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Apnea-hypopnea index and the polysomnographic risk factors for predicting 5- to 8-year mortality in patients with OSA

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Abstract

Background The purpose of this study was to investigate the long-term mortality rates of patients with obstructive sleep apnea (OSA) who received an overnight polysomnogram (PSG) for obtaining the diagnosis and to determine the relationship between PSG parameters and overall mortality.

Methods Between 2007 and 2013, patients who had overnight PSG and were diagnosed with OSA were included in the study. Factors which are thought to influence mortality were assessed for 5-year and overall survival using the log rank test and Kaplan-Meier survival curves. Using multivariable Cox regression analysis, a model was constructed for factors influencing 5-year and overall survival.

Results A total of 762 patients with a mean age of 52.7 (±10.8) and a dominance of men (74.7%) were studied. Gender, OSA severity subgroups, and apnea hypopnea index (AHI) were not statistically significantly associated with either 5-year or overall mortality ($p<0.05$ for both). Age, having a cardiovascular comorbidity, proportion of rapid eye movement (%REM), and total sleep time with an oxyhemoglobin saturation of less than 90% (T90) all showed a significant correlation with overall all-cause mortality in the model. For 5-year mortality and overall mortality, the hazard ration (HR) for T90 was 3.6 (95% CI (1.6–8.0) $p=0.001$) and 3 (95% CI (1.6–5.7) $p=0.001$), respectively.

Conclusion The study findings suggest that not AHI but PSG parameters of hypoxia, mainly T90, having cardiovascular comorbidity, and %REM sleep were significant risk factors for all-cause mortality in patients with OSA. The association of OSA, hypoxia, and mortality is an area that deserves further study.

Keywords Sleep apnea · Obstructive · Apnea · Hypoxia · Mortality · Polysomnography

Introduction

Obstructive sleep apnea (OSA) is a significant health issue which is recognized as a separate risk factor for mortality and morbidity [1]. Sleep fragmentation and intermittent hypoxia are the hallmarks of the condition. Every system, including the cardiovascular, nervous, respiratory, and endocrine systems, is impacted by OSA. The relative risks of major adverse cardiac events, stroke, and all-cause mortality increase by 2.04, 2.15, and 1.54 respectively, when OSA is untreated [2]. A 1.9-fold elevated risk of all-cause mortality and a 2.65-times increased risk of cardiovascular mortality have both been linked to severe OSA [3]. Aging and comorbidity, such as cardiovascular diseases, chronic kidney disease, and moderate-to-severe chronic obstructive pulmonary disease, have been suggested as significant factors in increased mortality in OSA, in addition to the severity of the disease [4].

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The sum of the apnea and hypopnea indexes per hour is used to calculate the apnea hypopnea index (AHI), which is used to categorize the severity of OSA [5]. There is growing evidence that AHI does not accurately estimate the risk of CV diseases, even though AHI is used to diagnose and evaluate the severity of OSA. Hypoxic burden (HB) specific to OSA and heart rate variability have recently been found to be powerful indicators of overall CV morbidity and mortality in OSA [6]. There is evidence that a desaturation rate of 2% is linked to all-cause mortality and a desaturation rate of 4% is related to an increased risk of hypertension [7, 8]. However, not all published studies have consistently shown an association between OSA parameters and all-cause mortality [6]. We therefore hypothesize that in individuals with OSA identified by overnight PSG, AHI is not a reliable indicator of all-cause mortality.

The goal of this study was to look for the 5- to 8-year mortality rates of patients with OSA by overnight PSG and the correlation between PSG parameters and all-cause mortality.

Methods

Study design

In this retrospective cohort study, the demographic characteristics, body mass index (BMI), Epworth score, and polysomnographic findings were collected from the inpatient reports during 2007–2013 in our hospital sleep laboratory. This research study followed the guidelines of the Declaration of Helsinki and was conducted using information obtained for clinical purposes. Our University Hospitals Ethics Committee provided its approval.

Participant characteristics

Patients hospitalized for OSA having overnight PSG during 2007–2013 in our hospital sleep laboratory were considered for inclusion in the study. The hospital archive contains the data of every patient who underwent PSG for one night in our clinic. Patients' symptoms, family history, associated diseases, and Epworth survey results are noted while they are hospitalized. But if the patient's file contained missing data, that patient was excluded from the trial. BMI and number of comorbidities were obtained from the medical records. Diagnosis of coronary heart disease and those with cardiovascular disease risk factors like hypertension, diabetes, and dyslipidemia, or their combination, were referred to as cardiovascular (CV) comorbidity. Other rare comorbidities were not included in the analysis. Participants were divided into two groups according to survival (deceased and survived). OSA severity was calculated with AHI score and the severity of OSA was classified as mild, moderate, and severe (5≤ AHI <15, 15≤ AHI <30, AHI ≥30) respectively.

Mortality data of patients with OSA were obtained from the hospital online data system, and these data were also checked over the data of the social insurance institution.

Polysomnography

Using the Epworth sleepiness scale higher than 10, excessive daytime sleepiness was determined [9]. All patients underwent overnight PSG using an Astro-Med Inc. Product Group, Grass Technologies Comet Series EEG/PSG and Grass Technologies Twin software version 4. The overnight PSG included four electroencephalography channels, four tibialis anterior electromyography channels, a finger pulse oximeter, and one chin electromyography channel. A nasal thermistor, a digital microphone to detect snoring, a nasal airflow, strain gauges to detect thoracoabdominal movements, and a single electrocardiography lead were also included in the PSG system. The American Academy of Sleep Medicine's (AASM) standard criteria were applied to PSG recordings, which were measured for oxygenation, breathing, and sleep in 30-s intervals (epochs) [10]. A 90% cessation of oro-nasal airflow for at least 10 s was considered to be obstructive apnea, while there was chest wall motion. Hypopnea was defined by AASM criteria. The total number of apneas and hypopneas per hour of sleep was used to calculate AHI. PSG findings were used for the diagnosis of OSA, according to guidance of the International Classification of Sleep Disorders 2 [11]. Patients with an AHI <5 were excluded, and the severity of OSA was classified as mild, moderate, and severe (5≤ AHI <15, 15≤ AHI <30, AHI ≥30) respectively.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, Inc., Chicago IL), version 22 Windows software was used to analyze the data. To ascertain whether the data were normally distributed or not, the Shapiro-Wilk test was applied. The results were presented as mean (±standard deviation) and median (min–max). Mann-Whitney *U* test and Student *t* test were used for comparing continues parameters between the groups. To compare categorical data between groups, the chi square and exact tests were used, and the results were presented in number and percentage (%). Cut-off values for the continuous variables affecting mortality in the comparisons between mortality groups were determined by evaluating the AUC and Youden index values using the ROC analysis method. According to these cut-off values, patients were grouped

for mortality risk. With these risk groups whose cut-off values were determined, comorbidity, gender, OSA severity, and AHI value groups, which are thought to have an effect on mortality, were evaluated for 5-year survival and overall survival using the log rank test in Kaplan-Meier survival curves. For multivariable modeling, in univariable analysis and in intergroup comparisons, parameters such as age, BMI, comorbidity, REM%, Min O2 Sat, and desaturation time with an alpha value of less than 0.1 were used. This model was then analyzed to determine risk factors for 5-year and overall mortality in multivariable Cox regression analysis. The results were presented with 95% CI. In all statistical analyses, p value of <0.05 was accepted as statistical significance.

Results

After exclusions, 762 patients were enrolled in the study. There was a male dominancy (74.7%) with a mean age of 52.7 (±10.8) in our cohort. Baseline characteristics and polysomnographic results of the participants are shown in Table 1. In this population, mean AHI was 43.4 (±31.5), 5-year survival rate was 91.9%, and 8-year survival rate was 88.2%. When we compared the demographic and clinical characteristics of survived and deceased patients, we found that age, BMI, and having a CV comorbidity were significantly different between two groups (p<0.001, p=0.001, p<0.001 respectively). In addition, PSG parameters %REM, minimum oxygen saturation during sleep, and T90 were significantly different between survived and deceased patients (p<0.001, p<0.001, p<0.001 respectively.) AHI was not statistically significantly different between survived and deceased patients (p=0.99) (Table 2).

In the evaluation of possible risk factors for mortality prediction (in the ROC analysis), age and BMI were statistically significantly associated with 5-year mortality (p<0.001, p=0.002, respectively). Also, %REM, minimum O2 saturation, and T90 during PSG were statistically significantly associated with 5-year mortality (p<0.001, p=0.003, p<0.001 respectively). Likewise, age, BMI, %REM, and minimum O2 saturation, T90 (p<0.001 for all) were significantly correlated with 8-year mortality in patients with OSA. In addition, Epworth score was not correlated with 5-year mortality (p=0.22) but found to be correlated with 8-year mortality (p=0.047). AUC, sensitivity, and specificity of these possible risk factors for mortality prediction are summarized in Table 3.

Regarding the factors affecting 5-year survival and overall survival using Kaplan-Meier curves and the log rank test, we found that gender, OSA severity subgroups, and AHI were not statistically significantly related with mortality both 5-year and overall all-cause mortality (Table 4). Age, CV comorbidity, BMI, %REM, and hypoxemic features (T90 and minimum oxygen saturation) were found related both with 5-year and 8-year mortality (Table 4). Patients younger than

Table 1 Baseline characteristics and polysomnographic results of the participants

Age (years) mean±SD (min–max)	52.7±10.8 (16.0–78.0)
BMI kg/m^2 mean±SD (min–max)	33.0±6.5 (18.4–60.0)
Male/female *n* (%)	569/193 (74.7%/25.3%)
Survivors/mortality *n* (%)	637/125 (83.6%/16.4%)
8-year survival /mortality *n* (%)	672/90 (88.2%/11.8%)
5-year survival/mortality *n* (%)	700/62 (91.9%/8.1%)
Follow-up time (months) mean±SD (min–max)	116.7±38.4 (1.2–154.0)
CV comorbidity *n* (%)	394 (51.7%)
Obesity *n* (%)	480 (63.0%)
Epworth score mean±SD (min–max)	9.0±5.5 (0–24)
AHI mean±SD (min–max)	43.4±31.5 (5.0–369.0)
OSA severity *n* (%)	
Mild	157 (20.6%)
Moderate	166 (21.8%)
Severe	439 (57.6%)
%REM mean±SD (min–max)	10.5±11.6 (0–217.0)
Min $SatO_2$ mean±SD (min–max)	76.1±12.4 (8.0–97.0)
Desaturation time (T90) (min) mean±SD (min–max)	70.0±97.4 (0–477.0)

Cv, cardiovascular; *BMI*, body mass index; *AHI*, apnea hypopnea index; *OSA*, obstructive sleep apnea; *REM%*, the ratio of rapid eye movement period; *Min $SatO_2$*, minimum oxygen saturation during sleep; *T90*, total sleep time with oxyhemoglobin saturation below 90%

Table 2 Comparison of demographic and clinical characteristics of survived and deceased patients

	Deceased *n*=125	Survivors *n*=637	*p* value
Age (years) mean±SD	60.9±8.9	51.1±10.4	**<0.001**
BMI mean±SD	35.4±8.2	32.6±6.1	**0.001**
Gender			0.134
Male	100 (80.0%)	469 (73.6%)	
Female	25 (20.0%)	168 (26.4%)	
Follow-up time mean±SD	66.7±44.6	126.5±28.1	**<0.001**
Cv comorbidity	96 (76.8%)	298 (46.8%)	**<0.001**
Obesity	89 (71.2%)	391 (61.4%)	**0.038**
Epworth score median (min–max)	10.0 (1–19)	8.0 (0–24)	0.062
AHI median (min–max)	37.2 (5.4–123.7)	37.0 (5.0–369.0)	0.991
OSA severity, *n* (%)			
Mild	26 (20.8%)	131 (20.6%)	0.958
Moderate	26 (20.8%)	140 (22.0%)	
Severe	73 (58.4%)	366 (57.5%)	
REM% median (min–max)	6.4 (0–217.0)	10.3 (0–113.1)	**<0.001**
Min $SatO_2$ median (min–max)	75.5 (8.0–97.0)	80.0 (24.0–94.0)	**<0.001**
Desaturation time (T90) (min) median (min–max)	67.9 (0–475.1)	15.0 (0–477.0)	**<0.001**

Values in bold are statistically significant

Cv, cardiovascular; *BMI*, body mass index; *AHI*, apnea hypopnea index; *OSA*, obstructive sleep apnea; *REM%*, the ratio of rapid eye movement period; *Min* $SatO_2$, minimum oxygen saturation during sleep; *T90*, total sleep time with oxyhemoglobin saturation below 90%

Table 3 Evaluation of possible risk factors for mortality prediction (ROC analysis)

	AUC	95% CI	*p* value	Cut-off	Sensitivity (%)	Specificity (%)
5-year mortality						
Age	0.779	0.722–0.836	**<0.001**	57.50	73.3	69.4
BMI	0.623	0.545–0.702	**0.002**	33.99	60.3	64.2
AHI	0.484	0.410–0.558	0.671	-	-	-
Epworth score	0.547	0.476–0.619	0.229	-	-	-
%REM	0.650	0.582–0.718	**<0.001**	8.35	69.4	58.4
Min $SatO_2$	0.615	0.541–0.690	**0.003**	80.50	72.1	47.7
Desaturation time (T90)	0.689	0.618–0.761	**<0.001**	21.45	80.3	53.6
8-year mortality						
Age	0.758	0.707–0.809	**<0.001**	58.50	64.4	75.0
BMI	0.639	0.570–0.707	**<0.001**	33.99	60.0	65.2
AHI	0.517	0.456–0.578	0.601	-	-	-
Epworth score	0.565	0.507–0.624	**0.047**	7.50	66.7	44.5
REM%	0.651	0.591–0.711	**<0.001**	8.45	67.8	59.1
Min $SatO_2$	0.641	0.579–0.703	**<0.001**	79.50	70.5	53.7
Desaturation time (T90)	0.689	0.631–0.748	**<0.001**	16.95	80.9	50.5

Values in bold are statistically significant

BMI, body mass index; *AHI*, apnea hypopnea index; *OSA*, obstructive sleep apnea; *%REM*, the ratio of rapid eye movement period; *Min* $SatO_2$, minimum oxygen saturation during sleep; *T90*, total sleep time with oxyhemoglobin saturation below 90%

58.5 years of age compared to older ones (≥59) (147.3 (95% CI 145.0–149.5) vs 125.6 (95% CI 118.9–132.2), $p<0.001$) had a longer overall survival. Also, patients with BMI< 34 compared to patients with BMI ≥ 34 (145.1 (95% CI 142.3–147.8) vs 133.8 (95% CI 128.6–139.0), $p<0.001$) had a longer overall survival. In addition, patients without CV comorbidities compared to patients with CV comorbidities had a longer overall survival (147.9 (95% CI 145.2–150.7)

Table 4 Factors affecting 5-year survival and overall survival (Kaplan-Meier analysis and log rank test)

5-year survival (143.8 months, 95% CI 141.4–146.3)				Overall survival (140.9 months, 95% CI 138.3–143.5)			
	OS	95% CI	*p* value		OS	95% CI	*p* value
Age (years)			**<0.001**	Age (years)			**<0.001**
<57.5	149.5	147.7–151.6		<58.5	147.3	145.0–149.5	
>57.5	132.6	126.8–138.5		>58.5	125.6	118.9–132.2	
Gender			0.814	Gender			0.334
Male	143.5	140.6–146.4		Male	140.2	137.1–143.3	
Female	144.7	140.1–149.2		Female	143.1	138.4–147.8	
OSA groups			0.893	OSA groups			0.802
Mild	142.8	137.2–148.4		Mild	141.9	136.1–147.6	
Moderate	143.7	138.7–148.8		Moderate	140.9	135.5–146.3	
Severe	144.1	140.9–147.3		Severe	140.5	137.0–144.0	
CV comorbidity			**<0.001**	CV comorbidity			**<0.001**
–	149.0	146.4–151.6		–	147.9	145.2–150.7	
+	139.0	135.0–143.0		+	134.4	130.1–138.6	
BMI (kg/m^2)			**0.001**	BMI (kg/m^2)			**<0.001**
<34.0	147.0	144.5–149.6		<34.0	145.1	142.3–147.8	
>34.0	138.3	133.4–143.2		>34.0	133.8	128.6–139.0	
AHI			0.660	AHI			0.640
>30.0	143.4	139.6–147.2		>30.0	141.5	137.6–145.5	
<30.0	144.1	140.1–147.3		<30.0	140.5	137.0–144.0	
%REM			**<0.001**	%REM			**<0.001**
>8.35	148.5	146.1–150.9		>8.45	146.6	144.0–149.2	
<8.35	137.9	133.4–142.5		<8.45	133.8	129.1–138.6	
Min $SatO_2$			**0.002**	Min $SatO_2$			**<0.001**
>80.5	148.0	145.2–150.8		>79.5	146.1	143.2–149.1	
<80.5	140.3	136.5–144.1		<79.5	135.6	131.3–139.9	
Desaturation time (T90) (min)			**<0.001**	Desaturation time (T90) (min)			**<0.001**
<21.45	150.0	147.8–152.1		<16.95	149.0	146.6–151.3	
>21.45	137.2	132.8–141.6		>16.95	133.5	129.1–138.0	
				Epworth score			**0.049**
				<7.50	143.9	140.4–147.5	
				>7.50	139.1	135.5–142.8	

Values in bold are statistically significant

CV, cardiovascular comorbidity; *BMI*, body mass index; *%REM*, the ratio of rapid eye movement period; *Min $SatO_2$*, minimum oxygen saturation during sleep; *T90*, total sleep time with oxyhemoglobin saturation below 90%

vs 134.4 (95% CI 130.1–138.6), $p<0.001$) (Table 4 and Figs. 1 and 2). Other factors affecting 5-year and overall mortality are summarized in Figs. 1 and 2. There was no difference in 5-year and overall survival between the OSA severity groups and the AHI groups (Table 4, Figs. 1 and 2).

In our cohort, AHI and OSA severity groups were not correlated with survival; therefore, we did not put these variables into the multivariable Cox regression analysis. In our model, there was a statistically significant association between age (HR 3.6, 95% CI 2–6.5, $p<0.001$), REM% (HR 1.9, 95% CI 1.1–3.3, $p=0.024$), and T90 (HR 3.6, 95% CI 1.6–8.0, $p=0.001$) and 5-year all-cause mortality (Table 5). In our overall mortality model, there was a statistically significant association between age (HR 2.7, 95% CI 1.7–4.2, $p<0.001$), Cv comorbidity (HR 2.6, 95% CI 1.4–4.5, $p=0.001$), REM% (HR 1.7, 95% CI 1.1–2.7, $p=0.019$), and T90 (HR 3, 95% CI 1.6–5.7, p=0.001) and overall all-cause

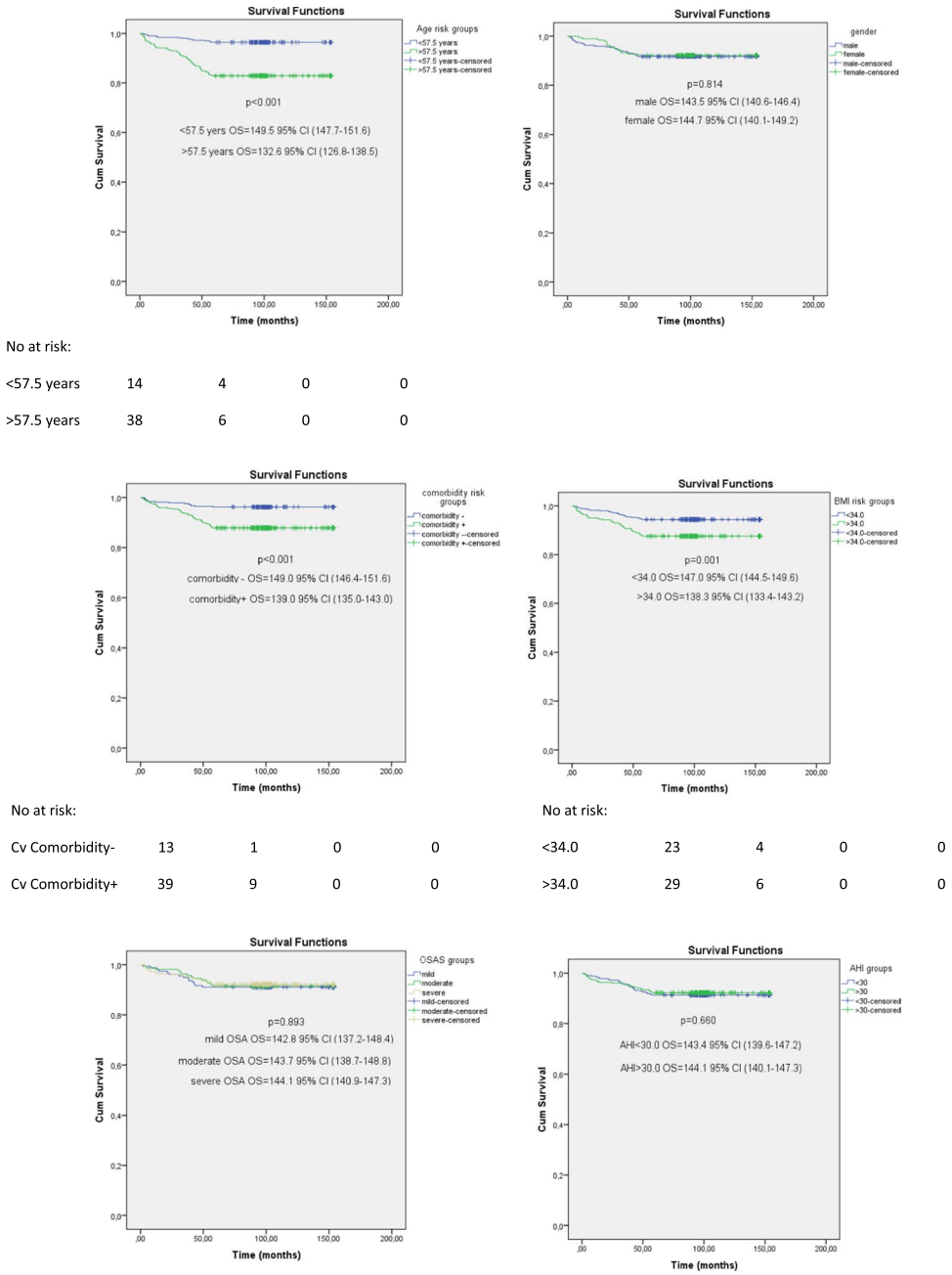

Fig. 1 Kaplan-Meier curves for 5-year mortality of patients with OSA regarding age, gender, comorbidity, BMI, OSA severity, and AHI groups

mortality (Table 5). HR for total sleep time with oxyhemoglobin saturation below 90% under PSG was 3.6 (95% CI 1.6–8.0) for 5-year mortality and 3 (95% CI 1.6–5.7) for overall mortality (Table 5).

Discussion

In our study, we examined the factors affecting 5–8-year mortality in patients with OSA. The findings suggest that having a CV comorbidity, T90%, and %REM sleep were associated with mortality in patients with OSA.

Previous research has linked OSA to an increased risk of death from any cause. In a metanalysis done by Pan et al., it was shown that patients with OSA had a significantly higher risk of death from any cause [12]. They included twelve prospective cohort studies involving 34,382 participants and showed OSA is a separate risk factor for all-cause mortality. The main contributing factors of the link between OSA risk and all-cause mortality are not clearly identified. The relationship can be explained by some pathophysiological mechanisms associated with OSA. OSA may cause intermittent hypoxia with sleep fragmentation, fluid redistribution, swings in negative intrathoracic pressure, alterations in

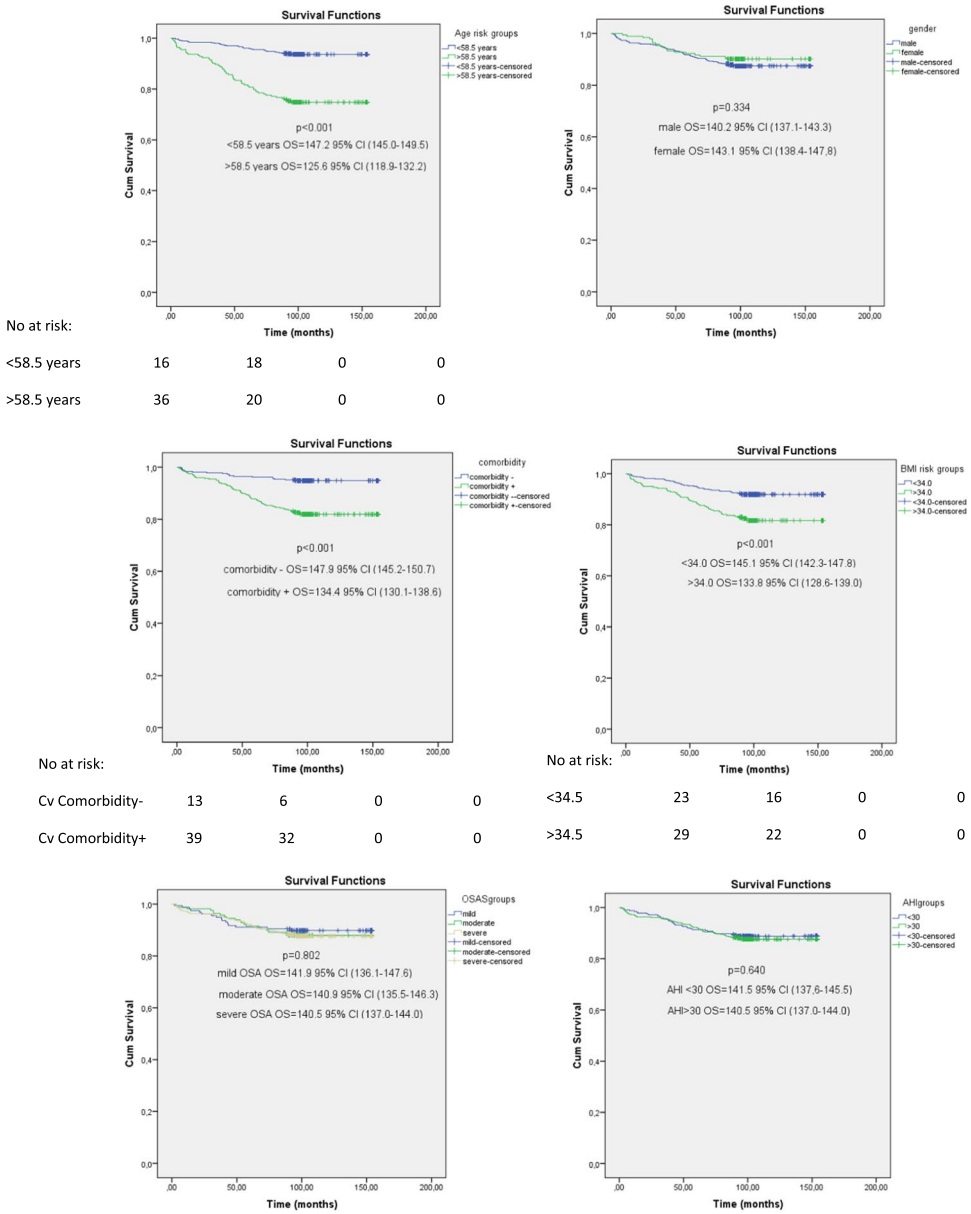

Fig. 2 Kaplan-Meier curves for 8-year mortality of patients with OSA regarding regarding age, gender, comorbidity, BMI, OSA severity, and AHI groups

sympathetic activity, and increased systemic inflammation, Also aging, having more comorbidities and obesity may play a role in the mechanisms underlying mortality risk. All these components may foster multi-organ damage and may cause patient death [12].

Long-term mortality is affected by many factors like age, gender, and obesity. There are different results in the literature regarding gender and OSA mortality. Female patients with OSA had a lower mortality than males in some studies. However, in Labarca's study, gender did not influence all-cause, cardiovascular, or cancer mortality [13, 14]. We believe that aging increases OSA mortality, although different results have been obtained in different studies. Patients with severe hypoxemic OSA were statistically significantly older compared to patients with mild hypoxemic OSA [14, 15]. Age turned out to be a significant risk factor affecting mortality in this study, as was expected. Another significant risk factor for the development of OSA and the progression of diseases is obesity. Theoretically, a higher BMI could worsen OSA and raise mortality. However, there is still disagreement regarding how obesity affects all-cause mortality based on BMI [12]. In this study, although BMI was considered a potential risk factor, it was not found to affect all-cause mortality in the multivariable regression analysis model.

In most of the previous studies, AHI was used as the indicator of the severity of sleep apnea [16–18]. In this study, T90, not AHI, was shown to be an independent risk factor for OSA all-cause mortality. He and colleagues analyzed mortality and the severity of OSA using only the apnea

Table 5 Identification of risk factors for 5-year mortality and overall mortality (multivariable Cox regression analysis)

5-year mortality				Overall Mortality			
	HR	95% CI	*p* value		HR	95% CI	*p* value
Age (years)				Age (years)			
<57.5 years vs **>57.5 years**	3.6	2.0–6.5	**<0.001**	<58.5 years vs >58.5 years	2.7	1.7–4.2	**<0.001**
BMI (kg/m^2)				BMI (kg/m^2)			
<34.5 vs **>34.5**	1.4	0.8–2.4	0.181	<34.5 vs **>34.5**	1.4	0.9–2.2	0.110
CV comorbidity				CV comorbidity			
No vs **yes**	1.8	0.9–3.4	0.075	No vs **yes**	2.6	1.4–4.5	**0.001**
%REM				REM%			
>8.35 vs **<8.35**	1.9	1.1–3.3	**0.024**	>8.35 vs **<8.35**	1.7	1.1–2.7	**0.019**
Min $SatO_2$				Min $SatO_2$			
>80.5 vs **<80.5**	0.8	0.4–1.6	0.485	>80.5 vs **<80.5**	1.0	0.6–1.7	0.954
Desaturation time (T90) (min)				Desaturation time (T90) (min)			
<21.45 vs **>21.45**	3.6	1.6–8.0	**0.001**	<21.45 vs **>21.45**	3.0	1.6–5.7	**0.001**
				Epworth			
				<7.5 **vs >7.5**	1.0	0.6–1.6	0.978

Values in bold are statistically significant

BMI, body mass index; *AHI*, apnea hypopnea index; *OSA*, obstructive sleep apnea; *%REM*, the ratio of rapid eye movement period; *Min $SatO_2$*, minimum oxygen saturation during sleep; *T90*, total sleep time with oxyhemoglobin saturation below 90%

index. They discovered that an apnea index of 20 was linked to a higher mortality rate in patients under 50 but was less clearly linked to a higher mortality rate in patients over 50 [19]. This may be because younger patients typically have fewer complicating medical conditions, making it simpler to detect the comparatively lower association between OSA severity and all-cause mortality. The significance of the AHI in the categorization of OSA severity has been questioned in light of new data on etiology, epidemiology, and prognosis. A multicomponent grading system decision, the Baveno classification, incorporating symptoms and comorbidities was recently presented to define OSA and direct treatment options [20]. Because it integrates patient-related symptoms on the one hand and prognostic factors on the other, compared to the traditional OSA classification based on AHI, the Baveno classification method is probably preferable. According to Baveno groups, percentage of sleep time with T90 and mean oxygen saturation were statistically significantly different between groups. Additionally, Azarbarzin et al.'s study demonstrated that patients with OSA who present an increased heart rate response are more susceptible to experiencing cardiovascular morbidity and mortality [21]. Trzepizur et al. demonstrated that patients with OSA who have a high level of OSA-specific hypoxic burden are more likely to develop a cardiovascular event and have a high overall mortality rate [6]. Labarca et al. included 889 patients in the analysis describing four clinical phenotypes of patients with moderate to severe OSA and concluded that in addition to the AHI, oximetric parameters are useful for describing a different phenotype that has a high risk of mortality [14]. Over the past 3 years, hypoxic burden (HB) has shown promise across these metrics in both community and clinical populations. HB consistently enhanced risk prediction for cardiovascular events, compared to conventional measures of OSA severity [22]. Long-term prospective studies are needed to predict which hypoxemic parameter can better determine mortality and OSA severity, and to understand its effect with comorbidities.

It is clearly known that OSA is linked to a variety of disorders and in comparison, to patients without comorbidities, patients with OSA and any comorbidity may have a higher risk of death. In a large-scale cohort study, it was revealed that the most predominant cause of death was cardiovascular events, followed by infection and cancer [23]. It is obvious that the best-defined health outcomes of OSA relate to the cardiovascular system. Hypertension, arrhythmias, cerebrovascular events, cardiac failure, and coronary artery disease have a strong association with OSA. Patients with these comorbidities should be evaluated for the possibility of OSA, especially if they exhibit the recognizable symptoms and physical exam findings of OSA. The treatment of OSA also contributes to the treatment of concomitant diseases [24]. The diagnosis and treatment of OSA are an important point in the context of the relationship between comorbid diseases and mortality.

REM sleep has drawn attention in terms of its relationship with increased sympathetic activity and cardiovascular instability in healthy people compared to non-rapid eye movement (NREM) sleep, and this association is even stronger in patients with OSA. Contrary to NREM sleep,

significant changes to the autonomic nervous system and the cardiorespiratory system take place during REM sleep. All evidence points to the possibility that REM sleep-related OSA may have more negative cardiometabolic effects than non-REM sleep [25]. Although the patients in this study were not classified as REM-related OSA, it can be suggested that patients with OSA and low REM% may have higher mortality due to the pathophysiological process described above. In this study, %REM was associated with long-term mortality but not with 5-year mortality. Although not enough studies have been done to support this, lower %REM during sleep may be a metric indicating that the REM sleep cycle may have an impact on longer-term mortality.

There are limitations to the current study. This is a single-center retrospective cohort study and may not represent the whole population of patients with OSA. Our center is one of the biggest sleep centers in the region and works as a referee center. Therefore, we may represent more severe patients and this knowledge cannot be generalized to patients with mild OSA. Despite the study's large sample size and extensive follow-up period, there may still be several confounding factors that affect mortality, such as the effect of treatment on mortality results, which this study was unable to demonstrate due to the challenges and unpredictability in gathering PAP adherence data. A strength of this study is that all patients underwent overnight PSG in-hospital settings with direct observation during the night. Therefore, the diagnosis of the patients is certain and documented by objective data.

Conclusion

This study showed a strong correlation between hypoxemic features, having CV comorbidity, %REM sleep, and long-term all-cause mortality in patients with OSA diagnosed by overnight PSG. AHI was not determined to be a risk factor for 5- to 8-year all-cause mortality in individuals with OSA. Additional studies are needed to explain the link between OSA patients' polysomnographic characteristics and all-cause mortality.

Data availability The corresponding author will provide the datasets produced and/or analyzed during the current study upon reasonable request.

Declarations

Ethical approval The Suat Seren Chest Diseases and Surgery Education and Training Hospital's institutional and national research committees, as well as the 1964 Helsinki Declaration and its later amendments or comparable ethical standards, were all followed when conducting studies involving human subjects. Formal consent is not required because the demographic data, BMI, Epworth score, and polysomnographic results were obtained from inpatient reports that were analyzed retrospectively. The article contains no information that could be used to identify any participants.

Conflict of interest The authors declare no competing interests.

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