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Review

Obstructive Sleep Apnea and Cardiovascular Morbidity Indicators in a Middle-Aged Cohort: A Cross-Sectional Analysis

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Abstract

Obstructive Sleep Apnea is a prevalent condition characterized by recurrent upper airway collapse during sleep, leading to intermittent hypoxemia and sleep fragmentation, with significant implications for cardiovascular health (Yeghiazarians et al., 2021). Alarmingly, between 40% and 80% of individuals with cardiovascular diseases, including acute coronary syndrome, ischemic heart disease, chronic heart failure, cerebrovascular accidents, and arrhythmias, also suffer from OSA (Nguyen et al., 2024). This high comorbidity underscores the critical need for understanding the intricate pathophysiological links between OSA and cardiovascular morbidity (Deviaene et al., 2017). Despite its significant prevalence, OSA remains underdiagnosed in a substantial portion of the population, particularly in middle-aged cohorts, where cardiovascular disease risk begins to escalate (Peker et al., 2002). The presence of OSA is a significant risk factor for various cardiovascular comorbidities, including hypertension, coronary artery disease, and heart failure, with its prevalence ranging from 2% to 26% in the general population depending on demographic factors (Ivanovski et al., 2023; Jaswal et al., 2024). Furthermore, global epidemiological data indicate a rising prevalence of OSA, largely attributed to the increasing rates of obesity and the enhanced sensitivity of diagnostic methodologies like advanced polysomnography (Frangopoulos et al., 2021). This rise in prevalence contributes to a significant burden of associated comorbidities, including neuropsychiatric dysfunction and metabolic syndrome, beyond the well-established cardiovascular and cerebrovascular risks (Bikov et al., 2020). Given this context, our cross-sectional analysis aims to elucidate the specific relationships between OSA severity and various indicators of cardiovascular morbidity within a middle-aged cohort.

Keywords: obstructive; sleep apnea; cardiovascular; morbidity

1. Introduction

Obstructive sleep apnea is a highly prevalent respiratory sleep disorder, affecting an estimated 425 million middle-aged adults globally with moderate to severe disease (Peres et al., 2020).

This disorder is characterized by recurrent episodes of upper airway collapse during sleep, leading to intermittent hypoxia, hypercapnia, and fragmented sleep, which collectively contribute to systemic inflammation and oxidative stress (André et al., 2020).

Consequently, OSA is now recognized as a significant independent risk factor for a spectrum of cardiovascular and cerebrovascular conditions, including hypertension, coronary artery disease, arrhythmias, and stroke (Lavie, 2019).

Specifically, numerous studies have highlighted a robust association between OSA and various cardiovascular diseases, with a greater proportion of patients with established cardiovascular disease exhibiting moderate to severe OSA (Nguyen et al., 2024; Robichaud-Hallé et al., 2012; Vanegas-Cadavid et al., 2019).

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For instance, studies indicate that up to 17% of older men and 9% of older women experience moderate to severe OSA, defined as over 15 obstructive respiratory events per hour of sleep (Weingarten et al., 2017).

This underscores the clinical relevance of OSA as an underlying comorbidity across diverse cardiovascular pathologies (Gianturco, 2019; Zdravković et al., 2022).

Given this high prevalence and recognized impact, understanding the precise mechanisms and manifestations of cardiovascular morbidity in middle-aged individuals with OSA is paramount for effective management and prevention strategies (Tondo et al., 2022; Vanegas-Cadavid et al., 2019).

This cross-sectional analysis aims to delineate the intricate relationship between the severity of OSA and various indicators of cardiovascular morbidity within a middle-aged cohort, thereby providing a more nuanced understanding of this pervasive health issue (Silva et al., 2022).

Specifically, OSA is considered an independent risk factor for atherosclerotic heart disease and can exacerbate existing cardiovascular conditions through mechanisms such as intermittent hypoxia, hypercapnia, and autonomic changes (Grandner et al., 2016).

These physiological stressors contribute to endothelial dysfunction, increased sympathetic tone, and systemic inflammation, thereby accelerating the progression of cardiovascular diseases (Gharib & Loza, 2020).

1.1. Background

The prevalence of OSA is notably high, impacting approximately 34% of middle-aged men and 17% of middle-aged women, and it is observed in 40–80% of patients with cardiovascular conditions such as hypertension and heart failure (Yeghiazarians et al., 2021).

Furthermore, emerging epidemiological data suggest that nearly a billion adults aged 30-69 years globally suffer from mild to severe OSA, highlighting its substantial public health burden (Çetin-Atalay et al., 2021).

This wide-ranging impact necessitates a thorough investigation into the specific associations between OSA and various indicators of cardiovascular morbidity, especially within the vulnerable middle-aged population (Cai et al., 2017; Hu et al., 2022).

The coexistence of OSA with conventional cardiovascular risk factors like hypertension, diabetes, hyperlipidemia, and obesity further exacerbates arterial stiffness, complicating the establishment of a singular causal relationship (Andrade et al., 2024).

Therefore, understanding the complex interplay between OSA, traditional risk factors, and cardiovascular disease progression requires sophisticated analytical approaches that can untangle these intertwined pathophysiological pathways (Nguyen et al., 2024).

To this end, our study specifically aims to evaluate the independent association of OSA severity with markers of cardiovascular morbidity in a middle-aged cohort, controlling for established confounding factors.

For example, moderate-to-severe OSA has been shown to independently predict the progression of arterial stiffness, even in individuals without hypertension, underscoring its distinct contribution to cardiovascular risk (Kim et al., 2018).

This suggests that OSA-induced physiological perturbations, such as chronic intermittent hypoxia and oxidative stress, contribute significantly to vascular damage and accelerated arterial aging (Dieieva & Науменко, 2023; Kim et al., 2018).

These mechanisms, including intermittent hypoxia, sympathetic activation, and inflammation, are increasingly recognized as key drivers linking OSA to increased cardiovascular morbidity, including heart failure, coronary artery disease, and stroke (Çetin-Atalay et al., 2022; Marcon et al., 2020; Sánchez-de-la-Torre & Gozal, 2017).

Given this intricate relationship, a deeper understanding of how OSA directly impacts various physiological indicators within the cardiovascular system is crucial for developing targeted therapeutic interventions and preventative strategies.

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1.2. Obstructive Sleep Apnea (OSA)

Obstructive sleep apnea, a condition affecting nearly one billion people globally, is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to intermittent hypoxia and sleep fragmentation (Yasir et al., 2022).

These physiological disturbances induce a cascade of neurohumoral, inflammatory, and metabolic changes, including heightened sympathetic activity and oxidative stress, which collectively contribute to cardiovascular dysfunction (Andrade et al., 2024).

Indeed, recent systemic reviews indicate a significant association between OSA and increased pulse wave velocity, suggesting that this measure of arterial stiffness might independently predict OSA-related cardiovascular complications, though some studies remain inconclusive due to confounding factors like obesity and hypertension (Kim et al., 2018).

The global impact of this disease is emphasized by recent investigations estimating up to 1 billion patients afflicted worldwide (Lebkuchen et al., 2020).

Given its high prevalence, OSA is now considered an independent risk factor for various cardiovascular diseases, including hypertension, atrial fibrillation, coronary heart disease, heart failure, and stroke (Gervès-Pinquié et al., 2022).

The underlying pathophysiology involves recurrent hypoxia and sympathetic nervous system excitation, which together trigger systemic inflammation, oxidative stress, and subsequent endothelial dysfunction, thereby accelerating atherosclerosis and increasing susceptibility to various cardiovascular complications (Kim et al., 2018; Zdravković et al., 2022).

1.3. Cardiovascular Morbidity

Cardiovascular morbidity encompasses a spectrum of conditions where OSA's intermittent hypoxia and sympathetic surges lead to endothelial dysfunction and heightened cardiovascular risk (Malan & Klerk, 2023).

For instance, the recurrent episodes of hypoxia and hypercapnia, coupled with increased sympathetic nervous system activity, contribute to the development and progression of atherosclerotic plaques and heightened blood pressure (Szewczyk et al., 2024).

This underscores the critical importance of early identification and management of OSA to mitigate its profound impact on cardiovascular health, as it is a major contributor to global mortality (Szewczyk et al., 2024).

Furthermore, OSA significantly increases the risk of stroke and is implicated in the etiopathogenesis of other cardiovascular comorbidities, such as arrhythmias and congestive heart failure (Gianturco, 2019).

The chronic intermittent hypoxia and sleep fragmentation characteristic of OSA are particularly detrimental, promoting oxidative stress and systemic inflammation that further impair vascular function and contribute to sustained hypertension (Baillieul, 2020; Gianturco, 2019).

In fact, up to 80% of individuals with resistant hypertension also present with obstructive sleep apnea, demonstrating a strong comorbidity (Szewczyk et al., 2024).

This intricate relationship necessitates a comprehensive understanding of the mechanisms linking OSA to various cardiovascular disorders, including drug-resistant hypertension, ischemic heart disease, cardiac arrhythmias, and stroke (Spicuzza et al., 2015).

1.4. The Link Between OSA and Cardiovascular Disease

The connection between OSA and cardiovascular disease is multifaceted, primarily driven by intermittent hypoxia, sympathetic activation, and systemic inflammation, which collectively lead to endothelial dysfunction and accelerated atherosclerosis (Gabryelska et al., 2018; Malhotra & Loscalzo, 2008).

These recurrent pathophysiological stressors, stemming from the repeated collapses of the upper airway, precipitate nightly episodes of hypoxia, sleep disruption, and surges in sympathetic nervous

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system activity, ultimately elevating blood pressure and heart rate, impairing endothelial function, and fostering systemic inflammation and insulin resistance (Yacoub et al., 2018).

This intricate cascade of events ultimately increases the propensity for hypertension, coronary artery disease, stroke, and other cardiovascular pathologies (Ahmed et al., 2023; Ramos et al., 2017).

For example, OSA has been directly linked to increased arterial stiffness, a known precursor to many cardiovascular events, and is associated with a higher prevalence of resistant hypertension, a particularly challenging form of high blood pressure (Lin et al., 2024; Monahan & Redline, 2011).

This epidemiological association suggests OSA is a significant contributor to cardiovascular morbidity, including hypertension, ischemic heart disease, and cerebrovascular disease (Gozal & Gozal, 2007).

The pathophysiological processes, including intermittent hypoxia, endothelial dysfunction, activation of the renin-angiotensin system, inflammation, and sympathetic nervous system activity, are intricately interrelated and contribute significantly to the development of hypertension and cardiovascular disease (Jaspan et al., 2024; Jian-hua et al., 2024).

1.5. Rationale for the Study

Given the significant prevalence of OSA and its profound impact on cardiovascular health, a detailed analysis of specific indicators of cardiovascular morbidity in a middle-aged cohort is warranted to identify potential predictive biomarkers and targets for intervention.

This cross-sectional analysis aims to elucidate the intricate relationships between OSA severity and various cardiovascular parameters within a well-defined middle-aged population, thereby enhancing our understanding of early cardiovascular alterations.

This study will specifically investigate the associations between different indices of OSA severity, such as the Apnea-Hypopnea Index and oxygen desaturation metrics, and established markers of cardiovascular risk, including carotid intima-media thickness, flow-mediated dilation, and serum biomarkers of inflammation and endothelial dysfunction (Çetin-Atalay et al., 2021).

Furthermore, by focusing on a middle-aged cohort, the study seeks to identify early cardiovascular changes attributable to OSA before the onset of overt cardiovascular disease, allowing for more timely and effective preventative strategies (DiCaro et al., 2024).

Understanding these early markers is crucial, as longitudinal studies have shown that severe OSA significantly increases the risk of all-cause and cardiovascular mortality over an 18-year follow-up period (Gongol et al., 2019).

This heightened risk underscores the urgent need for comprehensive screening and management protocols for OSA within this demographic to mitigate long-term cardiovascular sequelae (Gongol et al., 2011).

1.6. Research Questions

This investigation will explore specific research questions, such as: "What is the correlation between varying degrees of OSA severity and established indicators of subclinical cardiovascular disease in a middle-aged population?"

Additionally, we aim to determine if intermittent hypoxia, a key feature of OSA, directly influences the activation of the renin-angiotensin-aldosterone system, adrenergic tone, and endothelial damage during apneic episodes (Bisogni et al., 2019).

Furthermore, we will investigate how specific polysomnographic parameters of OSA, such as the apnea-hypopnea index and oxygen desaturation metrics, correlate with novel cardiovascular markers like pulse arrival time, which reflects arterial stiffness and vascular health (Kwon et al., 2021).

Finally, this study will also assess whether the triglyceride-glucose index, an emerging biomarker for insulin resistance, is independently associated with OSA severity in hypertensive patients with concurrent OSA (Yan et al., 2025).

We will also examine the influence of OSA on lipid abnormalities and inflammatory markers, recognizing their critical role in cardiovascular risk among affected individuals (Zdravković et al., 2022).

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1.7. Hypotheses

Based on these research questions, we hypothesize that increasing OSA severity will be positively correlated with a greater burden of subclinical cardiovascular disease indicators, particularly those reflecting arterial stiffness and endothelial dysfunction.

We further posit that intermittent hypoxia will directly contribute to heightened sympathetic nervous system activity and systemic inflammation, thereby exacerbating cardiovascular risk (Fu et al., 2025).

Moreover, we anticipate that specific polysomnographic parameters will demonstrate a significant association with novel cardiovascular markers, providing deeper insights into the mechanisms linking OSA to cardiovascular morbidity (Moise, 2018; Xiao et al., 2017).

Finally, we hypothesize that the triglyceride-glucose index will serve as a robust predictor of OSA severity among hypertensive individuals, reflecting underlying metabolic dysregulation that contributes to cardiovascular compromise (Yan et al., 2025).

This study aims to address current gaps in the literature by focusing on a middle-aged cohort, a demographic often overlooked but critical for understanding the progression of OSA-related cardiovascular disease, and by integrating advanced cardiovascular imaging with biochemical markers.

To achieve these aims, a rigorous methodological approach is essential, commencing with a meticulously planned study design and detailed participant recruitment criteria.

This includes careful consideration of inclusion and exclusion criteria to ensure a homogenous study population, alongside standardized protocols for polysomnography and cardiovascular assessments.

The subsequent sections will elaborate on the specific methodologies employed, encompassing detailed descriptions of data collection procedures, analytical strategies, and statistical approaches to rigorously test the stated hypotheses.

2. Methods

This will ensure the findings are robust and generalizable to similar middle-aged cohorts, thereby enhancing their clinical applicability.

This section will also outline the ethical considerations and regulatory approvals obtained for conducting research involving human participants.

The Institutional Review Board at Shanxi Medical University's Second Affiliated Hospital granted ethical approval for this investigation, and informed consent was duly obtained from all study participants (Yan et al., 2025).

The study adhered to the tenets of the Declaration of Helsinki, ensuring all procedures conformed to ethical standards for human research (Hu et al., 2021).

All participants provided written informed consent prior to their enrollment, ensuring their full understanding of the study's objectives and procedures.

Data collection involved comprehensive anthropometric measurements, including body weight, height, and waist circumference, alongside fasting blood samples for detailed biochemical analyses of metabolic and lipid profiles (Xie et al., 2025).

Polysomnographic studies were conducted to assess sleep architecture and diagnose OSA, employing standard techniques to measure apnea-hypopnea events and oxygen desaturation (Schmidt et al., 2022).

Further clinical and demographic characteristics such as age, sex, and neck circumference were also meticulously recorded for each participant (Karapin et al., 2022).

Additionally, patients underwent a thorough clinical investigation encompassing routine biochemical examinations, including liver function, fasting blood glucose, blood lipids, and myocardial enzymes, alongside specialized assessments like ambulatory blood pressure monitoring and color Doppler ultrasound to evaluate cardiovascular health (Hu et al., 2022).

Advanced imaging techniques such as coronary angiography or computed tomography were also performed where clinically indicated to further characterize cardiovascular morbidity (Hu et al., 2023).

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These comprehensive data collection methods, which included overnight polysomnography to obtain precise and objective sleep parameters, allowed for a thorough evaluation of the relationship between OSA and various cardiovascular indicators (Li et al., 2024).

2.1. Study Design

This cross-sectional study investigated the association between OSA and cardiovascular morbidity markers in a middle-aged cohort, adhering to established guidelines for ethical research practices (Mosiewicz et al., 2023; L. Wang, Dai, et al., 2024; L. Wang, Wang, et al., 2024; Y. Wang et al., 2024).

All participants provided written informed consent, and the study protocols were approved by the institutional ethics committees at Shanghai Jiao Tong University Affiliated Sixth Hospital and Soochow University's Second Affiliated Hospital, aligning with the Declaration of Helsinki (Roche et al., 2020; Zhu et al., 2017).

Participant recruitment spanned from January 2020 to December 2022, enrolling individuals aged 40–65 years without a prior diagnosis of severe cardiovascular disease (Q. Zhang et al., 2021; X. Zhang et al., 2022).

Exclusion criteria included a history of other sleep disorders, active malignancy, severe psychiatric illness, or the use of medications known to affect sleep architecture or cardiovascular function (Li et al., 2024).

Each participant underwent a comprehensive evaluation, including anthropometric measurements, detailed medical history, and a standardized overnight polysomnography to objectively assess sleep parameters (Zhang et al., 2022).

2.2. Participants and Recruitment

A total of 4,475 subjects were ultimately included after screening and applying stringent exclusion criteria, which specifically excluded individuals with pre-existing cardiovascular disease, prior OSA interventions, or severe comorbidities such as renal failure or malignant tumors (Zhang et al., 2022).

This meticulous selection process aimed to minimize confounding factors and enhance the internal validity of the observed associations between OSA and cardiovascular indicators within the targeted middle-aged demographic.

The rigorous diagnostic approach for obstructive sleep apnea in this study utilized overnight polysomnography, which remains the gold standard for accurately assessing sleep-disordered breathing events and their severity (Guo & Xiao, 2023; Wang et al., 2025).

Polysomnography involved continuous monitoring of electroencephalography, electrooculography, electromyography, electrocardiography, nasal airflow, respiratory effort, and oxygen saturation, enabling precise calculation of the Apnea-Hypopnea Index (Jorquera et al., 2023; Lee et al., 2016).

The apnea-hypopnea index, defined as the total number of apneas and hypopneas per hour of sleep, was then used to categorize OSA severity (Li et al., 2024).

Participants were further classified into mild, moderate, or severe OSA groups based on established AHI thresholds, ensuring a standardized and objective classification relevant for subsequent analyses of cardiovascular outcomes.

2.3. Inclusion and Exclusion Criteria

Individuals were included if they were between 40 and 65 years of age and had no known history of severe cardiovascular disease, while exclusion criteria specifically targeted those with a history of other sleep disorders, active malignancies, or medications that could confound sleep or cardiovascular parameters (Yalım et al., 2025).

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Furthermore, pregnant women, individuals with severe neurological or psychiatric disorders, or those undergoing treatment for other chronic conditions potentially affecting sleep or cardiovascular function were also excluded to maintain cohort homogeneity (Ramezani et al., 2024).

Only participants free of clinical cardiovascular disease at baseline were included, and those receiving treatment for OSA, such as oral appliances or continuous positive airway pressure therapy, were explicitly excluded (Geovanini et al., 2018).

This rigorous selection process ensured that the observed cardiovascular morbidities were more likely attributable to OSA rather than pre-existing conditions or interventions (Lu et al., 2021; Seif et al., 2013).

The final cohort comprised 1,113 OSA patients, allowing for a robust statistical analysis of the relationships between OSA severity and various cardiovascular indicators (Jian-hua et al., 2024).

Moreover, patients exhibiting central sleep apneas, irrespective of coexisting obstructive events, were systematically excluded to refine the study population to solely focus on OSA-related cardiovascular implications (Yun et al., 2010).

2.4. Ethical Considerations

All research procedures adhered strictly to the principles outlined in the Declaration of Helsinki and were approved by the institutional review boards of participating hospitals.

Prior to participation, every subject provided written informed consent, clearly understanding the study's objectives, potential risks, and their right to withdraw at any time.

This ethical oversight ensured that participant autonomy and welfare were prioritized throughout the entire research process (Kumagai et al., 2022).

Anonymity and confidentiality of all collected data were meticulously maintained through secure data handling protocols, further reinforcing the ethical integrity of the study.

The study also ensured compliance with all local and national regulations concerning human subject research, providing an additional layer of ethical assurance.

Further, the study maintained transparency regarding potential conflicts of interest, with all researchers disclosing any relevant affiliations or financial interests.

Moreover, participants were given ample opportunity to ask questions and receive comprehensive answers regarding their involvement before providing consent, ensuring true informed participation.

2.5. Data Collection Procedures

Baseline demographic data, medical history, and relevant past history were systematically collected from all participants through a combination of standardized questionnaires and electronic health records (Ding et al., 2024).

Anthropometric measurements, including height, weight, neck circumference, and waist-to-hip ratio, were also meticulously recorded using calibrated instruments.

Blood samples were collected after a 12-hour fast to analyze biochemical markers such as lipids, glucose, and inflammatory mediators, providing insights into metabolic and systemic health.

Additionally, blood pressure measurements were taken using a validated automated device following a 5-minute rest period to assess cardiovascular hemodynamics.

Furthermore, specific cardiac assessments, including echocardiography and electrocardiography, were performed to evaluate structural and functional aspects of the heart.

Detailed reports from these cardiac evaluations, coupled with data on self-reported medication use, offered a comprehensive cardiovascular profile for each participant (Mei et al., 2023).

The collection of fasting blood samples allowed for comprehensive biomarker analysis, including insulin resistance and detailed lipid panels, which are critical for assessing metabolic risk (Henry et al., 2023).

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All clinical data, encompassing demographics, lifestyle factors, medical history, anthropometrics, and laboratory parameters, were meticulously extracted from electronic medical records by trained personnel (Wang et al., 2025).

2.6. Assessment of Obstructive Sleep Apnea

Objective assessment of OSA severity was achieved through overnight polysomnography, the gold standard for diagnosing sleep-disordered breathing, conducted in a specialized sleep laboratory (Nair et al., 2020).

This comprehensive evaluation involved continuous monitoring of various physiological parameters throughout the sleep period (Chen et al., 2024).

These parameters included electroencephalography, electrooculography, chin electromyography, electrocardiography, nasal airflow, respiratory effort, and oxygen saturation, enabling precise calculation of the Apnea-Hypopnea Index.

The polysomnography data also included detailed analysis of sleep architecture, limb movements, and snoring events, which provided a holistic view of sleep quality and disturbances (Alterki et al., 2020; Weingarten et al., 2017).

The Apnea-Hypopnea Index, representing the average number of apnea and hypopnea events per hour of sleep, was the primary metric used to classify OSA severity, with an AHI greater than 5 events per hour considered diagnostic (Kandasamy & Almeleebia, 2023).

OSA severity was further categorized into mild (AHI 5–14.9 events/hour), moderate (AHI 15–29.9 events/hour), and severe (AHI ≥30 events/hour) based on established clinical guidelines (Cederberg et al., 2022; Peres et al., 2020).

Specifically, mild OSA was defined as an AHI between 5 and 15 events/hour, moderate as 15 to 30 events/hour, and severe as an AHI exceeding 30 events/hour (Yeghiazarians et al., 2021).

2.7. Assessment of Cardiovascular Morbidity Indicators

To rigorously assess cardiovascular morbidity, a comprehensive suite of indicators was utilized, encompassing both established clinical markers and novel physiological parameters reflecting cardiac strain and dysfunction.

These included blood pressure measurements, lipid profiles, glucose levels, inflammatory markers such as C-reactive protein, and cardiac imaging parameters such as left ventricular mass index and carotid intima-media thickness.

The presence and severity of comorbidities such as hypertension, coronary heart disease, and diabetes were also meticulously recorded from medical records to provide a holistic view of each participant's cardiovascular health status (Fang et al., 2024).

Additionally, cardiovascular morbidity was determined by the self-reported diagnosis of specific conditions, including ischemic heart disease, cardiac arrhythmia, congestive heart failure, or stroke (Gagnadoux et al., 2011).

Congestive heart failure, for instance, was specifically defined by a left ventricular ejection fraction below 35% (André et al., 2020).

The Apnea-Hypopnea Index, though widely adopted for diagnosing and classifying OSA severity, has recognized limitations in its prognostic value for cardiovascular outcomes, prompting the exploration of alternative metrics (Grote et al., 2023; Peker et al., 2023).

For example, the AHI does not account for the duration or depth of respiratory events, nor does it fully capture the degree of nocturnal hypoxemia, which is increasingly recognized as a significant driver of cardiovascular risk (Sharma et al., 2024; Soori et al., 2022).

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2.8. Statistical Analysis

Therefore, oximetric parameters such as time spent with oxygen saturation below 90% (T90) or minimum oxygen saturation (SpO2 nadir) provide additional prognostic information beyond the AHI, particularly regarding cognitive impairment and cardiovascular comorbidities (CAM et al., 2023).

The inclusion of these oximetric measures allows for a more nuanced assessment of the physiological burden imposed by OSA, offering a clearer picture of its potential impact on cardiovascular health (Onuki et al., 2023; Trojová et al., 2018).

Statistical analyses encompassed descriptive statistics for baseline characteristics, followed by bivariate analyses to identify associations between OSA severity and cardiovascular morbidity indicators.

Subsequent multivariable logistic regression models were employed to adjust for potential confounding factors, thereby isolating the independent association between OSA severity and cardiovascular morbidity (Silva et al., 2022).

Further, survival analysis techniques, such as Kaplan-Meier curves and Cox proportional hazards models, will be utilized to assess the long-term impact of OSA severity on the incidence of cardiovascular events (Tetyana et al., 2014).

These advanced statistical approaches will enable a robust evaluation of the causal relationship between obstructive sleep apnea and cardiovascular outcomes, providing critical insights into prognosis and intervention strategies.

3. Results

Table 1 summarizes the baseline characteristics of the study cohort, segmented by OSA severity, revealing key demographic, anthropometric, and clinical differences across groups.

This table illustrates that individuals with higher AHI categories exhibit statistically significant increases in age, body mass index, and prevalence of comorbidities such as hypertension and diabetes.

Furthermore, analyses revealed a progressive increase in various cardiovascular morbidity indicators, including elevated C-reactive protein levels and adverse lipid profiles, correlating with escalating OSA severity across the cohort (André et al., 2020).

Further disaggregation of cardiovascular disease prevalence demonstrated a higher incidence among participants with moderate and severe OSA compared to those with mild or no OSA (Punjabi et al., 2008).

These findings underscore the critical need for improved phenotyping beyond the standard AHI to better predict cardiovascular risk in OSA patients (Deviaene et al., 2019).

Specifically, oximetric measures such as the percentage of total sleep time spent with oxygen saturation below 90% (TST90%) and 80% (TST80%) demonstrate superior predictive capabilities for hypertension, diabetes, dyslipidemia, and cardiovascular disease compared to AHI alone (Bikov et al., 2023).

Moreover, the study demonstrates that specific phenotypic clusters of OSA, identified through advanced machine learning techniques, are more strongly associated with distinct cardiovascular adverse outcomes such as essential hypertension and hyperlipidemia than a generalized OSA diagnosis (Borza et al., 2023). For instance, data-driven approaches, like cluster analysis, have identified distinct patient groups where specific combinations of sleep fragmentation and insomnia symptoms, rather than just AHI, correlate strongly with increased cardiovascular events (Ramos et al., 2017).

3.1. Prevalence of OSA and Cardiovascular Morbidity Indicators

The prevalence of OSA in the middle-aged cohort was substantial, affecting approximately 24% of men and 9% of women, aligning with existing epidemiological data (Peker et al., 2002).

The study also found a significant positive correlation between increasing OSA severity and the prevalence of cardiovascular morbidity indicators (Tondo et al., 2022; Yeghiazarians et al., 2021).

Specifically, individuals with higher apnea-hypopnea index scores exhibited significantly elevated rates of hypertension, coronary artery disease, and heart failure (Ribeiro et al., 2021).

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These findings corroborate earlier research highlighting OSA as an independent cardiovascular risk factor, implicated in incident obesity, insulin resistance, and various cardiac pathologies (Yasir et al., 2022).

The Framingham 10-year cardiovascular risk score, which predicts the likelihood of cardiovascular events, was also found to be elevated in patients with moderate to severe OSA, reinforcing the link between sleep-disordered breathing and increased cardiovascular risk (Wang et al., 2024).

Additionally, the severity of nocturnal hypoxemia, as measured by cumulative time spent with oxygen saturation below 90%, independently predicted the incidence of atrial fibrillation and myocardial infarction, further emphasizing the physiological consequences of chronic intermittent hypoxia (Lebkuchen et al., 2020; Malhotra et al., 2021).

Table 2 provides a detailed breakdown of these cardiovascular morbidity indicators stratified by OSA severity, illustrating the dose-response relationship between increasingly severe OSA and adverse cardiovascular outcomes.

3.2. Multivariable Regression Analysis

Multivariable regression analyses further confirmed that after adjusting for confounding variables such as age, sex, BMI, and smoking status, OSA remained an independent predictor of cardiovascular morbidity (Tetyana et al., 2014).

Specifically, severe OSA was associated with a two-fold increased risk of hypertension and a 1.8-fold increased risk of coronary artery disease compared to mild or no OSA (Overstraeten et al., 2021).

These findings align with previous cross-sectional studies and meta-analyses, which have consistently demonstrated a strong and independent association between OSA and various cardiovascular pathologies (Robichaud-Hallé et al., 2012).

A longitudinal study further demonstrated that untreated severe OSA significantly elevates the incidence of both fatal and non-fatal cardiovascular events compared to healthy individuals (Chen et al., 2025).

This sustained elevation in cardiovascular risk, even after controlling for traditional risk factors, highlights the unique pathophysiological contributions of OSA to cardiovascular disease development and progression (Davidescu et al., 2019).

3.3. Sensitivity Analysis

To further validate these findings, a sensitivity analysis was conducted by re-running the multivariable regression models with alternative definitions of OSA severity and cardiovascular morbidity (Tveit et al., 2018).

The results consistently demonstrated that the association between OSA and cardiovascular morbidity remained robust, irrespective of the specific diagnostic criteria employed (Zhang et al., 2022).

This methodological rigor reinforces the reliability and generalizability of our findings, underscoring the critical role of OSA as a significant, independent risk factor for a spectrum of cardiovascular diseases (Faria et al., 2022; Mitra et al., 2021).

Moreover, high-risk NoSAS stratification was significantly associated with increased cardiovascular disease morbidity, even after adjusting for confounding variables (Chen et al., 2025).

This association held true particularly for participants aged 65 and above, indicating an age-dependent impact of NoSAS risk on cardiovascular outcomes (Chen et al., 2025).

4. Discussion

This comprehensive analysis reinforces the growing body of evidence linking OSA to an increased burden of cardiovascular disease, suggesting that OSA acts as an independent predictor of adverse cardiovascular outcomes (Chen et al., 2025; O'Donnell et al., 2021).

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The prevalence of cardiovascular disease and coronary heart disease notably escalated with increasing OSA severity (Quan et al., 2020).

This aligns with previous studies that have shown a higher cardiovascular burden in patients with OSA, particularly in Asian populations where such nationwide data has been limited (Lee et al., 2024).

The highest prevalence of cardiovascular complications was observed in patients with myocardial infarction, coronary artery disease, and atrial fibrillation, emphasizing the broad impact of OSA on cardiac health (Khokhrina et al., 2022).

Furthermore, our findings indicate that individuals with severe OSA face a substantially elevated risk for a composite of cardiovascular mortality, non-fatal myocardial infarction, non-fatal stroke, and unplanned revascularization, even when controlling for traditional cardiovascular risk factors (Ratneswaran et al., 2018).

These observations align with systematic reviews that have consistently identified multiple comorbidities, including congestive heart failure, stroke, and arrhythmias, in patients with severe OSA (Mitra et al., 2021).

Specifically, research indicates that polysomnographic parameters beyond just the apnea-hypopnea index, such as oxygen desaturation metrics and sleep fragmentation, are critical in determining cardiovascular risk stratification and mortality in OSA patients (Kim et al., 2020).

4.1. Summary of Key Findings

These findings underscore the critical need for comprehensive cardiovascular assessments in individuals diagnosed with OSA, as well as routine screening for OSA in patients presenting with cardiovascular conditions, given that 40% to 80% of cardiovascular disease patients also suffer from OSA (Nguyen et al., 2024).

This bidirectional relationship necessitates integrated clinical approaches to manage both conditions effectively.

Thus, early identification and management of OSA, potentially through therapies like continuous positive airway pressure, could mitigate cardiovascular morbidity and improve long-term health outcomes in affected individuals (Patil et al., 2023; Tetyana et al., 2014).

However, it is important to note that while treatment for OSA is essential, previous randomized controlled trials have not consistently demonstrated a beneficial effect of continuous positive airway pressure treatment on cardiovascular outcomes, based on primary endpoints, suggesting the need for further investigation into optimal therapeutic strategies and patient stratification (Murata & Kasai, 2017).

4.2. Comparison with Previous Research

Our findings corroborate earlier research that established a significant correlation between OSA and various cardiovascular ailments, including hypertension, atrial fibrillation, and coronary artery disease (Javaheri et al., 2024; Peker et al., 2023).

For instance, severe OSA in individuals with pre-existing cardiovascular disease has been linked to a more than doubled risk for recurrent cardiovascular events, even after adjusting for key confounders (Mokhlesi & Varga, 2017).

This association is largely mediated by physiological disruptions such as intermittent hypoxia, heightened oxidative stress, and systemic inflammation, which are characteristic of OSA and directly contribute to atherosclerotic processes and myocardial dysfunction (Nguyen et al., 2024; Zdravković et al., 2022).

The nocturnal heart rate response to hypoxemia, specifically, has been identified as a significant predictor of acute myocardial infarction in OSA patients (Huang et al., 2022).

Moreover, the presence of both obstructive sleep apnea and type 2 diabetes mellitus acts as an independent and cumulative risk factor for cardiovascular mortality, exceeding the risk posed by either condition alone (Paschou et al., 2022).

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Indeed, the convergence of these conditions exacerbates cardiovascular risk factors, leading to a higher incidence of adverse cardiac events (Eldaboosy et al., 2021).

This synergistic relationship is driven by shared pathological mechanisms, including accelerated atherosclerosis and endothelial dysfunction, compounded by chronic hyperglycemia, systemic inflammation, and oxidative stress (Vacelet et al., 2021).

4.3. Mechanisms Linking OSA and Cardiovascular Morbidity

The intermittent hypoxia and sleep fragmentation characteristic of OSA instigate a cascade of physiological responses, including increased sympathetic nervous system activity, systemic inflammation, and endothelial dysfunction, all of which contribute to the progression of cardiovascular disease (Dieieva & Науменко, 2023).

These mechanisms collectively promote arterial stiffness, exacerbate hypertension, and foster the development of atherosclerosis, thereby elevating the risk of adverse cardiovascular events (DiCaro et al., 2024).

Sympathetic nervous system overactivity, coupled with reduced parasympathetic tone, further contributes to this cardiovascular burden by increasing heart rate and blood pressure, thereby imposing greater cardiac workload and risk of myocardial injury (Nguyen et al., 2024).

Furthermore, the resultant oxidative stress and systemic inflammatory mediators, such as C-reactive protein and interleukin-6, exacerbate endothelial dysfunction and contribute to the development of atherosclerosis, directly linking OSA to cardiovascular morbidity (Gervès-Pinquié et al., 2022; Stepan et al., 2022).

This chronic inflammatory state, evidenced by elevated C-reactive protein levels, accelerates atherogenesis and can lead to structural and functional alterations in the heart, predisposing individuals to conditions like heart failure and myocardial infarction (Tang et al., 2021; Zdravković et al., 2022).

4.4. Strengths and Limitations

In addition, impaired glucose tolerance, often observed in OSA patients due to sleep-associated oxygen desaturation, further amplifies cardiovascular risk independent of obesity, highlighting a critical metabolic pathway (Chew et al., 2022).

This metabolic dysregulation creates a vicious cycle with OSA, where intermittent hypoxia exacerbates insulin resistance, and conversely, insulin resistance can worsen OSA severity, thereby accelerating cardiovascular deterioration (Heffernan et al., 2024; Passàli et al., 2025).

For instance, OSA participants with diabetes exhibited a higher incidence of cardiovascular events over a 42-month follow-up period (Su et al., 2021).

Table 1 summarizes the demographic and clinical characteristics of the study cohort, segmented by OSA severity, illustrating key differences in baseline cardiovascular risk factors.

Figure 1, conversely, presents a visual representation of the prevalence of various cardiovascular morbidities across different OSA severity groups, providing a clear graphical overview of the disease burden.

Similarly, Table 2 illustrates the association between specific cardiovascular risk factors and OSA severity, emphasizing the dose-dependent relationship observed in this cohort (Zdravković et al., 2022).

Finally, Figure 2 elucidates the mechanistic pathways through which OSA contributes to increased arterial stiffness, a critical intermediate phenotype for cardiovascular disease (Marcon et al., 2020).

4.5. Clinical Implications

These findings underscore the critical need for routine screening for OSA in patients presenting with cardiovascular risk factors, enabling timely intervention and potentially mitigating the progression of cardiovascular disease.

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Furthermore, early detection and management of OSA, particularly in high-risk groups, may reduce the burden of cardiovascular disease and improve overall patient outcomes (Chen et al., 2025).

Specifically, addressing OSA in patients with prediabetes or type 2 diabetes could significantly reduce their heightened cardiovascular risk (Paschou et al., 2022).

Given the complex interplay between OSA and cardiovascular disease, comprehensive interdisciplinary management strategies are imperative to optimize patient care and improve long-term prognosis.

This approach should integrate lifestyle modifications, pharmacological interventions, and advanced OSA therapies to address the multifaceted nature of these interconnected conditions effectively.

Such strategies must consider the nuanced interactions among sleep apnea severity, metabolic dysregulation, and cardiovascular health to optimize intervention efficacy (André et al., 2020; Song et al., 2024).

Additionally, personalized treatment plans, informed by detailed phenotypic characterization of both OSA and cardiovascular disease, are essential for maximizing therapeutic benefits and minimizing adverse events (Kim et al., 2018; Nguyen et al., 2024).

Ultimately, a deeper understanding of the molecular and cellular mechanisms underpinning the cardiovascular complications of OSA will pave the way for novel therapeutic targets and more precise interventions.

This includes exploring novel pharmacological agents that target inflammation, oxidative stress, or sympathetic overactivity pathways, alongside advanced sleep apnea treatments tailored to individual patient profiles.

4.6. Future Research Directions

Further studies are warranted to investigate the long-term efficacy of combined therapeutic modalities in attenuating cardiovascular morbidity in OSA patients, particularly focusing on objective cardiovascular endpoints rather than surrogate markers (Ayas et al., 2014).

Research should also prioritize identifying specific biomarkers that predict cardiovascular risk in OSA patients, facilitating earlier and more targeted interventions (Ayas et al., 2014; Nguyen et al., 2024).

Moreover, randomized controlled trials evaluating the long-term benefits of continuous positive airway pressure and other emerging therapies are crucial to establish definitive causal links and inform clinical guidelines (Kwon et al., 2019; Sawanyawisuth et al., 2022).

Additionally, investigating the bidirectional relationship between OSA and comorbidities such as metabolic syndrome and diabetes is essential for developing comprehensive management strategies that address the intertwined pathologies (Li et al., 2025; McNicholas & Pevernagie, 2022; Tenda et al., 2024; Valensi et al., 2025).

Future research should also delve into the phenotypic variations of OSA and their differential impact on cardiovascular outcomes, utilizing large-scale cohorts and advanced genetic and molecular analyses (Ramos et al., 2017).

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