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Research Article

Do Cardiac Patients with Obstructive Sleep Apnea Have a Higher Prevalence of Atrial Fibrillation?

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Abstract

Study Objectives: Obstructive sleep apnea (OSA) is a growing health concern amongst all populations. The relationship between sleep apnea and heart health is also of particular interest in clinical populations. Thus, the aim of this study was to examine if OSA in cardiac patients leads to a higher prevalence of atrial fibrillation (AF).

Methods: Data was retrospectively analyzed from the Sleep Heart Health Study (SHHS). Patients with cardiovascular disease were divided into an OSA group or a control group who did not have OSA. Demographic and descriptive statistics were completed on all subjects and a chi-square analysis was used to determine prevalence among the groups. The alpha level was set at < 0.05 for significance.

Results: No statistically significant difference ($p = .120$) was seen in atrial fibrillation prevalence for cardiac patients with OSA ($n = 271$) compared to cardiac patients without OSA ($n = 34$).

Conclusion: Cardiac patients with OSA displayed a higher AF prevalence rate of 17.8% when compared with cardiac patients without OSA who had an AF prevalence rate of 13.8%. This difference was not calculated to be statistically significant although limitations unique to this study should be considered when interpreting data.

Keywords: *Obstructive Sleep Apnea; Atrial Fibrillation; Cardiac Patients; Prevalence*

Abbreviations

AF: Atrial Fibrillation, an irregular heart rhythm marked by various time intervals between heart beats rather than consistent rhythmic time intervals between cardiac cycles [18]; AHI: Apnea Hypopnea Index, the gold standard measurement for diagnosing sleep apnea. Apnea hypopnea index measures the average number apneas and hypopneas within a 1-hour time span during sleep. Three severity levels of sleep apnea exist, all of which are diagnosed using the apnea hypopnea index [1,2,21]; BMI: Body Mass Index, currently still the gold standard for defining health from a body weight standpoint. Body mass index compares a person's weight relative to their height, without considering any other characteristics [19]; OSA: Obstructive Sleep Apnea, a disordered sleep condition marked by periods of reduced breathing and cessation of sleep. Obstructive sleep apnea may involve cessation of breathing that results in reduced tissue oxygenation

levels [21]; SHHS: Sleep Heart Health Study, a large multi-cohort study involving adults over the age of 40 which was mainly focused on disordered sleeping patterns and the implications of those disorders on cardiovascular specific outcomes. The study had two cycles, the first from 1995 to 1998 and the second lasted from 2001 to 2003, tracking of cardiovascular outcomes finished in 2010 [22].

Brief Summary

Current knowledge/study rational: Patients with cardiovascular disease typically are diagnosed with other comorbidities such as obesity or sleep apnea. Both atrial fibrillation and sleep apnea are seen in cardiac patients independent of other risk factors, however, the prevalence of atrial fibrillation in cardiac patients with sleep apnea is not comprehensive.

Study impact: Cardiac patients who are diagnosed with obstructive sleep apnea will want to pay careful attention to the possible impacts of sleep apnea as it pertains to cardiac health.

Introduction

Cardiovascular disease remains the leading cause of the death worldwide and is highly associated with other comorbidities particularly atrial fibrillation (AF) and obstructive sleep apnea (OSA) [1]. Patients with AF are at a five-fold increased risk of stroke compared to patients without AF, thus preventative methods for the development of AF are crucial [5,13,27]. Both AF and OSA are common conditions amongst patients with cardiovascular diseases [5]. Recently authors have attempted to examine the prevalence of AF in the general population with estimates at roughly 1 - 2% of the general population [24]. Furthermore, researchers have observed prevalence rates of AF as high as 7.6% in patients with OSA [15].

The prevalence of AF in patients with OSA has not been extensively researched and furthermore the prevalence of AF in cardiac patients with OSA is further limited. The prevalence of OSA in patients with AF has been examined and some rates as high as 82.7% - 85% have been noted [1,25]. When prevalence is examined in a reverse manner, the rates of AF in patients with OSA is drastically lower, closer to 10.44% [15].

Some mechanisms have been postulated to explain a physiological connection between OSA and AF. One major mechanism is that drops in blood and tissue oxygen saturation during sleep can trigger alterations in the electrical aspect of the cardiovascular system [16,18]. Another hypothesis is that changes in both intra-thoracic pressure and Vagus nerve stimulation may also lead to mechanical and electrical alterations of heart rate [23]. With these considerations, the aim of this study was to establish the prevalence of AF in cardiac patients with OSA and if that prevalence is higher than those without OSA.

Methods

Study population and sample selection

The authors of this study conducted a retrospective analysis of conditionally defined eligible cardiovascular rehabilitation patients, selected from the Sleep Heart Health Study (SHSS) existing database. Access was first granted by the owners of the original dataset. Patients selected all had one or more of the following conditions: myocardial infarction, previous valve repair or replacement, coronary artery bypass graft, stable angina, congestive heart failure, previous stent placement, or other confirmed cardiovascular disease. Selected participants with diagnosed sick-sinus syndrome, aortic valve disorders, or post-operative atrial fibrillation were disqualified and thus excluded from the current study. Males and females were eligible for inclusion towards the final analysis of the study.

After applying inclusion and exclusion criteria to the original SHHS dataset which included over 5800 participants, a sample population (N = 2740) was determined, with eligible participants only for the study. The data was stored on an encrypted hard drive. Four groups

were created which participants were divided into. Groups consisted of obstructive sleep apnea without atrial fibrillation, obstructive sleep apnea with atrial fibrillation, atrial fibrillation without obstructive sleep apnea, and a control group which contained participants with neither diagnosis.

Data collection

Authorization for the use of data was granted by the SHHS prior to any data being utilized. Once access was granted, the original dataset was downloaded in spreadsheet format. Over 1000 variables are included in the original dataset from the SHSS, however the authors of this study only used variables that were necessary to the overall outcome of this study. Eligible subjects were identified first, and non-necessary variables were removed. Data points include age, gender, height, weight, body mass index (BMI), blood pressure, OSA diagnosis (including severity), AF diagnosis, history of stroke, and other pertinent medical diagnoses.

Atrial fibrillation and obstructive sleep apnea diagnoses

Participants whose medical diagnosis of atrial fibrillation, as per methods outlined in the Sleep Heart Health Study, were cross-referenced with available 12-lead electrocardiograms from the SHHS database [22]. Those who had an atrial fibrillation diagnosis that was attributable to a known heart valve problem were excluded.

Obstructive sleep apnea was defined as either a "yes" or "no", indicated on the SHHS database as well as cross-referenced to the apnea-hypopnea index (AHI) of each participant. Any participant with an AHI above 5 is considered to have OSA [1,2,21]. Detailed descriptions of the design and methods of the SHHS have been previously described [22].

Data analysis

For data analysis, IBM SPSS© statistical software was used. Participants were divided into four groups: (a) OSA without AF, (b) OSA with AF, (c) AF without OSA, and (d) a control group. Descriptive statistics were included as well as inferential statistics to show a positive and linear correlation of the independent variables (OSA and AF diagnoses). A chi-square analysis was used to examine the relationship between OSA diagnosis and prevalence of atrial fibrillation. An alpha level of .05 was used to indicate statistical significance in this study.

Results

Population demographics

The data is expressed as total counts (N) with mean (M) and standard deviations. The total number of eligible participants (N = 2740) was subdivided into three health descriptive categories, (a) OSA (n = 2088), (b) AF (n = 34), and (c) OSA and AF (n = 271), and one control group category (n = 347). The mean severity of OSA, using apnea hypopnea index as a measurement, was found to be moderate (19.64 ± 16.71). The average BMI indicated overweight (28.74 ± 5.34), while the average age was 66.64 ± 10.49. Detailed study population characteristics with chi-square analyses for significant differences across groups are seen in table 2.

	N	Mean	Standard Deviation
Systolic BP	2702	134.17	20.19
Age	2740	66.64	10.49
Body Mass Index	2723	28.74	5.34
Body Mass Index New	2696	27.94	4.94
Weight (KG)	2702	79.67	16.40
Waist (CM)	2619	99.09	13.59
Height (CM)	2724	167.25	9.57
Ahi	2740	19.64	16.71

Table 1: *Descriptive statistics.*

BP: Blood Pressure; KG: Kilograms, CM: Centimeters, AHI: Apnea Hypopnea Index.

		Experimental Groups		
	Control	OSA	AF	OSA_AF
	(n = 347)	(n = 2088)	(n = 34)	(n = 271)
Gender % (n)				
Male, n (%)	89a (25.60%)	1131b (54.20%)	13a,b (38.20%)	139b (51.3%)
Female, n (%)	258a (74.40%)	957b (45.80%)	21a,b (61.80%)	132b (48.70%)
Missing	0	0	0	0
Total	347 (100%)	2088 (100%)	34 (100%)	271 (100%)
Race: % (n)				
White, n (%)	258a (74.40%)	1793b (85.90%)	24a (70.60%)	235b (86.70%)
Black, n (%)	63a,c (18.20%)	202b (9.70%)	10a (24.90%)	35b,c (12.90%)
Other, n (%)	26a (7.50%)	93b (4.50%)	1 (0%)	1c (0.40%)
Missing	0	0	0	0
Total, n (%)	347 (100%)	2088 (100%)	34 (100%)	271 (100%)
Stroke				
No, n (%)	317a (96.10%)	1927a (94.50%)	31a,b (91.20%)	240b (90.90%)
Yes, n (%)	13a (3.90%)	113a (5.50%)	3a,b (8.80%)	24b (9.10%)
Missing	17	48	0	7
Total, n (%)	330 (100%)	2040 (100%)	34 (100%)	264 (100%)
Age				
Mean (SD)	62.00a (11.17)	66.00b (10)	73.00c (7)	74.00c (8)
Smoking Status				
Never, n (%)	171a (50.00%)	970a,b (46.60%)	11b (32.40%)	118a,b (43.70%
Current, n (%)	40a (11.70%)	158b (7.60%)	3a,b (8.80%)	14b (5.2%)
Former, n (%)	131a (38.30%)	952b (45.80%)	20b (58.80%	138b (51.10%)
Missing	5	8	0	1
Total, n (%)	342 (100%)	2080 (100%)	34 (100%)	270 (100%)
Hypertension				
No, n (%)	38a (11.00%)	205a,b (9.80%)	2a,b (5.90%)	17b (6.30%)
Yes, n (%)	309a (89.00%)	1883a,b (90.20%)	32a,b (94.10%)	254b (93.70%)
Missing	0	0	0	0
Total, n (%)	347 (100%)	2088 (100%)	34 (100%)	271 (100%)
Ethnicity				
Hisp./Lat., n (%)	16a (4.60%)	67a (3.20%)	0[1]	1b (0.40%)
Non Hisp., n (%)	331a (95.40%)	2021a (96.80%)	34[1] (100%)	270b (99.60%)
Missing	0	0	0	0
Total, n (%)	347 (100%)	2088 (100%)	34 (100%)	271 (100%)
Body Mass Index				
Mean (SD)	26.50a∓ (4.4)	29.10b (5.50	27.20a,c (3.7)	28.70b,c (4.9)

Body Mass Index New Formula				
Mean (SD)	28.10a (5.3)	28.00a (4.9)	28.30a,b (5.8)	27.00b (4.4)

Table 2: *Study population characteristics.*

OSA = Obstructive Sleep Apnea; AF = Atrial Fibrillation; OSA_AF = Obstructive Sleep Apnea and Atrial Fibrillation; SD = Standard Deviation

Note: Values in the same row and sub table not sharing the same subscript are significantly different at p < .05 in the two-sided test of equality for column proportions.

Cells with no subscript are not included in the test. Tests assume equal variances.

Atrial fibrillation prevalence

The major purpose of this study was to examine if cardiac patients with OSA had a higher prevalence of atrial fibrillation versus patients without OSA. A chi-square analysis with frequencies was completed to examine any statistically significant differences among these groups, as seen in table 3. No significant difference in atrial fibrillation diagnosis was seen in patients with OSA versus patients without OSA. One important aspect that should be taken into consideration was the significant difference (p = <.05) in age between the control group (62 ± 11.17), the OSA group (66 ± 10), the AF group (73 ± 7), and the OSA_AF group (74 ± 8).

		AFIB Present					
		No		**Yes**			
		n	**%**	**n**	**%**	**X2**	**p**
OSA Present	No	213[a]	86.20%	34[a]	13.80%	2.419	.120
	Yes	1252[a]	82.20%	271[a]	17.80%		

Table 3: *Frequencies and chi-square results for atrial fibrillation among subjects.*

Note: Values in the same row and sub-table not sharing the same subscript are significantly different at p < .05 in the two-sided test of equality for column proportions. Cells with no subscript are not included in the test. Tests assume equal variances.

Discussion

The major purpose of this study was to examine the prevalence of AF in cardiac patients with OSA and compare that prevalence to cardiac patients without OSA. No statistically significant difference was seen in AF prevalence in patients with OSA versus those without OSA. There was also no increased risk of stroke in patients with both OSA and AF when the data was analyzed with covariates. The researchers of this study hypothesized that patients with OSA would have a higher prevalence of AF, and thus have failed to reject the null hypothesis.

Chronic cardiovascular, pulmonary, and metabolic conditions have been linked in a cyclical fashion to OSA, where OSA worsens metabolic conditions, which then worsens OSA [17]. OSA is becoming increasingly more prevalent in most populations and is being linked to other chronic diseases such as obesity and heart disease [1,7,11,12,14]. Studies examining the prevalence of OSA have been conducted prior to this study with researchers placing national prevalence anywhere from 3 - 24% of the American population [18,26]. Discrepancies with prevalence figures in OSA have been attributed to factors such as diagnostic testing (including frequency and type of test used), sleep apnea type, and specific sample populations [18,26]. The prevalence of OSA in the sample population of this study was 76.2%. The current research study utilized a protocol where the primary sample size was patients with OSA thus drastically increasing the prevalence of the sample population and should not be extrapolated to the general population.

One of the most common cardiac arrhythmias is AF which is a known risk factor for stroke and is also associated with other comorbidities [8,9,15,24]. The primary thought process of the authors in this study was that OSA would cause intra-thoracic pressure differences as well as oxygen saturation differences that would then influence the sympathetic nervous system to stimulate cardiac involvement thus resulting in disturbances to the cardiac rhythm [18,20,23]. The resultant disturbance would be AF and henceforth patients with OSA would have higher prevalence of AF. The prevalence of AF in OSA patients in this study was 17.8%, which is lower than some current research (26%) but still higher than what other researchers have found [3,11]. More recently, researchers have observed an AF prevalence of as low as 7.6% [15]. This large range in prevalence has been attributed to numerous factors in previous research such as proper medical diagnosis, screening, etc [1]. Determining the prevalence of AF in OSA patients is important from a health and medical standpoint because individuals with AF are five times more likely to develop a stroke [5,10,13]. Furthermore, AF continues to be a key independent risk factor in the medical and clinical stroke risk assessment [3].

Few research studies have been conducted examining the prevalence of AF in eligible cardiac rehabilitation patients with OSA. The authors of this research study did not observe a higher prevalence of AF in OSA patients even though previous research has been done where researchers have observed higher comorbidities in individuals with OSA [4,7,19]. Although the results of this study were not statistically significant (p = .120), the slight increase in AF in patients with OSA versus those without OSA leads the researchers to infer a trend. The slight increase in AF incidence lends to a phenotype of patients with OSA that includes other comorbidities such as obesity, hypertension, chronic kidney conditions and stroke, all of which are independent risk factors for cardiovascular disease [5,6,25,27]. Future research studies should examine the relationship of OSA, AF, and stroke more closely in the cardiac population.

The researchers of this study did note that when considering covariates, there was a statistically significant (OR = 1.055, CI 95% [1.035 - 1.075], p < .001) increased risk of stroke with age. Although the researchers in this study did not designate age as an independent variable, there was value in considering age as a covariate and future studies should aim to age-match groups to avoid the variance of error. The same can be said for race as there was a statistically significant increase in stroke risk for individuals of White or Black race when compared to others (White: p = .013; Black: p = .011; Other: p = .103), further studies are necessary to examine these aspects further (Table 4).

Variable	B	S.E.	Wald	df	p	Exp(B)	95% CI for EXP(B)	
							LL	UL
Experimental Groups			0.841	3	.840			
OSA	0.175	0.312	0.314	1	.576	1.191	0.646	2.196
AF	0.259	0.679	0.146	1	.702	1.296	0.343	4.901
OSA_AF	0.334	0.375	0.792	1	.373	1.396	0.669	2.912
Gender	-0.114	0.178	0.41	1	.522	0.892	0.629	1.265
Race (White)			8.692	2	**.013**			
Race (Black)	0.585	0.231	6.402	1	**.011**	1.794	1.141	2.822
Race (Other)	1.021	0.626	2.659	1	.103	2.777	0.814	9.48
Age	0.054	0.01	29.394	1	**.000**	1.056	1.035	1.077
Never Smoker			0.659	2	.719			
Current Smoker	0.18	0.358	0.254	1	.614	1.197	0.594	2.413
Former Smoker	0.135	0.181	0.555	1	.456	1.144	0.803	1.631
Hypertension	0.445	0.354	1.573	1	.210	1.56	0.779	3.125
Ethnicity	1.798	1.181	2.317	1	.128	6.035	0.596	61.055

BMI	0	0.018	0	1	.985	1	0.966	1.035
Constant	-9.051	1.556	33.824	1	.000	0		

Table 4: *Binary logistic regression for stroke risk with covariates.*

Note. CI = Confidence Interval; LL = Lower Limit; UL = Upper Limit.

a Male = 1, female = 2. b No = 0, Yes = 1, Unknown = 8. c Hispanic or Latino = 1, Non-Hispanic or Latino = 2. Values are statistically significant at p < .05.

Limitations of the Study

The original dataset from the SHHS contained over 1000 variables related to sleep, cardiovascular health, metabolic health, and medicine. One variable which was not utilized in this study was sleep apnea severity. There are 4 classifications of OSA: none, mild, moderate, and severe. This aspect of OSA was not a point of focus in this study but should be used in further research. Other limitations to this study include not being able to control or account for certain medications, a small final sample size, and the secondary (retrospective) aspect of the study from a medical standpoint and data collection standpoint.

Conclusion

To conclude, the authors of this study did not find a statistically significant increase in AF prevalence in cardiac patients with OSA versus cardiac patients without OSA. The authors did notice a trend that individuals with OSA also had a higher incidence of AF although not statistically significant. This trend lends credence to a certain phenotype in cardiac patients with OSA that should be considered more closely. Other factors such as age and race should be considered more closely in future studies. Additionally future studies should aim for larger samples for experimental conditions.

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