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The Intersection of Sleep Apnea and Severe Mental Illness in Veterans

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Abstract

Background: Individuals with serious mental illness (SMI) have a high prevalence of risk factors for sleep apnea, but these risk factors often go unrecognized, partly due to the overlap among sleep apnea, somatic conditions, and symptoms (e.g., obesity, daytime sleepiness), leading to potential under-recognition of sleep apnea in a high-risk population.

Objective: The objective of our study was to compare sleep apnea prevalence and clinical features among Veterans with and without SMI.

Method: Data for the current analyses were drawn from an administrative dataset of 33,818 United States Military Veterans with a primary care visit in calendar year 2007. The medical record data included demographic characteristics, and medical, psychiatric, and sleep diagnoses.

Results: Veterans with SMI had a significantly higher prevalence of sleep apnea than those without SMI. Younger Veterans with SMI had a higher prevalence of sleep apnea relative to older Veterans with SMI and Veterans with SMI and sleep apnea had a greater number of medical comorbidities than Veterans with SMI and no sleep apnea.

Conclusion: In a large sample of Veterans, those with SMI were at greater risk of having comorbid sleep apnea. Furthermore, Veterans with comorbid SMI and sleep apnea were at greater risk for increased rates of comorbid medical disorders. Sleep apnea appears to be a key risk factor for increased morbidity in Veterans with an SMI diagnosis, highlighting the importance of treating sleep apnea in a challenging patient population.

Keywords

sleep disorders; schizophrenia; bipolar disorder

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INTRODUCTION

Sleep apnea is characterized by repeated pharyngeal obstruction during sleep, causing airflow cessation or reduction and resulting in fragmented sleep, hypoxia, and sympathetic hyperarousal. This constellation of physiological processes often leads to immediate and long-term health consequences, such as reduced daytime vigilance, sleepiness and fatigue, depressed mood, and increased cardiovascular and cerebrovascular morbidity and mortality.[1,2] Sleep apnea affects approximately 6% of the general population,[3] but prevalence estimates are significantly higher in certain clinical populations, such as patients with cardiovascular disease, hypertension, and smokers, suggesting a common underlying pathophysiology with specific conditions.[4]

These disorders are also common among individuals with serious mental illness (SMI), such as bipolar disorder, schizophrenia, and schizoaffective disorder. Assessing rates of comorbidity and associated characteristics in patients with SMI and sleep apnea is a priority, given the considerable overlap between symptoms of SMI and sleep apnea (e.g., daytime sleepiness, psychomotor slowing, and depressed mood) and the high prevalence of risk factors for sleep apnea in SMI patients (e.g., obesity, tobacco use, cardiovascular disease, diabetes).[5,6,7] However, the reported prevalence of sleep apnea and SMI varies greatly, depending on the definition of SMI adopted and the treatment setting. High rates of sleep apnea (46.2 % of men and 57.1% of women) have been described in patients with schizophrenia referred for an inpatient sleep consult,[8] but these rates reflect a high *a priori* suspicion of apnea. In an outpatient setting, 58% of individuals with schizophrenia or schizoaffective disorder were at high-risk of obstructive sleep apnea (OSA) per the STOP measure and 15% had a diagnosis of OSA.[9] On the other hand, a lower prevalence of sleep apnea in individuals with SMI than in non-SMI individuals has been reported in a large cohort of US Military Veterans (4.5%).[10]

A better understanding of the relationship between SMI and sleep apnea would inform treatment planning and provide novel treatment targets to improve medical and functional outcomes in individuals with SMI. Our study sought to address some of these gaps in the SMI and sleep apnea literature by assessing the prevalence of sleep apnea in a large cohort of Veterans. Specifically, we compared the prevalence of sleep apnea in Veterans with and without SMI, determined if Veterans with SMI had a greater likelihood of being diagnosed with sleep apnea than those without SMI, and explored clinical correlates of sleep apnea in Veterans with SMI.

METHOD

The current study is a secondary analysis of data from an administrative dataset of 33,818 Veterans who attended a primary care visit at the Department of Veterans Affairs (VA) Pittsburgh Healthcare System in calendar year 2007. This study was approved by the VA Pittsburgh Healthcare System's Institutional Review Board. Medical record data was pulled for those Veterans in the 2007 cohort retrospectively to 2001, or earliest records available after 2001, and prospectively until 2011, or the last date of care before 2011. The medical record data included demographics (e.g., age, gender, race); service information

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(e.g., combat exposure); and medical, psychiatric, and sleep diagnoses (e.g., insomnia, sleep apnea).

In our sample, SMI was defined using the International Classification of Diseases (ICD-9) codes for diagnoses of schizophrenia, schizoaffective disorder, and/or bipolar disorder. For the current analysis, we required ≥2 lifetime diagnoses to be present in the medical record, consistent with methods used in other studies of VA administrative data.[11,12] A diagnosis of sleep apnea was defined by the presence of ≥2 lifetime diagnoses of a breathing-related sleep disorder (ICD-9 codes: 327.21, 327.23, 327.27, 780.57) in the medical record. Medical comorbidities were defined based on ICD-9 codes organized by organ systems and identified as chronic or acute. At least 2 instances of a chronic ICD-9 code within an organ system were required for an organ system to be considered impacted by chronic disease. This coding system was developed at the study site and used similar methods as the Chronic Condition Indicator, developed as part of the Healthcare Cost and Utilization Project by the Agency for Healthcare Research and Quality.[13] With this medical comorbidity data, a dichotomous (yes/no) variable was derived to indicate if an individual had a health condition commonly associated with sleep apnea (medical risk for sleep apnea). Codes of 1 were assigned to individuals with at least 1 of the following systems impacted by a chronic condition: cardiac, hypertension, vascular, respiratory, upper gastrointestinal, and endocrine-metabolic. Codes of 0 were assigned to individuals who had no chronic conditions impacting the above-listed systems.

Analysis Plan

Descriptive statistics were calculated as means and standard deviations for continuous measures, and as frequencies and percentages for categorical measures. Independent samples *t*-tests and chi-square analyses were used to determine differences in demographic and clinical characteristics in Veterans with and without SMI. Binary logistic regression analysis was used to determine whether Veterans with SMI had an increased likelihood of being diagnosed with sleep apnea. Variables were included in the model using the enter method. Covariates (variables with significant bivariate associations with sleep apnea diagnosis) and SMI diagnosis were entered simultaneously. Presence or absence of sleep apnea was the dependent variable.

RESULTS

Demographic and clinical characteristics of our sample are reported in Table 1. In the total sample, 6.2% of Veterans had SMI and 8.8% of Veterans had sleep apnea. Veterans with SMI were significantly younger than those without SMI and there were significantly more female Veterans with SMI, proportionally, than female Veterans without SMI. Veterans with SMI also had a notably higher rate of chronic medical comorbidities, despite being younger, as well as a higher rate of psychiatric comorbidities. Insomnia disorder was diagnosed with a similar prevalence among Veterans with and without SMI. The prevalence of a sleep apnea diagnosis was significantly higher among Veterans with SMI compared to Veterans without SMI. On average, Veterans with both SMI and sleep apnea had a significantly higher number of medical comorbidities (M =10.19, SD = 2.32) than those with SMI but no sleep apnea (M

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= 8.16, SD = 2.96, $p < 0.001$, Cohen's $d = 0.76$, Hedge's $g = 0.70$) as well as those with sleep apnea but no SMI ($M = 9.45$, SD = 2.46, Cohen's $d = 0.31$, Hedge's $g = 0.30$). Table 2 shows the prevalence of sleep apnea across age groups in individuals with and without SMI. Sleep apnea is highly prevalent among all age deciles among the SMI group, but shows an inverse-U shaped distribution in the non-SMI group, consistent with that reported for the general population.[14]

Age, sex, race, marital status, medical risk, number of comorbid psychiatric disorders, and SMI diagnosis were all significantly associated with a sleep apnea diagnosis at the bivariate level (data not shown). To promote a parsimonious model and because a very small proportion (<5%) of the sample had no medical risk for sleep apnea, this variable was excluded from the logistic regression analysis. All other significant variables were included in the final logistic regression model. Because age was not linearly associated with sleep apnea, we converted age into a categorical variable (<60, ≥60) based on cut points in the sample age distribution.

The overall logistic regression model was statistically significant ($p < 0.001$). Age, sex, race, marital status, psychiatric comorbidities, and SMI diagnosis were significantly associated with sleep apnea diagnosis, both individually and in combination (all p values < 0.05; see Table 3). Veterans with SMI were 26% more likely to have diagnosed sleep apnea. Also, older age was associated with a lower likelihood of having sleep apnea. Veterans who identified as male, Black, and married were more likely to have sleep apnea as were Veterans with a greater number of non-SMI psychiatric comorbidities.

DISCUSSION

Comparable to what has been reported by most recent general population epidemiology studies, our study showed a high prevalence of sleep apnea (8.8%) in a large cohort of Veterans[15] and the prevalence was higher among Veterans with SMI (13.7%), consistent with findings by Alam et al.,[16] and Annamalai et al.,[9] although in a larger sample. Our findings also show that, of Veterans with sleep apnea, those with SMI are younger than those without SMI. Earlier onset of cardiovascular disease and other chronic conditions that lead to premature mortality in individuals with SMI has previously been reported.[6,17] However, this is, to the best of our knowledge, the first report to show that (1) individuals with SMI have a higher prevalence of sleep apnea at a younger age than those without SMI, and (2) that individuals with SMI and sleep apnea have higher rates of medical and psychiatric comorbidities than those with SMI and no sleep apnea.

Ancoli-Israel et al.,[18] and Winlkeman[8] have previously reported high rates of sleep apnea in patients with schizophrenia. However, they reported on small samples of older patients[18] and hospitalized patients.[8] Sharafkanen et al.,[10] reported on a national sample of Veterans, although they found a surprisingly low prevalence of sleep apnea among patients diagnosed with schizophrenia and schizoaffective disorder. The discrepancy between these and our findings could be explained in several ways. One possibility is that clinicians have become more willing to diagnose sleep apnea during the time our study data were collected (2001–2011) compared to the time that data for the Sharafkanen et al. study were collected (1998

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– 2001). In addition, the use of portable home testing for diagnosing sleep apnea may have helped to circumvent the problem of limited access to sleep laboratories.[19,20] In other words, our cohort may have experienced more widespread access to sleep apnea assessment and, hence, may have benefitted from increased efforts to identify sleep apnea, compared to patients seeking care in the late 1990s and early 2000s. In fact, rates of sleep apnea reported for the general population in the late 1990s (6 – 7%) were also lower than what we found in our Veteran cohort without SMI (8.4%).

Of note, both the values reported by Sharafkanen et al.[10] and those from the current study reflect the rates at which OSA was recognized and diagnosed and likely still represents an underestimate of the true prevalence. Several steps are required for the recognition, diagnosis, and treatment of a condition, and factors such as access to care, finances, other medical comorbidities, may differentially affect individuals with SMI. Some of our previous work and work conducted by colleagues would in fact point in that direction. For example, a study conducted in an academic primary care clinic setting found that, of 100 adult patients with schizophrenia or schizoaffective disorder, 69% were at high-risk for sleep apnea *via* the STOP-Bang screening questionnaire, but only 16% had been previously diagnosed with sleep apnea, per objective testing, and only 6% were currently using positive airway pressure therapy.[16] Similarly, in a study of 72 individuals with bipolar I disorder and schizoaffective disorder, 54.1% were deemed at high-risk for sleep apnea based on the Berlin Questionnaire, but none of them had been previously diagnosed,[7] suggesting that the very same cluster of symptoms that would prompt a sleep evaluation in the general population, is not readily recognized in patients with SMI. Importantly, sleep apnea and SMI can share clinical features, which may mask sleep apnea. For example, daytime sleepiness[18] and poor cognitive performance due to sleep apnea[21,22] may be attributed to negative symptoms of SMI, such as apathy and cognitive slowing, or medication side effects, even if sleep apnea is present. A number of additional factors related to patients, providers, and systems may also be responsible for fewer sleep apnea diagnoses in patients with SMI.[23] Patient factors can include amotivation, fearfulness of novel environments, social instability, poverty, unemployment, and incarceration. Provider factors include discomfort with patients with severe psychiatric problems, poor coordination of care, and misperception about the ability of individuals with SMI to adhere to care recommendations. System factors include disparities in health care access, utilization, and provision of sleep apnea treatments, limited funding, and fragmentation and discontinuity of care between general health, mental health, and sleep-related care.[18] Importantly, OSA is independently associated with increased morbidity and mortality in the general population[24] and in light of the widening mortality gap between individuals with SMI and the general population,[25] novel targets for prevention and intervention of sleep apnea need to be identified. Appropriate detection, diagnosis, and management of sleep apnea may help to reduce morbidity and mortality risk in individuals with SMI. Furthermore, targeting overlapping symptoms and behaviors of SMI and sleep apnea, such as sedentary behaviors and cognitive slowing can potentially improve use of positive airway pressure therapy and result in better apnea outcomes.

Some key limitations of our study include the cross-sectional and naturalistic nature of the data and the fact that a large Veteran cohort may not necessarily be generalizable to a community sample. Another limitation of our study is that body mass index (BMI) was not

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a variable collected from the medical records as a part of this dataset. Obesity (BMI ≥30) is one of the main risk factors for sleep apnea and the rising prevalence of obesity is likely partially responsible for the increased prevalence of sleep apnea in the past 3 decades.[26,27] Obesity is also a known problem for SMI patients[28] and it may be one of the contributors to the higher prevalence of sleep apnea at a younger age. It is worth noting that obesity rates in the VA population are up to 49% in middle age men, over 50% in women, and up to 72% among Veterans diagnosed with sleep apnea.[29] Thus, it seems unlikely to be an exclusive characteristic of the SMI group.

However, patients with SMI may be more likely to experience rapid weight gain, and subsequent increase in BMI, due to psychotropic medications and higher rates of sedentary behaviors. The higher rate of OSA could represent a byproduct of recent and rapid weight gain, which is more likely to happen in the SMI population.

Our results are important in several ways. First, this is one of the few large sample size reports on the prevalence of sleep apnea in individuals with SMI. Although it is possible that this still reflects an under-estimate of the true prevalence, it highlights how the overlap of SMI and sleep apnea constitutes a double adversity and increases the likelihood of other medical and psychiatric comorbidities. At the same time, sleep apnea is a treatable condition and treating sleep apnea may result in improvements in quality of life and cardiovascular risks in individuals with SMI.[30] An enhanced recognition of the overlap between OSA and SMI would ideally foster increased attention and more vigilant screening and referral from mental health providers to primary care and sleep providers for diagnostic workup. The wider availability of home sleep testing and technology for remote positive airway pressure adherence monitoring could be leveraged to create novel integrated care models that could allow easier access to care for individuals with SMI.

In summary, our data show high prevalence of sleep apnea in Veterans with SMI, even in younger groups. The higher prevalence of sleep apnea at an earlier age could be one of the pathways to high cardiovascular morbidity and premature mortality in Veterans with SMI and may offer a new target intervention for risk reduction. Considering the elevated rates, future research focused on the potential synergistic effects of sleep apnea and SMI is needed, as is research on the role of treating OSA in individuals with SMI and the impact on functional outcomes, quality of life, morbidity, and mortality. Additionally, epidemiology and observational studies are needed that can identify valuable clinical correlates and social determinants of health in this vulnerable population to develop promising targets for prevention and intervention.

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TABLE 1.

Descriptive Statistics and Bivariate Analyses of Demographic and Clinical Characteristics of Veterans With and Without SMI (N = 33,818)

	SMI diagnosis				Analysis	
	No (*n* = 31715; 93.8%)		Yes (*n* = 2103; 6.2%)		Test statistic	*p*-value
Age, M ± SD	66.5 ± 13.5		55.6 ± 11.9		$T(2476.4) = 40.2$	<0.001
Age group					$\chi^2(6) = 1527.9$	<0.001
18–29 y	517	(1.6%)	45	(2.1%)		
30–39 y	756	(2.4%)	130	(6.2%)		
40–49 y	1889	(6.0%)	400	(19.0%)		
50–59 y	6420	(20.2%)	862	(41.0%)		
60–69 y	7696	(24.3%)	407	(19.4%)		
70–79 y	8413	(26.5%)	182	(8.7%)		
≥80 y	6024	(19.0%)	77	(3.7%)		
Sex					$\chi^2(1) = 170.4$	<0.001
Male	30,846	(97.3%)	1939	(92.2%)		
Female	869	(2.7%)	164	(7.8%)		
Race					$\chi^2(1) = 146.5$	<0.001
Black	3214	(10.1%)	390	(18.5%)		
Non-Black	28,501	(89.9%)	1713	(81.5%)		
Marital status					$\chi^2(1) = 846.5$	<0.001
Married	17,970	(56.7%)	507	(24.1%)		
Single/Previously married/Never married	13,745	(43.3%)	1596	(75.9%)		
Sleep apnea diagnosis					$\chi^2(1) = 69.8$	<0.001
Yes	2672	(8.4%)	289	(13.7%)		
No	29,043	(91.6%)	1814	(86.3%)		
Medical risk for sleep apnea					$\chi^2(1) = 7.54$	0.01
Yes	30,321	(95.6%)	2037	(96.9%)		
No	1394	(4.4%)	66	(3.1%)		
Number of psychiatric comorbidities (not SMI)					$\chi^2(3) = 1213.60$	<0.001
0	25,353	(79.9%)	1056	(50.2%)		
1	4561	(14.4%)	605	(28.8%)		

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	SMI diagnosis				Analysis	
	No (*n* = 31715; 93.8%)		**Yes (*n* = 2103; 6.2%)**		**Test statistic**	***p*-value**
2	1388	(4.4%)	311	(14.8%)		
≥3	413	(1.3%)	131	(6.2%)		

SMI = serious mental illness.

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TABLE 2.

Prevalence of Sleep Apnea Within Age Groups of Individuals With SMI and Without SMI

	−SMI, +Sleep Apnea *n* (%)	**+SMI, +Sleep Apnea *n* (%)**
18–29 y	26 (5.0%)	4 (8.9%)
30–39 y	79 (10.4%)	17 (13.1%)
40–49 y	250 (13.2%)	69 (17.3%)
50–59 y	874 (13.6%)	114 (13.2%)
60–69 y	843 (11.0%)	59 (14.5%)
70–79 y	441 (5.2%)	22 (12.1%)
≥80 y	159 (2.6%)	4 (5.2%)

SMI = serious mental illness.

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TABLE 3.

Logistic Regression Model With Sleep Apnea Regressed on Covariates and SMI

		Odds ratio and 95% Confidence intervals			
	B(SE)	**Odds ratio**	**Lower**	**Upper**	***p*-value**
Included					
Constant	−3.07 (0.13)				
Age (≥60)	−0.56 (0.04)	0.57	0.53	0.62	<0.001
Sex (Male)	0.57 (0.13)	1.77	1.38	2.27	<0.001
Race (Black)	0.18 (0.06)	1.19	1.06	1.34	0.003
Marital status (married)	0.42 (0.04)	1.53	1.41	1.65	<0.001
Number of psychiatric comorbidities (not SMI)					<0.001
1	0.72 (0.05)	2.06	1.87	2.26	<0.001
2	0.86 (0.07)	2.35	2.04	2.71	<0.001
≥3	1.08 (0.11)	2.94	2.36	3.66	<0.001
SMI diagnosis	0.23 (0.07)	1.26	1.10	1.45	0.001

Note: $\chi^2(8) = 804.64$, $p < 0.001$; $R^2 = 0.02$ (Cox & Snell), $R^2 = 0.05$ (Nagelkerke).