



Age-Related Clinical Phenotypes and Mortality Predictors in Obstructive Sleep Apnea: Insights from Extreme Age Groups

Obstrüktif Uyku Apnesinde Yaşa Bağlı Klinik Fenotipler ve Mortalite Belirleyicileri: Ekstrem Yaş Gruplarından Bulgular

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Abstract

Objective: Obstructive sleep apnea (OSA) is a heterogeneous disorder, yet age-related differences in clinical presentation and prognostic determinants remain insufficiently characterized, with younger OSA patients particularly underrepresented in the literature. This study compared two extreme age groups (≤ 35 and ≥ 65 years) to identify distinct phenotypic patterns and age-specific predictors of mortality.

Materials and Methods: This retrospective observational study included 659 patients aged ≤ 35 ($n = 405$) or ≥ 65 years ($n = 254$) who underwent overnight polysomnography between 2011 and 2016. Clinical, laboratory, and polysomnographic data were extracted from electronic records, and mortality data were obtained from a national registry. Within the ≥ 65 group, multivariable Cox regression models were constructed using different OSA severity metrics, including apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and time spent with $SpO_2 < 90\%$ (T90).

Results: Older patients had a greater comorbidity burden, higher AHI (33.0 vs. 20.8 events/h), longer T90 (42.5 vs. 4.8 min), and higher mortality rate (39% vs. 2%; all $p < 0.001$). In multivariable Cox regression analyses restricted to patients aged ≥ 65 years, age, male sex, neck circumference, diabetes mellitus, and red cell distribution width (RDW)-coefficient of variation were independently associated with increased mortality, whereas higher sleep efficiency was protective. AHI, ODI, and T90 were each independently associated with mortality, although the effect sizes were modest.

Öz

Amaç: Obstrüktif uyku apnesi (OUA) heterojen bir hastalık olmakla birlikte, klinik prezentasyondaki yaşa bağlı farklılıklar ve prognostik belirleyiciler yeterince tanımlanmamıştır; özellikle genç OUA hastaları literatürde yeterince temsil edilmemektedir. Bu çalışmada, farklı fenotipik özellikleri ve yaşa özgü mortalite belirleyicilerini ortaya koymak amacıyla iki uç yaş grubu (≤ 35 ve ≥ 65 yaş) karşılaştırılmıştır.

Gereç ve Yöntem: Bu retrospektif gözlemsel çalışmaya, 2011–2016 yılları arasında gece polisomnografisi uygulanan, ≤ 35 yaşında ($n = 405$) veya ≥ 65 yaşında ($n = 254$) toplam 659 hasta dahil edilmiştir. Klinik, laboratuvar ve polisomnografik veriler elektronik hasta kayıtlarından elde edilmiş, mortalite verilerine ise ulusal bir kayıt sistemi aracılığıyla ulaşılmıştır. ≥ 65 yaş grubunda; apne-hipopne indeksi (AHI), oksijen desatürasyon indeksi (ODI) ve $SpO_2 < 90\%$ olarak geçirilen süre (T90) dahil olmak üzere farklı OUA şiddet ölçütlerinin kullanıldığı çok değişkenli Cox regresyon modelleri oluşturulmuştur.

Bulgular: Yaşlı hastalarda komorbidite yükü daha fazla, AHI daha yüksek (33,0'a karşı 20,8 olay/saat), T90 daha uzun (42,5'e karşı 4,8 dakika) ve mortalite oranı daha yüksek (%39'a karşı %2) bulunmuştur (tüm karşılaştırmalar için $p < 0,001$). ≥ 65 yaşındaki hastalarla sınırlı çok değişkenli Cox regresyon analizlerinde; ileri yaş, erkek cinsiyet, boyun çevresi, diabetes mellitus ve eritrosit dağılım genişliği (RDW) varyasyon katsayısının mortalite artışıyla bağımsız olarak ilişkili olduğu, daha yüksek uyku etkinliğinin ise koruyucu olduğu saptanmıştır. AHI, ODI ve T90'ın

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Conclusion: OSA demonstrates substantial age-related heterogeneity, with younger and older adults representing distinct clinical phenotypes. In older adults, mortality risk appears to be more strongly associated with systemic vulnerability and comorbidity burden than with conventional event-based severity metrics.

Keywords: Obstructive sleep apnea; aging; mortality, RDW

her biri mortalite ile bağımsız olarak ilişkili bulunmakla birlikte, etki büyüklükleri sınırlı düzeyde kalmıştır.

Sonuç: OUA, yaşa bağlı belirgin bir heterojenite göstermekte olup genç ve yaşlı erişkinler farklı klinik fenotipleri temsil etmektedir. Yaşlı erişkinlerde mortalite riskinin, geleneksel olay temelli OUA şiddet ölçütlerinden ziyade sistemik kırılabilirlik ve komorbidite yükü ile daha güçlü ilişkili olduğu görülmektedir.

Anahtar Kelimeler: Obstrüktif uyku apnesi, yaşlanma, mortalite, RDW

Introduction

Obstructive sleep apnea (OSA) is a heterogeneous disorder characterized by substantial variability in symptoms, physiological mechanisms, comorbidities, and clinical outcomes, resulting in clinically meaningful differences among patients (1,2). Aging not only increases the prevalence of OSA but also alters its clinical presentation, pathophysiological mechanisms, and associated comorbidity patterns, suggesting that OSA in older individuals may represent a distinct phenotype (3). Despite these observations, OSA is still commonly evaluated as a relatively uniform condition, and age-specific differences in clinical and prognostic characteristics remain insufficiently explored.

Previous studies have shown that older patients with OSA tend to present with fewer typical symptoms, a higher burden of comorbidities, and distinct polysomnographic features compared to younger individuals (3). Similar variability in clinical presentation has also been observed across other demographic factors, such as sex and reproductive aging (4). Phenotype-based approaches further support the concept that OSA consists of distinct clinical subgroups with varying symptom burden, comorbidity profiles, and treatment responses, which are also associated with demographic characteristics such as age (5). Moreover, different OSA phenotypes have been linked to distinct clinical and cardiovascular outcomes, suggesting that variations in phenotype distribution across age groups may influence disease prognosis (6).

However, the available evidence regarding OSA in older adults remains limited, heterogeneous, and often inconclusive, with older individuals being underrepresented in clinical studies (7). In addition, OSA-related intermittent hypoxia has been implicated in accelerating biological aging processes and contributing to the progression of age-related diseases, further complicating the interaction between OSA and aging (8).

Although several studies have identified predictors of mortality in OSA (9,10), these analyses have largely been conducted in mixed-age populations, potentially obscuring age-specific differences in prognostic determinants. Given the distinct clinical and pathophysiological characteristics observed in older individuals, it is plausible that the factors associated with mortality may differ across age groups. To better capture this heterogeneity, we focused on individuals at the extremes of the age spectrum (≤ 35 and ≥ 65 years), deliberately excluding the middle-aged group in which OSA prevalence peaks. Epidemiological data, including the Wisconsin Sleep Cohort, indicate that OSA is most prevalent during the 4th to 6th decades

of life (11). By selecting younger and older age groups, we aimed to enhance the contrast between potentially distinct phenotypes and allow a clearer evaluation of age-related differences.

Therefore, this study aimed to compare the clinical and demographic characteristics of younger and older patients with OSA and to investigate age-specific predictors of mortality, with a particular emphasis on older adults.

Materials and Methods

Study design and population

This retrospective observational study was designed to compare two extreme adult age groups. Among all patients who underwent overnight polysomnography (PSG) in a tertiary sleep laboratory at niversity of Health Sciences Türkiye Başakşehir Çam and Sakura City Hospital between January 2011 and January 2016, only individuals aged ≤ 35 years or ≥ 65 years at the time of PSG were eligible for inclusion. Patients aged 36–64 years were not considered for the study, as the objective was to maximize phenotypic contrast between younger and older adults rather than to evaluate the entire adult age spectrum. A total of 659 patients met these predefined age-based eligibility criteria, including 405 (61.5%) patients aged ≤ 35 years and 254 (38.5%) patients aged ≥ 65 years. Follow-up duration was defined as the time from PSG to death or last follow-up (January 2026). The median follow-up duration was 136 months (interquartile range: 120–155), corresponding to approximately 11.3 years.

The study protocol was approved by the Ethics Committee of niversity of Health Sciences Türkiye Başakşehir Çam and Sakura City (approval number: 2026-6, date: 12.02.2026). The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design of the study and the use of anonymized data, the requirement for written informed consent was waived by the ethics committee.

Data Collection

Demographic characteristics, comorbidities, anthropometric measurements, laboratory parameters, and PSG-derived variables were extracted from electronic medical records. Mortality data were obtained from the national death notification system, ensuring complete ascertainment of all-cause mortality during follow-up.

PSG

All patients underwent overnight attended PSG using a standard multichannel recording system. Recorded signals included electroencephalography, electrooculography, electromyography, electrocardiography, airflow (nasal pressure transducer and oronasal thermal sensor), thoracoabdominal respiratory effort,

body position, and pulse oximetry. Sleep stages and respiratory events were scored manually by experienced technologists according to the American Academy of Sleep Medicine criteria in effect at the time of recording. Apnea was defined as a $\geq 90\%$ reduction in airflow lasting at least 10 seconds. Hypopnea was defined as a $\geq 30\%$ reduction in airflow lasting at least 10 seconds, associated with $\geq 3\%$ oxygen desaturation or arousal. The apnea–hypopnea index (AHI) was calculated as the number of events per hour of sleep. The oxygen desaturation index (ODI) was defined as the number of desaturation events per hour of sleep.

Definitions

Comorbid conditions, including diabetes mellitus, hypertension, coronary artery disease, chronic obstructive pulmonary disease (COPD), and others, were defined based on documented clinical diagnoses in medical records. Overlap syndrome (OS) was defined as the coexistence of OSA and COPD.

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables are presented as median (interquartile range), and categorical variables as counts and percentages. As most continuous variables were not normally distributed, comparisons between groups were performed using the Mann–Whitney U test. Categorical variables were compared using the chi-square test. Baseline characteristics were compared between age groups (≤ 35 vs. ≥ 65 years) and between survivors and non-survivors within the ≥ 65 group. Multivariable Cox regression analyses were performed to identify factors associated with mortality in patients aged ≥ 65 years. Candidate variables were selected based on univariable group comparisons ($p < 0.20$), clinical relevance, and effect size. To minimize multicollinearity, highly correlated variables ($r > 0.70$) were not included simultaneously in the same model. Three separate models were constructed to evaluate the impact of different OSA severity metrics. All models included the same set of covariates [age, sex, neck circumference, diabetes mellitus, red cell distribution width–coefficient of variation (RDW-CV), and sleep efficiency], with the addition of one severity parameter per model: time spent with $\text{SpO}_2 < 90\%$ (T90) (Model 1), AHI (Model 2), or ODI (Model 3). Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported. A two-sided p value < 0.05 was considered statistically significant. All statistical analyses were performed using Jamovi (version 2.6.19).

Results

A total of 659 patients were included, of whom 405 (61.5%) were aged ≤ 35 years and 254 (38.5%) were aged ≥ 65 years. The proportion of male patients was higher in the younger group (91.7% vs. 61.9%, $p < 0.001$). OSA phenotypes differed between age groups ($p < 0.001$), with positional OSA more frequent in younger patients (35.1% vs. 19.1%) and general OSA more common in older patients (72.5% vs. 55.2%). OS, obesity hypoventilation syndrome (OHS), and sleep-related movement disorders were more prevalent in the ≥ 65 group

(all $p < 0.001$). Periodic limb movement (PLM) disorder and restless legs syndrome (RLS) were also more frequent among older patients. Comorbid conditions were more common in patients aged ≥ 65 years, including diabetes mellitus (35.6% vs. 3.6%), hypertension (61.9% vs. 5.0%), coronary artery disease (16.1% vs. 0.0%), hyperlipidemia (5.9% vs. 0.7%), COPD (26.7% vs. 1.1%), and hypothyroidism (7.2% vs. 1.4%), (all $p < 0.01$). A history of ear, nose, and throat (ENT) surgery was more frequent in younger patients (32.6% vs. 5.9%, $p < 0.001$). Older patients had higher body mass index (BMI) and larger waist and hip circumferences, while Epworth Sleepiness Scale (ESS) scores and neck circumference were similar between the groups (Table 1).

PSG parameters showed higher AHI and ODI values in the ≥ 65 group (both $p < 0.001$), along with lower minimum and average SpO_2 values and a longer T90 (all $p < 0.001$). Non-supine AHI, rapid eye movement (REM) AHI, and non-rapid eye movement (NREM) AHI were higher in older patients, whereas supine AHI did not differ significantly. Total sleep time and sleep efficiency were lower, and sleep onset latency was longer in the ≥ 65 group (all $p < 0.001$). The N1 percentage was higher, while the N3 and REM percentages were lower in older patients. The PLM index was also higher in the ≥ 65 age group (Table 1).

Laboratory findings showed higher glucose, urea, creatinine, C-reactive protein (CRP), and RDW-CV levels in the ≥ 65 age group, while aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), ferritin, serum iron, hemoglobin, hematocrit, and platelet counts were lower (all $p < 0.05$). High-density lipoprotein (HDL) levels were higher in older patients, whereas low-density lipoprotein (LDL) and total cholesterol did not differ significantly (Table 1). Device report rates and regular follow-up attendance were higher in the ≥ 65 age group, and mortality was more frequent among older patients (39% vs. 2%, $p < 0.001$) (Table 1).

Characteristics by mortality status in patients aged ≥ 65 years

Among patients aged ≥ 65 years, the non-surviving group was older compared to survivors [median (IQR) age: 70 (67–73) vs. 67 (65–70) years, $p < 0.001$] and included a higher proportion of male patients (76.8% vs. 63%, $p = 0.05$). OS, OHS, PLM disorder, diabetes mellitus, and COPD were more frequent among non-survivors (all $p \leq 0.05$). Sleep hypoventilation syndrome, sleep-related movement disorder, RLS, hypertension, coronary artery disease, hyperlipidemia, hypothyroidism, and history of ENT surgery did not differ significantly between groups. Non-survivors had higher BMI and larger neck, waist, and hip circumferences (all $p \leq 0.01$), while ESS scores were similar between groups (Table 2).

PSG parameters showed higher AHI and ODI values in non-survivors ($p = 0.003$ and $p < 0.001$, respectively), along with lower average SpO_2 and longer T90 ($p = 0.002$ and $p = 0.01$, respectively). Non-supine AHI was higher in non-survivors ($p = 0.004$), whereas supine AHI, REM AHI, and NREM AHI did not differ significantly. Total sleep time and sleep efficiency were lower in non-survivors ($p = 0.001$ and $p < 0.001$, respectively).

Table 1. Baseline characteristics by age group (≤ 35 vs. ≥ 65 years).

Parameter	≤ 35 years n = 405 (61.5%)	≥ 65 years n = 254 (38.5%)	p-value
Male sex	255 (91.7%)	146 (61.9%)	<0.001
OSA classification			<0.001
Positional OSA	98 (35.1%)	45 (19.1%)	
REM OSA	27 (9.7%)	20 (8.5%)	
OSA	154 (55.2%)	171 (72.5%)	
Overlap syndrome (OSA+COPD)	1 (0.4%)	60 (25.4%)	<0.001
Obesity hypoventilation syndrome	10 (3.6%)	29 (12.3%)	<0.001
Sleep hypoventilation syndrome	0 (0.0%)	3 (1.3%)	0.095
Sleep-related movement disorder	24 (8.6%)	62 (26.3%)	<0.001
PLM disorder	16 (5.7%)	48 (20.3%)	<0.001
RLS	10 (3.6%)	20 (8.5%)	0.029
Diabetes mellitus	10 (3.6%)	84 (35.6%)	<0.001
Hypertension	14 (5.0%)	146 (61.9%)	<0.001
Coronary artery disease	0 (0.0%)	38 (16.1%)	<0.001
Hyperlipidemia	2 (0.7%)	14 (5.9%)	<0.001
COPD	3 (1.1%)	63 (26.7%)	<0.001
Hypothyroidism	4 (1.4%)	17 (7.2%)	0.001
ENT surgery	91 (32.6%)	14 (5.9%)	<0.001
Body mass index	29.4 (26.6-34.0)	33.3 (28.7-38.3)	<0.001
Epworth Sleepiness Scale	9.0 (6.0-13.0)	9.0 (5.5-13.0)	0.187
Neck circumference	39.0 (37.0-41.0)	39.0 (36.0-42.0)	0.402
Waist circumference	100.0 (93.0-108.0)	108.0 (100.0-120.0)	<0.001
Hip circumference	105.0 (100.0-110.0)	106.0 (100.2-116.0)	0.032
PSG parameters			
AHI (events/h)	20.8 (9.4-44.2)	33.0 (17.3-52.5)	<0.001
ODI (events/h)	18.8 (7.3-41.0)	31.0 (16.0-51.4)	<0.001
Minimum SpO ₂	85.0 (78.2-89.0)	79.0 (68.0-86.0)	<0.001
Average SpO ₂	94.0 (91.2-95.0)	91.0 (88.0-93.0)	<0.001
Time with SpO ₂ <90 % (min)	4.8 (0.3-44.5)	42.5 (8.3-134.7)	<0.001
Supine AHI (events/h)	40.0 (15.4-68.2)	46.6 (22.4-68.8)	0.185
Non-supine AHI (events/h)	6.9 (1.9-30.9)	19.1 (6.3-42.5)	<0.001
REM AHI (events/h)	24.2 (9.0-49.6)	42.8 (24.4-58.3)	<0.001
NREM AHI (events/h)	19.8 (7.3-45.7)	30.4 (13.4-54.3)	0.003
Total sleep time (min)	405.0 (349.5-436.5)	328.0 (271.9-369.2)	<0.001
Sleep efficiency (%)	89.1 (78.6-93.4)	70.9 (59.9-79.7)	<0.001
Sleep onset latency (min)	10.0 (4.5-18.9)	17.0 (7.0-31.5)	<0.001
N1 %	6.80 (4.90-9.90)	10.8 (6.80-16.6)	<0.001
N2 %	51.3 (45.7-56.6)	52 (44.8-59.1)	0.300
N3 %	21.7 (16.9-27.4)	19.1 (11.7-26.8)	0.001
REM %	17.8 (13.4-22)	15.4 (10.4-19.8)	<0.001
PLM index	1.4 (0.0-6.3)	3.4 (0.0-20.2)	<0.001
Laboratory parameters			
Glucose (mg/dL)	93 (87 - 99.5)	106 (94-127.03)	<0.001
Urea (mg/dL)	28 (24-33)	38 (31.08-45.25)	<0.001
Creatinine (mg/dL)	0.8 (0.72-0.9)	0.9 (0.76-1.09)	<0.001

Table 1. Continued

Parameter	≤35 years n = 405 (61.5%)	≥65 years n = 254 (38.5%)	p-value
AST (U/L)	22 (19-28)	19 (16-23)	<0.001
ALT (U/L)	30 (20-45)	18 (14-24)	<0.001
GGT	32 (23-50)	24 (17-38)	<0.001
Total cholesterol (mg/dL)	200 (178-225.5)	208.95 (172-239.25)	0.069
Triglycerides (mg/dL)	149 (107-215)	132 (99.75-184)	0.029
HDL (mg/dL)	40 (35-46)	46 (40-54)	<0.001
LDL (mg/dL)	124 (101-146.75)	130 (99-157.25)	0.147
CRP (mg/L)	3 (1-5)	4.25 (2-8)	<0.001
Ferritin (ng/mL)	60 (32-90.2)	36.5 (20.1-59.6)	<0.001
Serum iron (µg/dL)	90 (67-124.75)	78 (56-102)	<0.001
WBC (×10 ³ /µL)	8.04 (6.76-9.33)	7.58 (6.5-9.17)	0.073
Hemoglobin (g/dL)	15.4 (14.7-16.2)	13.75 (12.7-14.8)	<0.001
Hematocrit (%)	46.15 (44.1-48.32)	42.3 (39.1-44.62)	<0.001
Platelet count (×10 ³ /µL)	252.5 (213.75-302.25)	225 (196.75-283)	<0.001
RDW-CV (%)	13.7 (12.3-15.1)	14.1 (12.88-15.22)	0.017
PAP therapy initiation	90 (22.2%)	147 (56.9%)	<0.001
Regular follow-up attendance	38 (9.4%)	42 (16.7%)	0.005
Non-surviving patients	8 (2.0%)	99 (39.0%)	<0.001

Values are presented as n (%) for categorical variables and as median (interquartile range) for continuous variables.

OSA: Obstructive sleep apnea, REM: Rapid eye movement, COPD: Chronic obstructive pulmonary disease, ENT: Ear, nose, and throat, BMI: Body mass index, PSG: Polysomnography, AHI: Apnea–hypopnea index, ODI: Oxygen desaturation index, SpO₂: Peripheral oxygen saturation, REM AHI: Apnea–hypopnea index during REM sleep, NREM AHI: Apnea–hypopnea index during non-REM sleep, PLM: Periodic limb movements, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gamma-glutamyl transferase, CRP: C-reactive protein, WBC: White blood cell count, RDW-CV: Red cell distribution width–coefficient of variation.

Table 2. Baseline characteristics of patients aged ≥65 years stratified by mortality status.

Parameters	Non-survivors n = 99 (39%)	Survivors n = 155 (61%)	p-value
Age (years)	70 (67-73)	67 (65-70)	<0.001
Male sex	76 (76.8%)	97 (63.0%)	0.050
Overlap syndrome (OSA+COPD)	38 (38.4%)	22 (14.2%)	<0.001
Obesity hypoventilation syndrome	16 (16.2%)	13 (8.4%)	0.050
Sleep hypoventilation syndrome	1 (1.0%)	2 (1.3%)	0.800
Sleep-related movement disorder	29 (29.3%)	36 (23.2%)	0.200
PLM disorder	26 (26.3%)	24 (15.5%)	0.030
Restless legs syndrome	7 (7.1%)	14 (9.0%)	0.500
Diabetes mellitus	49 (49.5%)	41 (26.5%)	<0.001
Hypertension	66 (66.7%)	89 (57.4%)	0.100
Coronary artery disease	19 (19.2%)	23 (14.8%)	0.300
Hyperlipidemia	4 (4.0%)	12 (7.7%)	0.200
COPD	41 (41.4%)	25 (16.1%)	<0.001
Hypothyroidism	7 (7.1%)	10 (6.5%)	0.800
ENT surgery	3 (3.0%)	11 (7.1%)	0.100
Epworth Sleepiness Scale	9 (6-13)	8 (5-13)	0.600
Body mass index	33.8 (29.4-41.5)	32.4 (28.2-37.2)	0.010
Neck circumference	41 (38-43)	38 (35.8-40)	<0.001
Waist circumference	108 (102-119)	105 (99.5-114)	0.006
Hip circumference	112 (102-124)	106 (97-113)	<0.001

Table 2. Continued

Parameters	Non-survivors n = 99 (39%)	Survivors n = 155 (61%)	p-value
PSG parameters			
AHI (events/h)	38.2 (20.9-60)	20.7 (11.3-45.5)	0.003
ODI (events/h)	37.8 (19.9-58.5)	22 (9.8-43.8)	<0.001
Minimum SpO ₂	77 (67.3-85)	81 (71-87)	0.400
Average SpO ₂	90 (86-92.5)	92 (89.8-93.8)	0.002
T90 (min)	59.5 (12.6-160)	24.9 (3.77-86.8)	0.010
Supine AHI (events/h)	46.6 (29.1-68.3)	35.5 (13-66)	0.100
Non-supine AHI (events/h)	29.3 (11.8-51.4)	12.4 (4-31.4)	0.004
REM AHI (events/h)	42.9 (22.4-60)	38.8 (18.4-56)	0.300
NREM AHI (events/h)	35.9 (17.6-60.9)	18.1 (7.65-43.8)	0.900
Total sleep time (min)	312 (248-353)	337 (287-376)	0.001
Sleep efficiency (%)	68 (58-74.9)	73.1 (62.4-81)	<0.001
Sleep onset latency (min)	19 (7.25-33.3)	17.3 (8-32.1)	0.500
N1 %	13.1 (7.6-18.8)	9 (6.4-15.2)	<0.001
N2 %	53 (44.9-60.1)	51.9 (45-58.6)	0.900
N3 %	18.7 (9.6-27.9)	19.1 (13.1-26)	0.700
REM %	14.7 (8.3-19)	16.1 (12.1-20.2)	0.010
PLM index	5.4 (0.2-26.1)	2.3 (0-14.7)	0.100
Laboratory parameters			
Glucose (mg/dL)	113 (96.5-143)	103 (94-115)	<0.001
Urea (mg/dL)	40 (33.5-50)	36 (30-43)	<0.001
Creatinine (mg/dL)	0.97 (0.8-1.10)	0.85 (0.69-1)	0.700
AST (U/L)	18 (15.5-22)	19 (17-23)	0.070
ALT (U/L)	17.3 (14-21)	19 (13.5-25)	0.090
GGT	24 (18.5-35)	23 (16-38)	0.500
Total cholesterol (mg/dL)	204 (169-240)	216 (179-240)	0.300
Triglycerides (mg/dL)	141 (99.5-192)	126 (98.5-174)	0.300
HDL (mg/dL)	44 (38-50.5)	49 (42-59)	<0.001
LDL (mg/dL)	122 (91-155)	132 (101-158)	0.800
CRP (mg/L)	5 (2.6-10)	4 (1.98-8)	0.300
Ferritin (ng/mL)	34.8 (20.8-64.4)	39.2 (20.1-57.3)	0.700
Serum iron (µg/dL)	73 (54-92.5)	81.5 (62.3-109)	0.010
WBC (×10 ³ /µL)	8.14 (6.96-9.57)	7.33 (6.2-8.67)	0.001
Hemoglobin (g/dL)	13.8 (12.6-14.9)	13.8 (12.8-14.8)	0.800
Hematocrit (%)	42.3 (38.4-45.3)	42.4 (39.4-44.4)	0.900
Platelet count (×10 ³ /µL)	222 (196-279)	229 (197-283)	0.900
RDW-CV (%)	14.6 (13.4-15.7)	13.7 (12.6-15)	0.002
PAP therapy initiation	60 (60.6%)	87 (56.1%)	0.400
Regular follow-up attendance	16 (16.5%)	26 (16.9%)	0.900

Values are presented as n (%) for categorical variables and as median (interquartile range) for continuous variables. OSA: Obstructive sleep apnea, REM: Rapid eye movement, COPD: Chronic obstructive pulmonary disease, ENT: Ear, nose, and throat, BMI: Body mass index, PSG: Polysomnography, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, SpO₂: Peripheral oxygen saturation, T90: Time spent with SpO₂ <90%, REM AHI: Apnea-hypopnea index during REM sleep, NREM AHI: Apnea-hypopnea index during non-REM sleep, PLM: Periodic limb movements, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gamma-glutamyl transferase, CRP: C-reactive protein, WBC: White blood cell count, RDW-CV: Red cell distribution width-coefficient of variation.

The N1 percentage was higher and the REM percentage was lower among non-survivors, while N2 and N3 percentages were similar between groups. PLM index did not differ significantly (Table 2).

Laboratory findings showed higher glucose, urea, serum iron, white blood cell count, and RDW-CV in non-survivors (all $p \leq 0.01$), while HDL levels were lower ($p < 0.001$). Creatinine, AST, ALT, GGT, total cholesterol, triglycerides, LDL, CRP, ferritin, hemoglobin, hematocrit, and platelet counts were similar between groups (Table 2).

Positive airway pressure (PAP) therapy initiation rates and regular follow-up attendance did not differ significantly between survivors and non-survivors (Table 2).

In multivariable Cox regression analyses performed to identify independent predictors of mortality in patients aged ≥ 65 years, the six covariates retained across all models were selected based on their univariable associations with mortality, clinical relevance, and avoidance of multicollinearity. BMI was not included because of its strong correlation with neck circumference ($r = 0.80$); therefore, neck circumference was retained as the anthropometric variable in the multivariable models. Across all three models, age, male sex, neck circumference, diabetes mellitus, RDW-CV, and sleep efficiency were consistently associated with mortality. Age was a strong independent predictor of mortality in all models (HR: 1.08, 95% CI: 1.05–1.12; $p < 0.001$). Male sex was associated with a significantly increased risk of mortality, with HRs ranging from 1.92 to 2.00 across models (all $p \leq 0.008$). Similarly, diabetes mellitus was independently associated with higher mortality risk (HR: 2.13–2.38; all $p \leq 0.001$). Neck circumference was also positively associated with mortality (HR: 1.03 in all models; $p \leq 0.002$), while RDW-CV showed a modest but significant association (HR: 1.13–1.16; $p \leq 0.03$). In contrast, sleep efficiency was inversely associated with mortality, indicating a protective effect (HR 0.97, 95% CI: 0.96–0.99; $p < 0.001$ in all models). Regarding OSA severity metrics, T90 was significantly associated with mortality in Model 1 (HR: 1.20, 95% CI: 1.05–1.37; $p = 0.009$).

In Model 2, AHI showed a statistically significant but small effect size (HR: 1.01, 95% CI: 1.00–1.02; $p = 0.02$). Similarly, in Model 3, ODI was also associated with mortality with a modest effect (HR: 1.01, 95% CI: 1.00–1.02; $p = 0.04$) (Table 3).

Discussion

In this study, we demonstrated that OSA exhibits marked age-related differences in clinical presentation, disease severity, and prognostic determinants. By comparing two extreme age groups (≤ 35 and ≥ 65 years), we aimed to capture distinct phenotypic patterns rather than intermediate variations. Although aging is a well-established risk factor for OSA, a substantial proportion of patients in our cohort were aged ≤ 35 years, underscoring that clinically significant OSA is not confined to older populations. Younger patients were characterized by a phenotype with male predominance, a higher frequency of positional OSA, lower comorbidity burden, and relatively preserved oxygenation and sleep architecture, suggesting a more localized and position-dependent form of the disease. In contrast, older patients exhibited a more complex phenotype, with substantially higher comorbidity burden, more severe respiratory disturbance, greater hypoxic exposure, and impaired sleep architecture. These differences were accompanied by a markedly higher mortality rate in the older group. Furthermore, within this group, age, sex, neck circumference, diabetes mellitus, RDW-CV, and sleep efficiency emerged as independent predictors of mortality, indicating that prognostic profiles in OSA differ across age groups.

These findings are particularly noteworthy given that OSA is traditionally considered a disorder of older individuals. However, epidemiological data indicate that moderate-to-severe sleep-disordered breathing is also present in younger adult populations, with prevalence estimates reaching approximately 10% in men and 3% in women aged 30–49 years (11). Despite this, most epidemiological studies have examined broad adult age ranges (12), often grouping younger individuals with middle-aged populations, thereby limiting insights into early-

Table 3. Multivariable Cox regression models evaluating factors associated with mortality using different OSA severity metrics.

Parameters	Model 1		Model 2		Model 3	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (years)	1.08 (1.05-1.12)	<0.001	1.08 (1.05-1.12)	<0.001	1.08 (1.05-1.12)	<0.001
Male sex	2.00 (1.25-3.23)	0.004	1.92 (1.19-3.03)	0.008	1.92 (1.19-3.13)	0.007
Neck circumference (cm)	1.03 (1.02-1.05)	<0.001	1.03 (1.01-1.05)	0.002	1.03 (1.01-1.05)	0.002
Diabetes mellitus	2.13 (1.39-3.33)	0.001	2.38 (1.56-3.70)	<0.001	2.33 (1.52-3.57)	<0.001
RDW-CV (%)	1.13 (1.01-1.26)	0.030	1.16 (1.03-1.29)	0.010	1.14 (1.02-1.28)	0.010
Sleep efficiency (%)	0.97 (0.96-0.99)	<0.001	0.97 (0.96-0.99)	<0.001	0.97 (0.96-0.99)	<0.001
Time with SpO ₂ <90% (hours)*	1.20 (1.05-1.37)	0.009	-	-	-	-
AHI (events/hour)	-	-	1.01 (1.00- 1.02)	0.020	-	-
ODI (events/hour)	-	-	-	-	1.01 (1.00-1.02)	0.040

Values are presented as hazard ratios (HR) with 95% confidence intervals (CI). Model 1 includes time spent with SpO₂ <90% (T90), Model 2 includes apnea–hypopnea index (AHI), and Model 3 includes oxygen desaturation index (ODI). *T90 was entered into the regression models as hours. HR: Hazard ratio, CI: Confidence interval, RDW-CV: Red cell distribution width–coefficient of variation, SpO₂: Peripheral oxygen saturation, T90: Time spent with SpO₂ <90%, AHI: Apnea–hypopnea index, ODI: Oxygen desaturation index.

onset OSA. By specifically focusing on patients aged ≤ 35 years, our study provides novel insights into this underexplored subgroup. Beyond clinical differences, marked demographic variations were also observed between age groups. In particular, the higher proportion of female patients in the older group is consistent with prior evidence indicating that the risk of OSA increases significantly in women after menopause, likely due to hormonal changes affecting respiratory control and upper airway stability (4).

In line with previous studies, positional OSA in our cohort was more prevalent among younger patients with a lower comorbidity burden (1,13,14). This phenotype has been consistently associated with younger age, lower BMI, milder disease severity, and reduced hypoxic burden. Emerging evidence further suggests that positional OSA may represent an early stage in the natural history of the disease, with a subset of patients transitioning to non-positional OSA over time in association with increasing age, weight, and disease severity (13,14). However, it remains unclear whether this pattern reflects true disease progression or the presence of distinct, age-related phenotypes. Consistent with these phenotypic differences, PAP therapy was less frequently initiated in younger patients, particularly those with positional OSA and low comorbidity burden. This likely reflects real-world clinical decision-making, in which treatment strategies are influenced not only by AHI but also by symptom profile, comorbidities, and perceived disease impact. In contrast, older patients with more severe and non-positional disease, as well as a higher comorbidity burden, were more likely to receive PAP therapy. These findings support the concept that OSA management is inherently phenotype-driven and may vary substantially across age groups.

A similar pattern was observed in terms of comorbidity burden, with older patients exhibiting substantially higher rates of cardiometabolic and respiratory conditions (1,3). This difference may reflect, at least in part, the cumulative effects of prolonged exposure to OSA. However, it should also be interpreted in the context of aging itself, as OSA-related manifestations and age-related multimorbidity substantially overlap in older adults. In addition, age-related alterations in sleep architecture are well established, with reductions in slow-wave and REM sleep, increased lighter sleep stages, and decreased sleep efficiency observed with advancing age (15). Consistent with these findings, older patients in our cohort demonstrated a more fragmented and less restorative sleep profile.

Physiological studies further support that OSA in older adults represents a distinct entity driven by different underlying mechanisms. Trait-based analyses have shown that aging is associated with increased upper airway collapsibility, whereas ventilatory control instability and respiratory drive are reduced compared to younger individuals. In contrast, younger patients tend to exhibit relatively preserved airway anatomy but greater ventilatory instability, indicating that different physiological traits predominate across age groups. Together, these findings suggest that OSA in younger and older individuals may arise from fundamentally different pathophysiological mechanisms rather than representing a single uniform disease spectrum (16).

This mechanistic divergence may help explain the more severe respiratory disturbance, greater hypoxic burden, and impaired sleep architecture observed in older patients in our cohort.

An additional notable finding was that conventional OSA severity metrics, including AHI and ODI, were independently associated with mortality in the older group, albeit with modest effect sizes. In contrast, factors reflecting systemic burden and physiological reserve, such as age, neck circumference, diabetes mellitus, RDW-CV, and sleep efficiency, showed stronger and more consistent associations across models. These findings suggest that in older adults, mortality risk may be more closely related to overall biological vulnerability and comorbidity burden than to the frequency of respiratory events alone. This pattern indicates a relative shift in prognostic relevance from event-based severity metrics toward markers of systemic dysregulation. Although indices such as AHI and ODI capture the frequency of respiratory disturbances, they may not fully reflect the downstream consequences of intermittent hypoxia, including oxidative stress, inflammation, and accelerated biological aging. In this context, elevated RDW-CV may represent an integrative marker of chronic systemic stress, capturing both age-related vulnerability and the cumulative physiological impact of OSA.

Intermittent hypoxia and sleep fragmentation in OSA promote oxidative stress, systemic inflammation, and pathways linked to cellular senescence (17). In parallel, RDW is increasingly recognized as a marker of chronic inflammation and biological aging and has been consistently associated with increased mortality risk in the general population (18). Moreover, elevated RDW levels are linked to a broad spectrum of cardiovascular and metabolic conditions, supporting its role as an integrative marker of systemic disease burden (19). Taken together, these findings suggest that the interaction between age-related physiological changes and OSA-related inflammatory processes may underlie the increased mortality observed in older patients in our cohort.

Despite the relatively low rates of regular clinical follow-up and PAP therapy initiation, no significant difference in mortality was observed according to treatment status or follow-up adherence in the older group. This finding should be interpreted with caution, as treatment was not randomly assigned and may be subject to confounding by indication, whereby patients with more severe disease and higher baseline risk are more likely to receive treatment. Importantly, mortality ascertainment in this study was complete through the national death notification system, minimizing bias related to loss to follow-up and strengthening the validity of outcome assessments.

Beyond this methodological consideration, our findings may also reflect a broader pathophysiological shift in older individuals with OSA. While OSA in younger patients may predominantly represent a mechanical and potentially reversible disorder, in older adults it may instead reflect the cumulative burden of aging-related physiological decline. By the time of diagnosis, systemic processes such as chronic inflammation, metabolic dysregulation, and vascular damage may already be established, potentially attenuating the impact of OSA-targeted therapies on long-term outcomes. In this context, mortality risk in older

patients may be driven less by conventional OSA severity metrics and more by markers of overall biological vulnerability and reduced physiological reserve.

Overall, these findings highlight that OSA is not a uniform disorder but varies substantially across age groups in terms of clinical presentation, underlying mechanisms, and prognostic implications. Recognizing these age-related differences may have important clinical implications, particularly for risk stratification and individualized management strategies. Future studies are needed to further elucidate age-specific disease trajectories and optimize personalized approaches to OSA care.

Study Limitations

This study has several limitations. First, its retrospective single-center design may have introduced selection bias and may limit the generalizability of the findings beyond a sleep laboratory population. Second, mortality analyses were based on all-cause mortality, and cause-specific mortality data were not available, limiting further interpretation of underlying mechanisms. Finally, although information on regular follow-up attendance was available, detailed objective data on treatment adherence, particularly to PAP therapy, were not consistently accessible.

Conclusion

In conclusion, OSA exhibits substantial age-related differences in clinical presentation, pathophysiology, and prognostic determinants. Younger and older patients appear to represent distinct clinical profiles, highlighting the need for age-specific approaches to risk assessment and management.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of University of Health Sciences Türkiye Başakşehir Çam and Sakura City (approval number: 2026-6, date: 12.02.2026). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Due to the retrospective design of the study and the use of anonymized data, the requirement for written informed consent was waived by the ethics committee.

Footnotes

Authorship Contributions

Surgical and Medical Practice: D.A.Y., Concept: D.A.Y., S.N.S., Design: S.N.S., C.S., S.N.K., C.Ö., Data Collection or Processing: D.A.Y., S.N.S., C.S., Ş.A., S.N.K., Analysis or Interpretation: D.A.Y., C.S., Literature Search: C.S., Ş.A., S.N.K., Writing: D.A.Y., S.N.S., Ş.A., S.N.K., C.Ö.

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