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Obstructive sleep apnea and acute respiratory failure: An analysis of mortality risk in patients with pneumonia requiring invasive mechanical ventilation ☆

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ABSTRACT

Purpose: Although obstructive sleep apnea (OSA) is common and pneumonia is a frequent cause of acute respiratory failure requiring admission to the intensive care unit, little is known about the effect of OSA on this patient population. This study examined outcomes associated with OSA in patients with pneumonia requiring invasive mechanical ventilation.
Materials and methods: The Nationwide Inpatient Sample was investigated for discharges with a primary diagnosis of pneumonia requiring invasive mechanical ventilation between 2009 and 2011. Persons aged 18 to 75 years with OSA were compared with patients without OSA. Outcomes included in-hospital mortality and nonroutine discharges.
Results: Among 74032 hospitalizations, 13.8% (10227) were obese, and 10.3% (7610) had OSA. Obstructive sleep apnea patients had decreased in-hospital mortality (17.0% vs 25.8%; $P < .01$) and nonroutine discharge (74.4% vs 79.4%; $P < .01$) when compared with non-OSA patients. In adjusted logistic models, OSA was associated with a 27% decreased risk of in-hospital mortality (odds ratio, 0.73; 95% confidence interval, 0.68-0.79; $P < .01$) and a 21% decreased risk of nonroutine discharge (odds ratio, 0.79; 95% confidence interval, 0.74-0.84; $P < .01$).
Conclusions: In mechanically ventilated patients with pneumonia, OSA was associated decreased in-hospital mortality and nonroutine discharge. It is possible that differences in treatment pattern may partially explain improved survival.

1. Introduction

Obstructive sleep apnea (OSA) has been increasingly recognized as a significant comorbidity in critically ill patients. Persons with untreated OSA are at increased risk for metabolic dysfunction [1], pulmonary hypertension [2], arrhythmias [3], and cardiovascular disease [4]. Currently, there are limited data on the effects of OSA on mortality related to pulmonary disease [5,6].

Pneumonia is one of the most common infectious diseases and a significant cause of mortality [7,8]. Up to 20% of hospitalized patients diagnosed with pneumonia are transferred to the intensive care unit for supportive treatment with invasive mechanical ventilation (IMV) [8,9]. Invasive mechanical ventilation itself is associated with several complications and comorbidities, including ventilator-associated pneumonia [10], increased mortality [11], and prolonged duration of hospitalization resulting in substantially increased health care costs [12]. Early tracheostomy may shorten time on IMV and hospital length of stay (LOS) [13], but its impact on mortality in critically ill patients is under constant investigation [13-16].

To our knowledge, there are no studies that have examined mortality risk in persons with OSA who present with pneumonia and acute respiratory failure requiring invasive ventilator support. The aim of the study was to assess the impact of OSA on outcomes of critically ill patients requiring IMV. Our primary outcome measures are in-hospital mortality and patient disposition at the time of discharge. Secondary outcomes included rate of tracheostomy, hospital LOS, and total monetary charges of hospitalization.

☆ Drs Jean, Gibson, Jean, and Ochieng were involved in the conception, hypothesis delineation, and design of the study. Dr Raymond A Jean was involved in the acquisition of the data, the analysis, and interpretation of such information. Dr Charlisa D Gibson drafted the submitted article and revised it critically for important clinical content. Drs Jean, Gibson, Jean, and Ochieng were substantially involved in its revision before submission. Dr Raymonde E Jean had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The authors report no funding sources and no financial conflicts of interest.

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2. Materials and methods

2.1. Data selection

The Nationwide Inpatient Sample (NIS) database over the years of 2009 to 2011 was used as the data source for this study. Developed by the Agency for Healthcare Research and Quality (AHRQ), the NIS contains a nationally representative 20% stratified sample of discharges throughout the United States [17]. The NIS records up to 25 diagnoses and up to 15 procedures for each hospitalization using *International Classification of Disease*, *Ninth Version* (*ICD-9*) codes. For procedural codes, NIS also provides the hospital day on which the procedure took place. The study population was selected based upon all discharges of patients aged 18 to 75 years, with a primary diagnosis of pneumonia (*ICD-9*, 480-486) as well as an *ICD-9* procedural code for IMV (*ICD-9 Clinical Modification*, 90.64, 96.7, 96.70, 96.71, and 96.72). Next, records were queried for secondary diagnosis codes for OSA (*ICD-9*, 327.23, 780.53, and 780.57), obesity (*ICD-9*, 278.8, 278.1, 278.00, and 278.01) and atrial fibrillation (AF) (*ICD-9*, 427.31). Procedural codes were queried for the incidence of tracheostomies (*ICD-9 Clinical Modification*, 31.1 and 31.2). Weighted estimates were used in calculations for the final study cohorts, and, therefore, the results can be considered to be nationally representative.

To further enrich our investigation, we sought to identify several complications and conditions of interest associated with critically ill hospitalizations. Because of the diversity of *ICD-9* procedure codes, the AHRQ created the Clinical Classification Software (CCS) series of numerical codes that can identify categories of diagnoses. Healthcare Cost and Utilization Project CCS codes were investigated for secondary diagnoses of these other conditions, including septicemia (CCS 2), shock (CCS 249), and lung cancer (CCS 19 and 20).

Primary outcomes of interest were the impact of OSA upon in-hospital mortality and discharge status. *Discharge* was defined as "routine" if discharged to home or self-care and as "nonroutine" if otherwise. Nonroutine discharges included in-hospital death as well as discharge to a short-term hospital, skilled nursing facility, intermediate care facility, home health care, or against medical advice [18]. Secondary outcomes were LOS, hospital charges, rates of tracheostomy, time to initiation of mechanical ventilation, and time to tracheostomy. Cases were excluded from analysis if there was a secondary diagnosis of intracranial injury (*ICD-9*, 850-854) or poisoning (*ICD-9*, 960-979). Finally, patients in whom IMV was initiated before admission were also excluded from analysis.

Patient information on age, sex, and race was organized into discrete categorical variables. Age was grouped into 3 groups of 18 to 40, 41 to 64, and 65 to 75 years. Race was classified according to AHRQ groupings as white, black, Hispanic, Asian or Pacific Islander, or other. Because a large percentage of discharges in the NIS are missing information about race, this was not used as a variable in any multivariate statistical analysis. To capture the impact of comorbidity in this patient population, the Deyo adaptation of the Charlson comorbidity index (CCI) score [19,20] was calculated for each discharge, based on the *ICD-9* diagnosis codes [21]. Charlson comorbidity index scores were grouped into 4 categories: none (CCI, 0), low (CCI, 1-2), moderate (CCI, 3-4), or severe (CCI, ≥ 5).

2.2. Statistical analysis

Descriptive statistics were used to identify significant differences between the OSA and non-OSA cohorts. χ^2 test was used to determine significant differences between categorical variables. Student *t* test and Mann-Whitney *U* tests were used to identify significant differences between normally distributed and nonnormally distributed continuous variables, respectively.

Next, multivariate logistic regression models were used to identify significant predictors for in-hospital mortality, nonroutine discharge, and tracheostomy. Finally, multivariate ordinary least squares linear regression models were used to calculate the impact of predictors on

Table 1
Baseline Characteristics

Category	Year							
	2009		2010		2011		Total	
n	26852	36.3%	23746	32.1%	23433	31.7%	74032	100.0%
Sex								
Male	14216	52.9%	12726	53.6%	12413	53.0%	39355	53.2%
Female	12636	47.1%	11020	46.4%	11020	47.0%	34677	46.8%
Age (y)								
Mean, SD	64.2 (16.9)		65.4 (16.4)		65.6 (16.5)		65.1 (16.7)	
18-40	3680	13.7%	2894	12.2%	2861	12.2%	9436	12.7%
41-64	13877	51.7%	12070	50.8%	11708	50.0%	37655	50.9%
65-75	9295	34.6%	8782	37.0%	8864	37.8%	26940	36.4%
Race								
White	15207	56.6%	14420	60.7%	14697	62.7%	44325	59.9%
Black	3532	13.2%	3734	15.7%	3435	14.7%	10700	14.5%
Hispanic	2176	8.1%	1893	8.0%	1980	8.4%	6049	8.2%
Asian or Pacific Islander	754	2.8%	533	2.2%	655	2.8%	1942	2.6%
Other	886	3.3%	488	2.1%	491	2.1%	1866	2.5%
Missing	4297	16.0%	2677	11.3%	2176	9.3%	9150	12.4%
Conditions of interest								
OSA	2507	9.3%	2240	9.4%	2863	12.2%	7610	10.3%
obese/morbidly obese	3445	12.8%	3077	13.0%	3705	15.8%	10227	13.8%
Shock	4787	17.8%	4294	18.1%	4115	17.6%	13196	17.8%
Septicemia	8927	33.2%	7313	30.8%	6610	28.2%	22850	30.9%
Lung cancer	1452	5.4%	1464	6.2%	1447	6.2%	4363	5.9%
AF	3969	14.8%	3840	16.2%	4473	19.1%	12283	16.6%
Charlson comorbidity								
None	4424	16.5%	3663	15.4%	3290	14.0%	11377	15.4%
Low (1, 2)	11962	44.5%	10416	43.9%	9719	41.5%	32097	43.4%
Moderate (3, 4)	6271	23.4%	5572	23.5%	6157	26.3%	18000	24.3%
Severe (5+)	4195	15.6%	4095	17.2%	4268	18.2%	12558	17.0%
Discharge status								
In-hospital death	6698	24.9%	5946	25.0%	5754	24.6%	18399	24.9%
Nonroutine discharge	20744	77.3%	18942	79.8%	18695	79.8%	58381	78.9%