Postoperative Hypoxemia in Orthopedic Patients with Obstructive Sleep Apnea

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Received: 15 January 2010/Accepted: 22 April 2010/Published online: 28 May 2010
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Abstract Criteria to determine which patients with obstructive sleep apnea (OSA) require intensive postoperative monitoring are lacking. Our postoperative OSA patients are all intensively monitored in the PACU and can provide such data. Thus, we reviewed patient records to determine incidence and risk factors for postoperative hypoxemia in OSA patients and subsequent association with postoperative complications. Five hundred twenty-seven charts of patients with OSA based on preoperative ICD-9 codes were reviewed for outcomes including episodes of hypoxemia and hypercarbia. Univariate analysis, logistic regression, and propensity analysis were performed to determine

independent risk factors for hypoxemia and association with adverse outcomes. Thirty-three and 11 percent of these patients developed hypoxemia or hypercarbia. Risk factors for hypoxemia were hypercarbia, home bronchodilator use, BMI ≥ 35 , and estimated blood loss ≥ 250 ml. Patients with hypoxemia had significantly more respiratory interventions and increased intensity of care. Patients with hypoxemia had significantly increased length of stay and risk of wound infections. Severe hypoxemia was associated with significantly more interventions than mild hypoxemia. Propensity analysis confirmed significant association of hypoxemia with adverse outcomes after adjustment for pre-existing risk factors. We conclude that postoperative hypoxemia in OSA patients is associated with adverse outcomes. Risk factors for hypoxemia were identified to guide allocation of monitoring resources to high-risk patients.

Each author certifies that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article. All funding was provided by the Department of Anesthesiology, Hospital for Special Surgery.

Each author certifies that his or her institution has approved the reporting of these cases, that all investigations were conducted in conformity with ethical principles of research.

Level of Evidence: Prognostic study, level IV (retrospective study)

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Keywords orthopedic surgery · obstructive sleep apnea · hypoxemia · postoperative complications

Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder associated with increased morbidity such as hypertension, myocardial ischemia, stroke, heart failure, pulmonary hypertension, and sudden death [11]. In the general medical population, estimates for prevalence of mild OSA range from 17 to 26% of men and 9 to 28% of women, whereas estimates for prevalence for severe OSA ranges from 9 to 14% of men and 2 to 7% of women [4, 14]. In the surgical population, excluding bariatric surgery, estimates for prevalence of OSA range from 10 to 64% [4]. Not only is OSA prevalent among surgical patients, but episodes of apnea may be more severe due to documented perioperative disturbances in sleep architecture [6] and respiratory depressant effects of postoperative analgesics [3]. Practice guidelines for preoperative management of OSA have been created [7]. However, as noted in the guidelines and recent reviews [4, 11], recommendations were primarily based on

consultant opinion, as there was insufficient data for evidence-based findings. Thus, incidence and severity of postoperative hypoxemia in OSA patients has not been determined. Furthermore, association between hypoxemia and adverse outcomes is unclear.

The primary purpose of this study is to determine the frequency and severity of postoperative hypoxemia in patients with OSA. Our secondary purpose was to determine the risk factors for developing postoperative hypoxemia so as to identify patient groups that would selectively benefit from intensive monitoring. Finally, we wished to examine the association of postoperative hypoxemia with the need for respiratory interventions, increased intensity of care, incidence of wound infection, and length of hospital stay.

Patients and methods

Our institution has had a policy since December, 2005 that all patients with a preoperative diagnosis of OSA spend at least the night in the post-anesthesia care unit (PACU) for continual monitoring including pulse oximetry and frequent arterial blood gas sampling. We retrospectively reviewed charts of patients with a preoperative diagnosis of OSA to determine incidence and severity of postoperative hypoxemia, subsequent outcomes, and to determine risk factors for hypoxemia to aid in allocation of monitoring resources.

After obtaining Institutional Review Board approval, patient records from date December, 2005 to November, 2008 were identified by using ICD-9 codes 327.23 and 780.57 for OSA. Records were reviewed from 527 consecutive patients with a preoperative diagnosis of OSA. As expected in a population with diagnosis of OSA [11], our patients were predominantly male (69%), older (mean age 61), and overweight (mean BMI of 35). All patients spent at least the first postoperative night in the PACU with at least 2 l/min oxygen delivery via nasal cannula. Continual monitoring included standard non-invasive monitors and an arterial line for frequent arterial blood gas sampling. Outcomes were prospectively defined (Table 1) prior to chart review. Collected data included patient characteristics (Table 2), type of procedure, type of anesthetic, intra-operative data, postoperative course, and type of postoperative analgesia.

The primary outcome analyzed was the occurrence of postoperative hypoxemia (mild SpO₂ <95% or severe SpO₂ <90%). Descriptive analysis was initially performed to determine if any differences in perioperative characteristics (Tables 2, 3, and 4) were apparent between groups that had at least one episode of hypoxemia (mild or severe) versus those who did not. Perioperative characteristics that appeared to differ between groups were then compared with univariate analysis (*t* test or Chi square test) to screen for potential risk factors for hypoxemia. Potential risk factors that had a significance level of $p < 0.05$ on univariate analysis were then used for multivariate logistic regression to determine independent risk factors for hypoxemia (mild or severe). Logistic regression was performed with both discrete and continuous variables and was adjusted for type

Table 1 Definitions for outcomes

Outcome	Definition
Mild hypoxemia	SpO ₂ <95% on pulse oximeter. All readings over time were considered to be the same continuous episode until interrupted by a SpO ₂ ≥95%. Thus, readings of continued hypoxemia over 5 min or over 5 h were all considered a single episode
Severe hypoxemia	SpO ₂ <90% on pulse oximeter. Same definition as above for an episode
Hypoxemia	Both mild and severe combined
Hypercarbia	PCO ₂ >50 mm Hg on arterial blood gas. No definition of duration due to pm nature of blood gas sampling
Increased intensity of care	Transfer from SDU to ICU Change to 1:1 nursing Addition of bedside observer Additional diagnostic testing for respiratory function (e.g., chest radiograph or chest CT scan) Consultation with other services regarding hypoxemia
Wound infection	Positive wound culture

of procedure (Appendix). BMI is a continuous variable but a cutoff value of 35 was used to create a binary variable for logistic regression. This value is the World Health Organization cutoff for mild (Class I, BMI <35) vs moderate/severe obesity (Class II, III) [21]. Our patients with a diagnosis of OSA would be expected to have some degree of obesity, thus this cutoff value was selected for external clinical relevance.

Unadjusted association between hypoxemia (mild or severe) with adverse outcomes such as increased respiratory interventions, need for increased intensity of care, and major morbidities was tested with either Chi square or *t* test with hypoxemia as the independent variable. Then, we tested whether severity of hypoxemia was associated with increased severity or incidence of adverse outcomes by performing pairwise comparisons (no hypoxemia vs. mild, none vs. severe, and mild vs. severe) with Chi square or *t* test. A $p < 0.05$ after Bonferonni correction was considered significant.

Propensity analysis was used to examine association between hypoxemia (mild or severe) with adverse outcomes after adjustment for underlying risk factors identified above. Propensity scores were created based on risk factors identified in Tables 5 and 6 [17]. Logistic regression was performed for most dichotomous outcomes in Table 7 with propensity scores and hypoxemia as independent variables [5, 15]. However, “Administration of naloxone” and “Wound infection” had too few occurrences for analysis. Linear regression was used for “Hospital stay” as a continuous outcome variable again with propensity scores and hypoxemia as independent variables. Then, severity of hypoxemia was tested against increased severity or incidence of adverse outcomes by performing logistic or linear regression for the same outcomes with hypoxemia categorized as none, mild, or severe and controlling for propensity scores.

Table 2 Selected patient characteristics

Characteristic	No hypoxemia (n=353)	Any hypoxemia (n=174)	Mild (n=127)	Severe (n=47)
Age (years, mean/SD)	60±12	61±12	60±12	64±12
Gender (M/F, %)	71/29	66/34	67/33	62/38
BMI (mean/SD) ^a	33±7	36±7	36±7	35±7
ASA class (%) ^a				
1	2	0	0	0
2	46	36	35	37
3	51	63	64	61
4	1	1	1	2
Past medical history				
CPAP at home (%)	36	37	40	28
Hypertension (%)	58	60	60	60
COPD (%)	5	6	6	6
Asthma (%)	11	14	14	15
Home medications				
Anti-hypertensive (%)	55	60	58	68
Bronchodilators ^a (%)	13	22	21	23
Physical exam				
Airway class (%) 1/2/3/4	20/55/24/2	15/52/29/4	14/52/31/3	18/52/25/5

^a Identified as potential risk factor by univariate analysis

ASA class ≥3 identified as potential risk factor by univariate analysis

Results

Thirty-three percent of patients had at least one episode of hypoxemia, 11% of patients had at least one episode of hypercarbia, and 6% had both. In patients with hypoxemia, the median (mode) number of episodes of hypoxemia was 1

(1). The mean and standard deviation for duration of each episode was 143±178 min. In patients with hypercarbia, the median (mode) number of episodes of hypercarbia was 1 (1). Twenty-three percent of patients with hypoxemia had their initial episode on POD 0, and 56% had their initial episode by POD1 (Fig. 1). Each postoperative day began at 12:01 AM.

Table 3 Intraoperative characteristics

Characteristic	No hypoxemia (n=353)	Any hypoxemia (n=174)	Mild (n=127)	Severe (n=47)
Procedure				
Spine (%)	20	26	26	26
Hip replacement (%)	31	21	23	17
Knee replacement (%)	35	39	36	47
Foot/ankle (%)	8	8	8	8
Other lower extremity (%)	3	2	3	0
Shoulder replacement (%)	3	2	2	2
Other upper extremity (%)	0	2	2	0
Surgeons (N)	61	44	44	30
Anesthesia ^a				
General				
General only (%)	19	29	30	28
General + epidural only (%)	1	1	0	2
General + nerve block (%)	1	1	2	0
Regional				
Combined spinal epidural (%)	53	48	48	49
Combined spinal epidural + nerve block (%)	8	7	6	11
Spinal (%)	4	4	6	0
Spinal + nerve block (%)	1	1	0	2
Epidural (%)	8	5	4	6
Nerve block (%)	5	4	4	2
Anesthesiologists (N)	36	35	35	24
Intraoperative				
IV fluids ^a (ml, mean/SD)	1,855±692	2,022±1,024	2,010±1,064	2,054±916
Estimated blood loss ^a (ml, mean/SD)	253±294	382±525	397±582	340±322
Length of procedure ^a (min, mean/SD)	130±66	154±109	154±112	152±102

^a Identified as potential risk factor by univariate analysis

Table 4 Postoperative analgesia characteristics

Characteristic	No hypoxemia (<i>n</i> =353)	Any hypoxemia (<i>n</i> =174)	Mild (<i>n</i> =127)	Severe (<i>n</i> =47)
Primary analgesia technique				
Intravenous PCA (%)	28	32	35	26
Intravenous PCA + nerve block (%)	4	3	3	4
Epidural PCA (%)	44	39	42	30
Epidural PCA + nerve block (%)	18	17	13	28
Nerve block (%)	2	3	3	4
Continuous nerve block (%)	2	4	2	8
Oral opioid only (%)	2	2	2	0
Analgesic adjuncts				
Oral opioids (%)	52	44	49	30
NSAIDs (%)	24	20	22	13
IV Opioids (%)	13	12	12	11

PCA patient controlled analgesia

Univariate analysis indicated that initial patient characteristic risk factors for the development of hypoxemia included BMI ≥ 35 , ASA class ≥ 3 , and home use of bronchodilators. Univariate analysis indicated that initial intraoperative risk factors (Table 3) included use of general anesthesia, quantity of intravenous fluids, estimated blood loss, and length of procedure. None of the postoperative analgesia modalities qualified as an initial risk factor (Table 4). The final independent risk factors for hypoxemia after logistic regression were the occurrence of hypercarbia episodes, a history of home bronchodilator use, BMI ≥ 35 , and estimated blood loss ≥ 250 ml (Table 5). Table 6 displays the prevalence and risk for hypoxemia for all combinations of identified risk factors.

Patients with episodes of hypoxemia had significant association with increased adverse outcomes including need for respiratory interventions (emergent CPAP application, change in oxygen delivery, and intravenous naloxone), increased intensity of care, wound infection rates, and increased hospital length of stay (Table 7). Severe hypoxemia was associated with greater incidences of changes in oxygen delivery, intravenous naloxone, and increased intensity of care than mild hypoxemia (Table 7). Propensity analysis also indicated that hypoxemia was associated with adverse outcomes including emergent CPAP application, change in oxygen delivery, increased intensity of care, and increased hospital length of stay (Table 8) after adjustment for underlying risk factors. Outcomes of “Administration of naloxone” and “Wound infection” were not analyzed due to small number of occurrences. Propensity analysis also indicated that severe hypoxemia was associated with greater

risk of need for emergent CPAP, change in oxygen delivery, and increased intensity of care than mild hypoxemia (Table 8).

Discussion

Our purpose was to determine incidence and severity of postoperative hypoxemia in patients with a diagnosis of OSA, adverse outcomes associated with hypoxemia, and to determine risk factors for hypoxemia to aid in allocation of monitoring resources.

There are several limitations to our study. The data collection was retrospective and has typical limitations in that data may have been missed and that patients may have been treated differently due to pre-existing knowledge of the diagnosis of OSA. The diagnosis of OSA was based on ICD9 codes, which are commonly used as an efficient and effective means to identify patients with OSA [19, 20]. Disadvantages of using ICD-9 codes include the possibility of mis-coding [10, 22] and that severity of OSA could not be ascertained. Our primary measure of oxygen saturation via pulse oximetry was monitored continually but recorded intermittently. Finally, our case series does not include a control group, and all associations are inferential.

Incidences of hypoxemia was 33% and hypercarbia was 11% in OSA patients after elective orthopedic surgery. Hypoxemia was significantly associated with adverse outcomes including more frequent respiratory interventions, need for more intensive monitoring, length of hospital stay, and postoperative wound infections. Our findings are in agreement with a previous smaller retrospective survey of OSA patients diagnosed with polysomnography undergoing orthopedic surgery that reported a 21% incidence of hypoxemia and 7% incidence of hypercarbia [8]. Risk of postoperative hypoxemia is likely much greater in our patients with OSA versus those without the diagnosis. The previous smaller study in orthopedic patients reported an 8% incidence of hypoxemia in matched controls without diagnosis of OSA. A much larger observational study in 24,000 patients after mixed surgery including orthopedics

Table 5 Final risk factors for episodes of hypoxemia

Final independent risk factors for hypoxemia	Odds ratio (95% CI)
Hypercarbia episode	2.9 (1.6–5.2)
Home bronchodilators	2 (1.2–3.3)
BMI ≥ 35	1.9 (1.3–2.9)
Estimated blood loss ≥ 250 ml	1.2 (1.1–1.4)

Table 6 Incidence and risk of hypoxemia for individual and combinations of risk factors

Number of risk factors from Table 5	Risk factors combinations	Incidence of hypoxemia (% and number of patients)	Odds
0		No observations	0.21
1	BMI ≥ 35	40% (96)	0.41
	EBL ≥ 250 ml	38.89% (77)	0.26
	Home bronchodilators	46.34% (38)	0.42
	Hypercarbia	57.89% (33)	0.61
2	BMI ≥ 35	42.86% (39)	0.5
	+EBL ≥ 250 ml		
	BMI ≥ 35	47.73% (21)	0.81
	+Home bronchodilators		
	BMI ≥ 35	60% (15)	1.16
	+Hypercarbia		
	EBL ≥ 250 ml	50% (16)	0.52
	+Home bronchodilators		
	EBL ≥ 250 ml	57.14% (16)	0.75
	+Hypercarbia		
	Home bronchodilators	84.62% (11)	1.21
	+Hypercarbia		
3	BMI ≥ 35	56.25% (9)	1
	+EBL ≥ 250 ml		
	+Home bronchodilators		
	BMI ≥ 35	50% (4)	1.43
	+EBL ≥ 250 ml		
	+Hypercarbia		
	BMI ≥ 35	100% (6)	2.32
	+Home bronchodilators + hypercarbia		
	EBL ≥ 250 ml	71.43% (5)	1.48
	+Home bronchodilators + hypercarbia		
4	BMI ≥ 35	100% (2)	2.85
	+ EBL ≥ 250 ml		
	+Home bronchodilators + hypercarbia		

Odds were calculated from same logistic regression as Table 5. As there were no patients with zero risk factors, odds were estimated from the zero intercept. Individual odds ratios can be calculated for any pair. For example, the odds ratio for risk factor combination (BMI + Home bronchodilators + Hypercarbia) vs. risk factor (BMI ≥ 35) is $2.32/0.41=5.66$.

reported a postoperative incidence of hypoxemia of 0.8% [16] without specifying diagnoses of OSA.

Our findings are clinically relevant in that we identified combinations of risk factors to determine which patients may benefit most from allocating resources for intensive postoperative monitoring. Ability to select patients is important, as most institutions do not have the resources to intensively monitor all postoperative OSA patients. It has been estimated that each institution would need to spend at

least \$25,000 annually to be able to provide such monitoring [7]. Direct cause and effect between risk factors and hypoxemia are speculative, but all risk factors (episode of hypercarbia, increased BMI, home use of bronchodilators, and increased blood loss) can be reasonably linked to increased risk of respiratory compromise and resultant hypoxemia. Our results suggest that the peak period of monitoring for hypoxemia may extend through POD1. This is consistent with previous studies reporting that major

Table 7 Adverse outcomes associated with hypoxemia

Outcome	Total number of patients with adverse outcome	No hypoxemia (N=353)	Hypoxemia (N=174)	Mild (N=127)	Severe (N=47)
Need for CPAP	158	27%	36%	35%	38%
CPAP at home + subsequent routine PACU use	128	24%	25%	26%	21%
Emergent CPAP	15	2%	21%	14%	37%*
Change in oxygen delivery	121	9%	51%	39%	85%*
Administration of naloxone	7	1%	3%	1%	9%*
Increased intensity of care	131	15%	45%	36%	70%*
Wound infection	7	0%	3%	4%	2%
Hospital stay (days, mean/SD)	n/a	4.4 $\pm$ 2.3	6.0 $\pm$ 5.2	6.0 $\pm$ 5.9	5.9 $\pm$ 2.3

All values are significantly different ($p<0.05$) between No hypoxemia vs Hypoxemia groups. Mild hypoxemia=SpO₂<95%, Severe hypoxemia=SpO₂<90%

* $p<0.05$, Severe hypoxemia is significantly different from No hypoxemia and Mild hypoxemia

Fig. 1. This graph plots the time course of occurrence of hypoxemia episodes. POD postoperative day. The total number of patients evaluated per postoperative day is shown on bottom line (e.g., there were 527 patients on postoperative day0)

disturbances in sleep architecture in normal patients occur the night prior to and immediately after surgery [6]. Sleep disturbances over the preceding two nights could easily lead to somnolence and hypoxemia by POD1. Unfortunately, episodes of hypoxemia were not limited to POD1, as many patients continued to have episodes through POD5. This finding is also consistent with previous studies in normal postoperative patients reporting continued disturbance in sleep architecture with REM rebound through POD3 [18]. Thus, sleep disturbances may routinely continue for several days after surgery, and prolonged monitoring for hypoxemia may be required in high-risk patients.

Within our study population, hypoxemia was associated with several adverse outcomes. Every hypoxemic episode is severe enough to deserve clinical interventions, and our patients with hypoxemia did have an increased need for respiratory interventions ranging from the simple such as changing oxygen delivery to the more complex such as emergent application of CPAP. Although we did not determine a direct association, it is likely that clinically significant postoperative respiratory compromise from OSA led to these interventions, and multiple smaller retrospective surveys have also reported increased need for respiratory interventions in OSA vs. non-OSA patients after a variety of surgical procedures [4]. There was an association between hypoxemia and increased intensity of care. This would be expected to increase cost of care and was likely prompted by clinically significant compromised respiratory function due to OSA. Hypoxemia was associated with more serious

adverse outcomes including increased rate of wound infection and prolonged length of hospital stay. It would be reasonable to propose that hypoxemia impaired the immune system and perhaps created a more anaerobic environment promoting wound infection [12]. Alternatively, the typical dose of preoperative antibiotic may have been insufficient for our heavier patients. Hospital length of stay is multifactorial and may have been increased due to an increase in all of the above complications. Although this direct association is unclear, previous smaller retrospective surveys have also reported an increased length of hospital stay in postoperative OSA patients compared to non-OSA [4].

In conclusion, hypoxemia in patients with a diagnosis of OSA is associated with increased need for respiratory interventions, increased intensity of care, length of stay, and risk of wound infection. Severe hypoxemia was associated with increased incidences of complications. Our findings are in agreement with previous smaller surveys that also reported high incidence of hypoxemia and complications in OSA patients after orthopedic surgery. In our study characterization and capture of hypoxemia was more complete due to use of continual monitoring in the PACU. Our findings have enhanced clinical relevance in that we identified risk factors for hypoxemia to identify OSA patients that would most benefit from intensive postoperative monitoring.

Appendix: specifics of logistic regression

All statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC, USA). Model fitting for multivariate logistic regression started with a full model including all risk factors that were significant in univariate analysis. The full model consisted of an outcome variable of hypoxemia, five dichotomous (BMI ≥ 35 , episode of hypercarbia, use of home bronchodilators, ASA class ≥ 3 , and general versus regional anesthesia), and three continuous (IV fluids, estimated blood loss, and length of procedure) predictors and was adjusted for type of surgical procedure (spine, hip or knee replacement, lower extremity, and upper extremity). Continuous variables were tested for continuity and linearity and were virtually linear in a graphic analysis [9]. For each individual predictor, odds ratio, 95% confidence interval, and p value were computed. Multicollinearity was judged by checking the value inflation factor

Table 8 Adverse outcomes associated with hypoxemia after adjustment for underlying risk factors in Table 5 with propensity analysis

Outcome (odds ratio with 95% CI)	Hypoxemia	Mild	Severe
Need for emergent CPAP	8 (1.6–39.2)	5.6 (1.02–30.5)	17.4 (2.8–110)
Change in oxygen delivery	8.4 (5.1–13.6)	5.3 (3.1–9)	55.7 (20.1–154)
Increased intensity of care	3.9 (2.5–6.1)	2.9 (1.8–4.7)	10.7 (5–22.9)
Increased hospital stay (analyzed as continuous variable with linear regression)	$p < 0.001$	ND	ND

Mild hypoxemia = $\text{SpO}_2 < 95\%$. Severe hypoxemia = $\text{SpO}_2 < 90\%$. Outcomes of Administration of naloxone and Wound infection not analyzed due to small number of occurrences

ND not significantly different with increased severity of hypoxemia

and condition index, and standard criterion for absence of collinearity was sufficiently met (value inflation factor <10 and condition index <30) [2]. Multivariate logistic regression models were fitted and selected using backward elimination, and models with the lowest Akaike Information Criterion were selected [1]. The Hosmer–Lemeshow test of goodness-of-fit was performed and indicated that the final logistic model fit the data well ($p=0.43$) [1].

We also checked data for patient clustering effect by anesthesiologist or surgeon (e.g., whether a single subgroup of anesthesiologists or surgeons was involved with most patients). Chi square tests were conducted to compare the distributions of patient within each cluster (anesthesiologists or surgeons), and no significant association was found between hypoxemia and anesthesiologist ($p=0.33$) and surgeon ($p=0.65$). Furthermore, the generalized estimating equations (GEE) approach for logistic regression was also applied to identify risk factors for hypoxemia. Unlike standard logistic regression, GEE logistic regression allows for dependence within clusters, specifically clustering by anesthesiologist or surgeon in this case [13]. The same methods for model fitting and model selection for logistic regression were also applied to GEE. After analysis, both GEE logistic and standard logistic final models contained the same set of independent risk factors in Table 5 with nearly identical coefficient estimates. As neither the Chi square tests nor the GEE logistic regression indicated a clustering effect, results from standard logistic regression were used.

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