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Hospital outcomes in non-surgical patients identified at risk for OSA

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Abstract

Background: In-hospital respiratory outcomes of non-surgical patients with undiagnosed obstructive sleep apnea (OSA), particularly those with significant comorbidities are not well defined. Undiagnosed and untreated OSA may be associated with increased cardiopulmonary morbidity.

Study objectives: Evaluate respiratory failure outcomes in patients identified as at-risk for OSA by the Berlin Questionnaire (BQ).

Methods: This was a retrospective study conducted using electronic health records at a large health system. The BQ was administered at admission to screen for OSA to medical-service patients under the age of 80 years old meeting the following health system criteria: (1) BMI greater than 30; (2) any of the following comorbid diagnoses: hypertension, heart failure, acute coronary syndrome, pulmonary hypertension, arrhythmia, cerebrovascular event/stroke, or diabetes. Patients with known OSA or undergoing surgery were excluded. Patients were classified as high-risk or low-risk for OSA based on the BQ score as follows: low-risk (0 or 1 category with a positive score on the BQ); high-risk (2 or more categories with a positive score on BQ). The

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CRediT authorship contribution statement

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Declaration of Competing Interest

None declared.

primary outcome was respiratory failure during index hospital stay defined by any of the following: orders for conventional ventilation or intubation; at least two instances of oxygen saturation less than 88% by pulse oximetry; at least two instances of respiratory rate over 30 breaths per minute; and any orders placed for non-invasive mechanical ventilation without a previous diagnosis of sleep apnea. Propensity scores were used to control for patient characteristics.

Results: Records of 15,253 patients were assessed. There were no significant differences in the composite outcome of respiratory failure by risk of OSA (high risk: 11%, low risk: 10%, $p = 0.55$). When respiratory failure was defined as need for ventilation, more patients in the low-risk group experienced invasive mechanical ventilation (high-risk: 1.8% vs. low-risk: 2.3%, $p = 0.041$). Mortality was decreased in patients at high-risk for OSA (0.86%) vs. low risk for OSA (1.53%, $p < 0.001$).

Conclusions: Further prospective studies are needed to understand the contribution of undiagnosed OSA to in-hospital respiratory outcomes.

Keywords

Sleep; Obstructive sleep apnea; Health outcomes; Respiratory failure

Introduction

Obstructive sleep apnea (OSA) is prevalent, with rates estimated to be 23% in females, and 49% in males[1,2] and may be unrecognized in up to 24% of adult patients.[3] Untreated OSA is associated with cognitive decline,[4-7] and increased cardiovascular and cerebrovascular morbidity.[8-13] In the peri-operative period, untreated OSA has been associated with respiratory failure requiring admission to the intensive care unit, longer hospital stays, and increased healthcare costs.[14] Respiratory complications included hypoxemia, hypercapnia, pneumonia, as well as need for intubation and mechanical ventilation.[15-18] While these studies found OSA was associated with hypoxemia and hypercapnic respiratory failure, the relationship between undiagnosed OSA and in-hospital respiratory complications in non-surgical populations is not well defined.[19-21] This knowledge gap is significant given the prevalence of untreated OSA in hospitalized patients.[14] To address this gap, we analyzed records from a large health system that had implemented screening for OSA using the Berlin Questionnaire at admission. The Berlin Questionnaire has been used previously to predict postoperative complications in patients at risk for OSA.[22] We evaluated in-hospital outcomes of patients identified as at increased risk for OSA. We hypothesized that patients identified as high-risk for OSA by this screening tool would have worse respiratory outcomes, specifically greater in-hospital respiratory failure and respiratory-related complications.

Methods

We performed a retrospective study using electronic medical records of a large health system. The database contained information from 19 hospitals including a quaternary-care academic hospital and a tertiary-care academic hospital, with a total of approximately 3000

beds. Data were obtained from all adult hospitalized patients in the system, from January 1, 2010 to December 31, 2015, who were screened for OSA at admission using the Berlin Questionnaire. The Berlin Questionnaire was administered to all patients admitted to general medical wards who were under 80 years old and met at least one comorbid diagnosis identified by the health system's screening protocol: BMI greater than 30, Hypertension, Congestive Heart Failure, Acute Coronary Syndrome, Pulmonary hypertension, Arrhythmia, CVA, stroke, TIA, or Diabetes. Patients undergoing surgery or those with known OSA during the index hospitalization were also excluded.

Berlin questionnaire and risk of OSA

The Berlin questionnaire is an 11-question validated tool to predict OSA. It contains questions related to snoring, cessation of breathing, daytime sleepiness, hypertension, and body mass index (BMI). The tool has reported sensitivities and specificities of up to 86% and 87% respectively to detect OSA, with higher sensitivity in patients with vascular comorbidities.[23-26] We classified patients into risk categories for OSA using previously defined criteria: low-risk (none, or one category with a positive score on the Berlin questionnaire) or high-risk (two or more categories with a positive score on the questionnaire).[27] For this analysis, we only considered the index hospitalization when the questionnaire was first administered.

Outcomes

We queried the medical record system to obtain outcome variables. The primary outcome was respiratory failure during hospitalization. Respiratory failure was defined by any of the following: orders for mechanical ventilation or International Classification of Disease (ICD) 9 code, intubation procedure note or procedure code, tracheostomy procedure note or code; at least two instances of oxygen saturation less than 88% by pulse oximetry; at least two instances of respiratory rate over 30 breaths per minute; and/or any orders placed for non-invasive mechanical ventilation (continuous or intermittent non-invasive positive pressure ventilation) without a previous diagnosis of sleep apnea. Oxygen saturation and respiratory rate were included in the definition as they have been associated with increased risk of mechanical ventilation and failure of non-invasive ventilation.[28]

Secondary outcomes included emergency room visit within 30 days after hospital discharge, hospital readmission within 30 days, hospital length of stay (in days), in-hospital mortality, orders for pulmonary consultation, medication orders, diagnoses of encephalopathy or delirium. Other data collected included age, Body Mass Index (BMI), gender, race, smoking history, the presence of comorbid conditions including hypertension, pulmonary hypertension, diabetes, asthma, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), cerebrovascular accident (CVA), delirium, myocardial infarction, atrial fibrillation, congestive heart failure (CHF), as well as inpatient medication orders for opioids and benzodiazepines.

Statistical analysis

Categorical variables were summarized using frequencies, and continuous characteristics using mean and standard deviation. Summaries for characteristics were also calculated based

on risk of OSA (high versus low). Differences in characteristics by OSA risk status (low-risk: none, or one category with a positive score on the BQ vs. high-risk: two or more categories with a positive score), as appropriate, were tested using t-tests, Pearson's Chi-squared tests, or Fisher's exact tests. Further analyses were performed using propensity scores to control for different patient characteristics between the high- and low-risk group, based on a logistic regression that modeled the probability (propensity) of being classified as high-risk for OSA. Propensity score model of the log-odds of being classified as at high risk for OSA was fit using logistic regression. All patient characteristics were entered into propensity score model. Continuous covariates, age and BMI, were included in model as natural cubic splines with 5 and 6 knots respectively. Goodness of fit of propensity score model was tested using Supremum goodness of fit test. Propensity score matching was performed by sub-classification method using MatchIt package in R. Matching was done using 8 strata as this showed acceptable balance of propensity score distributions across the OSA risk groups. Within-stratum propensity score balance was assessed both graphically, and using Kolmogorov-Smirnov test. Covariate balance for the OSA risk groups within the 8 strata was assessed using mean differences as computed by the MatchIt package. Comparison of in hospital outcomes based on OSA risk status (high versus low), as appropriate, was performed using simple linear regression and logistic regression while adjusting for the propensity scores. Effects (mean differences or odds ratios) were estimated at the stratum-level, and then pooled using the Mantel–Haenzel method. Pooling of stratum-level estimates was performed only after showing that relationship between outcome and OSA risk status was not modified by stratum/sub-classification. Interaction effects were tested using likelihood ratio test. After showing null interaction, for each outcome, we calculated a pooled estimate along with a 95% confidence interval. Multiple testing was adjusted for using the Bonferroni method. Analysis was repeated with propensity score adjusted for the inverse probability weighting (IPW) approach. All statistical tests were carried out at the 0.05 alpha-level. Statistical analysis was performed using SAS version 9.4 and R version 3.4.2.

Results

We assessed medical records of 15,253 eligible patients. We categorized the patients into two groups based on their scoring of risk for OSA using the Berlin Questionnaire: low-risk with 0 or 1 positive category ($n = 8363$), and high-risk defined as more than 1 positive category ($n = 6890$).

Baseline characteristics of the study population are shown in Table 1. Patients in the high-risk group were significantly younger (high-risk: mean age 55 vs. low-risk: mean age 58, $p =< 0.001$), more likely to be male (high-risk: 46% vs. low-risk: 43%, $p = 0.001$), and African American (high-risk: 18% vs. low-risk: 14%, $p < 0.001$). The high-risk group was significantly more likely ($p < 0.001$) to be obese (high-risk: 57%, low-risk: 44%) or severely obese (high-risk: 18% vs. low-risk: 11%), have asthma (high-risk: 12% vs. low-risk: 10%, $p < 0.001$) and have a history of tobacco use (high-risk: 28% vs. low-risk: 27%, $p = 0.016$). Atrial fibrillation was also more common in the low-risk group (high-risk: 9.6% vs. low-risk: 12%, $p < 0.001$).

Outcomes

There were no significant differences in incidence of the composite outcome of respiratory failure between groups (high-risk: 743 (11%) vs. low-risk: 877 (10%), $p = 0.553$) (Table 2). When the analysis was limited to respiratory failure defined as orders, diagnosis codes, or procedure notes/codes for invasive or non-invasive mechanical ventilation or tracheostomy, more patients in the low-risk group received orders for invasive mechanical ventilation (high-risk: 1.8% vs. low-risk: 2.3%, $p = 0.041$). Mortality was decreased in the high-risk group (59 (0.86%) vs. low-risk: 128 (1.53%), p=<0.001), but there were no significant differences in other secondary outcomes including rates of pulmonary consultation or delirium. Disposition at discharge was significantly different between groups, with high risk for OSA associated with discharge home compared to low risk patients (high-risk: 88.9% vs. low-risk: 81.6%, $p < 0.001$).

After adjusting for patient characteristics through propensity scores, high risk for OSA was associated with longer mean hospital stays measured in days. Hospital length of stay was, on average, 0.05 (95% CI: 0.02–0.07) days longer in the high-risk group compared to low risk patients. High-risk patients also had lower odds of hospital mortality (OR: 0.69, 95% CI: 0.45–0.96). Odds of respiratory failure (OR 1.09 95% CI: 0.95–1.22), mechanical ventilation (OR 0.81 95%CI 0.63–1.03), hospital orders for non-invasive ventilation or invasive ventilation (OR 0.95 95%CI 0.82–1.11), ER visits (OR 1.0 95% CI: 0.86–1.12), and readmissions within thirty days (OR 0.98 95% CI: 0.85–1.1) were not significantly different between groups (Table 3).

Discussion

While untreated OSA is associated with increased pulmonary complications in the perioperative setting, the relationship between risk for OSA and respiratory outcomes in non-surgical patients is not well understood. We sought to fill this knowledge gap by analyzing the relationship between risk of OSA and respiratory failure in patients admitted to medical services. Using a propensity-score based statistical analysis, we found patients identified as high-risk for OSA by the Berlin Questionnaire did not differ from the low-risk group in our composite definition of respiratory failure. When analyzing respiratory failure outcomes by orders for mechanical ventilation or tracheostomy, however, patients at low-risk for OSA had statistically increased orders for invasive mechanical ventilation. In addition, the high-risk group had decreased hospital mortality, and, on average, slightly longer hospital stays compared to patients in the low-risk group. While our retrospective analysis is not able to definitively identify reasons for these findings, we hypothesize patients identified as high-risk by the BQ screening at admission received greater clinical attention.

Our findings may contribute to an understanding of a subset of the population: patients with significant cardiovascular comorbidities, at risk for OSA, and admitted for non-surgical care. In contrast with studies focusing on operative or pre-operative patients, risk of OSA and hospital outcomes in non-surgical patients are not well defined. Based on results of prior studies, we anticipated worse hospital outcomes in patients at high-risk for OSA. For example, in previous literature, patients with high-risk for OSA had longer hospital stays, and increased pulmonary and cardiovascular complications in the post-operative period.[29]

Other studies have found conflicting results in mortality, and rates of respiratory failure were higher in patients with OSA compared with those without the disorder.[30,31] In the cardiac surgery population, patients with OSA had a twofold higher risk of developing atrial fibrillation in the post-operative period and 33% higher odds of a major cardiovascular or cerebrovascular event.[32]

In contrast to these previously cited studies, high-risk for OSA in our population was associated with lower mortality. These findings may be due to closer monitoring of the patient previously identified as being at a higher risk for complications, and differences in mechanical ventilation use between low-risk and high-risk groups. If screening identified a patient at high-risk, the respiratory therapists may have communicated this information to the treating teams and given closer attention to these patients from a pulmonary hygiene perspective. Prior studies have also noted decreased mortality in obese postoperative patients.[16,33]

Our study has several important limitations due to the retrospective nature of the analysis. Firstly, given that our study was conducted utilizing an electronic database, adherence to administration of the questionnaire and its effects on clinical practice are not known. Data on opioids were limited to orders within the health record, rather than administered drugs and their indications. Granular data on implementation of the questionnaire was not collected, and whether clinicians were aware of the BQ screening results in all cases, and how this may have affected management of patients is not clear. At some sites, patients at high-risk for OSA were referred for outpatient sleep evaluation but outcomes from these referrals are not available. Furthermore, due to limitations of the database, specific indications for mechanical ventilation orders was not available for analysis. Secondly, only patients deemed at risk by prespecified criteria received screening, thereby selecting a group with significant comorbidities.

Thirdly, our institution utilized the Berlin Questionnaire for screening; it is possible that we may have found greater differences between high risk and low risk populations if a different tool, such as STOP-BANG, or diagnosis by polysomnogram had been utilized.[34,35] The Berlin Questionnaire was validated in the sleep clinic and surgical populations and its sensitivity in non-surgical patients is likely limited. Our study also excluded those with diagnosed OSA; these patients are likely highest risk for complications and may have resulted in significant differences between high and low risk outcomes. Furthermore, due to the retrospective nature of our study, we were not able to report on differences in management between patients. While Berlin Questionnaire results are displayed under the respiratory tab of the electronic medical record, we are unable to assess what percentage of providers were aware of these findings and whether they affected inpatient management or led to greater outpatient referrals for polysomnography. Our study also has notable strengths, including our focus on a non-operative population, furthering our understanding of hospital outcomes in patients without a known diagnosis of OSA, a large cohort for conducting the analysis, and utilizing real-time clinical workflow-based data.

In summary, we found nuanced association between OSA risk as predicted by the Berlin Questionnaire and respiratory complications in non-surgical patients. While patients

identified to be at low vs. high risk for OSA did not differ in overall respiratory failure events, the low-risk group had increased need for invasive mechanical ventilation, while the high-risk group had longer hospital stays, and decreased odds of hospital mortality. Further prospective studies are needed to better understand the reason for these differences in outcomes between groups in specific at-risk populations.

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Table 1

Demographics, body mass index and comorbidities of patients in the overall sample and categorized by risk status.

Characteristics	All patients *N* = 15,253	Low risk* *N* = 8363	High risk** *N* = 6890	*P*-value
Demographics				
Age in years, mean (SD)	57 (16)	58 (16)	55 (14)	<0.001
African–American, *n* (%)	2344 (15)	1137 (14)	1207 (18)	<0.001
Female, *n* (%)	8522 (56)	4772 (57)	3750 (54)	0.001
Body mass index				<0.001
Underweight (%)	119 (0.8)	106 (1.4)	13 (0.2)	
Normal (%)	1035 (7.3)	781 (10)	254 (3.9)	
Overweight (%)	3947 (28)	2612 (34)	1335 (21)	
Obese (%)	7103 (50)	3413 (44)	3690 (57)	
Severely obese (%)	2053 (14)	858 (11)	1195 (18)	
Comorbidities				
CHF (%)	1220 (8.0)	682 (8.2)	538 (7.8)	0.432
MI (%)	680 (4.5)	358 (4.3)	322 (4.7)	0.242
CVA(%)	1041 (6.8)	595 (7.1)	446 (6.5)	0.118
Dementia (%)	27 (0.2)	21 (0.3)	6 (0.1)	0.016
Diabetes mellitus (%)	2457 (16)	1306 (16)	1151 (17)	0.069
Hypertension (%)	5517 (36)	2995 (36)	2522 (37)	0.311
Pulmonary hypertension (%)	1003 (6.6)	553 (6.6)	450 (6.5)	0.840
Atrial fibrillation (%)	1643 (11)	982 (12)	661 (9.6)	<0.001
COPD (%)	2427 (16)	1348 (16)	1079 (16)	0.441
Asthma (%)	1723 (11)	868 (10)	855 (12)	<0.001
Tobacco use, including	4179 (27)	2225 (27)	1954 (28)	0.016

Data shows n (%) unless otherwise specified.

*Low-risk: none, or one category with a positive score on the Berlin questionnaire.

**High-risk: two or more categories with a positive score on the questionnaire. CHF: congestive heart failure; MI: myocardial infarction; CVA: cerebrovascular accident; COPD: chronic obstructive pulmonary disorder; SD: standard deviation.

Table 2

Respiratory, clinical, healthcare utilization and medication outcomes by berlin questionnaire risk category.

Outcomes	All patients *N* = 15,253	Low-risk *N* = 8363	High-risk *N* = 6890	*P* value
Primary outcome				
Respiratory failure, * *n* (%)	1620 (11)	877 (10)	743 (11)	0.553
Mechanical ventilation (invasive), ** *n* (%)	314 (2.1)	190 (2.3)	124 (1.8)	0.041
Non-invasive ventilation, *** *n* (%)	787 (5.2)	456 (5.5)	331 (4.8)	0.072
Secondary outcomes				
Hospital mortality, *n* (%)	187 (1.23)	128 (1.53)	59 (0.86)	<0.001
Length of stay, days (SD)	4.4 ± 4.2	4.4 ± 4.2	4.4 ± 4.2	0.967
Discharge disposition Home, *n* (%)	12,954 (84.9)	6827 (81.6)	6127 (88.9)	<0.001
Other facility, *n* (%)	2299 (5.1)	1536 (18.4)	763 (11.1)	
Pulmonary consultation, *n* (%)	520 (3.41)	293 (3.50)	227 (3.29)	0.479
Healthcare utilization				
Hospital readmission within 30 days, *n* (%)	1590 (10.4)	900 (10.8)	690 (10.0)	0.133
ER Visit within 30 days post-discharge, *n* (%)	1513 (9.92)	833 (9.96)	680 (9.87)	0.851
Other outcomes				
Delirium, *n* (%)	1576 (10)	888 (11)	688 (10)	0.201
Medications				
Opioid order, *n* (%)	7345 (48)	3831 (46)	3514 (51)	<0.001
Benzodiazepine order, *n* (%)	125 (0.8)	63 (0.8)	62 (0.9)	0.318

*Defined as presence of any of the following: orders or procedure codes or notes for mechanical ventilation, intubation, or tracheostomy; at least two recorded oxygen saturations less than 88%; at least two recorded respiratory rates over 30 breaths per minute; any orders placed for non-invasive positive pressure ventilation in the absence of known obstructive sleep apnea.

**Defined as presence of any of the following: orders or procedure codes or notes for mechanical ventilation, intubation, or tracheostomy.

***Defined as presence of any of the following: any orders placed for non-invasive positive pressure ventilation in the absence of known obstructive sleep apnea. Low risk: 0 or 1 category with a positive score on the BQ. High-risk: 2 or more categories with a positive score on BQ.

Table 3

Propensity score analysis results of outcomes in high risk vs. low risk for OSA.

Outcome	Odds ratio (95% CI)
Respiratory failure	1.09 (0.95–1.22)
Invasive mechanical ventilation	0.81 (0.63–1.03)
Non-invasive mechanical ventilation	0.95 (0.82–1.11)
In-hospital mortality	0.69 (0.45–0.96)
30-day hospital readmission	0.98 (0.85–1.11)
30-day emergency department visits	1.0 (0.86–1.12)