

Sleep Apnea Patients do not have an Elevated Risk of Complications or Length of Stay Post-Lobectomy

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Abstract

Obstructive Sleep Apnea (OSA) has been associated with an increased risk of postoperative complications. The complication rate and length of hospital stay in patients with OSA undergoing lung resection has not specifically been evaluated. We postulate that OSA may be associated with an increased length of stay and risk of complications post-lobectomy.

Three hundred and twenty patients who underwent lobectomy between January 2009 and December 2011 were reviewed. Those with either a hospital coding of OSA, or medical history of OSA, were deemed as having OSA. Age, gender, a variety of preoperative co-morbidities, and lung function were used as covariates. Data analysis was performed using independent t-test/Kruskal-Wallis test for continuous variables, and the Chi square/ Fisher exact test for categorical variables. Multiple logistic regression method and linear regression were used to estimate the effect of OSA on complications and length of stay, controlling for the effects of potential confounders.

Out of 320 patients, 25 carried the diagnostic code of OSA. The two groups were equivalent in regards to age, FEV1, DLCO and smoking status, but differed in Body Mass Index (BMI). Four out of the 25 patients with OSA developed post-lobectomy complications compared to 55 in the OSA negative group (16.0% vs. 18.6%, p-value>0.9). Length of stay in the OSA group was 4.16 ± 3.68 days compared to 4.32 ± 3.14 days in OSA negative group (p-value=0.639).

After adjusting for comorbidities, OSA is not associated with an increase in complications or length of hospital stay following major lung resection.

Keywords: Obstructive sleep apnea; Thoracic surgery; Lung resection; Complications

Introduction

Obstructive Sleep Apnea (OSA) is a common condition characterized by repetitive upper airway obstruction associated with oxygen desaturation and frequent arousals. Obstructive sleep apnea is present in 2-9% of the general population [1-3], but may be more common in a general surgical population when screened using the Berlin questionnaire [4,5]. Recently, there have been reports of an increased risk of postoperative complications occurring with OSA [6-10]. In instances when the diagnosis is known preoperatively, and peri-operative management is not optimized, the risk of perioperative complications may be elevated [10]. OSA patients may be uniquely susceptible to the effects of neuromuscular blockers on reduced upper airway muscular tone leading to worsened obstruction of the upper airway [11-13]. In addition, the use of postoperative narcotics may reduce ventilatory drive and arousal threshold in response to hypoxia [14-16].

Lung resection is a procedure known to have significant morbidity and mortality and is commonly performed on patients with emphysema. The risk of lung resection in patients with sleep apnea is not known. Certainly, there is reason to be concerned that the post-operative management of pain, the presence of coexisting underlying lung disease, and peri-operative hypoxemia may increase the risk of complications. We hypothesized that patients undergoing lobectomy with a known diagnosis of OSA may have more complications than those without.

Materials and Methods

We performed a retrospective review of all patients who underwent lobectomy between January 2009 and December 2011. Sleep apnea

patients at Case Medical Center are asked to bring in their home positive pressure ventilation systems, and they are routinely used in the postoperative setting for such patients. Patients were deemed to have OSA by searching through preoperative medical history and the admitting ICD 9 codes. Other factors entered into the database were age, diabetes, hypertension, peripheral vascular disease, coronary artery disease, and history of congestive heart failure, gender, Body Mass Index (BMI), smoking status, Forced Expiratory Volume in one second (FEV1) and Diffusing Capacity of the Lung for Carbon Monoxide (DLCO). These variables and perioperative outcomes were collected prospectively as part of our institutions participation in the Society of Thoracic Surgery (STS) Database. The IRB committee at our institution approved this study. All data collection and patient follow up were performed by a nurse and/or physician assistant. Only patients who underwent elective lobectomy were included in the analysis.

The primary outcome variables were hospital length of stay and the incidence of postoperative complications which included air leak, pneumonia, ARDS, cardiac events, new renal failure, thromboembolic events, delirium, sepsis, urinary tract infection, ileus and other complications as recorded in the STS database. Prolonged air leak was

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defined as an air leak lasting greater than 5 days. Pneumonia was defined as a patient having at least two of the following criteria: fever greater than 38 or WBC greater than 10,000, infiltrate on CXR, positive sputum gram stain and culture. DLCO and FEV1 were measured according to ATS standards.

Baseline characteristics are presented as mean ± standard deviation for continuous measurements and frequency for categorical factors. The difference of continuous variables between groups was analyzed using Student's t-test/Kruskal-Wallis test, and the association between two categorical variables was estimated using Chi square/ Fisher exact test. Multiple linear regression for continuous measurements (e.g. length of hospital stay) and logistic regression for binary outcomes (e.g. complications) were used to probe for potential confounders. All

| Variables | Non-OSA (n=295) | OSA (n=25) | P-Value |
|-----------------------|-----------------|--------------|---------|
| Age | 67.2 ± 12.2 | 64.3 ± 11.4 | 0.17 |
| Gender n(%) | | | |
| Male | 170 (57.6) | 11 (44.0) | 0.18 |
| Race n(%) | | | |
| Caucasian | 242(82.0) | 23(92.0) | 0.28 |
| Black | 53(17.8) | 2(8.0) | |
| BMI kg/m ² | 27.11 ± 6.12 | 30.54 ± 5.03 | 0.002 |
| Smoking status n(%) | | | |
| Never | 63(21.4) | 6 (24.0) | 0.34 |
| Quit >1month | 144 (48.9) | 15 (60.0) | |
| Current | 88 (29.8) | 4 (16.0) | |
| FEV1 % | 85.4 ± 18.1 | 81.0 ± 19.5 | 0.26 |
| DLCO % | 80.6 ± 22.3 | 83.0 ± 24.1 | 0.74 |
| Comorbidities n(%): | | | |
| Diabetes | 42(14.2) | 3(12) | >0.99 |
| Hypertension | 171(56) | 16(64) | 0.56 |
| PVD | 23(7.5) | 0 | 0.23 |
| CAD | 54(17.7) | 8(32) | 0.11 |

Definition of abbreviations: BMI= Body Mass Index, FEV1= Forced Expiratory Volume in one second, DLCO= Carbon Monoxide Diffusing Capacity, PVD = Peripheral Vascular Disease, CAD = Coronary Artery Disease

Table 1: Baseline characteristics.

| Postoperative Events | Non-OSA | OSA | P value |
|---------------------------------|-------------|-------------|---------|
| Number of Patients with event | 55 (18.6%) | 4 (16.0%) | >0.999 |
| Length of Stay (days) | 4.32 ± 3.14 | 4.16 ± 3.68 | 0.639 |
| Cardiac: | | | |
| CHF | 7(2.4%) | 0 | |
| Atrial Arrhythmia | 13(4.4%) | 2 (8.0%) | |
| Respiratory: | | | |
| Prolonged Air Leak | 20(6.8%) | 2 (8.0%) | |
| Pneumonia | 5(1.7%) | 0 | |
| Bronchopleural fistula | 0 | 0 | |
| Empyema | 1(0.3%) | 0 | |
| Atelectasis | 4(1.4%) | 1 (4.0%) | |
| Tracheotomy | 2(0.7%) | 0 | |
| Deaths (in-hospital or <30days) | 1(0.34%) | 0 | |

Definition of abbreviation: CHF = Congestive Heart Failure

Table 2: Patients Post-Operative Events.

| Variable | Parameter Estimate | p-value | Odds Ratio | 95% Confidence Limits |
|---|--------------------|---------|------------|-----------------------|
| OSA (Yes vs. No) | -1.004 | 0.234 | 0.367 | (0.070, 1.916) |
| Age | 0.022 | 0.212 | 1.022 | (0.988, 1.057) |
| Gender (Male vs. Female) | 0.538 | 0.160 | 0.712 | (0.809, 3.623) |
| BMI (per one unit increase) | -0.010 | 0.752 | 0.990 | (0.932, 1.052) |
| FEV1 | -0.022 | 0.054 | 0.978 | (0.956, 1.000) |
| DLCO | -0.013 | 0.191 | 0.987 | (0.967, 1.007) |
| HTN (Yes vs. No) | -0.653 | 0.080 | 0.520 | (0.250, 1.081) |
| CHF (Yes vs. No) | 0.719 | 0.460 | 2.052 | (0.305, 13.797) |
| CAD (Yes vs. No) | -0.067 | 0.892 | 0.936 | (0.359, 2.436) |
| PVD (Yes vs. No) | 0.665 | 0.286 | 1.943 | (0.573, 6.591) |
| COPD (Yes vs. No) | 0.056 | 0.899 | 1.058 | (0.446, 2.511) |
| Smoking (Yes vs. Never) | 0.654 | 0.229 | 1.924 | (0.662, 5.591) |
| Diabetes (yes vs. No) | -0.718 | 0.210 | 0.488 | (0.159, 1.498) |
| Procedure time (per minute increase) | 0.00005 | 0.231 | 1.000 | (1.000, 1.000) |
| Operative approach (Thoracotomy vs. VATS) | 0.165 | 0.715 | 1.179 | (0.487, 2.856) |

Table 3: Multiple logistic regression of preoperative factors with post operative events.

tests are two-sided and p-value less than 0.05 were pre-designated as statistically significant. P values >0.05-0.15 are designated as marginally significant. The statistical analysis was performed using SAS program (SAS Institute Inc., Cary, NC, USA)

Results

Baseline patient characteristics are listed in Table 1. A total of 320 lobectomy patients were included in the analysis. All had elective lobectomy as a part of management of lung cancer or lung nodule\ except one lobectomy which was performed for lung abscess. Among this group, 25 patients carried the diagnosis code of obstructive sleep apnea. The demographics and co-morbidities were similar in both groups. Mean BMI in the OSA group (30.54 ± 5.03) was higher than the control group (27.11 ± 6.12, p=0.002). Twenty four patients with OSA and 264 patients from the control group had FEV1 measurement obtained before surgery. There was no difference between groups in FEV1 and DLCO.

Four patients had five postoperative complications in the OSA group (one patient had both a prolonged air leak and an atrial arrhythmia, one had a prolonged air leak, one patient had atelectasis requiring bronchoscopy and one had an atrial arrhythmia requiring treatment) compared to 55 postoperative events in the control group (16.0% vs. 18.64%, p>.999) (Table 2). Multivariable analysis showed that preoperative FEV1 (p= .054) and hypertension (HTN) (p= .08) showed a trend toward an association with adverse postoperative events, while OSA did not. (Table 3) The in-hospital length of stay was not significantly different between the two groups. It was 4.16 ± 3.68 days in the OSA group compared to 4.32 ± 3.14 days in OSA negative group (p value=0.639). Multivariable analysis showed that age (p= .009) and history of congestive heart failure (CHF) (p= .052) predicted a prolonged length of stay, while OSA did not (Table 4). Both groups were similarly matched in regards to T and N stage (Table 5).

Discussion

The results of this retrospective study do not suggest that a pre-existing diagnosis of OSA results in an increased length of stay or

| Variable | Parameter Estimate | Standard Error | p-value |
|--|--------------------|----------------|---------|
| OSA (Yes) | -0.409 | 0.719 | 0.569 |
| Age (per year increase) | 0.049 | 0.019 | 0.009 |
| Gender (Male) | 0.129 | 0.435 | 0.766 |
| BMI (per one unit increase) | -0.043 | 0.033 | 0.197 |
| FEV1 (% Pred) | -0.013 | 0.013 | 0.300 |
| DLCO (% Pred) | -0.002 | 0.011 | 0.836 |
| HTN (Yes) | -0.137 | 0.417 | 0.743 |
| CHF (Yes) | 2.232 | 1.143 | 0.052 |
| CAD (Yes) | 0.099 | 0.528 | 0.852 |
| PVD (Yes) | 0.098 | 0.796 | 0.903 |
| COPD (Yes) | 0.417 | 0.522 | 0.425 |
| Smoking (Yes) | 0.670 | 0.510 | 0.191 |
| Diabetes (Yes) | -0.393 | 0.587 | 0.504 |
| Procedure time (per minute increase) | 0.00007 | 0.00005 | 0.183 |
| Operative approach (Thoractomy vs. VATS) | 0.333 | 0.550 | 0.546 |

Table 4: Multiple linear regression of preoperative factors with post operative length of stay.

| Variables | Non-OSA ^a (n=295) | OSA ^b (n=25) | P-Value ^c |
|---------------------|------------------------------|-------------------------|----------------------|
| T stage n(%) | | | |
| T1 | 132 (56.41) | 13 (54.17) | 0.755 |
| T2 | 65 (27.78) | 9 (37.50) | |
| T3 | 31 (13.25) | 2 (8.33) | |
| T4 | 6 (2.56) | 0 (0.00) | |
| N stage n(%) | | | |
| N0 | 202 (86.32) | 18 (75.00) | 0.238 |
| N1 | 23 (9.83) | 4 (16.67) | |
| N2 | 9 (3.85) | 2 (8.33) | |

^a 61 subjects have no staging ; ^b 1 subject has no staging.
^c p-value from Fisher exact test

Table 5: Frequencies of T stage and N Stage.

increased risk of complications following lobectomy. Prior reports suggesting an increased risk of complications following surgery in patients with OSA were limited by lack of inclusion of a significant number of lung surgery patients. Prior studies also measured outcomes such as episodes of oxygen desaturation which may not carry a significant adverse impact. In one such study, OSA was an independent predictor of postoperative complications in patients admitted for elective surgery. The most common complication, however, was transient oxygen desaturations. These OSA patients required a higher number of respiratory treatments and interventions than the control group [8]. In another study, OSA, as ascertained by preoperative evening oxygen desaturation index, was an independent predictor of postoperative respiratory complications in patients undergoing elective non-thoracic surgery, but length of hospital stay was similar [6]. The majority of complications in this study were simple oxygen desaturations, and, as might be expected, OSA patients required more interventions for these desaturations. The length of stay, however, was identical, consistent with a lack of increase in serious complications. Complications in our cohort were generally limited to those with a significant negative impact, such as pneumonia, prolonged air leak, or atelectasis requiring a bronchoscopy.

In patients undergoing cardiac surgery, the incidence of encephalopathy, infection and ICU length of stay was higher in patients with OSA. The higher incidence of infection was manifest as a higher

incidence of mediastinitis, to be expected in a more obese population [9]. A higher postoperative complication rate was also seen in patients who underwent knee and hip replacement surgery [10]. In one of the most detailed reports to date, 282 OSA patients undergoing surgery (only 4.3% had thoracic surgery) were compared to an OSA negative group. OSA was associated with increased risk of postoperative hypoxemia, overall complications, higher incidence of ICU transfer, and longer hospital length of stay. Interestingly, the severity of OSA as measured by Apnea/ Hypopnea Index (AHI) did not correlate with the incidence of postoperative complications [7].

In our cohort, while the BMI was, as expected, greater in the OSA cohort, they were otherwise well matched, with no significant difference between the groups in regards to age, lung function, smoking status or other co-morbidities. The lack of a significant relationship between OSA and postoperative complications in our lobectomy cohort may be attributed to the relatively low complication rates in the both groups (16.0-18.6%). The low incidence of complications in our OSA patients undergoing lobectomy may also be a result of the general intensive perioperative respiratory care given to all our post-lobectomy patients – care that may not routinely be administered to non-thoracic surgical patients. First, all patients are admitted to a dedicated telemetry thoracic surgery postoperative floor with a 1:5 nursing ratio. Second, postoperatively, patients are routinely assessed by dedicated thoracic surgery practitioners and respiratory therapists for any needed therapies.

This study has inherent limitations. While the retrospective nature of the study is a limitation, information on preoperative risk factors (aside from OSA) and perioperative adverse events was collected prospectively, helping to insure the thorough capture of postoperative events. A second limitation was the relatively small number of patients with OSA in our population. We used ICD-9 code as well as the chart documented preoperative history to determine the OSA status in our patients. The non-OSA patients were not routinely screened for silent OSA. It is possible that some of the OSA negative patients may have had undiagnosed OSA, thus confounding the results. Additionally, it is unclear how many OSA patients were diagnosed using polysomnograms, considered the gold standard in OSA diagnosis.

Our analysis of patients undergoing major lung resection and cared for in a dedicated respiratory unit showed no difference in length of stay or complications between patients with and without OSA. Prospective studies may be needed to delineate the relationship between OSA and complications, to determine whether severity of OSA affects the incidence of complications, and to evaluate whether using noninvasive ventilation in the postoperative period would affect the incidence of complications.

References

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, et al. (1993) The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 328: 1230-1235.
2. Durán J, Esnaola S, Rubio R, Iztueta A (2001) Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. *Am J Respir Crit Care Med* 163: 685-689.
3. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, et al. (2001) Prevalence of sleep-disordered breathing in women: effects of gender. *Am J Respir Crit Care Med* 163: 608-613.
4. Finkel KJ, Searleman AC, Tymkew H, Tanaka CY, Saager L, et al. (2009) Prevalence of undiagnosed obstructive sleep apnea among adult surgical patients in an academic medical center. *Sleep Med* 10: 753-758.
5. Chung F, Ward B, Ho J, Yuan H, Kayumov L, et al. (2007) Preoperative identification of sleep apnea risk in elective surgical patients, using the Berlin questionnaire. *J Clin Anesth* 19: 130-134.

6. Hwang D, Shakir N, Limann B, Sison C, Kalra S, et al. (2008) Association of sleep-disordered breathing with postoperative complications. *Chest* 133: 1128-1134.
7. Kaw R, Pasupuleti V, Walker E, Ramaswamy A, Foldvary-Schafer N (2012) Postoperative complications in patients with obstructive sleep apnea. *Chest* 141: 436-441.
8. Liao P, Yegneswaran B, Vairavanathan S, Zilberman P, Chung F (2009) Postoperative complications in patients with obstructive sleep apnea: a retrospective matched cohort study. *Can J Anaesth* 56: 819-828.
9. Kaw R, Golish J, Ghamande S, Burgess R, Foldvary N, et al. (2006) Incremental risk of obstructive sleep apnea on cardiac surgical outcomes. *J Cardiovasc Surg (Torino)* 47: 683-689.
10. Gupta RM, Parvizi J, Hanssen AD, Gay PC (2001) Postoperative complications in patients with obstructive sleep apnea syndrome undergoing hip or knee replacement: a case-control study. *Mayo Clin Proc* 76: 897-905.
11. Bouillon T, Schmidt C, Garstka G, Heimbach D, Stafforst D, et al. (1999) Pharmacokinetic-pharmacodynamic modeling of the respiratory depressant effect of alfentanil. *Anesthesiology* 91: 144-155.
12. Knill RL, Clement JL (1984) Site of selective action of halothane on the peripheral chemoreflex pathway in humans. *Anesthesiology* 61: 121-126.
13. Eastwood PR, Platt PR, Shepherd K, Maddison K, Hillman DR (2005) Collapsibility of the upper airway at different concentrations of propofol anesthesia. *Anesthesiology* 103: 470-477.
14. Dahan A, Sarton E, Teppema L, Olivier C (1998) Sex-related differences in the influence of morphine on ventilatory control in humans. *Anesthesiology* 88: 903-913.
15. Catley DM, Thornton C, Jordan C, Lehane JR, Royston D, et al. (1985) Pronounced, episodic oxygen desaturation in the postoperative period: its association with ventilatory pattern and analgesic regimen. *Anesthesiology* 63: 20-28.
16. Clyburn PA, Rosen M, Vickers MD (1990) Comparison of the respiratory effects of i.v. infusions of morphine and regional analgesia by extradural block. *Br J Anaesth* 64: 446-449.