CME 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.

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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 morbidity[1] 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

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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)
3. EMBASE (1980–2007)
4. Cochrane Database of Systematic Reviews (1st Quarter 2007)
5. ACP Journal Club (1991–March 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. Despite 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 studies[6–9] 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/m^2, 6.10; 95% CI 2.86–13.00; women: OR for age >60 yr, 6.04; 95% CI 1.75–20.0),[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

Study location and population	Numbers (*n*)	Age range (yr)	Estimated prevalence (%) of mild OSA (AHI >5) (95% CI)		Estimated prevalence (%) of moderate OSA (AHI >15) (95% CI)	
			Males	Females	Males	Females
Wisconsin (state employees)[6]	602 M = 352 F = 250	30–60	24 (19–28)	9 (6–12)	9 (6–11)	4 (2–7)
Pennsylvania (household population)[7,8]	1741 M = 741 F = 1000	20–100	17 (15–20)	—	7 (6–9)	2 (2–3)
Spain (general population)[9]	2148 M = 1050 F = 1098	30–70	26 (20–32)	28 (20–35)	14 (10–18)	7 (3–11)

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

Surgical patient population	Age and gender	Methods used to diagnose OSA	No. of patients with OSA (percentage in brackets)
General surgery (excluding cardiac and OSA surgery)[27]	44 ± 17 yr 212 F, 221 M	Symptoms & PSG	41/433 (9.5%) patients with 2 or more symptoms of OSA AHI >5: 14/433 (3.2%)
Surgery for intracranial tumor[26]	54 ± 18 yr 8 M, 3 F	PSG	AHI >5: 7/11 (64%) AHI >20: 6/11 (55%)
Bariatric surgery[24]	7 M, 34 F, F: 43 yr (25–60 yr) M: 50 yr (19–58 yr)	PSG	AHI >5: 29/41 (71%)
Epilepsy patients undergoing surgical treatment[25]	With OSA: 40 ± 9 yr 9 M, 4 F without OSA: 33 ± 10 yr 9 M, 17 F	PSG	AHI >5: 13/39 (33%) AHI >20: 5/39 (13%)

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/m^{-2}) 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 studies[24–27] 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,[24,28]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, dexmedotomidine'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 trials[52,53] 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 CO_2.[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.[56]

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.[64] 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.[65] Furthermore, the hypoxic episodes occur earlier in the sleep period and SaO_2 levels may not return to normal after the long apneas that were induced by alcohol consumption. It was proposed that alcohol has a depressant effect on the respiratory centers that control pharyngeal muscle tone, thus increasing the likelihood of pharyngeal collapse during sleep.[65] This reduction in pharyngeal tone with alcohol ingestion is coupled with the prolongation of time to arousal after airway occlusion.[66] A similar reduction in pharyngeal tone and increased arousal threshold to hypoxia occurs after administration of sedatives, anesthetics and analgesics. Investigation of the actions of sedatives, anesthetics and analgesics points to the pharynx as a primary site of obstruction after anesthesia.[67–70] It has been proposed that airway obstruction with sedation and anesthesia follows a similar course as that seen with obstructive apneas during sleep; that is, increased airway collapsibility due to an increase in the critical closing pressure,[36] loss of tonic activity in pharyngeal muscle[41] and failure of the phasic activation of upper airway muscles before diagphragmatic activity.[71] This suggests that respiration in OSA patients may also be more susceptible to drugs used during the perioperative period.

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.[72] 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.[72] Similarly, in the postoperative setting, analgesia with oxycodone in healthy, nonobese ASA class I-II females without a history of OSA did not result in apnea. In this study, SaO_2 was decreased during the first postoperative night but levels above 90% were maintained.[73]

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.[74] 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.[56] Postoperative epidural morphine in a patient with a history suggestive of OSA was documented to result in apneas, respiratory depression and cyanosis.[75]

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.[76] 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 SaO_2 <80% were observed to be primarily associated with obstructive apnea and paradoxical breathing,[52] and no correlation was found between the duration of anesthesia and postoperative SaO_2 levels[52] 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 hypopnic events.[77] Moreover, increased numbers and duration of apneic events is observed in healthy volunteers and asymptomatic nonsurgical patients[78–80] after sedation with

various sedative medications such as midazolam, fentanyl,[78,79] and flurazepam.[80] 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.[1,2,81–83] Untreated OSA patients are at a greater risk of developing cardiovascular disease (OR 3.1, 95% CI 1.2–8.3),[84] including heart failure,[85] arrhythmias (2–4 fold increase),[86] hypertension (10-fold increase),[87] and stroke (OR 4.33, 95% CI 1.32–14.24, $P < 0.02$).[88] 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.[89] The impact of OSA is also seen on $Paco_2$ levels and the coagulation systems.[90–92] In a large observational cohort study,[93] 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 (SaO_2 <80%) when they were monitored for 16 h after surgery.[50] These occurred only while the patients were asleep and were associated with disturbances in ventilatory pattern such as obstructive apnea (144 episodes), paradoxic breathing and periods of slow ventilatory rate.[52,75,94] In patients with OSA-associated severe postoperative respiratory events, the need for postoperative reintubation has been documented.[95] However, since OSA is a risk factor for increased difficulty with tracheal intubation,[96] 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.[97] 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 O_2 Sat 71.9% vs 77.8%, $P < 0.01$).[98] 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.[99] Pang et al.[100] 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%).[103] 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.[103] However, the risk factor of an OSA diagnosis was not studied in this population.[103]

Apart from respiratory complications, sustained arrhythmias and hypertension[104] 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[105] have been reported in OSA patients undergoing gastric bypass surgery.[106] The hemodynamic instability associated with arrhythmias can significantly affect postoperative morbidity. Morphine infusion in asymptomatic surgical patients has been shown to increase the

Table 3. Summary of Perioperative Outcomes Associated With OSA

Study design and evidence level	Study subjects	Patient history	Finding and perioperative/postoperative outcome
Case report; Level IV[75]	Male (65 yr) with prostatic carcinoma aborted radical prostatectomy.	History suggestive of OSA. No formal diagnosis.	Morphine 5 mg, epidural for analgesia. 8 h later, patient found unresponsive, with apneic spells and cyanosis. Patient made a complete recovery.
Case report; Level IV[109]	Male(38 yr) emergency mastoidectomy.	History of loud snoring and subsequently diagnosed with OSA.	Patient developed severe upper airway obstruction upon extubation. Reintubated but airway obstruction reoccurred.
Case report; Level IV[111]	3 cases. Ages 41–66. 2 orthopedic surgery, 1 ventral hernia repair.	All 3 diagnosed with OSA before surgery.	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.
Case report; Level IV[112]	Male (74 yr) aortic reconstructive surgery.	Preoperative oximetry suggested severe, previously undiagnosed OSA.	IV morphine for analgesia. Severe respiratory obstruction and large fluctuations in systolic and diastolic blood pressure 4 h after extubation.
Observational study; Level IV[121]	80 patients major surgery.	All patients had a history suggestive of OSA confirmed by preop oximetry.	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% Spo_2.
Retrospective review; Level IV[102]	347 patients, uvulopalatopharyngoplasty (UPPP) and associated procedures for OSA treatment.	All study patients had PSG-confirmed OSA diagnosis.	5 of the patients had postop airway complications. Preop AHI and SaO_2 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.
Retrospective review; Level IV[122]	109 patients upper airway surgery for OSA treatment.	All patients had a preexisting diagnosis of OSA.	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.
Case report; Level IV[113]	A subset of three patients, laparoscopic weight reduction surgery.	All patients were diagnosed with OSA.	Patients developed postop prolonged heart block during sleep.
Case report; Level IV[108]	Obese male (42 yr) ear surgery.	Previous diagnosis of OSA.	Cardiac arrest noted 3 h after IM morphine. Severe hypoxic encephalopathy and brain death.
Retrospective; Level IV[95]	101 OSA patients and 101 matched controls hip and knee surgery.	PSG OSA diagnosis before or after surgery. Controls did not undergo PSG.	Postop complications greater in OSA patients versus controls. Hospital stay significantly longer and requirement for ICU transfer greater in OSA patients.
Newsletter report; Level IV[110]	Composite cases based on 8 cases reviewed.	All patients eventually diagnosed with OSA.	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.
Observational; Level IV[119]	10 patients UPPP and septoplasty for OSA treatment.	All patients had an established OSA diagnosis. AHI range 2–30.	Night following surgery: increased AHI and decreased SaO2. Within 24h postop, significant increase in systolic and diastolic blood pressure (BP) and heart rate and increased urinary catecholamines during 1st postop night.
Retrospective; Level IV[101]	130 patients tonsillectomy with UPPP.	All patients had an established OSA diagnosis.	Patients spent an average of 18 h in the step down unit. Postoperative desaturation below 90% was observed in 8 patients (6.2%).
Retrospective; Level IV[117]	234 patients with OSA Outpatient surgical procedures and equal number of matched controls.	All study patients had PSG-confirmed OSA diagnosis. Control patients did not undergo PSG to exclude OSA diagnosis.	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.

(*Continued*)

Table 3. Continued

Study design and evidence level	Study subjects	Patient history	Finding and perioperative/postoperative outcome
Retrospective review; Level IV[98]	90 patients UPPP and associated procedures for OSA treatment.	All 90 had a PSG confirmed diagnosis of OSA.	Postop complications in 19 (21%) of patients & respiration complication in 12 (13%). Airway-related complications in 5 (6%), SaO_2 <90 in 8 (9%), bleeding in 7 (8%), ECG change in 1 (1%).
Retrospective review; Level IV[120]	110 OSA UPPP and associated procedures as outpatient surgical treatment of OSA.	All patients had a PSG confirmed diagnosis of OSA.	90 (82%) of patients discharged on same day. 20 (18%) kept for observation. Of the 25 patients with AHI >50: 5 (20%) admitted; 2 patients with AHI >90 admitted due to oxygen desaturation. Desaturation requiring admission in 3% of patients. 10 (10%) patients had minor postop complications No major complications.
Retrospective review; Level IV[100]	118 patients upper airway surgery for OSA treatment.	All patients had a preexisting diagnosis of OSA.	Combined perioperative complication rate of 14%, including oxygen desaturation, hypertension and upper airway compromise.
Retrospective review; Level IV[114]	37 OSA patients undergoing cardiac surgery.	All patients had a diagnosis of OSA.	Significantly greater occurrences of postoperative encephalopathy and infection and longer ICU stay.

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.

incidence of conduction abnormalities.[53] Furthermore, a preoperative diagnosis of OSA has been shown to be an independent predictor of atrial fibrillation after coronary bypass surgery.[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.[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.[114] Two reviews on anesthesia in OSA patients emphasize that these patients are at greater risk of perioperative adverse events.[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[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 surgical surgery is normally around 1%–2%.[118]

In contrast to the above findings, a retrospective matched case-controlled study of OSA patients undergoing hip or knee replacement surgery[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[95] suffers from many of the same limitations as the above study[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.[98,100–102,119–122] Postoperatively, there are reports of increased obstructions and desaturations[98,119,121] and changes in systolic and diastolic blood pressure.[119] It was further documented that postoperative complications were more frequent in OSA patients that had an

increased AHI 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 hypertension[104] 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[105] 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 blood pressure[123] in patients not undergoing surgery. In a population of middle-aged adults with subclinical sleep-disordered breathing, large fluctuations in systolic blood pressure (23 $\pm$ 10 mm Hg) and diastolic pressure (13 $\pm$ 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 hypoxemia[98,119,121] while decreases in arterial oxygen saturation (Spo_2) have been found to be significantly higher on postoperative nights than preoperatively[128,129] (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 study[130] 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 setting[138,139] 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%

vs 2.6%, $P < 0.05$).[96] In OSA patients undergoing ear, nose, and throat surgery, a 44% prevalence of difficult intubation had similarly been reported.[142] Furthermore, patients with severe OSA (AHI ≥40) were found to have a much higher prevalence of difficult intubation.[143] 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.[144] The corollary of the relationship is also true, that is, patients with difficult tracheal intubation have also been shown to be at greater risk of having OSA.[145] In a small retrospective study of 15 patients with difficult intubation, 53% (8 of 15) of patients were diagnosed with OSA.[145] In a prospective study, 66% of patients with difficult intubation were subsequently found to have AHI >5.[146] 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.[147] 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,[148] restoration of quality of life,[149] improvement in vigilance,[150] concentration and memory,[151] lessening of fatigue,[152] reduction in health care usage,[1] and a decrease in traffic accidents.[148]

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.[153] There are a number of reports of serious postoperative hypertensive events in OSA patients.[100,112,119] The efficacy of long-term CPAP treatment in reducing arterial blood pressure in OSA patients not undergoing surgery has been demonstrated.[154–157] 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).[158,159] However, the literature is not without controversy as others[160] have reported that acute CPAP does not alter blood pressure. Apart from one case report[112] 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[133,161,162] and the beneficial effects of CPAP on sinus arrest and episodes of heart block during sleep have been reported.[163] In a study of 17 patients, CPAP treatment reduced the number of arrhythmias from 1575 to 165 episodes per night ($P < 0.01$).[163] 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[164–166] 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.[167] 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.[168] 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,[169] one case report[109] and one retrospective study.[95] 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.[170] 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[171] and another in abdominal surgery patients without a history of OSA,[172] 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[3] 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.[173] 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.[174–177] 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.[10,178] 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.[31]

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.[179] When incorporating BMI more than 35 kg/m^{-2} (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 $\geq$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 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 *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 preoperative 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

week.[188] 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[189] and, consequently, apneas are of larger duration and are associated with a greater degree of hypoxemia during REM sleep than non-REM sleep.[190] 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.[191] Coincidentally, numerous ventilatory disturbances, including apneas and hypopneas, have been observed on the second and third postoperative nights.[192] 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.[77] 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.[52] More recent studies have documented that the more serious complications occurred within the first 24 h after surgery in OSA patients.[95] In a study of non-OSA surgical patients,[193] 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[111,113,194–197] 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 analgesics have different margins of safety and result in varying levels of respiratory depression. A relatively recent study[36] 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.[97] 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.[198,199] 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.[200]

Premedication sedatives, especially benzodiazepines, such as flunitrazepam or midazolam, have been shown to cause postoperative airway obstruction.[41] 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.[201] 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.[202] Contributing factors were the concurrent use of a background

Table 4. Strategies for Reducing Use of Postoperative Opioids

Agent/technique	Study level	Subject group	Study results
IV NSAIDS–ketoprofen (5 mg/kg/24)	Nonrandomized study; Level III[210]	22 tonsillectomy patients and 31 UPPP patients.	Over 90% of patients reported that ketoprofen was effective.
Dexmedetomidine premedication	Case report; Level IV[45]	Morbidly obese patient undergoing gastric bypass surgery.	Patient-controlled analgesia requirement on the first postop day was reduced by 1/3 compared to the second postop day.
Oral clonidine premedication	Randomized, double-blind prospective study; Level II[201]	30 OSA patients undergoing ENT surgery.	Postoperatively, pain scores and total analgesic consumption were reduced.
Transcranial magnetic stimulation (TMS)	Randomized, controlled study; Level II[211]	20 gastric bypass surgery patients and matched controls.	TMS allowed a 40% reduction in total morphine use.

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

infusion of opioids, advanced age, concomitant administration of sedative or hypnotic medications and a preexisting 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 analgesia[203] 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 negative 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 analgesics[210] 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 dexmedetomidine[45] 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 anesthesia technique, general anesthesia, regional anesthesia or monitored anesthesia care in OSA patients undergoing surgery or studies on different analgesic or adjuvants.

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,[76] 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 corticosteroids[213] 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[184] 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.[214] 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 long-standing 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),[215] and a 0.4% to 1.6% incidence of mortality has been reported.[216,217] Airway-related postoperative complications occur in about 6% of patients, oxygen desaturations in 9% and electrocardiogram changes in 1%.[98] Others have documented that about one-third of the complications involve the airway.[102] Cardiac complications, such as hypertension, have also been commonly reported.[122] 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[3] 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.[3]

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 from OSA.[3] The use of postoperative supplemental oxygen has been suggested[76] 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.[3] 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.[218] 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 postoperative risk in OSA patients.

Other postoperative strategies for reducing postoperative 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.[219] The lateral position improves upper airway stability during sleep which may allow reduction of the therapeutic levels of CPAP.[220] The study by Penzel et al. also supported the idea that lower CPAP pressure was needed during lateral positions versus supine positions.[221] However, the ASA guidelines recommend a semi-upright position for extubation and recovery in OSA patients[3] 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[101,183] 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.[120] 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.[102,122,222] 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.[223,224]

From the consultants in the ASA guidelines,[3] 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

Table 5. Summary of Perioperative Management Suggestions for OSA Patients Undergoing Surgery

Recommendations from ASA guidelines
Extubate only after patient is fully conscious and upper airway obstruction seems unlikely.
Supplemental oxygen use if desaturation occurs, but only for as long as necessary to maintain appropriate arterial oxygen levels.
Continuous monitoring of oxygen saturation is necessary only in ICU or step down unit.
There is no consensus agreement on whether CPAP should be administered if there is evidence of apneas and desaturation or if hypoxia persists with supplemental oxygen. This is especially controversial for patients who were not previously treated with CPAP.
Consider use of nonopioid medications (such as NSAIDS) instead of or in conjunction with opioids to decrease the need for analgesia. Use of regional analgesic techniques rather than systemic opioids can reduce the likelihood of adverse respiratory events.
Avoid supine position for postoperative recovery. Consider placing at-risk patients in a sitting position to reduce OSA episodes and improve oxygen saturation.
OSA patients without significant comorbid factors can be monitored in an ambulatory care postoperative unit with proper nursing support and oxygen desaturation monitoring, but only if surgery is superficial or minor, and involves local or regional anesthesia.

OSA = obstructive sleep apnea; CPAP = constant positive airway pressure; NSAIDS = nonsteroidal antiinflammatory drugs.

types of surgeries,[3] 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 postoperative 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[3] 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[3] 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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STOP Questionnaire

A Tool to Screen Patients for Obstructive Sleep Apnea

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Background: **Obstructive sleep apnea (OSA) is a major risk factor for perioperative adverse events. However, no screening tool for OSA has been validated in surgical patients. This study was conducted to develop and validate a concise and easy-to-use questionnaire for OSA screening in surgical patients.**

Methods: **After hospital ethics approval, preoperative patients aged 18 yr or older and without previously diagnosed OSA were recruited. After a factor analysis, reliability check, and pilot study; four yes/no questions were used to develop this screening tool. The four questions were respectively related to *s*noring, *t*iredness during daytime, *o*bserved apnea, and high blood *p*ressure (STOP). For validation, the score from the STOP questionnaire was evaluated *versus* the apnea–hypopnea index from monitored polysomnography.**

Results: **The STOP questionnaire was given to 2,467 patients, 27.5% classified as being at high risk of OSA. Two hundred eleven patients underwent polysomnography, 34 for the pilot test and 177 for validation. In the validation group, the apnea–hypopnea index was 20 ± 6. The sensitivities of the STOP questionnaire with apnea–hypopnea index greater than 5, greater than 15, and greater than 30 as cutoffs were 65.6, 74.3, and 79.5%, respectively. When incorporating body mass index, age, neck circumference, and gender into the STOP questionnaire, sensitivities were increased to 83.6, 92.9, and 100% with the same apnea–hypopnea index cutoffs.**

Conclusions: **The STOP questionnaire is a concise and easy-to-use screening tool for OSA. It has been developed and validated in surgical patients at preoperative clinics. Combined with body mass index, age, neck size, and gender, it had a high sensitivity, especially for patients with moderate to severe OSA.**

OBSTRUCTIVE sleep apnea (OSA) is the most prevalent breathing disturbance in sleep,[1] affecting 2–26% of the general population depending on sex, age, and the definition of criteria.[2] OSA is associated with significant morbidity, including excessive daytime sleepiness, loud snoring during sleep, refractory hypertension, and impaired quality of life. Studies have also shown that OSA is associated with a high risk for traffic accidents and cardiovascular disease.[3,4]

The prevalence of OSA in the surgical population is higher than in the general population and varies with different surgical populations. In particular, approximately 7 of every 10 patients undergoing bariatric surgery were found to have OSA,[5] presumably because of 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,[5,6] most cases were not diagnosed, and careful screening was not implemented before surgery.[6] One of the barriers to study the prevalence of OSA in surgical patients is the difficulty with recruiting patients to undergo polysomnography before surgery. Fidan *et al.*[7] screened 433 surgical patients; only 18 of 41 invited patients agreed to undergo polysomnographic testing, and 14 patients (3.2% of all screened patients) were diagnosed with OSA. In another study conducted by Chung *et al.*,[8] 24% of 305 surgical patients were classified as being at high risk of having OSA using the Berlin questionnaire, and 13 patients were confirmed as having OSA by polysomnography, 4.2% of the total number of patients screened.

It is estimated that nearly 80% of men and 93% of women with moderate to severe sleep apnea are undiagnosed.[9] Undiagnosed OSA may pose a variety of problems for anesthesiologists. A number of case reports have documented an increase in the incidence of postoperative complications and deaths among patients suspected of having OSA.[10] Untreated OSA patients are known to have a higher incidence of difficult intubation, postoperative complications, increased intensive care unit admissions, and greater duration of hospital stay.[11–13] Identifying patients with OSA is the first step in preventing postoperative complications due to OSA.

In-laboratory polysomnography is the accepted standard for diagnosing OSA.[14] However, polysomnography is a time-consuming and costly procedure. Further, the growing awareness of sleep apnea has exacerbated the long waiting list in many sleep laboratories.[15] To deal with this issue, a number of screening questionnaires and clinical screening models have been developed to help identify patients with OSA.[16–25] However, a significant limitation to the aforementioned studies is that patients were preselected because most studies were conducted in the sleep laboratory setting.[16,18,19,26] Furthermore, clinical models designed for OSA screening usually require the assistance of a computer and may not be suitable for clinical practice. One of the most widely

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used questionnaires, the Berlin questionnaire, has not been validated as a screening instrument in surgical patients. The American Society of Anesthesiologists (ASA) checklist, a screening instrument recommended by the ASA Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea, has not been validated. Besides the fact that no predictive model or questionnaire for identifying OSA has been validated in the surgical patient population, most questionnaires have numerous items with a confusing scoring system. As a result, they are not suitable for a busy clinical setting, such as preoperative clinics.

The purpose of the study was to develop and validate a concise and easy-to-use questionnaire for OSA screening in surgical patients.

Materials and Methods

Patient Population of the Study

The study was conducted in the preoperative clinics of Toronto Western Hospital and Mount Sinai Hospital, Toronto, Ontario, Canada. Ethics approval was obtained from both institutions. Patients aged 18 yr or older who had an ASA physical status of I–IV and were scheduled to undergo elective procedures in general surgery, gynecology, orthopedics, urology, plastic surgery, ophthalmology, or neurosurgery were included in the study. Patients who were unwilling or unable to give informed consent, patients previously diagnosed with OSA or any other sleep breathing disorder, or patients who were expected to have abnormal electroencephalographic findings (*e.g.*, brain tumor, epilepsy surgery, patients with deep brain stimulator) were excluded. All patients who visited the preoperative clinics for their scheduled surgery and met the inclusion criteria were approached by the research staff. After informed consent was obtained, patients were asked to complete a questionnaire and were invited to undergo an overnight polysomnographic study.

Development of the STOP Questionnaire

To keep the questionnaire concise and easy to use, the questions were designed in yes/no format. Based on our previous work with the Berlin questionnaire,[8] consensus from a group of anesthesiologists and sleep specialists, and a literature review, four questions (STOP Q1–4) related to snoring, tiredness during the daytime, stopped breathing during sleep, and hypertension were designed. They were phrased in English at a fifth-grade reading level by using the Flesch-Kincaid reading-level determination method built into Microsoft Word (Microsoft, Redmond, WA).

To examine the association of the questions with the underlying constructs that the questions were designed to reflect, these four yes/no questions were combined with items 1–10 (Berlin Q1–10) from the Berlin questionnaire to make a question list consisting of 14 questions. The question list was administered to 278 patients to answer. Of these patients, 254 answered all of the questions. Factor analysis with the SAS procedure Factor was based on the responses from these 254 patients. After a significant level of association was demonstrated, these four yes/no questions were accepted to form the STOP questionnaire (appendix 1). The four-item STOP questionnaire is a self-report, forced-choice (yes/no), paper-and-pencil scale that takes approximately 1 min to complete. It consists of the following four questions: S—"Do you *s*nore loudly (louder than talking or loud enough to be heard through closed doors)?" T—"Do you often feel *t*ired, fatigued, or sleepy during daytime?" O—"Has anyone *o*bserved you stop breathing during your sleep?" P—"Do you have or are you being treated for high blood *p*ressure?"

The STOP questionnaire was given to 592 preoperative clinic patients as a pilot study. All patients who answered the STOP questionnaire were invited to undergo an overnight, technician-supervised polysomnographic study. According to the interim analysis of the data from pilot study, the cutoff point of the STOP questionnaire had been decided and the sample size had also been adjusted.

To check the reliability of the questionnaire, 55 patients answered the STOP questionnaire twice at different time intervals of 1–27 days (median, 8 days). Because these four questions reflected four different dimensions of OSA morbidity, internal consistency checking was not applicable.

Validation of the STOP Questionnaire

After the pilot study, 1,875 patients were screened and asked to complete the STOP questionnaire. All patients, regardless of their score on the STOP questionnaire, were invited to undergo an overnight polysomnographic study. The data from patients who completed the polysomnographic study was used to validate the STOP questionnaire. The predictive parameters of the STOP questionnaire *versus* the apnea–hypopnea index (AHI) obtained from polysomnography in all patients of the validation group and in subgroups with different clinical characteristics—such as body mass index (BMI), age, neck circumference, and gender—were analyzed. An alternative scoring model incorporating *B*MI, *a*ge, *n*eck circumference, and *g*ender into the STOP questionnaire, termed the STOP-Bang (appendix 2), was also presented.

Sleep Study

A one-night, in-laboratory polysomnographic study was conducted before surgery at Toronto Western Hospital Sleep Laboratory. The result of polysomnography was used to evaluate the validity of the STOP questionnaire. During the overnight polysomnographic study, every patient went to bed at his or her usual bedtime.

Collection of continuous sleep architectural data was accomplished using a standard electroencephalographic montage consisting of an electroencephalogram, electrooculogram, submental electromyogram, and electrocardiogram using surface electrodes. Ancillary channels were used to specifically record respiratory parameters, including respiratory effort by thoracoabdominal excursion, respiratory inductive plethysmography, and oronasal airflow by nasal airflow pressure. Oxygen saturation was measured with a pulse oximeter.

One certified polysomnographic technologist with 10 yr of experience scored all of the polysomnographic recordings. Her scoring was under the supervision of a sleep physician (C.M.S.). The reports had to be assessed and approved by the sleep physician (C.M.S.). The certified technologist was blinded to the results of the STOP questionnaire (*i.e.*, whether patients were at high or low risk of having OSA) and clinical information of the patients. Sleep stages and the AHI were scored according to standard criteria.[27,28] To avoid bias and inaccuracy from polysomnographic scoring, the polysomnographic recording of 10 randomly selected patients was rescored by another experienced certified polysomnographic technologist, who was blinded to the scores of other technologist. The scores from two technologists for the same patient were almost identical ($r = 0.984$, $P < 0.0001$).

The clinical diagnosis of OSA was defined as AHI greater than 5 with fragmented sleep and daytime sleepiness. According to the American Academy of Sleep Medicine practice guideline, the severity of OSA is determined by the AHI: 5–15, mild; greater than 15–30, moderate; greater than 30, severe.[27] After polysomnography, patients were scheduled to meet with a sleep specialist (C.M.S.) for follow-up assessment and clinical management, where necessary.

Data Analysis and Statistics

Sample Size Estimation. The calculation of sample size was performed according to the method reported by Obuchowski.[29] Briefly, the two separate calculations of sample size were performed based on either estimated sensitivity, the precision (potential error) of sensitivity, expected power, a type I error, and estimated prevalence; or specificity, the precision of specificity, expected power, type I error, and prevalence. The bigger number of the two is chosen as the sample size. Based on the literature on the Berlin questionnaire[30–32] and the prevalence of OSA,[33,34] a sensitivity of 0.88, a precision of 0.09, an OSA prevalence rate of 24%, a type I error of 0.05, and a power of 0.8 were used to calculated sample size. The result was 208. The number calculated based on a specificity of 0.80 was much smaller than 208. So 208 was initially chosen as the sample size. From the pilot study data, the sensitivity was 0.72 and the prevalence was 0.7. If the other parameters were kept the same, the sample size would be 137. However, a prevalence of 0.7 is very high. It may be biased because of the small number of patients in the pilot study. If, for safety, 0.55 were taken as the prevalence, the adjusted sample size would be 170.

For factor analysis, the minimum requirement for sample size is the bigger of 100 respondents or 5 times the number of variables. In our study, we had 14 questions (variables), so we needed at least 100 complete respondents. The list of 14 questions was given to 278 patients; 254 patients who answered all of the questions were used for the factor analysis.

Data Analysis. Data were entered into a specifically designed Microsoft Access database and checked for possible errors. SAS 9.1 for Windows (SAS Institute, Cary, NC) was used for data analysis. Categorical data were presented as frequency and percentage with 95% confidence interval (CI). The statistical significance was checked by chi-square test or Fisher exact test. Resampling with bootstrap was used to calculate the CI of the likelihood ratios. A logistic regression procedure was used to calculate the odds ratio and area under the receiver operating characteristic curve. Continuous data were presented as mean ± SD, and the Student *t* test or analysis of variance was used to calculate the *P* value. $P < 0.05$ was defined as significant. The SAS procedure Factor was used for factor analysis. The report from the principal components analysis with varimax rotations was presented. Factors with an eigenvalue greater than average were retained. Questions with factor loading of 0.3 or greater were chosen for interpretation of factors.

Results

Patient Screening

Over a period of 16 months at Toronto Western Hospital and Mount Sinai Hospital preoperative clinics, a total of 2,974 patients were willing to complete the questionnaire. Of these, 2,721 patients (91.5%) answered all of the items on the questionnaire completely and had complete documentation of gender, age, and BMI. Only these patients were included in the analysis.

Factor analysis was based on the response of 254 patients who answered all 14 questions from the STOP and Berlin questionnaires. After the STOP questionnaire was developed, it was administered to 2,467 patients. The STOP questionnaire classified 27.5% of patients (679 of 2,467) as being at high risk of having OSA. Of all patients who were invited to undergo the overnight monitored polysomnographic testing, 416 of 2,467 patients (17%) gave consent to participate. In total, 211 patients underwent polysomnography, whereas 205 did not show up at the laboratory (fig. 1). Of 211 patients who underwent polysomnography, the first 34 patients were included in a pilot study and the

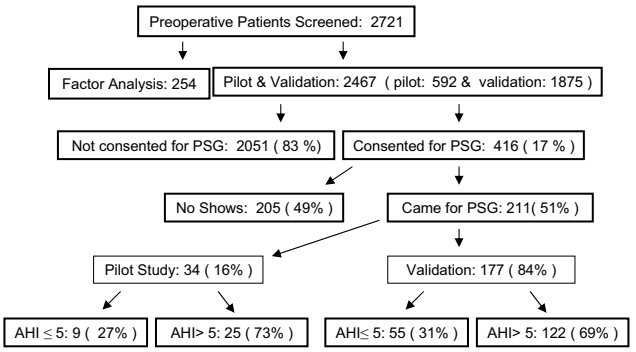

Fig. 1. Screening flow chart of surgical patients in preoperative clinic. The number in the figure shows the number and percentage of patients in the different groups. AHI = apnea–hypopnea index; PSG = polysomnography.

following 177 patients were for the validation of the STOP questionnaire.

Age, gender, and BMI of the different patient groups are shown in table 1. The patients who gave consent but did not actually undergo polysomnographic testing were younger than the group of patients who underwent the polysomnographic study. The BMI of patients who gave consent for polysomnography was significantly greater than that of the patients who did not give consent for polysomnography, regardless of whether the patient underwent polysomnographic testing. Compared with the patients who underwent polysomnographic testing, there was a higher rate of smoking in patients who gave consent but did not show up for the polysomnographic testing (26.8% *vs.* 14.7%; $P = 0.002$).

Development of the STOP Questionnaire

Four yes/no questions related to snoring, tiredness during the daytime, observed apnea during sleep, and hypertension were combined with 10 questions from the Berlin questionnaire and administered to 278 patients; 254 patients answered all of the questions. Demographic data are shown in table 1. Factor analysis demonstrated that four underlying factors were reflected by the 14 questions. These factors accounted for more than 95% of the total eigenvalue. Based on the category of questions with a loading factor greater than 0.3, four factors were identified: snoring, tiredness during daytime, cessation of breathing during sleep, and high blood pressure. The factor loading value for each question in the corresponding category is shown in table 2. The factor loading value of two questions related to falling asleep while driving (Berlin Q8 and Q9) is very low for all four factors.

Among the five questions related to snoring, although question 1 (STOP Q1) did not have the highest factor loading value, it still demonstrated a significant association with snoring. Because we wanted to develop a simple and easy-to-use questionnaire with questions in yes/no format, we chose question 1 to reflect snoring in our questionnaire. Using a similar rationale, question 6 was incorporated to reflect daytime tiredness. Regarding the cessation of breathing during sleep and high blood pressure, two questions in each category had similar factor loading values, so questions 12 and 14 were acceptable choices to reflect breathing cessation during sleep and high blood pressure in the STOP questionnaire. The final STOP questionnaire consisted of four yes/no questions: 1, 6, 12, and 14 (appendix 1).

Pilot Study

As a pilot study, the STOP questionnaire was administered to 592 preoperative clinic patients, and all patients were invited to undergo polysomnography. Thirty-four of these patients underwent the polysomnography study. The other patients either declined to give consent or gave consent but did not show up. Of 34 patients, 24 (70.5%) had an AHI greater than 5. According to the analysis of data from these 34 patients, using answering yes to two or more questions as the cutoff for the STOP questionnaire to classify the patients as high or low risk of having OSA demonstrated the best combination of sensitivity and specificity. The sensitivity of the STOP questionnaire was 72% (CI, 54.4–89.6), the specificity was 33.3% (CI, 2.5–64.1), the positive predictive value (PPV) was 75.0% (CI, 57.7–92.3), and the negative predictive value (NPV) was 30% (CI, 6.7–65.3).

To check the test–retest agreement, 55 patients answered the STOP questionnaire twice at a time interval of 1–27 days (median: 8 days); 53 (96.4%) patients were found to have the same score upon retesting with a κ coefficient of 0.923 (CI, 0.82–1.00).

Table 1. Characteristics of Screened Patients

	Total (n = 2,721)	Factor Analysis (n = 254)	No Consent (n = 2,051)	Consented, No Polysomnography (n = 205)	Polysomnography Done (n = 211)
Gender, M/F	1,305/1,416	126/128	967/1,084	106/99	106/105
Age, yr	57 ± 16	56 ± 17	57 ± 16	54 ± 13*	56 ± 13
BMI, kg/m^2	28 ± 6	28 ± 6	28 ± 6	30 ± 8*	30 ± 7*

Continuous data are presented as mean ± SD.

* $P < 0.05$ compared with Factor Analysis and No Consent groups.

BMI = body mass index.

Table 2. Summary of the Principal Components Analysis, Varimax Rotation

	Factor Loadings*
Snoring	
1. (STOP Q1). Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?	0.596
a. Yes	
b. No	
2. (Berlin Q1). Do you snore?	0.747
a. Yes	
b. No	
c. Don't know	
3. (Berlin Q2). Your snoring is:	0.825
a. Slightly louder than breathing	
b. As loud as talking	
c. Louder than talking	
d. Very loud—can be heard in adjacent rooms	
4. (Berlin Q3). How often do you snore?	0.795
a. Nearly every day	
b. 3–4 times a week	
c. 1–2 times a week	
d. 1–2 times a month	
e. Never or nearly never	
5. (Berlin Q4). Has your snoring ever bothered other people?	0.404
a. Yes	
b. No	
c. Don't know	
Tiredness during daytime	
6. (STOP Q2). Do you often feel tired, fatigued, or sleepy during daytime?	0.674
a. Yes	
b. No	
7. (Berlin Q6). How often do you feel tired or fatigued after your sleep?	0.805
a. Nearly every day	
b. 3–4 times a week	
c. 1–2 times a week	
d. 1–2 times a month	
e. Never or nearly never	
8. (Berlin Q7). During your waking time, do you feel tired, fatigued, or not up to par?	0.743
a. Nearly every day	
b. 3–4 times a week	
c. 1–2 times a week	
d. 1–2 times a month	
e. Never or nearly never	
Stop breathing during sleep	
11. (Berlin Q5). Has anyone noticed that you quit breathing during your sleep?	0.644
a. Nearly every day	
b. 3–4 times a week	
c. 1–2 times a week	
d. 1–2 times a month	
e. Never or nearly never	
12. (STOP Q4). Has anyone observed you stop breathing during your sleep?	0.606
a. Yes	
b. No	
High blood pressure	
13. (Berlin Q10). Do you have high blood pressure?	0.947
a. Yes	
b. No	
c. Don't know	
14. (STOP Q3). Do you have or are you being treated for high blood pressure?	0.945
a. Yes	
b. No	
Questions with low factor loading for all four factors	
9. (Berlin Q8). Have you ever nodded off or fallen asleep while driving a vehicle?	
a. Yes	
b. No	
10. (Berlin Q9). How often does nodding off or falling asleep while driving a vehicle occurs?	
a. Nearly every day	
b. 3–4 times a week	
c. 1–2 times a week	
d. 1–2 times a month	
e. Never or nearly never	

* Factor loadings are correlations between the original questions and their factors. Factor loadings greater than 0.30 in absolute value are considered to be significant.

Table 3. Demographic Data of Patients for Validation of STOP Questionnaire

		STOP	
	Total (n = 177)	Low Risk (n = 75)	High Risk (n = 102)
Gender (M/F)	88/89	38/37	50/52
Age, yr	55 ± 13	54 ± 15	56 ± 12
BMI, kg/m^2	30 ± 6	28 ± 6	31 ± 6*
BMI >35 kg/m^2, n	34	10	24
Neck circumference, cm	39 ± 6	38 ± 5	40 ± 7*
ASA physical status, n (%)			
I	11 (6)	8 (11)	3 (3)
II	101 (57)	47 (63)	54 (53)
III	63 (36)	18 (24)	45 (44)
IV	2 (1)	2 (3)	0
Average score	2.3 ± 0.6	2.2 ± 0.7	2.4 ± 0.6*
AHI	20 ± 6	12 ± 14	25 ± 27*
Minimum Sao_2	82 ± 11	84 ± 9	80 ± 10*
Existing conditions, n (%)			
Hypertension	72 (41)	22 (29)	50 (49)*
GERD	56 (32)	13 (17)	43 (42)*
Diabetes	32 (18)	9 (12)	23 (23)
Asthma	24 (14)	9 (12)	15 (15)
Depression	11 (6)	5 (7)	6 (6)

Categorical data are presented as frequency (percentage), and continuous data are presented as mean ± SD.

* $P < 0.05$, high risk *vs.* low risk.

AHI = apnea–hypopnea index; ASA = American Society of Anesthesiologists; BMI = body mass index; GERD = gastroesophageal reflux disease; Sao_2 = arterial oxygen saturation.

Validation of the STOP Questionnaire

Demographic Data and Sleep Study. Table 3 shows the demographic data of the patients who participated in the validation study, *i.e.*, they completed the questionnaires and underwent polysomnography. The patients classified by the STOP questionnaire as being at high risk of having OSA had a significantly higher frequency of hypertension and gastroesophageal reflux disease. They also had significantly higher average ASA physical status, larger BMI, larger neck circumference, and higher AHI.

Table 4. Characteristics of Patients Grouped by AHI >5 Cutoff

	AHI ≤5 (n = 55)	AHI >5 (n = 122)
Gender, M/F	18/37	70/52*
Age, yr	49 ± 14	58 ± 12*
BMI, kg/m^2	27 ± 6	31 ± 6*
Blood pressure		
Systolic	129 ± 21	142 ± 18*
Diastolic	78 ± 12	83 ± 14*
ASA physical status, n (%)		
I	7 (13)	4 (3)
II	39 (71)	62 (51)
III	9 (16)	54 (44)
IV	0	2 (2)
Average score	2.0 ± 0.5	2.4 ± 0.6*
Neck circumference	36 ± 4	40 ± 6*
AHI	3 ± 2	27 ± 24*

Categorical data are presented as frequency (percentage), and continuous data are presented as mean ± SD.

* $P < 0.01$, apnea hypopnea index (AHI) >5 *vs.* AHI ≤5.

ASA = American Society of Anesthesiologists; BMI = body mass index.

Table 5. Sleep Parameters of Patients for Validation

	Total (n = 177)	AHI ≤5 (n = 55)	AHI >5 (n = 122)
Total sleep time, min	351 ± 73	356 ± 76	348 ± 71
Sleep efficiency, %	78 ± 14	80 ± 12	77 ± 15
Wake percent, %	18 ± 13	16 ± 12	19 ± 13†
REM latency, min	124 ± 78	111 ± 67	131 ± 82
REM percent, %	14 ± 8	15 ± 6	13 ± 8†
Sleep stage 1, %	9 ± 9	8 ± 8	10 ± 9
Sleep stage 2, %	49 ± 13	47 ± 13	49 ± 13
Slow wave sleep, %	10 ± 7	13 ± 8	9 ± 7*
AHI	19.5 ± 22.9	2.5 ± 1.5	27.2 ± 23.8*
REM AHI	27.6 ± 23.1	8.6 ± 8.5	35.9 ± 22.6*
Arousal index	29.4 ± 18.3	23.2 ± 16.7	32.1 ± 18.4*
Minimum Sao_2	82 ± 11	87 ± 7	80 ± 11*

* $P < 0.05$, apnea–hypopnea index (AHI) >5 *vs.* AHI ≤5. † $P < 0.1$ *vs.* AHI ≤5.

REM = rapid eye movement; Sao_2 = arterial oxygen saturation.

Using an AHI greater than 5 as the cutoff for diagnosis of OSA, 122 patients (68.9%) were found to have OSA, 52 (29.4%) mild, 31 (17.5%) moderate, and 39 (22.0%) severe. As shown in table 4, there were clear differences between patients with an AHI of 5 or less and patients with an AHI greater than 5. There was a higher percentage of male patients with an AHI greater than 5 (57% male *vs.* 43% female; $P < 0.01$). The patients with an AHI greater than 5 were almost more than 10 yr older than patients with an AHI of 5 or less. They also had significantly higher average ASA physical status and blood pressure, greater BMI, and larger neck size.

Table 5 summarizes the sleep parameters in validation patients. Compared with the patients with an AHI of 5 or less, the patients with an AHI greater than 5 demonstrated a significantly increased arousal index, significantly lower minimum arterial oxygen saturation, and significantly decreased slow wave sleep, which is consistent with the sleep features of the patients with OSA.

STOP Questionnaire Effectively Identified the Patients with OSA. Predictive parameters for the STOP questionnaire at AHI greater than 5, greater than 15, and greater than 30 cutoff values are presented in table 6. Using AHI greater than 5 as a cutoff value to evaluate the STOP questionnaire, the sensitivity was 65.6%, the specificity was 60.0%, the PPV was 78.4%, and the NPV was 44.0%. The sensitivity and NPV were 74.3% and 76.0% at AHI greater than 15. They were 79.5% and 89.3% with AHI greater than 30 as the cutoff. This indicates that the STOP questionnaire was more sensitive in detecting the patients with moderate to severe OSA.

Further examination of the predictive parameters of the STOP questionnaire in the different patient groups demonstrates that the PPV with AHI greater than 5 as the cutoff was greatly increased in patients with a certain demographics: BMI greater than 35 kg/m^2, age older

Table 6. Predictive Parameters for STOP Questionnaire (n = 177)

AHI >5	
Sensitivity, %	65.6 (56.4–73.9)
Specificity, %	60.0 (45.9–73.0)
PPV, %	78.4 (69.2–86.0)
NPV, %	44.0 (32.6–56.0)
Likelihood ratio	1.639 (1.172–2.385)
Odds ratio	2.857 (1.482–5.507)
Area under ROC curve	0.703
AHI >15	
Sensitivity, %	74.3 (62.4–84.0)
Specificity, %	53.3 (43.4–63.0)
PPV, %	51.0 (41.3–60.7)
NPV, %	76.0 (64.8–85.1)
Likelihood ratio	1.590 (1.280–2.057)
Odds ratio	3.293 (1.707–6.352)
Area under ROC curve	0.722
AHI >30	
Sensitivity, %	79.5 (63.5–90.7)
Specificity, %	48.6 (40.0–63.0)
PPV, %	30.4 (21.7–40.3)
NPV, %	89.3 (80.1–95.3)
Likelihood ratio	1.545 (1.261–2.010)
Odds ratio	3.656 (1.636–9.054)
Area under ROC curve	0.769

Data are presented as average (95% confidence interval).

AHI = apnea–hypopnea index; NPV = negative predictive value; PPV = positive predictive value; ROC = receiver operating characteristic.

Table 7. Predictive Parameters for STOP-Bang (n = 177)

AHI >5	
Sensitivity, %	83.6 (75.8–89.7)
Specificity, %	56.4 (42.3–69.7)
PPV, %	81.0 (73.0–87.4)
NPV, %	60.8 (46.1–74.2)
Likelihood ratio	1.9160 (1.416–2.666)
Odds ratio	6.587 (3.217–13.489)
Area under ROC curve	0.806
AHI >15	
Sensitivity, %	92.9 (84.1–97.6)
Specificity, %	43.0 (33.5–52.9)
PPV, %	51.6 (42.5–60.6)
NPV, %	90.2 (78.6–96.7)
Likelihood ratio	1.629 (1.401–1.966)
Odds ratio	9.803 (3.654–26.300)
Area under ROC curve	0.782
AHI >30	
Sensitivity, %	100 (91.0–100.0)
Specificity, %	37.0 (28.9–45.6)
PPV, %	31.0 (23.0–39.8)
NPV, %	100 (93.0–100.0)
Likelihood ratio	1.586 (1.426–1.838)
Odds ratio	>999.999
Area under ROC curve	0.822

Data are presented as average (95% confidence interval).

AHI = apnea–hypopnea index; NPV = negative predictive value; PPV = positive predictive value; ROC = receiver operating characteristic.

than 50 yr, male gender, and neck circumference greater than 40 cm (fig. 2). The PPV of those ranked by the STOP questionnaire as being at high risk of having OSA was 84% in the patients with a BMI greater than 35 kg/m^2, 86.9% in patients older than 50 yr, 87.5% in male patients, 89.7% in male patients older than 50 yr, 94.3% in patients with neck circumference greater than 40 cm, and 100% in male patients older than 50 yr and with a BMI greater than 35 kg/m^2.

STOP-Bang, an Alternative Scoring Model Combining BMI, Age, Neck Circumference, and Gender with the STOP Questionnaire. To further improve the sensitivity of the STOP questionnaire to detect most patients with OSA, especially moderate and severe OSA, we developed an alternative scoring model, the STOP-Bang (appendix 2), which incorporated BMI, age, neck circumference, and gender into the scoring model of the STOP questionnaire. As shown in table 7, sensitivity and NPV are significantly increased by using the STOP-Bang. The sensitivities at AHI cutoffs of greater than 5, greater than 15, and greater than 30 were 83.6, 92.9, and 100%, respectively; the corresponding NPVs were 60.8, 90.2, and 100%.

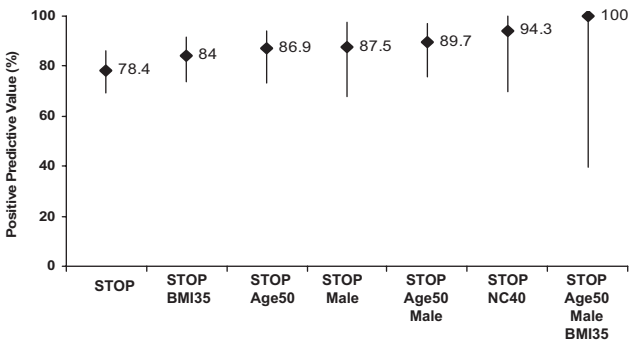

Fig. 2. Positive predictive value for STOP questionnaire in patients with the different clinical characteristics. The *y-axis* represents positive predictive value with 95% confidence interval, and the *x-axis* shows high risk of obstructive sleep apnea ranked by STOP questionnaire in patients with different clinical characteristics. BMI = body mass index; NC = neck circumference.

Discussion

In this study, the STOP questionnaire was developed and validated as an OSA screening tool for surgical patients. The STOP questionnaire is a self-administered screening tool that includes four yes/no questions (appendix 1). The STOP questionnaire was found to have a moderately high sensitivity and PPV at AHI greater than 5, greater than 15, and greater than 30 as cutoffs. In patients with certain clinical characteristics, such as male gender, age older than 50 yr, BMI greater than 35 kg/m^2, and neck circumference greater than 40 cm, the PPV was greatly increased. When incorporating BMI, age, neck circumference, and gender into the STOP scoring (STOP-Bang), the sensitivity and NPV significantly increased. They were both more than 90% for the patients with moderate and severe OSA.

Obstructive sleep apnea is known to diminish quality of life[35] and is associated with many common comorbid

conditions. Studies have documented an increased incidence of coronary artery diseases, hypertension, cerebrovascular accidents, gastroesophageal reflux disease, congestive heart failure, and myocardial infarction in OSA patients.[36,37] It is estimated that the average life span of an untreated OSA patient is 58 yr, which is 20 yr shorter than the average life span of the general population (men, 79 yr; women, 83 yr).[38] OSA is also associated with an increased incidence of postoperative adverse events.[11–13] Undiagnosed OSA in surgical patients have a serious impact on the postoperative outcome. Identifying patients with a high risk of OSA is the first step for the prevention of adverse health events, adverse perioperative outcomes, and its treatment. Screening tools work as a filter to separate the patients with a high risk of OSA from the patients with a low risk of OSA. A good screening tool should be validated in the target population against an accepted standard. It should be easy to use and have a high sensitivity and acceptable specificity.

Most screening tools for OSA so far have been validated in patients referred to sleep clinics or sleep laboratories. Seven predictive models, based on the different combinations of witnessed apneas, snoring, gasping, BMI, age, gender, and hypertension were developed and validated in the patients from sleep centers.[16,18,19,21,23,24,39,40] The Sleep Disorders Questionnaire,[41] Apnea Score,[25] and Global Sleep Assessment Questionnaire were all tested in patients mainly from sleep centers.[42] Patients referred to sleep centers are suspected of having sleep-related disorders, especially OSA. They are preselected patients. Screening tools for OSA developed and validated in the sleep center patient population cannot be applied to other patient populations without validation in the target patient population.

The Berlin questionnaire is one of the few questionnaires that have been validated in primary care patients.[30] However, instead of monitored polysomnography in a sleep laboratory, home portable sleep monitoring was used for the validation of the Berlin questionnaire. Home portable sleep monitoring has not been accepted as the standard for the diagnosis of OSA. The STOP questionnaire is currently the only questionnaire developed and validated in surgical patients. Although there was some self-selection from the patients' perspective, our study was designed to include all surgical patients in our preoperative clinics regardless of their score of the STOP questionnaire to avoid selection biases.

In most previous studies, reports from monitored polysomnography were used to validate models or questionnaires. However, the staff performing the polysomnography and scoring the polysomnography were usually not blinded to the score on the questionnaire.[18,19,23–25,39,40,42] This may have introduced bias into the scoring of polysomnography. In our study, in-laboratory polysomnography was used to evaluate the accuracy of the STOP questionnaire. The staff performing and scoring the polysomnography was blinded to the score on the STOP questionnaire. This practice avoided bias during polysomnographic scoring.

Ease of use is also very important for a screening tool in busy clinical settings. Prediction models need calculation and computer assistance. Most widely used questionnaires have a long question list with a complicated scoring system. Although the questions are similar, the number of questions among the different OSA screening tools varies. For example, there are 11 multiple-choice questions organized into three categories on the Berlin questionnaire,[30] and 14 items under three categories on the OSA checklist, which is recommended by the ASA.[43] Study has shown that the response rate among patients decreases with increasing length of the questionnaire.[44] Four questions on the STOP questionnaire were designed in yes/no format, and it takes less than 1 min to finish. As a result, it had a high completion rate (91.5%) and test–retest agreement (96.4%). The STOP questionnaire is based on questions referring to *s*noring, *t*iredness/sleepiness, *o*bserved stop of breathing during sleep, and blood *p*ressure. The alternative scoring model, the STOP-Bang, is based on eight items including four questions in STOP questionnaire, *B*MI, *a*ge, *n*eck circumference, and *g*ender. This creates the easy mnemonics STOP and STOP-Bang, which may serve as useful reminders for clinicians to use these instruments during the preoperative screening process.

To screen patients for a disease with an important health impact, a high sensitivity with an acceptable specificity is a basic requirement for a screening tool. The sensitivity and specificity of OSA screening tools have demonstrated considerable variability depending on the screening tool, the patient population, and the definition of OSA. For the prediction models tested in sleep center patients, the sensitivity varied from 76% to 96%, and the specificity ranged from 13% to 54%.[18,19,40] For the questionnaire tested in sleep center patients, the sensitivity varied from 70% to 93%.[25,41,42] The Berlin questionnaire is the most widely tested screening tool for OSA. The predictive parameters of the Berlin questionnaire largely varied in different patient populations. The sensitivity was 86% in primary care patients,[30] 62.5% in patients undergoing pulmonary rehabilitation, and 57–68% in sleep laboratory patients.[45] The wide variation in the sensitivity of the Berlin questionnaire also indicates the risk of transferring a screening tool between different patient populations without validation in the target patient population.

In terms of the predictive parameters, the STOP questionnaire itself demonstrated a moderately high level of sensitivity and specificity in surgical patients, and it was more sensitive to detect the patients with moderate to severe OSA. In the patients with certain clinical characteristics, such as male gender, age older than 50 yr, BMI greater than 35 kg/m^2, and neck circumference greater

than 40 cm, the high risk of OSA ranked by the STOP questionnaire could have a very high PPV for OSA (fig. 2). On the other hand, when incorporating BMI, age, neck circumference, and gender (Bang) into the STOP model (STOP-Bang); we could reach a very high level of sensitivity and NPV, especially for the moderate and severe OSA patients (table 6). Therefore, if a patient is ranked as low risk of OSA by the STOP-Bang scoring model, we would have a high confidence to exclude the possibility that the patient would have moderate to severe OSA.

This study has several limitations. In our study, the refusal rate for polysomnography was high. Self-selection from patients may exist because patients who had sleep symptoms might have selectively consented to the overnight polysomnography. The high refusal rate and dropout rate (49% of patients did not show up for their scheduled polysomnographic testing) also indicate the difficulty that the study faced. This may be due to the anxiety about surgery and the need to stay one night in the sleep laboratory. Other factors also played a role in patient refusal and dropout, *e.g.*, smokers and younger patients tended not to show up for their scheduled overnight polysomnography. The high prevalence of OSA in the group of patients who underwent polysomnography may reflect this self-selection. Currently, this tool has only been tested in surgical (noncancer) patients. It needs to be validated in the other settings.

In conclusion, the STOP questionnaire is a concise and easy-to-use screening tool to identify patients with a high risk of OSA. It has been validated in surgical patients at preoperative clinics as a screening tool. The STOP-Bang scoring model, which incorporates BMI, age, neck size, and gender with the STOP questionnaire, has demonstrated a higher sensitivity and NPV, especially for patients with moderate to severe OSA.

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Appendix 1: STOP Questionnaire

Height _____ inches/cm Weight _____ lb/kg
Age _____ Male/Female BMI _____
Collar size of shirt: S, M, L, XL, or _____ inches/cm
Neck circumference* _____ cm

1. *S*noring
   Do you *s*nore loudly (louder than talking or loud enough to be heard through closed doors)?
   Yes No
2. *T*ired
   Do you often feel *t*ired, fatigued, or sleepy during daytime?
   Yes No
3. *O*bserved
   Has anyone *o*bserved you stop breathing during your sleep?
   Yes No
4. Blood *p*ressure
   Do you have or are you being treated for high blood *p*ressure?
   Yes No

* Neck circumference is measured by staff.

High risk of OSA: answering yes to two or more questions
Low risk of OSA: answering yes to less than two questions

Appendix 2: STOP-Bang Scoring Model

1. *S*noring
   Do you *s*nore loudly (louder than talking or loud enough to be heard through closed doors)?
   Yes No
2. *T*ired
   Do you often feel *t*ired, fatigued, or sleepy during daytime?
   Yes No
3. *O*bserved
   Has anyone *o*bserved you stop breathing during your sleep?
   Yes No
4. Blood *p*ressure
   Do you have or are you being treated for high blood *p*ressure?
   Yes No
5. *B*MI
   *B*MI more than 35 kg/m^2?
   Yes No
6. *A*ge
   *A*ge over 50 yr old?
   Yes No
7. *N*eck circumference
   *N*eck circumference greater than 40 cm?
   Yes No
8. *G*ender
   *G*ender male?
   Yes No

High risk of OSA: answering yes to three or more items
Low risk of OSA: answering yes to less than three items