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Cardiovascular diseases across OSA phenotypes: A retrospective cohort study

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ABSTRACT

Background: Despite the considerable knowledge of Obstructive Sleep Apnea (OSA) implications for cardiac diseases, the evidence regarding cardiovascular complications across OSA phenotypes including Rapid Eye Movement OSA (REM-OSA) and Positional OSA (POSA) is limited. In this study, we aimed to evaluate the risk of cardiovascular diseases development and progression among patients with REM-OSA and POSA.

Methods: Based on a retrospective cohort analysis, we included polysomnography studies done in the sleep lab at the Jordan University Hospital. Regarding cardiovascular diseases, primary outcomes were Heart Failure, and 1-years Major Adverse Cardiac Events while secondary outcomes were atrial fibrillation, pulmonary hypertension, other arrhythmia, metabolic profile, and echocardiographic measurements of the heart.

Results: The total number of the included patients was 1,026 patients. POSA group had significantly lower percentage of patients with hypertension (P-value = 0.004). Additionally, systolic blood pressure and HbA1c were significantly lower among patients with POSA compared to the NPOSA group (P-value<0.050). Left ventricular end diastolic dimension was significantly higher among patients with POSA while ejection fraction was significantly lower (P-value<0.050). Patients with diabetes and mean HbA1c were significantly lower among patients with REM-OSA compared to patients with NREM-OSA (P-value = 0.015, P-value = 0.046). Multivariate regression analysis revealed that after adjusting for age, gender and preexisting comorbidities, POSA was significantly associated with lower ejection fraction and higher left ventricular diastolic diameter.

Conclusion: In conclusion, our findings indicate that POSA might be associated with huge and clinically significant heart strain and poor cardiac functions, yet it might not have a clinically significant atherogenic effect. This study should guide clinicians to identify OSA phenotypes to imply the best treatment plan to reduce its detrimental impact on cardiac muscle.

1. Introduction

Obstructive sleep apnea (OSA) is an increasingly common health concern. It is the most prevalent sleep-related breathing disorder that is characterized by recurrent episodes of upper airway collapse in which airflow significantly decreases (hypopnea) or completely ceases (apnea) resulting in intermittent hypoxemia, autonomic fluctuation, and sleep fragmentation [1,2].

OSA can be classified as Positional OSA (POSA) or Non-Positional OSA (NPOSA) according to whether the occurrence of respiratory events is associated with the body position during sleep, in which the number, and duration of apneas and hypopneas differ significantly with the changes in body position between these two phenotypes of OSA [3]. Moreover, OSA can be defined according to in which sleep stage the majority of apneas/hypopneas occur into Rapid Eye Movement OSA (REM-OSA) and Non-Rapid Eye Movement OSA (NREM-OSA). OSA patients are classified to have REM-OSA phenotype when the majority of the apneas/hypopneas occur in the REM stage of sleeping [4].

OSA has been associated with an increased incidence of development and progression of cardiovascular diseases [5]. OSA prevalence is as high as 40%–80% in patients with hypertension, heart failure, coronary artery disease, pulmonary hypertension, atrial fibrillation, and stroke

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[6]. The pathogenesis of cardiovascular disease in OSA includes sympathetic activation, fibrinolytic imbalance, vascular endothelial dysfunction, coagulation, oxidative stress, inflammation, and metabolic dysregulation [5]. Patients with OSA develop several physiological changes in the autonomic nervous system that have been implicated in the pathogenesis of cardiovascular disease development including an increased resting heart rate, decreased cardiac rhythm activity, and increased blood pressure variability [7]. These changes have also been linked to increased cardiovascular risk, elevated blood pressure, and impaired glucose metabolism [8]. Accordingly, OSA should be ruled out in patients with cardiovascular disease and be regarded as an important independent modifiable and treatable risk factor [9].

Despite the considerable knowledge of OSA implications for cardiac and vascular diseases, the evidence regarding cardiovascular complications across OSA phenotypes including REM-OSA and POSA is limited and much less understood. In this study, we aimed to evaluate the risk of cardiovascular diseases development and progression among patients with REM-OSA and POSA.

2. Methods

2.1. Data selection

Based on a retrospective cohort analysis, 1,092 polysomnography studies were done in the sleep lab at the Jordan University Hospital (JUH) between June 2016 and March 2022. Referral to the sleep study was based on the clinical suspicion of OSA (snoring, increased daytime sleepiness, witnessed apnea, and early morning headache) and preoperative evaluation of surgical patients. Patients with Apnea Hypopnea Index (AHI) $>$ 5 were considered to have OSA and were subsequently included in our study. Consequently, 55 patients were excluded.

2.2. Polysomnography and sleep data

The overnight study consisted of continuous recordings of an electrocardiographic lead, right and left electrooculographic leads, submental, and two electroencephalographic leads. Respiration was monitored throughout the night using thermocouples at the nose and mouth in addition to thoracic and abdominal strain gauges. Recordings of the oxyhaemoglobin saturation (SaO2) and duration of saturation below 90% SpO2 (minutes) were obtained. The biophysiological changes on the polysomnography (PSG) device were evaluated using the 2015 version of the American Academy of Sleep Medicine (AASM) manual for the scoring of sleep and associated events for studies performed before 2018 while all the studies done on and after 2018 were analyzed using the 2018 AASM manual. Obstructive apnea was defined as a reduction in the airflow greater than 90% with respiratory effort lasting at least 10 s. Hypopnea was defined as a reduction of more than 30% in the airflow associated with an electroencephalographic arousal or a drop of at least 3% in the SaO2. The AHI was calculated as the total number of apneas and hypopneas per hour of total sleep time. Sleep state-dependent indices (i.e., Non-Rapid Eye Movement AHI (NREM-AHI) and Rapid Eye Movement AHI (REM-AHI)) were also determined by dividing the number of events in NREM and REM sleep by the amount of NREM and REM time, respectively. The position during sleep was determined using position sensors. The Arabic version of the Epworth Sleepiness Scale (ESS), which was validated by Ahmed et al., was used to assess patient sleepiness [10]. Positional obstructive sleep apnea (POSA) was defined as the overall AHI>5, the overall AHI severity of at least 1.4 times the non-supine severity (Overall/NS-AHI) and a minimum amount of time (i.e., 20 min) in the supine and non-supine positions [11]. We chose this definition as it demonstrated the best consistency in detecting patients who were most likely to have reductions in sleep disordered breathing severity if supine sleep was avoided [11]. In addition, a previous study conducted in Jordan among OSA patients demonstrated that the Overall/NS-AHI criterion was valid, sensitive, specific and accurate in diagnosing OSA. Also, it showed superiority in terms of diagnostic measures over other criteria [12]. Moreover, we retested the differences between POSA and NPOSA while using Cartwright Criteria which defines POSA as a difference of 50% or more in AHI between supine and non-supine positions [12]. REM predominant OSA was defined as an overall AHI of $\geq$5 and a ratio of the AHI during REM sleep to the AHI during NREM sleep of $\geq$2 [13].

2.3. Clinical data and cardiovascular outcomes

Data about patients' demographics and comorbidities were collected including age, gender, Body Mass Index (BMI), diabetes, and chronic kidney disease. Clinical data from the patients follow up in the clinics including systolic and diastolic blood pressure were also obtained. Laboratory data including urea (mg/dl), creatinine (mg/dl), and Brain Natriuretic Peptide (BNP) (mg/dl) were also collected. Regarding cardiovascular diseases, primary outcomes were Heart Failure (HF), and 1-years Major Adverse Cardiac Events (1-year MACE) while secondary outcomes were atrial fibrillation, pulmonary hypertension, other arrhythmia, metabolic profile, and echocardiographic measurements of the heart. Heart failure was defined as clinical symptoms or signs suggestive of heart failure and elevation of BNP or echocardiographic evidence of pulmonary cardiac congestion. One year MACE was defined as the occurrence of myocardial infarction, cardiac death, congestive heart failure, percutaneous coronary intervention or coronary artery bypass surgery. Atrial fibrillation and arrhythmias were diagnosed based on Electrocardiography while pulmonary artery hypertension defined as pulmonary artery pressure higher than 20 mm Hg diagnosed using right sided heart catheterization. Metabolic profile included High Density Lipoprotein (mg/dl), Low Density Lipoprotein (mg/dl), and Glycated hemoglobin (HbA1c). Echocardiography measures included left atrial pressure, left ventricular end diastolic dimension in millimeters, ejection fraction, and pulmonary artery pressure were reviewed. All the data regarding patients' clinical data and cardiovascular outcomes were collected 1 year after the OSA diagnosis.

2.4. Data analysis

The patients' data was entered in Microsoft Office Excel 2019, then imported into IBM SPSS v.25 software to conduct the analysis. Continuous variables were summarized as mean and standard deviation while categorical variables were summarized as counts and percentages. The comparisons in categorical variables across the phenotypes of OSA were done using the chi-square test. Whereas the differences in continuous variables between the groups were examined using T-test. A P-value less than 0.050 was considered statistically significant across all the tests. The association between OSA Phenotypes and Left Ventricular End Diastolic Diameter as well as Ejection Fraction, when it was significant in the univariate analysis, was investigated using linear regression analysis while adjusting for age, gender and preexisting comorbidities.

3. Results

3.1. The characteristics of the included patients

The total number of the included patients was 1,026 patients. Of them 51.2% were males. The mean age of the patients was 59.78 $\pm$ 14.01. Around 60.0% of the patients had hypertension while 42.9% of the patients had diabetes. Moreover, 29.0% and 13.0% of the patients had hyperlipidemia and heart failure, respectively. Additionally, 4.7% of the patients had atrial fibrillation and 23.6% of them had MACE within 1 year after the diagnosis of OSA. The most frequent medications used by the patients were beta blockers (23.4%), insulin (23.9%), and angiotensin receptor blocker (19.4%). The mean systolic and diastolic blood pressure were 141.83 $\pm$ 13.84 and 83.24 $\pm$ 8.46, respectively. Furthermore, the mean HDL and LDL were 45.33 $\pm$ 20.9 and 113.44 $\pm$

39.4, respectively. The mean BNP was 53.67 ± 246.85 while the mean LVEDD was 29.63 ± 30.23 mm. In addition, the mean ejection fraction and pulmonary artery pressure were 53.43 ± 8.27 and 47.89 ± 14.06, respectively. Table 1 describes the characteristics, comorbidities, and cardiovascular echocardiography measurements.

3.2. Difference between POSA and NPOSA

Our analysis that investigated the differences between POSA and NPOSA patients showed that female patients were significantly higher among patients with POSA (54.8%) compared to their counterparts (45.2%) (P-value = 0.006). The mean age of the patients with POSA was significantly lower compared to the NPOSA group (P-value = 0.040). Moreover, the percentage of patients with hypertension was significantly lower among patients with POSA (54.8%) compared to patients with NPOSA (63.7%) (P-value = 0.004). Additionally, systolic blood pressure and HbA1c were significantly lower among patients with POSA compared to the other group (P-value = 0.026, P-value = 0.010). Left ventricular end diastolic dimension was significantly higher among patients with POSA (9.32 ± 6.99 mm) compared to patients with NPOSA (5.64 ± 2.43 mm) (P-value = 0.036). Patients with POSA had significantly lower ejection fraction (52.65 ± 8.57) compared to their counterparts (54.73 ± 7.61) (P-value = 0.014) (Table 2). The comparison between POSA and NPOSA groups while using the Cartwright Criteria showed similar findings (Table 3). Multivariate regression analysis revealed that after adjusting for age, gender and preexisting comorbidities, POSA was significantly associated with lower ejection fraction (Table 4; AB = −1.966; 95%CI: −3.706 to −0.226) and higher left ventricular diastolic diameter (Table 4; AB = 5.289; 95%CI: 0.711–9.868).

3.3. Difference between REM predominant and NREM predominant OSA

Our results showed that male patients were significantly higher among REM-OSA group (71.8%) compared to NREM (38.3%) (P-value = 0.000). The mean age was significantly lower among REM-OSA compared to the other group (P-value = 0.000). The percentage of patients with diabetes was significantly lower among patients with REM-OSA (32.7%) compared to patients with NREM-OSA (42.3%) (P-value = 0.015). Mean HbA1c was significantly lower among patients with REM-OSA (6.24 ± 1.39) compared to their counterparts (6.72 ± 1.58) (P-value = 0.001). HDL and LDL levels were significantly higher among patients with REM-OSA compared to patients with NREM-OSA (P-value = 0.025, P-value = 0.000). Urea levels were significantly lower among patients with REM-OSA (P-value = 0.003). Moreover, ejection fraction was significantly lower among patients with REM-OSA (31.06 ± 24.63)

Table 1
The general demographics of the participants.

Variable	Response	Frequency	Percentage (%)
Sex	Male	525	51.2
	Female	501	48.8
Hypertension	No	412	40.0
	Yes	617	60.0
Diabetes Mellitus	No	588	57.1
	Yes	442	42.9
Hyperlipidemia	No	731	71.0
	Yes	299	29.0
Heart Failure	No	889	87.0
	Yes	133	13.0
Chronic Kidney Disease	No	466	48.4
	Yes	49	5.1
Atrial Fibrillation	No	982	95.3
	Yes	48	4.7
Other Arrhythmias	No	506	70.6
	Yes	211	29.4
MACE	No	787	76.4
	Yes	243	23.6
Medications	Metformin	157	15.3
	Angiotensin Converting Enzyme Inhibitor	147	14.3
	Angiotensin Receptor Blocker	200	19.4
	Diuretics	143	13.9
	Insulin	245	23.8
	Beta Blockers	241	23.4
	Anti-platelet	131	12.6
	Anti-coagulants	157	15.2
	Calcium Channel Blockers	116	11.3
	Alpha Blockers	22	2.1
Type of Positional OSA	NPOSA	599	57.8
	POSA	431	41.6
Type of REM OSA	REM-OSA	211	26.1
	NREM-OSA	596	73.9

Variable	Mean	SD	Range
Age (years)	59.78	14.01	18–101
Creatinine (mg/dl)	1.43	0.72	0.34–5.21
Hb1AC	6.64	1.56	0.86–13.00
Systolic Blood Pressure	141.83	13.84	60–211
Diastolic Blood Pressure	83.24	8.46	30–140
High Density Lipoprotein	45.33	20.9	3–449
Low Density Lipoprotein	113.44	39.4	9–258
Triglyceride	165.48	89.25	31–738
Urea	122.75	437.60	2.23–616.52
Brain Natriuretic Peptide	53.67	246.85	0–3449.25
Left Atrial Pressure	4.48	0.86	2.6–9.0
Left Ventricular End Diastolic Diameter (millimeters)	29.63	30.23	4.00–503.00
Ejection Fraction	53.43	8.27	16–89
Pulmonary Artery Pressure	47.89	14.06	19–90

Table 2
Differences in the demographics between POSA and NPOSA according to overall/non-supine criteria.

Variable		NPOSA (n = 602)	POSA (n = 431)	P-value
Gender	Male	327 (54.8)	198 (46.2)	0.006*
	Female	270 (45.2)	327 (54.8)	
Age		60.57 ± 13.46	58.69 ± 14.69	0.040*
Hypertension	Yes	381 (63.7)	236 (54.8)	0.004*
	No	217 (36.3)	195 (45.2)	
Diabetes	No	333 (55.6)	255 (59.2)	0.253
	Yes	266 (44.4)	176 (40.8)	
Heart Failure	No	515 (86.4)	374 (87.8)	0.517
	Yes	81 (13.6)	52 (12.2)	
Hyperlipidemia	No	425 (71.0)	306 (71.0)	0.987
	Yes	174 (29.0)	125 (29.0)	
Chronic Kidney Disease	No	280 (50.0)	34 (6.1)	0.475
	Yes	65 (19.4)	15 (3.7)	
Atrial Fibrillation	No	569 (95.0)	413 (95.8)	0.532
	Yes	30 (5.0)	18(4.2)	
Other Arrhythmias	No	307 (71.7)	199 (68.9)	0.408
	Yes	121 (28.3)	90 (31.1)	
MACE	No	453 (75.6)	334 (77.5)	0.486
	Yes	146 (24.4)	97 (22.5)	
Creatinine (mg/dl)		0.31 ± 0.30	0.31 ± 0.28	0.785
Hb1AC		6.75 ± 1.58	6.49 ± 1.52	0.026*
Systolic Blood Pressure		142.95 ± 12.56	140.23 ± 15.38	0.010*
Diastolic Blood Pressure		83.53 ± 8.32	82.83 ± 8.67	0.259
High Density Lipoprotein		44.80 ± 23.67	46.00 ± 14.16	0.429
Low Density Lipoprotein		111.75 ± 38.92	115.62 ± 39.99	0.193
Triglyceride		168.41 ± 89.75	161.71 ± 88.59	0.319
Urea		23.66 ± 4.5	21.50 ± 4.1	0.952
Brain Natriuretic Peptide		64.30 ± 271.62	39.15 ± 207.88	0.171
Left Atrial Pressure		4.46 ± 0.82	4.50 ± 0.90	0.599
Left Ventricular End Diastolic Diameter (millimeters)		5.64 ± 2.43	9.32 ± 6.99	0.036*
Ejection Fraction		54.73 ± 7.61	52.65 ± 8.57	0.014*
Pulmonary Artery Pressure		48.33 ± 15.68	47.22 ± 11.59	0.786

Table 3
Differences in the demographics between POSA and NPOSA according to cartwright criteria.

Variable		NPOSA (n = 758)	POSA (n = 275)	P-value
Gender	Male	475 (62.7)	50 (18.2)	0.008*
	Female	283 (37.3)	225 (81.8)	
Age		63.43 ± 12.34	60.69 ± 13.12	0.032*
Hypertension	Yes	494 (65.2)	123 (44.7)	0.021*
	No	264 (34.8)	152 (55.3)	
Diabetes	No	405 (53.4)	186 (67.7)	0.109
	Yes	353 (46.6)	89 (32.3)	
Heart Failure	No	652 (86.0)	248 (90.2)	0.317
	Yes	106 (14.0)	27 (9.8)	
Hyperlipidemia	No	542 (71.5)	192 (70.0)	0.975
	Yes	216 (28.5)	83 (30.0)	
Chronic Kidney Disease	No	603 (79.5)	250 (90.8)	0.239
	Yes	155 (20.5)	25 (9.2)	
Atrial Fibrillation	No	719 (94.9)	266 (96.8)	0.279
	Yes	39 (5.1)	9 (3.2)	
Other Arrhythmias	No	434 (75.0)	208 (75.6)	0.918
	Yes	144 (25.0)	67 (24.4)	
MACE	No	401 (69.4)	209 (75.9)	0.751
	Yes	177 (30.6)	66 (24.1)	
Creatinine (mg/dl)		0.32 ± 0.29	0.32 ± 0.28	0.832
Hb1AC		6.81 ± 1.52	6.51 ± 1.51	0.021*
Systolic Blood Pressure		144.21 ± 13.12	141.23 ± 14.23	0.007*
Diastolic Blood Pressure		81.23 ± 8.12	82.12 ± 8.23	0.467
High Density Lipoprotein		45.12 ± 21.43	45.98 ± 20.59	0.518
Low Density Lipoprotein		109.89 ± 37.87	112.32 ± 38.35	0.287
Triglyceride		169.12 ± 88.65	162.32 ± 87.34	0.523
Urea		22.87 ± 4.0	22.50 ± 4.0	0.981
Brain Natriuretic Peptide		65.12 ± 272.89	42.13 ± 209.23	0.271
Left Atrial Pressure		4.43 ± 0.76	4.42 ± 0.213	0.765
Left Ventricular End Diastolic Diameter (millimeters)		4.89 ± 2.32	8.81 ± 6.87	0.046*
Ejection Fraction		55.12 ± 7.23	52.76 ± 8.13	0.024*
Pulmonary Artery Pressure		48.32 ± 15.23	47.56 ± 11.98	0.817

Table 4
Multivariate Linear Regression Analysis for the Association between POSA and Left Ventricular End Diastolic Diameter as well as Ejection Fraction Adjusted for Age, Gender and Preexisting Comorbidities.

Outcome	Exposure	AB (95% CI)	P-value
Left Ventricular End Diastolic Diameter (millimeters)	POSA	−1.966 (−3.706 to −0.226)	0.027[a]
Ejection Fraction	POSA	5.289 (0.711–9.868)	0.024[a]
Ejection Fraction	REM-OSA	1,612 (−3.411-6.636)	0.529

[a] P-value<0.050, AB: Adjusted B Coefficient.

compared to patients with NREM-OSA (54.09 ± 24.22) (P-value = 0.046) (Table 5). Multivariate regression analysis demonstrated that after adjusting for age, gender and preexisting comorbidities, REM-OSA was not associated with ejection fraction (Table 4; AB = 1,612; 95%CI: −3.411-6.636).

4. Discussion

OSA is a common sleep disorder with long-term major neurocognitive and cardiovascular sequalae [14]. Studies have characterized the heterogeneity of OSA into well-defined phenotypes based on the predominance of the disorder [15]. The importance of this classification stems from the basis of applying different treatment disorders to minimize the morbidity of the disease [16]. The treatment of OSA mainly

Table 5
Differences between REM-OSA and NREM-OSA patients.

Variable		NREM-OSA (n = 595)	REM-OSA (n = 209)	P-value
Gender	Male	228 (38.3)	150 (71.8)	0.000*
	Female	367 (61.7)	59 (28.2)	
Age		60.11 ± 13.33	54.99 ± 14.47	0.000*
Hypertension	Yes	353 (59.2)	113 (53.8)	0.172
	No	243 (40.8)	97 (46.2)	
Diabetes	No	344 (57.7)	142 (67.3)	0.015*
	Yes	252 (42.3)	69 (32.7)	
Heart Failure	No	527 (89.3)	191 (91.0)	0.504
	Yes	63 (10.7)	19 (9.0)	
Hyperlipidemia	No	432 (72.5)	149 (70.6)	0.604
	Yes	164 (27.5)	62 (29.4)	
Chronic Kidney Disease	No	262 (47.5)	28 (5.1)	0.148
	Yes	65 (19.4)	7 (3.5)	
Atrial Fibrillation	No	568 (95.3)	205 (97.2)	0.249
	Yes	28 (4.7)	6 (2.8)	
Other Arrhythmias	No	286 (68.9)	98 (73.7)	0.296
	Yes	129 (31.1)	35 (26.3)	
MACE	No	457 (76.7)	165 (78.2)	0.651
	Yes	139 (23.3)	46 (21.8)	
Creatinine (mg/dl)		0.34 ± 0.27	0.34 ± 0.25	0.657
Hb1AC		6.72 ± 1.58	6.24 ± 1.39	0.001*
Systolic Blood Pressure		141.80 ± 13.71	140.90 ± 12.54	0.470
Diastolic Blood Pressure		83.29 ± 8.26	83.13 ± 7.56	0.826
High Density Lipoprotein		44.43 ± 23.83	48.99 ± 14.23	0.025*
Low Density Lipoprotein		111.16 ± 37.65	125.21 ± 37.77	0.000*
Triglyceride		168.78 ± 93.18	156.34 ± 85.00	0.145
Urea		25.05 ± 4.19	5.26 ± 0.98	0.003*
Brain Natriuretic Peptide		38.47 ± 183.50	22.81 ± 97.55	0.346
Left Atrial Pressure		4.49 ± 0.87	4.41 ± 0.82	0.327
Left Ventricular End Diastolic Diameter (millimeters)		6.93 ± 2.42	9.05 ± 2.46	0.383
Ejection Fraction		54.09 ± 24.22	31.06 ± 24.63	0.046*
Pulmonary Artery Pressure		47.72 ± 13.22	52.83 ± 21.82	0.461

depends on CPAP however, positional therapy has been implied in the treatment of POSA [16]. OSA is associated with several adverse cardiovascular outcomes including coronary artery disease, heart failure, hypertension, and cardiac arrhythmias [17]. The aim of this study was to investigate the differences between OSA phenotypes in cardiovascular diseases.

Our study showed that patients with REM-OSA tended to be of younger age and to have lower percentage of diabetes. Previous studies have demonstrated that REM-OSA patients are of younger age group [18,19]. On the other hand, other studies showed that age was not significantly different between REM and NREM OSA groups [20]. Moreover, studies showed that type 2 diabetes is more prevalent among REM-OSA than NREM-OSA patients [21]. Additionally, HbA1c was significantly lower among REM-OSA patients while HDL and LDL were significantly lower. Studies showed that low REM latency was associated with higher HbA1c and fasting plasma glucose indicating that REM OSA phenotype has a high impact of glucose levels and control [22,23]. The plausible mechanism for the impact of REM-OSA on glucose levels was suggested by several studies. REM-OSA was associated with an increase in sympathetic activity and IL-1b which are both associated with increase in insulin resistance [24]. These differences between our findings and the aforementioned studies might be because of including patients without diabetes as studies showed that REM-OSA is associated with poor glycemic control measures only among patients with diabetes. Furthermore, studies showed that lifestyle modifications and weight loss was associated with reduction in HbA1c and improvement in diabetes control regardless of AHI reduction questioning the relationship between REM-OSA and diabetes and suggesting a huge impact of BMI on this relationship [25]. Previous studies showed that REM-OSA was associated with an increase in triglyceride and LDL but not HDL [22]. Another study demonstrated that the association between REM sleep disorder and metabolic parameters are poor and might be clinically

negligible [26]. On the other hand, a recent study showed that REM-OSA was associated with higher HDL and TG but not LDL [27]. The contradictions regarding these associations in the literature might be due to the differences in these studies in the criteria used to diagnose REM-OSA and the ethnic as well as genetic background [26]. However, studies showed controlling BMI as a confounding factor eliminated the impact of REM-OSA on lipid profile parameters [28]. In addition, our findings that showed increase in LDL and HDL among REM-OSA patients indicates that REM-OSA might not affect atheroma formation which is also evident by absence of association between REM-OSA and acute MACE events demonstrated by our study [29]. However, it is important to demonstrate that the rate of 1-year MACE among OSA patients was high in our study (24.6%). The role of the OSA in increasing cardiac events is well established in the literature [30]. In addition, managing OSA through upper airway surgery or CPAP was shown to reduce acute coronary syndrome while intolerance to CPAP increased the risk of mortality among patients with stroke [31,32]. Nevertheless, no randomized trials were able to demonstrate the efficacy of CPAP in reducing cardiovascular and cerebrovascular events [33,34].

Our results demonstrated that patients with POSA tended to be females and of younger age compared to NPOSA which is similar to previous studies in the literature [35,36]. Patients with POSA had significantly lower prevalence of hypertension and lower mean systolic blood pressure. Since POSA is considered a low OSA severity phenotype in terms of AHI, it is expected that patients with POSA exhibit lower sympathetic activity and thus lower blood pressure readings and prevalence of hypertension [37]. These findings were also demonstrated in previous studies [37,38]. In addition, patients with POSA had significantly lower HbA1c levels which is similar to previous studies. This relationship was implicated by the low BMI associated with patients with POSA, hence they are expected to have lower insulin resistance [39]. Moreover, patients with POSA had significantly higher left ventricular end diastolic dimension compared to patients with NPOSA. Previous studies showed that patients with heart failure have high prevalence of POSA [40] and studies has demonstrated that left ventricular end diastolic dimension is an indicator for impending heart failure [41]. In addition, studies showed that lateral sleeping position among those patients improve their heart failure condition [41]. Also, ejection fraction was significantly lower among patients with POSA The improvement of ejection fraction due to improvement in sympathetic tone among patients with heart failure was concluded by previous studies indicating the importance of using CPAP and positional therapy to improve OSA [42].

Although this is one of the first studies in the literature to explore the association, several limitations should be acknowledged. First, the retrospective nature of our study limits our conclusions to associations instead of causal relationships. Second, this study was conducted in a single center which limits the generalizability of our findings. Thus, future large multicentric well-conducted studies are needed. Furthermore, despite the fact that we used the most consistent definitions of POSA and REM-OSA and the ones that identifies patients with higher probability to benefit from therapy, several definitions were proposed to identify OSA phenotypes. Finally, the diagnosis of POSA and REM-OSA was made based on single night PSG and it is unknown if OSA phenotypes are stable night to night phenotype or not.

In conclusion, REM-OSA patients had lower HbA1c but slightly higher and might be clinically negligible HDL and LDL levels indicating that REM-OSA is not associated with clinically significant atherogenic effect. Moreover, Patients with POSA had higher prevalence of hypertension and systolic blood pressure. Also, POSA was significantly associated with lower ejection fraction and poor cardiac functions. Our findings indicate that POSA might be associated with huge and clinically significant heart strain and poor cardiac functions. This study should guide clinicians to identify OSA phenotypes to imply the best treatment plan to reduce its detrimental impact on cardiac muscle.

Data sharing

The data associated with this manuscript are available from the corresponding author upon reasonable request.

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Ethical approval

This study was approved by the institutional review board (IRB) of the Jordan University Hospital (JUH) (IRB#) and the IRB waived the need for consent from the participants. This study was conducted in accordance with the declaration of Helsinki.

CRediT authorship contribution statement

Khaled Al Oweidat: were involved in conceptualization, were involved in supervision and reviewing & editing the manuscript. **Ahmad A. Toubasi:** were involved in conceptualization. **Thuraya N. Al-Sayegh:** were involved in data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, and writing the original draft. **Rima A. Sinan:** were involved in data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft. **Sara H. Mansour:** were involved in data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft. **Hanna K. Makhamreh:** were involved in data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, were involved in supervision and reviewing & editing the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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