients with undiagnosed OSA would likely be identified at the time of the preoperative visit when there may not be time to do further testing before surgery. In this event, the ASA guidelines recommend that a presumptive diagnosis of OSA be made from criteria based on the signs and symptoms of OSA.

As maintenance of upper airway patency in OSA patients is a major consideration, caution is needed to ensure that extubation should only be done after the patient is fully conscious and airway patency is ensured. However, the ASA guidelines state that this need be the case only for patients at increased perioperative risk. The use of postoperative supplemental oxygen has been suggested for OSA patients undergoing upper airway surgery to maintain appropriate oxygen saturation. The ASA guidelines caution that oxygen supplementation should be used only until patients are able to maintain baseline oxygen saturation with room air. A side effect of the use of prolonged supplemental oxygen in patients with chronic obstructive pulmonary disease is the increased duration of obstructive apneas or hypopneas. The ASA guidelines further recommend that continuous oximetry may be used in the step down unit in patients with increased perioperative risk from OSA, but it does not support the need of continuous oxygen monitoring in all patients. There is no evidence-based determination if the cost of routine monitoring is warranted as there are no studies examining whether such monitoring reduces the perioperative risk in OSA patients.

Other postoperative strategies for reducing perioperative risk, such as the influence of sleep position on OSA, also warrant investigation. Lateral position is reported to improve the maintenance of the passive pharyngeal airway in patients with OSA. The lateral position improves upper airway stability during sleep which may allow reduction of the therapeutic levels of CPAP. The study by Penzel et al. also supported the idea that lower CPAP pressure was needed during lateral positions versus supine positions. However, the ASA guidelines recommend a semi-upright position for extubation and recovery in OSA patients and the use of a nonsupine position postoperatively. However, this position may not be feasible for certain orthopedic procedures.

Several nonrandomized follow-up studies in patients with upper airway surgery have assessed the effect of the appropriate setting of surgery for OSA patients. Based on these studies, it is recommended that OSA patients at low risk for adverse outcomes may be discharged home without ICU admission. One study proposed that upper airway surgery may be safely done as outpatient surgery and that more than 80% were discharged on the same day of surgery. A limitation of this study was that there was no information regarding postoperative follow-up and whether respiratory complications occurred in the days after surgery. Other studies, however, support the notion that ICU admission is not required and that respiratory complications, if they occur, do so a few hours after surgery. It is important to note that all OSA patients are carefully screened before undergoing upper airway surgery to improve the success of the treatment. As part of this screening process, younger nonobese OSA patients with AHI <40 are generally selected.

From the consultants in the ASA guidelines, there is an overall agreement that the level of perioperative risk is a function of OSA severity and type of surgery. The guidelines propose that the following types of surgeries can be performed safely on an outpatient basis: superficial surgeries using local or regional anesthesia, minor orthopedic surgery with local or regional anesthesia and lithotripsy. The consultants were equivocal or in disagreement regarding the other
types of surgeries, particularly with regards to upper airway surgery. The ASA guidelines further propose that the following factors need to be considered when determining outpatient care and the degree of perioperative risk: status of sleep apnea (e.g., treated or untreated), anatomical and physiologic abnormalities, level of co-morbidity (e.g., Are there OSA-associated comorbidities such as cardiovascular disorders and have these been appropriately managed?), type of surgery, anesthesia modality, postoperative opioid use (dosage, duration and length of administration, etc), patient age, how patients will be monitored after discharge and what facilities are available for outpatient monitoring.

The ASA guidelines emphasize the importance of increased perioperative risk in OSA patients and that additional measures of perioperative management need to be instituted in these patients. The guidelines identify several factors (above) that could increase the risk but there is no further elucidation of the degree of contribution of each factor. Certainly, surgeons and anesthesiologists have to treat each patient on a case-by-case basis, but an evidence-based algorithm to determine the actual level of risk would be a useful starting point. However, no clear definitions or grading schemes for “high” versus “low” risk for perioperative management are available in the literature and further studies are urgently needed in this area. The purpose of such research would be to identify and quantify the required measures in specifically assigning perioperative risk status in OSA patients. The appropriate classification and definition of level of perioperative risk would be an important step towards a concrete discernment of the degree of necessary perioperative monitoring and whether outpatient surgery could be conducted. Above all, the pressures to reduce health care expenditure dictate that the perioperative care of patients needs to be optimized to prevent unnecessary monitoring and depletion of limited resources.

A summary of the recommendations for OSA surgery from the ASA guidelines is shown in Table 5. The strength of the ASA guidelines is their use of expert-based consensus. However, it is important to note that their recommendations are not evidence-based and there is a paucity of research to substantiate the efficacy of these measures in improving perioperative outcome.

**CONCLUSIONS**

There is a frequent prevalence of undiagnosed OSA. Also, the severity of OSA varies among patient groups and perioperative complications are probably related to the interaction of the severity of the diseases and the degree of respiratory depression induced by opioids. Sleep apnea is associated with other preexisting medical conditions such as obesity, hypertension, coronary artery disease, and diabetes that negatively impact perioperative outcomes. It may be difficult to separate the impact of OSA per se from the other associated conditions.

Surgical patients with OSA may be vulnerable to sedation, anesthesia and analgesia. Episodic sleep-related desaturation and incidence of unexplained cardiorespiratory arrest may be attributable to undiagnosed OSA in surgical patients, but this connection needs to be tested within randomized, controlled trials. It also remains to be determined whether the perioperative risk of OSA patients could be reduced by appropriate screening to detect undiagnosed OSA and implementation of a perioperative management plan for OSA. Evidence-based research on perioperative management of OSA patients is sorely lacking.

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