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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ABSTRACT

Background and objectives Obstructive sleep apnea (OSA) is a risk factor for adverse postoperative outcome and perioperative professional societies recommend the use of regional anesthesia to minimize perioperative detriment. We studied the impact of OSA on postoperative complications in a high-volume orthopedic surgery practice, with a strong focus on regional anesthesia.

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 Overall, OSA was seen in 6.3% (n=1332) of patients with THA and 9.1% (n=1896) of patients with TKA. After adjustment for relevant covariates, OSA was significantly associated with 87% (OR 1.87, 95% CI 1.51 to 2.30), 52% (OR 1.52, 95% CI 1.13 to 2.04), and 44% (OR 1.44,95% CI 1.31 to 1.57) increased odds for pulmonary gastrointestinal complications, and prolonged LOS, respectively. The odds for other outcomes remained unaltered by OSA diagnosis.

Conclusion We showed that, even in a setting with almost universal regional anesthesia use, OSA was associated with increased odds for prolonged LOS, and pulmonary and gastrointestinal complications. This puts forward the question of how effective regional anesthesia is in mitigating postoperative complications in patients with OSA.

INTRODUCTION

Obstructive sleep apnea (OSA) is a condition characterized by repetitive episodes of upper airway obstruction accompanied by cessation in airflow and intermittent hypoxemia. While many cases are undiagnosed, the prevalence of OSA is estimated to be as high as 10% to 30% in surgical patients, especially among those undergoing orthopedic surgery.[1–3] Particularly troublesome is the association between OSA and increased risk of adverse postoperative outcomes.[2 4] These include pulmonary complications, postoperative cardiac events, and transfer to an intensive care unit as well as prolonged length of stay (LOS).[5 6] Guidelines issued by perioperative professional societies recommend the use of regional anesthesia to reduce postoperative complications in patients with OSA,[7–9] and studies have suggested improved postoperative outcomes with this approach in this patient population.[10–12] 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.[10]

To date, no data are available on outcomes among patients with OSA in a practice that focuses on regional anesthesia as a routine anesthetic for total joint arthroplasty. We therefore studied the 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

This is a retrospective cohort study using data from the Hospital for Special Surgery. Approximately 5000 THAs and 5000 TKAs are performed at this institution annually with around 90% regional anesthesia use.

Data sources and cohort

Hospital billing datasets were used to extract patient characteristics and medical history which contained information such as age, sex, dates of admission and discharge, and International Classification of Diseases, ninth revision (ICD-9) codes.

For the period of 2005 to 2014, we identified 56 351 cases with procedure codes for THA (81.51) and TKA (81.54). Exclusion criteria were missing type of anesthesia (n=10 138), pediatric patients (n=41), not the first procedure for the patient within the study time frame (n=4145; patients who had more than one surgery were included only once using data of their first visit), and surgeries that did not take place on the date of admission (n=261). The final study cohort consisted of 41 766 unique patients (21 022 THA; 20 744 TKA)(figure 1).

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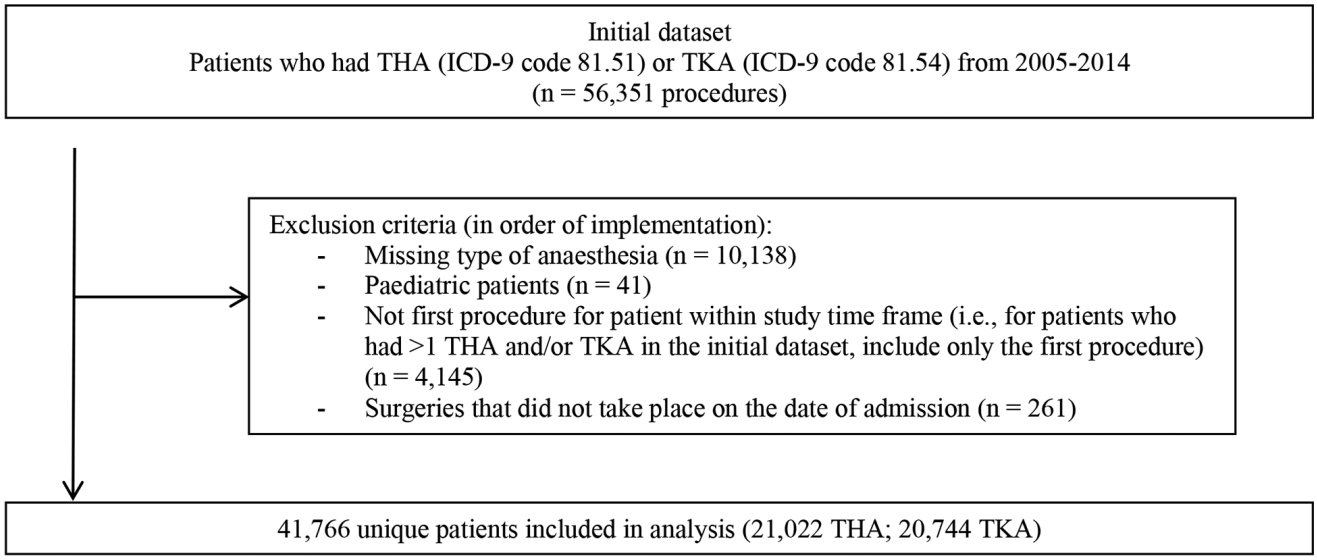

Figure 1 Summary of patient cohort and exclusion criteria ICD-9: International Classification of diseases, ninth revision THA: total hip arthroplasty TKA: total knee arthroplasty.

Study variables

The main effect of interest was OSA, which was defined as the presence of one or more of the following ICD-9 codes: 786.03, 780.53, 780.51, 780.57, 327.2X, or 278.03.

The main outcomes (defined by ICD-9 codes) were cardiac, pulmonary, gastrointestinal, renal/genitourinary, and thromboembolic complications as well as delirium. Online supplementary appendix 1 contains a list of ICD-9 codes that were used to identify complications (Supplemental Digital Content 1). Additionally, prolonged LOS (characterized as exceeding the 75th percentile of 4 days) was included as an outcome.

Categories for primary type of anesthesia were general or neuraxial; neuraxial anesthesia included combined spinal epidural, epidural, or spinal. Information on anesthesia type was extracted from a departmental anesthesia billing database.

Other study variables were age, sex, perioperative medications (benzodiazepines and ketamine), baseline laboratory values (hemoglobin, creatinine, international normalized ratio, and platelets), year of procedure (categorized every 2 years from 2005 to 2014), type of surgery (THA, TKA), and American Society of Anesthesiologists (ASA) physical status (I–II, III–IV). Individual comorbidities can be found in online supplementary appendix 2 (Supplemental Digital Content 2).

Statistical analysis

Descriptive summaries of patient characteristics were first considered. Categorical variables are presented as number (percent) and analyzed by OSA status using a χ^2 test. Continuous variables are presented as median (IQR) and are analyzed using a t-test. Frequencies of missing data are also reported for both categorical and continuous variables as number (percent).

Using the statistical software R V.3.3.3 and RStudio V.1.0.136,[13 14] we conducted multivariable logistic regression evaluating the impact of OSA on risk for the aforementioned outcomes.

All aforementioned study variables were included in the multivariable models except for obesity. A χ^2 test of independence between the OSA and obesity comorbidity variables suggested a significant association between diagnoses of OSA and obesity in this patient population. In the interest of maintaining a parsimonious model (especially due to the relatively low frequencies of the outcomes considered), we included OSA but not obesity as a covariate in our models.

We used multiple imputation methods to estimate missing values using the R statistical package "mice" (multivariate imputation by chained equations).[15] Frequencies of missing data are also reported for categorical and continuous variables as frequency (percent) (table 1). Results for multivariable logistic regression analyses were based on pooled estimates from five datasets generated from multiple imputation methods. Missing values were imputed using predictive mean matching (for continuous variables) and logistic regression imputation (for dichotomous variables).

The primary analysis was repeated as a sensitivity analysis in a subset of data that included only those patients with complete data (ie, excluding those with one or more missing values).

We report adjusted ORs and Bonferroni adjusted p values taking into account seven outcomes under study.

RESULTS

Of the 41 766 unique patients (21 022 THA and 20 744 TKA) included in this study, 7.7% (n=3228) 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 (table 1). 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.

Table 2 depicts results from the pooled multivariable logistic regression model after multiple imputation. After correcting for relevant covariates, OSA was significantly associated with an increased risk of pulmonary complications (OR 1.87, 95%

Table 1 Summary of baseline characteristics stratified by OSA status

	No OSA (n=38 538)	OSA (n=3228)	P value
Obesity	7972 (20.7)	1501 (46.5)	<0.001
ASA status			
I–II	35 827 (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	37 724 (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	10 582 (27.5)	1060 (32.8)	
Age	66.00 (58.00–74.00)	64.00 (57.00–71.00)	<0.001
Gender			
Female	23 427 (60.8)	1182 (36.6)	<0.001
Male	15 111 (39.2)	2046 (63.4)	
Type of surgery			
THA	19 690 (51.1)	1332 (41.3)	<0.001
TKA	18 848 (48.9)	1896 (58.7)	
Baseline laboratory 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)	
Perioperative benzodiazepines			
No	2038 (5.3)	152 (4.7)	<0.001
Yes	31 170 (80.9)	2705 (83.8)	
Missing	5330 (13.8)	371 (11.5)	
Perioperative ketamine			
No	25 361 (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 χ^2 test. Continuous variables are summarized as median (IQR) and are analyzed using t-test. Missing data are summarized as frequency (%).
ASA, American Society of Anesthesiologists; INR, international normalized ratio; LOS, length of stay; OSA, obstructive sleep apnea; THA, total hip arthroplasty.

CI 1.51 to 2.30; p≤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.

Additionally, table 2 presents data on complications stratified by anesthesia type in the overall group of patients with OSA and without OSA. The use of neuraxial anesthesia was associated with decreased odds for pulmonary complications (OR 0.50, 95% 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.

Results from the sensitivity analysis excluding cases with missing information (cohort n=27 690) showed a similar pattern and confirmed findings from the imputed data: odds

Table 2 Logistic regression models of postoperative outcomes by OSA status and anesthesia type after multiple imputation

	OSA status		Anesthesia type	
	Yes (reference=no)		Neuraxial (reference=general)	
	OR (95% CI)	P value	OR (95% CI)	P value
Cardiac complications	1.12 (0.88 to 1.43)	>0.999	0.74 (0.49 to 1.10)	0.938
Pulmonary complications	1.87 (1.51 to 2.30)	<0.007	0.50 (0.36 to 0.69)	<0.007
Gastrointestinal complications	1.52 (1.13 to 2.04)	0.042	0.68 (0.40 to 1.17)	>0.999
Renal/genitourinary complications	1.19 (0.95 to 1.48)	0.931	0.50 (0.36 to 0.68)	<0.007
Thromboembolic complications	1.17 (0.79 to 1.72)	>0.999	0.76 (0.39 to 1.50)	>0.999
Delirium	1.33 (1.03 to 1.72)	0.196	0.45 (0.32 to 0.63)	<0.007
Prolonged LOS	1.44 (1.31 to 1.57)	<0.007	0.51 (0.44 to 0.59)	<0.007

Model adjusted for OSA status, type of surgery (TKA or THA), age at surgery (in years), time period in which the surgery occurred (categorized every 2 years from 2005 to 2014), sex (male or female), baseline laboratory values (hemoglobin, creatinine, INR, and platelets), primary type of anesthesia (neuraxial or general), dichotomized perioperative medications (benzodiazepines and ketamine), and ASA status (dichotomized as ASA status I–II or III–IV).
ASA, American Society of Anesthesiologists; INR, International normalized ratio; LOS, Length of stay; OSA, Obstructive sleep apnea; THA, Total hip arthroplasty; TKA, Total knee arthroplasty.

for pulmonary complications, gastrointestinal complications, and prolonged LOS were significantly increased in patients with OSA (OR 2.16, 95% CI 1.69 to 2.73, p≤0.007; OR 1.72, 95% CI 1.19 to 2.42, p=0.021; and OR 1.57, 95% CI 1.41 to 1.76, p≤0.007, respectively) (table 3).

DISCUSSION

In this retrospective cohort study using data from a high-volume specialty practice with near universal regional anesthesia use, we demonstrated that OSA was associated with an increased risk of pulmonary complications, gastrointestinal complications, and prolonged LOS in patients undergoing THA and TKA while no significant associations were seen for postoperative delirium, cardiac, renal/genitourinary, and thromboembolic complications.

Similar to other reports, we found that, while overall more women had lower joint arthroplasties, patients with OSA were more likely to be male.[2] This finding may be explained by the fact that while female patients have a higher risk for osteoarthritis,[16 17] male patients have higher rates of OSA.[18 19]

Furthermore, our data show that patients with OSA were more likely to have a higher ASA score. Indeed, OSA can be associated with a variety of comorbidities.[20] These include arterial hypertension, coronary heart disease, atrial fibrillation, stroke, and pulmonary hypertension.[21–25]

As found in previous studies, patients with OSA undergoing THA or TKA were younger than patients without OSA.[26 27] This could be related to the strong association between OSA and obesity,[19 28] which is a predisposing factor for osteoarthritis of the lower extremity at a younger age.[29 30]

While both types of surgeries were performed with similar rates, patients with OSA were more prevalent in the TKA than the THA group. This too may be explained by the link between obesity and osteoarthritis of the knee.[31 32]

Table 3 Logistic regression models of postoperative outcomes by OSA status for the dataset excluding patients with missing data

	OSA status	
	Yes (reference=no)	
	OR (95% CI)	P value
Cardiac complications	1.16 (0.85 to 1.55)	>0.999
Pulmonary complications	2.16 (1.69 to 2.73)	<0.007
Gastrointestinal complications	1.72 (1.19 to 2.42)	0.021
Renal/genitourinary complications	1.14 (0.86 to 1.49)	>0.999
Thromboembolic complications	1.11 (0.64 to 1.82)	>0.999
Delirium	1.46 (1.07 to 1.95)	0.091
Prolonged LOS	1.57 (1.41 to 1.76)	<0.007

Model adjusted for type of surgery (TKA or THA), age at surgery (in years), time period in which the surgery occurred (categorized every 2 years from 2005 to 2014), sex (male or female), baseline laboratory values (hemoglobin, creatinine, INR, and platelets), primary type of anesthesia (neuraxial or general), dichotomized perioperative medications (benzodiazepines and ketamine), and ASA status (dichotomized as ASA status I–II or III–IV).
ASA, American Society of Anesthesiologists; INR, International normalized ratio; LOS, Length of stay; OSA, Obstructive sleep apnea; THA, Total hip arthroplasty; TKA, Total knee arthroplasty.

Pulmonary complications

OSA was independently associated with an increase in risk of pulmonary complications. This has been described extensively in the literature.[2 5 33] However, this is the first study investigating the impact of OSA on outcomes in a regional anesthesia setting, whereas in most other studies mainly general anesthesia was used. Theoretically, in a cohort of near universal neuraxial anesthesia use, minimal pulmonary risk differences between OSA groups are expected as neuraxial anesthesia is recommended by guidelines and has been shown to reduce perioperative pulmonary complications in patients with OSA.[12] However, the increased risk found in our study may indicate that the diagnosis of OSA itself increases the risk of pulmonary complications even when general anesthesia is avoided. Interestingly, the OR found in the current study (1.87) for pulmonary complications was lower than those described by Kaw *et al* in a 2012 meta-analysis investigating OSA and postoperative outcome. They calculated total ORs for patients with OSA (compared with non-OSA) of 2.43, 2.05, and 2.27 for the outcomes of respiratory failure, reintubation, and desaturation.[5] As the predominant anesthesia type in these publications was general, this comparison may reflect a reduced risk of pulmonary complications for patients with OSA when regional anesthesia is used, but also shows that this risk cannot be completely eliminated by choice of anesthetic alone.

Gastrointestinal complications

We found that patients with OSA had an increased risk of developing gastrointestinal complications, which has not been widely described. Looking at the frequency of specific ICD-9 codes, we found that the most common diagnosis was paralytic ileus (560.1).

Opioid consumption has been associated with the development of postoperative ileus.[34] In our dataset, patients with OSA had general anesthesia more often than patients with no OSA and therefore most likely received higher doses of opioids. Although we corrected for type of anesthesia in our multivariable regression model, an effect related to this variable might still be present. Additionally, some studies suggest that sleep fragmentation, insomnia, and desaturation, which can be related to OSA, may be associated with increased sensitivity to pain.[35–37] Patients with OSA may therefore require higher doses of opioids, which could directly influence the likelihood of opioid-related adverse effects like ileus. However, there are several publications that showed no difference or even a higher pain tolerance in patients with OSA.[38–40]

Another factor contributing to this finding may be the higher prevalence of irritable bowel syndrome among patients with OSA. Ghiasi *et al* found that OSA was independently associated with this condition.[41] Chronic constipation, one of the key symptoms of irritable bowel syndrome, has been established as a risk factor for postoperative ileus.[42]

Obesity might also be a link between OSA and postoperative ileus. Obesity has been identified as a risk factor for postoperative ileus; however, this was observed mainly in patients undergoing abdominal surgery and its relevance for the orthopedic patient might be limited.[43 44] There are investigations on postoperative ileus in joint arthroplasty patients, and Parvizi *et al* found that male gender, which is strongly associated with OSA, was a risk factor for postoperative ileus.[45] In a 2001 retrospective cohort study investigating patients who underwent THA and TKA, Bederman *et al* concluded that male patients were at increased risk of having a more prolonged ileus.[46]

Prolonged LOS

In addition to the increased risk of developing complications, we showed that OSA had an impact on prolonged LOS. This is similar to findings from large retrospective cohort studies using national data, showing an increase in resource use in patients with OSA undergoing orthopedic surgery.[26 47] Prolonged LOS may at least in part be a consequence of increased morbidity, as patients with OSA may have longer hospital stays because of complications and resulting treatments or transfers to intensive care units. However, it could also reflect planned monitoring of patients with OSA and use of continuous positive airway pressure devices with the goal to reduce complications as recommended by the ASA task force on perioperative care of patients with OSA.[7]

Limitations

Our study is subject to a number of limitations. Because it is a retrospective study, we cannot determine causal relationships, but only associations. Additionally, our data were not collected for research, but for administrative purposes, which results in a lack of clinical detail. OSA status and complications are based on ICD-9 codes and may be subject to coding bias. Under-reporting of diagnoses may be present, especially for the diagnosis of OSA. Furthermore, this study included data from a single institution and generalizability to a broader surgical population might be limited.

CONCLUSIONS

In 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.

Patient consent Not required.

Ethics approval This study was approved by our Institutional Review Board (IRB no. 2016-436) and considered exempt from obtaining patient consent as a retrospective study.

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