Society of Anesthesia & Sleep Medicine

SASM newsletter

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SASM

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Message from the President

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Dear SASM members,

Another exciting year full of successes for SASM has passed and I would like to express my gratitude to all of you, the SASM leadership as well as our administrative staff for the support you have given me and the society. I am truly honored to have had the opportunity to serve as President of our society and did so as best I could. The year has been marked by continued advances, but also challenges and changes, all which have helped our young society mature.

It is without a doubt that you, the members of SASM, have pushed the field of perioperative sleep medicine forward through the publications of research, presentation of lectures and dissemination of educational material. Wherever I visit our colleagues, I see the fruits of our hard work transforming healthcare systems. Only a few years ago, for example, just one in four health care institutions in North America had protocols to care for patients with sleep apnea. Although our work is far from done and adoption incomplete, encountering a department that is not routinely screening patients for sleep disordered breathing and has some plan in place to care for the needs of this patient population has become much less common. Supported by our activities and our published guidelines clear indications are available on how SASM is affecting positive change in our healthcare system.

Our society continues to thrive, attracting new members and pursuing new endeavors. SASM continues to be true to its multidisciplinary mission by seeking to harness the expertise of various subspecialties to advance the common goal of improving patient care. This year we have continued and expanded our work with experts in perioperative ultrasound who are offering courses at our annual meeting and designing studies to elucidate the utility to perform diagnostic airway and cardiovascular exams aiding in the treatment of patients with sleep apnea. Other collaborations are ongoing, such as with regional anesthesiologists. Leaders of the American Society of Regional Anesthesia and Pain Medicine will discuss the issues associated with perioperative pain management and the benefits of regional anesthesia, one of the few interventions shown to improve outcomes in patients with sleep apnea. My hope is that the synergy between perioperative sleep physicians, nurses, surgeons and anesthesiologists and other clinicians will provide the nidus for the development of the third and final SASM guidelines on postoperative care and monitoring of patients with sleep apnea.

Finally, as a dynamic society SASM does not only embrace and invite change in order to keep our activities at the front lines of innovation, we also welcome changes the representation of SASM and leadership in general. To that extent, I would like to welcome Dr. Toby Weingarten as the new section editor for sleep medicine in our official journal Anesthesia and Analgesia. Toby has served SASM for many years and is a well-known and accomplished academician. He is replacing Dr. David Hillman, a true giant in the field of perioperative sleep medicine who has served in this capacity for many years. SASM owes him a greatly for this and his other major contributions. As a founding member and past President he has helped shape SASM and guide it with passion. He will remain a great resource to us and support SASM for hopefully many years to come.

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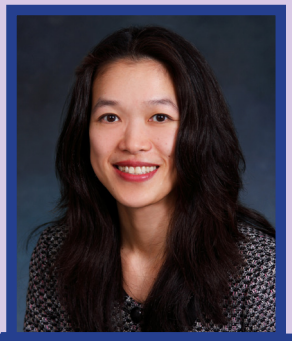

Welcome to the October edition of the SASM Newsletter. The SASM Annual Meeting in Orlando, Florida is quickly approaching. This issue of the newsletter features up-to-date and important topics we hope SASM members caring for patients with sleep disordered breathing during the perioperative period will find relevant to their practice. We would like to thank all of the contributors to this issue of the newsletter. These articles highlight areas for further research to improve perioperative management of patients with sleep disordered breathing.

Patients with OSA are at increased risk of postoperative adverse events. Previous investigators have explored several important indices and whether they can predict which OSA patients are at increased risk of the postoperative complications. Some of the indices found in the literature are AHI, ODI, CT90, minimum and maximum SpO2. Of these, AHI appears to have significant association with postoperative adverse events. These parameters may add value for risk stratification and minimization. In this issue, Colin Suen, MD, PhD provides a comprehensive summary of his recent article on "Sleep Study and Oximetry Parameters for Predicting Postoperative Complications in Patients with Obstructive Sleep Apnea" that was published in the Chest journal earlier this year.

The prevalence of obesity, which is a predisposing factor for OSA is increasing steadily among women. Obese women undergoing hysterectomy, may have an increased risk of OSA related postoperative complications. Jashvant Poeran, MD, PhD conducted a population-based analysis and found that OSA is associated with increased risk of postoperative complications, increased cost of hospitalization and length of hospital stay. Dr. Poeran provides a summary of this article that was published in Sleep Medicine.

SASM guidelines on intraoperative management of OSA patients (Anesth Analg 2018: 127:967-87) recommend regional anesthesia for OSA patients based on evidence of better postoperative outcomes. However, Lukas Pichler, MD critically analysed the postoperative outcomes associated with total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures in a high-volume orthopedic specialty practice with a strong focus on regional anesthesia. A summary of this article that was published in the journal Regional Anesthesia and Pain Medicine is featured in this issue of the newsletter.

The opioid epidemic has prompted many clinicians to use regional and multi-modal non-opioid analgesics to try to reduce the risk for opioid-induced respiratory depression (OIRD). In this issue, Kapil Gupta, MD outlines the prevalence, timing and various risk factors for opioid induced respiratory depression from his article that was recently published in the BMJ Open. OSA was found be an important risk factor for opioid induced respiratory depression. These risk factors will help develop a strategy for enhanced monitoring of high-risk surgical patients requiring opioid analgesia to prevent OIRD.

As ambulatory surgical procedures in hospitals continue to increase, it becomes imperative that patients take greater responsibility for their rehabilitation in the recovery process in the home. However, OSA patients can be challenging for anesthesiologists to manage during ambulatory surgery. Mahesh Nagappa, MD provides a comprehensive review of best practice for OSA patients during ambulatory surgical care. This was recently published in the journal, Current Opinions in Anesthesiology.

We look forward to seeing many of you at the upcoming SASM 9th Annual Meeting in Orlando, Florida on October 17-18, 2019. This year's SASM meeting offers the workshop on "Point of Care Ultrasound for OSA patients" by Stephen Haskins and "airway ultrasound and positive airway pressure" by Dennis Auckley and Mandeep Singh.

If you are interested in contributing an article or joining the Newsletter Subcommittee, please contact us as we welcome contributions from all SASM members.

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Finally, as my term as President comes to a close, I would like to welcome the new leadership of SASM who will without a doubt serve the society with dedication and great care. Dr. Dennis Auckley will assume the presidency this fall assisted by Dr. Krish Ramachandran in the role of president-elect. Both Krish and Dennis have been synonymous with our societies work and have dedicated many years to its success. I have no doubt that they will continue our mission and lead us into the next chapter of success.

In conclusion, I want to thank all of you and all my colleagues at SASM for the opportunity to serve you. With a committed membership and strong leadership in place, SASM has a bright future ahead as we confront our challenges and continue to pursue our mission.

With deep gratitude,
Stavros G. Memtsoudis

Sleep Study and Oximetry Parameters for Predicting Postoperative Complications in Patients with Obstructive Sleep Apnea

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Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder characterized by recurring episodes of complete or partial upper airway obstruction during sleep. In the surgical setting, the administration of opioids, sedatives and intravenous fluids may augment patient predisposition to sleep apnea by exacerbating upper airway collapse, depressing the arousal response and intensifying rostral fluid shifts leading to upper airway edema and reduced patency. These nocturnal respiratory events and episodic hypoxemia have been found to be associated with significant postoperative sequelae including cardiac ischemia and arrhythmias.[1,2] The severity and duration of hypoxemia is also important, as they have been correlated with the likelihood of myocardial ischemia.[2] In the postoperative period, eighty percent of death or near-death events in patients with OSA are observed within the first 24h after surgery with the majority of these events occurring on the hospital ward, a vulnerable period when patients are not meticulously monitored.[3] In addition to polysomnography (PSG), high-resolution nocturnal oximetry has been suggested as a low-cost preoperative screening tool for OSA.[4] For risk stratification in patients with OSA, it is unclear what, if any, specific parameters derived from the PSG or overnight oximetry are associated with postoperative complications. We performed a narrative review to determine the association between parameters extracted from portable, in-laboratory PSG, or overnight oximetry and postoperative adverse events.

We conducted a systematic literature search to obtain pertinent articles to include studies with adult surgical patients diagnosed for OSA with portable, in-laboratory PSG, or overnight oximetry that reported on specific sleep parameters and at least one adverse outcome. The search yielded 1,810 papers, of which 21 were included in the review. Preoperative apnea hypopnea index (AHI) and measurements of nocturnal hypoxemia such as oxygen desaturation index (ODI), cumulative sleep time percentage with SpO_2 < 90% (CT90), minimum SpO_2, mean SpO_2, and longest apnea duration were associated with postoperative complications.

This review highlighted several parameters that may be of importance to forewarn postoperative complications. AHI was the primary parameter derived from PSG used to determine the presence or absence of OSA and the severity.[5] In the current review, a diagnosis of AHI (AHI ≥ 5/h) alone was a predictor of postoperative complications[6] (Figure 1), although, data from multivariate logistic regression analysis[7] and direct comparisons between AHI categories (mild, moderate and severe)[8,9] did not support a linear relationship between increasing AHI and the incidence of postoperative complications. However, an association has been shown between a higher AHI and increased postoperative events. Among patients with diagnosed OSA, the mean AHI in the postoperative complication groups ranged from 37 to 68 events/hr. The majority of this evidence was based on patients undergoing upper airway corrective surgery for OSA, a population at greater risk of postoperative upper airway edema and obstruction following surgery.[10] Other respiratory, cardiac and cerebrovascular complications were rare. Postoperative atrial fibrillation was more prevalent in those patients undergoing cardiac surgery with an increasing AHI.[11]

Measurements of hypoxemia including CT90, mean and minimum SpO_2 levels were also reported. A number of studies in OSA populations suggest that the severity of nocturnal oxygen desaturation may be of similar or greater utility than the AHI for determination of cardiac dysfunction,[12] endothelial impairment[13], hypertension,[14] new onset and incident atrial fibrillation,[15,16] and poor prognosis following myocardial infarction.[17] In a large study by Chung et al (n = 543) that included oximetry data, the thresholds for predicting postoperative complications were an ODI >29/h, CT90 >7% and mean SpO_2 <93% (Figure 1).[4] Hwang et al. found that patients with ODI ≥ 5 and CT90 >21% experienced more postoperative complications. The rate of complications increased with the severity of OSA as determined by ODI. In patients for OSA surgery, several studies demonstrated that the lowest SpO_2 was associated with postoperative adverse events.[7,18]

In summary, AHI and measurements of nocturnal hypoxemia (ODI, CT90, minimum and mean SpO_2) are indices of OSA, which provide an imperfect assessment of the risk of postoperative complications. A significant association between the AHI and postoperative adverse events exists. Complications may be more likely to occur in the category of moderate-to-severe OSA (AHI ≥ 15). Other parameters from PSG or overnight oximetry such as ODI, CT90, mean and minimum SpO_2, and longest apnea duration have been shown to be associated with postoperative complications and may provide additional value in risk stratification and minimization. These parameters can be incorporated into clinical decision tools for risk minimization.

Full article can be accessed from: Suen, C., Ryan, C., Mubashir, T., Ayas, N., Abrahamyan, L., Wong, J., Mohklesi, B., Chung, F. Sleep Study and Oximetry Parameters for Predicting Postoperative Complications in Patients with Obstructive Sleep Apnea. (2019) Chest 155(4):855-867. https://doi.org/10.1016/j.chest.2018.09.030

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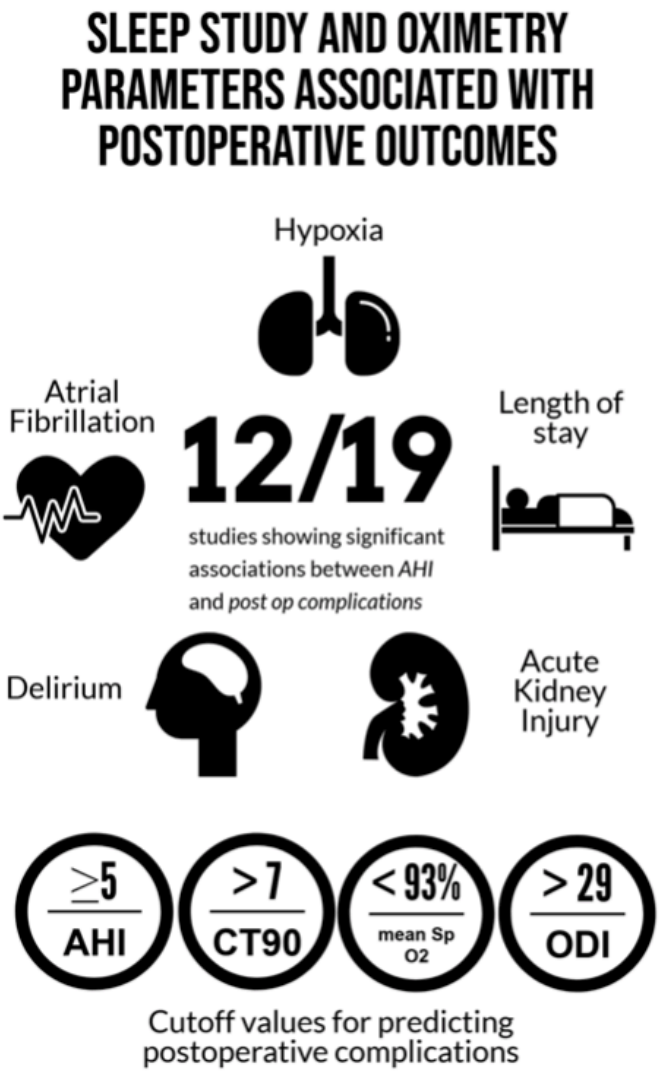

Figure 1. Summary of sleep study and oximetry parameters associated with postoperative outcomes

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Impact of Obstructive Sleep Apnea on Perioperative Complications Among Patients Undergoing Hysterectomy: A Population-Based Analysis

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Introduction: Although obstructive sleep apnea (OSA) has been established as a risk factor for perioperative complications in various patient cohorts, there is a lack of data on the prevalence of OSA and its association with outcomes in hysterectomies. With one out of nine women undergoing hysterectomy in her lifetime, this procedure is one of the most frequent surgeries among women.[1] Given that the prevalence of obesity - one of the major predisposing factors for OSA[2] - has steadily increased among women in the last decades, patients undergoing hysterectomy may represent a large patient cohort at risk for OSA-related complications.[3] We therefore analyzed the impact of OSA on perioperative outcomes among patients undergoing hysterectomy using a large national cohort. Analogous to other surgeries, we hypothesized that OSA would be associated with an increased risk of perioperative complications, increased cost of hospitalization and length of hospital stay.

Materials and methods: We extracted data on patients who underwent a hysterectomy between 2006 and 2014 from a large nationwide administrative database covering over 600 national hospitals (Premier Healthcare Database, Premier Inc., Charlotte, NC). [8]. OSA patients (identified by ICD-9 CM codes) were compared to non-OSA patients regarding perioperative outcomes including, cardiac, central-nervous, gastrointestinal, genitourinary, renal, respiratory, and thromboembolic complications; as well as opioid prescription, need for blood transfusion, cost of hospitalization, length of stay and ICU admission. Patient-related variables included age, race, obesity, and Deyo-Charlson Comorbidity Index (DCCI) to quantify overall comorbidity burden. In addition to the overall comorbidity burden separate variables were created for history of substance use/abuse, chronic pain conditions and psychiatric comorbidities as these are known to affect opioid prescription [13]. Healthcare related variables included insurance type, hospital location, hospital size, teaching status and mean annual number of hysterectomies per hospital. Procedure related variables included procedure year and procedure type. Anesthesia/analgesia variables included the type of anesthesia, use of patient-controlled analgesia (PCA) and the use of non-opioid analgesics (intravenous acetaminophen, NSAID, COX-2 inhibitor, ketamine, pregabalin/ gabapentin). Odds ratios (OR) and 95% confidence intervals (CI) were reported.

First, in univariable analyses we compared OSA patients to non- OSA patients regarding all study variables and outcomes using Chi-square and t-tests (or non-parametric tests where appropriate) for categorical and continuous variables, respectively. Subsequently, multilevel multivariable modeling was performed including variables that were found significant at the $P < 0.15$ level in the univariable analysis, and variables that were deemed to be clinically relevant.

Results: Of 459,508 patients undergoing a hysterectomy, 11,936 (2.67%) had a diagnosis code for OSA. Notably, the proportion of patients with a diagnosis of OSA undergoing a hysterectomy gradually increased from 2006 to 2014.

When adjusting for all relevant variables, OSA was associated with significantly higher odds for ICU admission (OR 2.28; 95% CI 1.77-2.94, $P < 0.05$) and renal (OR 1.98; 95% CI 1.70-2.32, $P < 0.05$) or respiratory complications (OR 3.25; 95% CI 2.97-3.56, $P < 0.05$) in particular. Additionally, OSA status was associated with modest but significant increases in cost of hospitalization (+6.2%; $P < 0.0001$), length of stay (+2.6%; $P < 0.0001$), and opioid prescription (+1.2%; $P = 0.04$), compared to patients without OSA. However, the odds for OSA patients to receive a blood transfusion was significantly reduced (OR 0.88; 95% CI 0.82-0.94, $P < 0.05$).

Conclusions: In patients undergoing hysterectomies, OSA was associated with substantially increased risk of complications and modestly increased resource utilization. While routine perioperative screening for OSA seems recommendable in patients undergoing hysterectomies, further research is needed to assess currently used perioperative care strategies in this patient population to improve perioperative outcomes.

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Table 1. Study variables by OSA status

	Diagnosis of Sleep Apnea				
	Yes (n=11,936)		No (n=447,572)		
	n	%	n	%	P value**
PATIENT RELATED					
Mean Age *	52.3	11.4	48.4	12.1	<0.0001
Race:					
White	7855	65.8	278992	62.3	<0.0001
Black	1941	16.3	68520	15.3	
Hispanic	263	2.2	17103	3.8	
Other	1877	15.7	82957	18.5	
Mean Deyo-Charlson Comorbidity Index*	1.13	1.8	0.55	1.5	<0.0001
History of Substance	1585	13.3	54395	12.2	0.00021
Use/Abuse					
Pain Conditions	4420	37.0	89322	20.0	<0.0001
Psychiatric Comorbidities	3436	28.8	55841	12.5	<0.0001
Obesity	6489	54.2	55650	12.4	<0.0001
HEALTHCARE RELATED					
Insurance Type					
Commercial	7338	61.5	310835	69.4	<0.0001
Medicaid	1123	9.4	43245	9.7	
Medicare	2850	23.9	62834	14.0	
Uninsured	252	2.1	15265	3.4	
Unknown	373	3.1	15393	3.4	
Hospital Location					
Rural	849	7.1	46501	10.4	<0.0001
Urban	11087	92.9	401071	89.6	
Hospital Size					
<300 beds	3174	26.6	145675	32.5	<0.0001
300-499 beds	4605	38.6	165753	37.0	
≥500 beds	4157	34.8	136144	30.4	
Hospital Teaching Status					
Non-Teaching	5852	49.0	266041	59.4	<0.0001
Teaching	6084	51.0	181531	40.6	
Mean number of hysterectomies/year per hospital*	263.3	159.7	310.6	213.3	<0.0001

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Table 1 ***continued.*** Study variables by OSA status

	Diagnosis of Sleep Apnea				
	Yes (n=11,936)		No (n=447,572)		
	n	%	n	%	P value**
PROCEDURE RELATED					
Year of Procedure					
2006	521	4,4	38381	8,6	<0.0001
2007	1111	9,3	63667	14,2	
2008	1205	10,1	57177	12,8	
2009	1388	11,6	58486	13,1	
2010	1537	12,9	55764	12,5	
2011	1668	14,0	54092	12,1	
2012	1768	14,8	48051	10,7	
2013	1523	12,8	40085	9,0	
2014	1215	10,2	31869	7,1	
Procedure Type					
Abdominal	6245	52.3	226833	50.7	<0.0001
Laparoscopic to Open	1152	9.7	22794	5.1	
Laparoscopic	3229	27.1	119999	26.8	
Vaginal	1310	11.0	77946	17.4	
Diagnosis of Malignancy	1801	15.1	24480	5.5	<0.0001
Robotic Assisted	1770	14.8	38674	8.6	<0.0001
Use of Morcellator	267	2.2	11704	2.6	0.01049
ANESTHESIA/ANALGESIA					
Anesthesia Type					
General	9733	81.5	370289	82.7	<0.0001
General + Neuraxial	1944	16.3	62678	14.0	
Unknown/Missing	259	2.2	14605	3.3	
Analgesia					
Intravenous Acetaminophen	1187	9.9	30495	6.8	<0.0001
PCA	3612	30.3	150301	33.6	<0.0001
NSAIDs	8234	68.8	335919	75.1	<0.0001
COX-2 Inhibitors	305	2.5	9746	2.2	0.00623
Ketamine	312	2.6	7710	1.7	<0.0001
Pregabalin/Gabapentin	835	7.0	11162	2.5	<0.0001

**Continuous variable mean and standard deviation reported, instead of N and %, respectively*
***Chi-square test for categorical variables, t-test for continuous variables*

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Table 2. Outcomes by OSA status

	Diagnosis of Sleep Apnea				
	Yes (n=11,936)		No (n=447,572)		
	n	%	n	%	P value**
Cardiac Complications	97	0.8	1811	0.4	<0.0001
Central Nervous System Complications	45	0.4	652	0.1	<0.0001
Gastrointestinal Complications	647	5.4	16714	3.7	<0.0001
Genitourinary Complications	181	1.5	6221	1.4	0.2446
Intensive Care Unit Utilization	1241	10.4	23537	5.3	<0.0001
Renal Complications	263	2.2	1885	0.4	<0.0001
Respiratory Complications	789	6.6	5254	1.2	<0.0001
Thromboembolic Complications	36	0.3	643	0.1	<0.0001
Blood Transfusion	1272	10.7	38159	8.5	<0.0001
Oral Morphine Equivalents (mg)*	334	162-454	311	155-415	<0.0001
Length of Hospital Stay (days)*	3	2-3	2	1-3	<0.0001
Cost of Hospitalization (USD)*	$10,464	$6,387-$12,236	$7,984	$5,077-$9,312	<0.0001

**Continuous variable median and interquartile range reported, instead of N and %, respectively*
***Chi-square test for categorical variables, Kruskal-Wallis test for continuous variables*

Table 3. Results from multivariable modeling; odds ratios (or % change) demonstrating the association between OSA and outcomes (reference is non-OSA patients). Odds ratios for binary outcomes and % change for continuous outcomes.

OUTCOME VARIABLE	DIAGNOSIS OF SLEEP APNEA
Cardiac Complications	1.18 (0.95; 1.48)
Central Nervous System Complications	1.37 (0.98; 1.90)
Gastrointestinal Complications	0.97 (0.89; 1.07)
Genitourinary Complications	0.97 (0.83; 1.13)
Intensive Care Unit Utilization	2.28 (1.77; 2.94)*
Renal Complications	1.98 (1.70; 2.32)*
Respiratory Complications	3.25 (2.97; 3.56)*
Thromboembolic Complications	1.16 (0.81; 1.67)
Blood Transfusion	0.88 (0.82; 0.94)*
Oral Morphine Equivalents	1.2% (0.1; 2.4%)*
Length of Hospital Stay	2.6% (2.1; 3.1%)*
Cost of Hospitalization	6.2% (4.9; 7.6%)*

Models adjusted for age, race, Deyo-Charlson comorbidity Index, history of substance use/abuse, chronic pain conditions, psychiatric comorbidities, and obesity, insurance type, hospital location, size, teaching status and hysterectomy volume, year of procedure, type of procedure, robotic use, morcellator use, anesthesia type, use of intravenous acetaminophen, PCA, NSAIDs, COX-2 inhibitors, ketamine, and pregabalin/gabapentin. ***P-value <0.05***

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Perioperative Impact of Sleep Apnea in a High-Volume Specialty Practice with a Strong Focus on Regional Anesthesia: A Database Analysis

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Background

Obstructive sleep apnea (OSA) is characterized by repetitive episodes of upper airway obstruction accompanied by cessation in airflow and intermittent hypoxemia. Particularly troublesome is the association between OSA and increased risk of adverse postoperative outcomes.[1-3] These include pulmonary complications, postoperative cardiac events, and transfer to an intensive care unit as well as prolonged length of stay (LOS). Guidelines issued by perioperative professional societies recommend the use of regional anesthesia to reduce postoperative complications in patients with OSA,[4-6] based on evidence suggesting improved postoperative outcomes.[7-9] Although lower joint arthroplasties are uniquely amenable to the use of neuraxial anesthesia, the majority of patients with OSA on a national level undergo this procedure under general anesthesia.[7]

We therefore studied outcomes associated with total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures in a high-volume orthopedic specialty practice with a strong focus on regional anesthesia. We hypothesized that under these circumstances, OSA may still be associated with an increased risk of adverse postoperative outcomes, but to a limited extent.

Methods

After Institutional Review Board approval, 41 766 cases of primary total hip and knee arthroplasties (THAs/TKAs) from 2005 to 2014 were extracted from institutional data of the Hospital for Special Surgery (approximately 5000 THAs and 5000 TKAs annually, of which around 90% under neuraxial anesthesia). The main effect was OSA (identified by the International Classification of Diseases, ninth revision codes); outcomes of interest were cardiac, pulmonary, gastrointestinal, renal/genitourinary, thromboembolic complications, delirium, and prolonged length of stay (LOS). Multivariable logistic regression models provided ORs, corresponding 95% CIs, and p values.

Results

Of the 41 766 unique patients (21, 022 THA and 20, 744 TKA) included in this study, 7.7% (3,228) had a diagnosis of OSA. OSA was more prevalent in patients with TKA than THA (9.1% and 6.3%, respectively; p≤0.001). The vast majority of surgeries (97.8%; n=40 852) were performed under neuraxial anesthesia. We observed that patients with OSA had general anesthesia more often than patients without OSA (3.1% and 2.1% general anesthesia, respectively; p≤0.001). Patients with OSA were younger, more likely to be men, classified with a higher ASA status, and had obesity more often than patients with no OSA. Univariable results also showed that patients with OSA had a higher incidence of pulmonary, gastrointestinal, and renal/genitourinary complications and prolonged LOS, but not delirium, cardiac, or thromboembolic complications. Cardiac, or thromboembolic complications. After correcting for relevant covariates, OSA was significantly associated with an increased risk of pulmonary complications (OR 1.87, 95% CI 1.51 to 2.30; $p \leq 0.007$), gastrointestinal complications (OR 1.52, 95% CI 1.13 to 2.04; $p = 0.042$), and prolonged LOS (OR 1.44, 95% CI 1.31 to 1.57; p≤0.007). No significant associations were observed for the other outcomes. The use of neuraxial anesthesia was associated with decreased odds for pulmonary complications (OR 0.50, 95%

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CI 0.36 to 0.69; p≤0.007), renal/genitourinary complications (OR 0.50, 95% CI 0.36 to 0.68; p≤0.007), delirium (OR 0.45, 95% CI 0.32 to 0.62; p≤0.007), and prolonged LOS (OR 0.51, 95% CI 0.44 to 0.59; p≤0.007), but not for cardiac, gastrointestinal, and thromboembolic complications.

Conclusion

We showed that in a regional anesthesia setting, OSA was associated with an increased risk of prolonged LOS, and pulmonary and gastrointestinal complications, but not for delirium, thromboembolism, cardiac, and renal/genitourinary complications. This underlines that, while regional anesthesia may improve postoperative outcomes in patients with OSA, some complications cannot be eliminated. Future studies should try and investigate if among neuraxial techniques one has a better potential to reduce the risk of complications in patients with OSA than other neuraxial techniques. Furthermore, as we know that patients with OSA undergoing lower joint arthroplasty are at risk even in a regional anesthesia setting, other interventions that could potentially lead to a better outcome in this patient group should be investigated.

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Table 1. Summary of baseline characteristics stratified by OSA status.

	No OSA (n = 38538)	OSA (n = 3228)	p-value
Obesity	7972 (20.7)	1501 (46.5)	<0.001
ASA PS			
I-II	35827 (93.0)	2427 (75.2)	<0.001
III-IV	2706 (7.0)	801 (24.8)	
Missing	5 (0.0)	0 (0.0)	
Type of anesthesia			
General	814 (2.1)	100 (3.1)	<0.001
Neuraxial	37724 (97.9)	3128 (96.9)	
Time period			
2005-2006	2762 (7.2)	143 (4.4)	<0.001
2007-2008	7010 (18.2)	491 (15.2)	
2009-2010	8388 (21.8)	704 (21.8)	
2011-2012	9796 (25.4)	830 (25.7)	
2013-2014	10582 (27.5)	1060 (32.8)	
Age	66.00 [58.00, 74.00]	64.00 [57.00, 71.00]	
Gender			
Female	23427 (60.8)	1182 (36.6)	<0.001
Male	15111 (39.2)	2046 (63.4)	
Type of surgery			
Total hip replacement	19690 (51.1)	1332 (41.3)	<0.001
Total knee replacement	18848 (48.9)	1896 (58.7)	
Baseline lab values			
Hemoglobin	13.30 [12.40, 14.30]	13.70 [12.70, 14.60]	<0.001
Missing	5526 (14.3)	464 (14.4)	
Creatinine	0.90 [0.70, 1.00]	0.90 [0.80, 1.10]	<0.001
Missing	5613 (14.6)	470 (14.6)	
INR	0.99 [0.97, 1.03]	1.00 [0.97, 1.03]	<0.001
Missing	5646 (14.7)	474 (14.7)	
Platelets	251.00 [212.00, 297.00]	241.00 [201.00, 284.00]	<0.001
Missing	5537 (14.4)	465 (14.4)	

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Table 1 ***continued***. Summary of baseline characteristics stratified by OSA status.

	No OSA (n = 38538)	OSA (n = 3228)	p-value
Perioperative benzodiazepines			
No	2038 (5.3)	152 (4.7)	<0.001
Yes	31170 (80.9)	2705 (83.8)	
Missing	5330 (13.8)	371 (11.5)	
Perioperative ketamine			
No	25361 (65.8)	2139 (66.3)	<0.001
Yes	3634 (9.4)	476 (14.7)	
Missing	9543 (24.8)	613 (19.0)	
Postoperative outcomes			
Cardiac	855 (2.2)	76 (2.4)	0.660
Pulmonary	839 (2.2)	113 (3.5)	<0.001
Gastrointestinal	419 (1.1)	55 (1.7)	0.002
Renal/genitourinary	869 (2.3)	94 (2.9)	0.020
Thromboembolic	327 (0.8)	30 (0.9)	0.704
Delirium	851 (2.2)	71 (2.2)	1.000
Prolonged LOS (> 4 days)	7344 (19.1)	782 (24.2)	<0.001

Categorical variables are summarized as frequency (%) and are analyzed using a chi-square test. Continuous variables are summarized as median (interquartile range) and are analyzed using a t-test. Missing data are summarized as frequency (%)

Table 2: Logistic regression models of postoperative outcomes by OSA status in the imputed dataset.

	OSA status	
	YES (reference=NO) OR [95% CI]	P-value
Cardiac complications	1.119 [0.876, 1.430]	0.367
Pulmonary complications	1.867 [1.514, 2.303]	<0.001*
Gastrointestinal complications	1.515 [1.128, 2.035]	0.006*
Renal/genitourinary	1.187 [0.949, 1.484]	0.133
Thromboembolic complications	1.165 [0.788, 1.721]	0.444
Delirium	1.334 [1.032, 1.724]	0.028
Prolonged LOS	1.438 [1.313, 1.574]	<0.001*

Risk Factors for Opioid Induced Respiratory Depression in Surgical Patients: A Systematic Review and Meta-Analyses

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Opioids are the cornerstone therapy for the management of moderate to severe postoperative pain, but they have numerous adverse effects, the most serious being opioid-induced respiratory depression (OIRD).[1] The major cause of opioid-related death is OIRD, which leads to hypoxia and hypercapnia, further accentuating the vicious cycle, finally causing cardio-respiratory arrest.

The definitions of OIRD vary resulting in a widely varied reported incidence ranging from 0.04-0.5% when naloxone utilization is used as a surrogate to 23-41% when OIRD is assessed by hypoxemia or bradypnea.[2,3,12,13,4–11]

The primary objective of this systematic review and meta-analysis (SRMA) was to evaluate the published literature to identify the potential associations between patient and procedural characteristics and post-operative OIRD in order to enable the health care providers to take appropriate precautions, titrate the dose of opioids and use enhanced monitoring in high-risk patients.

Methods

This systematic review included observational studies that reported both OIRD events and risk factors that predicted or were associated with OIRD, along with a control group. OIRD was defined by including the definitions of OIRD from all the included studies.[2,3,12,13,4–11] i.e. naloxone administration for reversal of respiratory depression (respiratory rate < 8/min and/or oxygen saturation < 90% and/or apnea ≥ 10 sec), excessive sedation or upper airway obstruction.

For the purpose of meta-analysis, data collection to evaluate the risk factors for OIRD were divided into the following categories: 1) demographic risk factors 2) medical comorbidities 3) type of surgery 4) opioid-related risk factors: types, doses (morphine equivalent daily dose [MEDD]), routes of delivery [patient-controlled (PCA), epidural, intravenous, oral, nurse-administered analgesia] and concomitant administration of sedatives 5) types of anesthesia and 6) LOS. Meta-analyses were performed to identify the potential risk factors for developing OIRD across demographics, medical comorbidities, types of surgery and anesthesia and opioid-related characteristics.

Results

Out of 8,690 citations, 6,984 records were screened by titles and abstracts, and 125 articles were extracted for full-text reviews. Twelve observational studies met the inclusion criteria for the systematic review.[2,3,12,13,4–11] These studies were comprised of 841,424 surgical patients, out of which 4,194 patients (0.5%) developed post-operative OIRD, with an incidence of 5.0 cases per 1,000 anesthetics delivered (95%CI: 4.83–5.14). Among post-operative OIRD events, 80% (3,333/4,194) occurred within first 12 hours (h) and 85% (3,567/4,194) within first 24h (Table 1).

Five studies provided data on OIRD and control groups for inclusion in the meta-analysis. There was no significant difference between OIRD vs control group in terms of age, gender, BMI and ASA physical status (Figure 2). In 3,706 patients with post-operative OIRD, the prevalence of cardiac disease was 45%,[5,8,12] respiratory disease 17%,[5,8,11,12] and OSA 18%OSA was 18%,[3–5,8–13] OSA was found to be significantly associated with OIRD (OR: 1.4; 95%CI: 1.2–1.7; I2: 31%; p=0.0003) (Figure 2). The MEDD of post-operative opioids was higher in OIRD than control (OIRD vs. control: 24.7±14 mg and 18.9±13.0 mg; MD: 2.8; 95%CI: 0.4–5.3; I2: 98%; p=0.02). Nearly 40% of OIRD patients had background continuous infusion of intravenous opioids in addition to PCA.[7,9,12,13] Approximately 56% of patients with OIRD received concomitant sedation in addition to opioids [3,5,7,11,13.]

No significant difference in the incidence of OIRD existed between general anesthesia and general anesthesia supplemented by neuraxial analgesia.

Discussion

To date, this is the first SRMA which evaluated the risk factors associated with OIRD in surgical patients. The incidence of post-operative OIRD in our study population was 5.0 cases per 1,000 anesthetics delivered, where 85% of cases occurred within the first 24hr. Three patient risk factors were identified: coexisting cardiac disease (1.79-fold), pulmonary disease (2.27-fold), and OSA (1.49-fold) that were associated with an increased risk for post-operative OIRD. Patients with OIRD received 23% higher MEDD than controls.

Our SRMA indicated that OSA was associated with 1.4-fold higher odds of OIRD compared to control group. Up to 50% of surgical patients who died within first 24h due to critical respiratory events had OSA diagnosis.[8] In a closed claims analysis, OSA or suspected OSA was present in 24% of patients with post-operative OIRD.[7]

In patients with OSA, opioids attenuate the arousal response to hypoxia and prolongs airway obstruction.[14,15] The physiologic phenotype of OSA with a high arousal threshold may be more sensitive to the sedative effects of opioids and anesthetic drugs with a higher risk of developing OIRD.[14] The Society of Anesthesia and Sleep Medicine Guidelines recommend

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that an institutional protocol for patients with known or suspected OSA should be developed, including type of anesthesia, choice of medications, postoperative analgesic regimens and monitoring.

Weingarten et al. highlighted that the administration of higher doses of intra-operative opioids [MEDD 40 mg (29-50mg), P<0.001] was significantly associated with a higher incidence of OIRD, with a 22% higher risk of OIRD with every 10mg IV MEDD.[3]

Chung et al. reported that 72h total opioid dose is a predictive factor for post-operative sleep disordered breathing.[16] A significant increase in central sleep apnea occurred in patients on high doses of opioids(MEDD >200mg/day) for chronic pain.[15] With higher doses of opioids, the increase in sleep-disordered breathing can be an important contributor to OIRD.

This meta-analysis showed that the majority of OIRD is reported within the first 12h and 24h accounting for 80% and 85% OIRD respectively. Similar to these results, 88% of insurance claims were related to post-operative OIRD within 24h.7 The highest risk period for OIRD is the first 6h post-surgical period[3–5] with 34% of the critical respiratory events.8 This is probably due to a combination of the residual effects of anesthetic medications Enhanced monitoring during this period in the vulnerable patients will mitigate OIRD.[16–18]

To prevent OIRD, the use of sedatives like benzodiazepines and gabapentin together with opioids should be minimized. Continuous background infusion of opioids should be avoided while using PCA. Multi-modal analgesia and an opioid sparing strategy with use of non-opioid analgesics will decrease risk of OIRD.[19]

In the post-operative period, enhanced monitoring of levels of sedation and ventilation (respiratory rate, pulse oximetry and capnography) especially in patients with high-risk of OIRD such as cardio-pulmonary diseases and OSA will enable us to detect OIRD and intervene earlier.[19,20]

This meta-analysis has the limitations inherent to observational studies. As naloxone administration was used to measure OIRD in 75% of studies,[3,5–8,10–13] mild cases of OIRD may not be reported.

In conclusion, the incidence of post-operative OIRD was 0.5% and 85% which occurred within the first 24h. Increased risk for OIRD was associated with pre-existing cardiac disease, pulmonary disease, and obstructive sleep apnea. The administration of higher doses of opioids is associated with an elevated risk of OIRD. These findings should be used to develop strategies for enhanced monitoring of high-risk surgical patients requiring opioid analgesia to prevent OIRD.

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Table 1. Demographic data of opioid induced respiratory depression

Study ID et al. [Year] [country]	Total patients (n)	Total OIRD n (%)	OIRD within 12 hr- n (%)	OIRD within 24 hr- n (%)	OIRD group		
					Age (year)	Females (n)	BMI (kg/m2)
[6]Etches et al.[1994] [Canada]	1,600	11 (0.69%)	6 (55%)	9 (82%)	55 ± 16	3	NA
[14]Gordon et al.[2005] [USA]	10,511	44 (0.53%)	NA	25 (57%)	60 ±16	36	NA
[13]Shapiro et al.[2005] [Israel]	1,524	18 (1.18%)	NA	NA	51 ± 24	14	25.4 ± 6.5
[5]Taylor et al.[2005] [USA]	-	62	35 (56%)	48 (77%)	68 ± 16	38	NA
[12]Overdyk et al.[2007] [USA]	178	73 (41%)	NA	NA	NA	NA	NA
[11]Ramachandran et al.[2011] [USA]	85,650	32 (0.04%)	NA	27 (84%)	52 ± 17	18	32.5 ± 9.2
[9]Khelemsky et al.[2015] [USA]	442,699	433 (0.10%)	NA	NA	60 ± 16	260	27 ± 7
[10]Lee et al.[2015] [USA]	9,799 claims	92 claims	NA	81 (88%)	50 ± 18	52	NA
[8]Weingarten et al.[2015] [USA]	84,533	134 (0.16%)	78 (58%)	110 (82%)	65 ± 15	78	28.9 ± 6.8
[7]Weingarten et al.[2015] [USA]	11,970	2836 (23.70%)	2836 (100%)	2836 (100%)	65 ± 12	1434	31 ± 6
[3]Rosenfeld et al.[2016] [USA]	28,151	108 (0.38%)	NA	66 (61%)	64± 16	56	NA
[4]Weingarten et al.[2016] [USA]	164,809	413 (0.25%)	413 (100%)	413 (100%)	61 ± 16	221	28 ± 7
Total n (%)	841,424	4,194 (0.5%)	3,333 (0.4%)	3,567 (0.42%)	58 ± 6	2,210	28.8 ± 3

OIRD- opioid induced respiratory depression, BMI- body mass index, n-number

Gupta K, Nagappa M, Prasad A, Abrahamyan L, Wong J, Weingarten TN, Chung F. Risk factors for opioid-induced respiratory depression in surgical patients: a systematic review and meta-analyses. BMJ Open, 2018 Dec 14; 8 (12): e024086. DOI: 10.1136/bmjopen-2018-024086.

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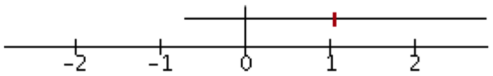
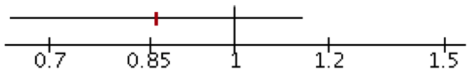
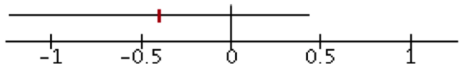
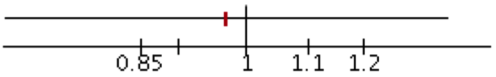
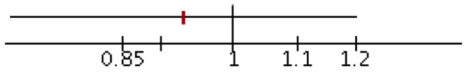
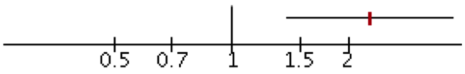
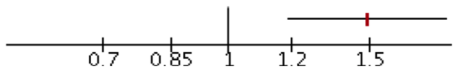
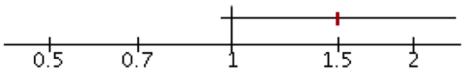
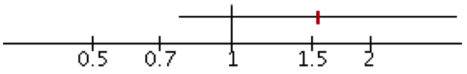
Figure 2: Meta-analysis evaluating the risk factors for respiratory events between OIRD and control groups in patients undergoing surgery. The pooled OR for each risk factor is plotted along with the 95% CI summarises the effect size using the inverse variance random effects model. Age and BMI represented as mean±SD. ASA, American Society of Anesthesiologists; BMI, body mass index; I^2, heterogeneity; OIRD, opioid-induced respiratory depression; OSA, obstructive sleep apnoea.

[Trials]Risk factor[I2 (%)]	OIRD Group	Control Group	Pooled estimate OR(95% CI)	
Demographic risk factor				
[5]Age[84]	64±1/3501	61±2 /10346	1.06 (-0.71, 2.83)	
[5]Female[86]	1775/3501	5849/10346	0.86 (0.65, 1.15)	
[3]BMI[87]	29±1/3383	22±12/10228	-0.40 (-1.23, 0.43)	
[2]ASA I & II[91]	2245/3249	7197/9960	0.97 (0.69, 1.36)	
[2]ASA > III[84]	2245/3249	7197/9960	0.93 (0.72, 1.19)	
Medical Comorbidities				
[2]Cardiac Disease[0]	84/196	98/330	1.79 (1.23, 2.60)	
[3]Pulmonary Disease[0]	45/252	40/386	2.27 (1.39, 3.70)	
[5]OSA[31]	511/2735	942/5779	1.49 (1.19, 1.87)	
[2]Diabetes Mellitus[0]	46/190	57/324	1.50 (0.96, 2.34)	
[2]Renal Disease[0]	23/118	16/118	1.54 (0.77, 3.10)	

Best Perioperative Practice in Management of Ambulatory Patients with Obstructive Sleep Apnea

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Introduction

Obstructive sleep apnea (OSA) is characterized by cyclical upper airway obstruction resulting in a low hemoglobin oxygen concentration and is of considerable concern to anesthesiologists, as it is associated with a range of clinical conditions, such as myocardial ischemia, congestive cardiac failure, hypertension, arrhythmias, chronic obstructive pulmonary disease, diabetes mellitus, stroke, gastroesophageal reflux and obesity.[1*] As perioperative physicians, anesthesiologists play an important role in selecting patients for ambulatory surgical procedures. Currently, in the United States, approximately 60-65% of all surgical procedures are being performed on an outpatient basis.[2]age and sex of the patients, and geographic regions. Major categories of procedures and diagnoses are shown by age and sex. Selected estimates are compared between 1996 and 2006. METHODS The estimates are based on data collected through the 2006 National Survey of Ambulatory Surgery by the Centers for Disease Control and Prevention's National Center for Health Statistics (NCHS As ambulatory surgeries continue to increase, there is a need to address the needs of OSA patients undergoing ambulatory surgery to ensure perioperative safety.

The type of anesthetic technique, airway management practice and anesthetic agents used, can potentially impact the perioperative outcome in this subset of ambulatory patients. We have reviewed the best perioperative practices in the management of OSA patients undergoing ambulatory surgical procedures.

A systematic review of 61 studies conducted by the Society of Anesthesia and Sleep Medicine (SASM) Task Force reported higher adverse outcomes among patients with OSA compared to the control group.[3**] The scientific literature regarding the safety of ambulatory surgery in OSA patients is sparse and of limited quality

Failure to recognize (or diagnose) OSA preoperatively may be one of the major causes of perioperative complications.[4] Both ASA and SASM strongly recommend preoperative screening of OSA patients.[5,6]V2, P14\nBiddle C, 1994, CRNA, V5, P97\nBIRO P, 1995, J CLIN ANESTH, V7, P417, DOI 10.1016/0952-8180(95 The Society of Anesthesia and Sleep Medicine has recently released its guideline on the intraoperative management of adult patients with OSA, presenting recommendations based on current scientific evidence.[7**]

The following are the considerations for OSA patients undergoing ambulatory surgery Preoperative considerations:
Diagnosis of OSA:
Polysomnography is considered to be the gold standard for the diagnosis of OSA. The severity of OSA is graded according to the recorded abnormal breathing events per hour of sleep and classified as mild (AHI ≥5 to <15), moderate (AHI ≥15 to <30) or severe (AHI ≥30).[8]as defined in the International Classification of Sleep Disorders, Third Edition, requires an increased frequency of obstructive respiratory events demonstrated by in-laboratory, attended polysomnography (PSG As PSG is expensive and time consuming, preoperative screening of OSA plays an important role in identifying high risk OSA surgical patients.

Preoperative screening of OSA patients
Routine preoperative screening for OSA in patients presenting for surgery may identify the majority of OSA patients and may provide opportunities for potential risk reduction by implementing appropriate preoperative, intraoperative and postoperative interventions. Screening tools such as STOP-Bang[9–11]*, the perioperative sleep apnea prediction (P-SAP) score[12], the Berlin questionnaire[13]a practical screening tool for surgical patients is required. This study was conducted to validate the Berlin questionnaire and the American Society of Anesthesiologists (ASA and the ASA Checklist[13]a practical screening tool for surgical patients is required. This study was conducted to validate the Berlin questionnaire and the American Society of Anesthesiologists (ASA can be used as preoperative screening tools to identify patients with suspected OSA.[6]

The STOP-Bang screening tool is validated across multiple populations and has been shown to have high sensitivity and **low to moderate specificity.**[9,10,14*] Patients at high-risk for OSA (STOP-Bang ≥3), identified using the STOP-Bang questionnaire, were found to have a higher rate of perioperative complications vs. patients with low-risk OSA (STOP-Bang 0-2).[1*] A recent meta-analysis evaluating the association of STOP-Bang with postoperative complications, favoured STOP-Bang as a perioperative risk stratification tool.[1*]

Intraoperative considerations:
Difficult airway in OSA patients:
The difficult airway in OSA patients is considered to be a main contributing factor to the higher rate of adverse respiratory events.[15] Many of the anatomical features like oropharyngeal crowding; narrowing of the upper airway, macroglossia, thick neck and mandibular anatomy are the common risk factors for both OSA and difficult airway. In the recent SASM intraoperative guidelines, known or suspected OSA was considered to be an independent risk factor for either difficult intubation or difficult mask ventilation, or both.[7**]

It is imperative to take specific precautions

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during airway management in patients with OSA. Head-elevated laryngoscopy position, adequate preoxygenation (end-tidal oxygen, ETO2 >90%), application of CPAP during bag and mask ventilation, transnasal humidified rapid-insufflation ventilatory exchange (THRIVE), apneic oxygenation and use of video laryngoscopy are helpful in avoiding rapid desaturation during a difficult direct laryngoscopy in this subset of patients.

Residual neuromuscular blockade in OSA patients

Residual neuromuscular blockade can can impair upper airway dilator muscle function in OSA patients aggravating postoperative upper airway obstruction.[16] It is important to avoid, or perhaps minimize the use and dosage of these medications. If administered, monitoring the level of neuromuscular blockade and completely reversing it before extubation is important in OSA patients to avoid postoperative respiratory complications.

In a randomized controlled trial with a sample size of 74 patients, OSA patients receiving sugammadex had fewer postoperative respiratory complications compared to non-OSA patients receiving neostigmine.[7,17]**

Opioid administration in OSA patients:

Chronic intermittent hypoxia and sleep fragmentation causes upregulation of mu opioid receptors, which results in increased sensitivity and hyperalgesia in OSA patients.[18] The intermittent hypoxia in OSA patients increases systemic inflammatory mediators like IL6, IL1b, and TNF-alpha.[19] These increased systemic inflammatory mediators may cause increased sensitivity to opioids leading to post-operative OIRD.[20–22]*

OSA patients are at increased risk of postoperative OIRD. In the closed claims analyses, OSA was present in 45% of patients with OIRD.[23] In another retrospective study, OSA was present in 38% of the patients with OIRD and 50% of patients who died as a result of OIRD had OSA.[24] In a recent systematic review of case reports of the death, or near-death, OSA patients had received a morphine equivalent dose of less than 10 mg per day.[25]*

Whenever possible, regional anesthesia is preferable in OSA patients undergoing surgery.[7,26,27] Regional anesthesia provides an opioid-sparing effect and reduce opioid-related side effects in the first postoperative day. If general anesthesia (GA) is administered, it may be preferable to use short acting opioids, which result in a faster return of the respiratory status to the baseline. Patient-controlled analgesia (PCA) should be used with caution and monitoring. The use of the multimodal analgesia with non-opioid analgesics may be the best analgesic solution.

Propofol for sedation in OSA patients

Propofol is the main medication used for drug-induced sleep endoscopy and gastroenterological endoscopy. Based on the moderate level of evidence, it was strongly recommended to use a small initial dose of propofol to avoid drug-induced airway obstruction or central apnea.[7]** Hypoxic events and oversedation during propofol administration can be minimised by monitoring ventilation via capnography vs. standard monitoring.[7]**

Fluid Management in OSA patients

It is important to minimize the excessive fluid administration in OSA patients as it may cause rostral shift of fluid from the legs towards the neck and upper airway during supine position, aggravating postoperative upper airway obstruction.[28,29]** Fluids with less salt content like ringer's lactate may be preferred over normal saline. Postoperatively a semi-recumbent position and active mobilization should be encouraged to prevent rostral fluid shift and fluid accumulation in the legs respectively.

Postoperative considerations:

Monitoring:

The American Patient Safety Foundation (APSF) recommendation, based largely on consensus opinion, encourages continuous monitoring of all patients receiving opioids for OIRD in the post-operative period. Recurrent respiratory events (episodes of apnea ≥10 sec, bradypnea <8 breaths/min, pain–sedation mismatch, or repeated oxygen desaturation <90%) in the postanesthesia care unit are indications for continuous postoperative monitoring.[30]

In a recent meta-analysis, continuous capnography monitoring identified 8.6% more OIRD events than pulse oximetry monitoring (CO2 group vs. SpO2 group: 11.5% vs. 2.8%, p<0.00001).31* Although the lack of resources may challenge universal continuous monitoring, it is important to ensure that all OSA surgical patients receiving opioids are being monitored for OIRD to advance perioperative safety.[31]*

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Summary and Conclusion

This review highlights concerns, and best practices based on the current literature and guidelines for the management of OSA patients undergoing ambulatory surgery. Screening should be a part of standard preoperative evaluation; the choice of anesthetic technique should be carefully considered for safe and efficient recovery; and patients should be monitored closely for OIRD, oxygen desaturation and apneic episodes.

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