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OBSTRUCTIVE SLEEP APNEA, SLEEP FRAGMENTATION AND CARDIOVASCULAR AUTONOMIC DYSFUNCTION: MECHANISMS AND CLINICAL IMPLICATIONS

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder associated with significant cardiovascular morbidity. Recurrent upper airway obstruction during sleep leads to intermittent hypoxia and repeated arousals, resulting in sleep fragmentation (SF). Increasing evidence suggests that both processes contribute to dysregulation of the autonomic nervous system and adverse cardiovascular outcomes.
Methods: A narrative literature review was conducted using PubMed and Google Scholar to identify relevant studies published up to 1 March 2026. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to sleep fragmentation, obstructive sleep apnea, autonomic dysfunction, and cardiovascular outcomes. Eligible studies included randomized controlled trials, cohort studies, systematic reviews, meta-analyses, and clinical guidelines involving adult populations.
Results: Recurrent microarousals from sleep fragmentation disrupt sleep continuity and increase sympathetic activity, manifesting as altered heart rate variability and sympathetic dominance. Sleep fragmentation alone can destabilize autonomic regulation independently of hypoxia. In obstructive sleep apnea, intermittent hypoxia adds oxidative stress and hypothalamic-pituitary-adrenal axis activation. Persistent sympathetic overactivity causes hemodynamic instability, impaired nocturnal blood pressure dipping, vascular stiffness, and cardiac remodeling, raising the risk of hypertension, arrhythmias, heart failure, and other cardiovascular events.
Conclusions: Sleep fragmentation and intermittent hypoxia are central mechanisms linking obstructive sleep apnea to cardiovascular autonomic dysfunction. They drive sustained sympathetic activation and progressive cardiovascular damage, highlighting the need for comprehensive diagnosis and therapies targeting both apnea reduction and improvements in sleep continuity and autonomic balance.

KEYWORDS

Sleep Apnea, Obstructive, Sleep Fragmentation, Cardiovascular Diseases, Autonomic Nervous System, Intermittent Hypoxia

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1. Introduction

Obstructive sleep apnea (OSA) is an increasing medical problem in the global population. An apnea-hypopnea index (AHI) of ≥ 5 occurs in up to 24% of middle-aged men and 9% of women, whereas full-blown OSA syndrome affects 4% of men and 2% of women [1]. The global epidemiology is exacerbated by the growing problem of obesity. Each 1 kg/m² increase in body mass index (BMI) raises the risk of developing the disease by 14% [1]. Male sex is a strong non-modifiable predisposing factor; however, the situation changes after menopause, when the risk rises significantly in women and becomes comparable to that in men [1]. It should be noted that the risk of OSA increases with age up to 65 years, after which it reaches a plateau [1]. The underlying mechanism of this disorder is excessive reduction of tone in the muscles responsible for patency of the upper airways. This leads to complete or partial obstruction of airflow, resulting in recurrent apneas or hypopneas [2]. Recurrent apneas are associated with episodes of hypoxia, hypercapnia, and swings in intrathoracic pressure. The cornerstone of OSA diagnosis is polysomnography (PSG) or portable monitoring [2]. These methods allow assessment of the respiratory disturbance index (RDI), defined as the number of apneas, hypopneas, and respiratory-effort-related arousals per hour of sleep [2]. Sleep fragmentation (SF) is a disruption of sleep architecture characterized by frequent awakenings that interrupt the continuity of sleep during the night [3]. Hypoxia occurring in OSA stimulates chemoreceptors and, as a consequence, generates an activating impulse to the brainstem centers and the sympathetic nervous system, triggering a protective response in the form of micro-arousals of the cerebral cortex [4]. This forced arousal allows restoration of normal muscle tone in the upper airways and resumption of airflow, however, its direct consequence is an immediate transition to lighter stages of sleep or brief periods of wakefulness [4]. In obstructive sleep apnea, hypoxia induces sympathetic overactivity in patients with cardiovascular disease, leading to blood-pressure surges and chronic vasoconstriction [5]. The aim of this review is to examine how sleep fragmentation and obstructive sleep apnea disturb autonomic balance of the cardiovascular system, resulting in sympathetic overactivity and parasympathetic withdrawal, and to outline the clinical consequences of these changes-especially an increased risk of arterial hypertension, arrhythmias, and other cardiovascular complications.

2. Materials and Methods

2.1. Search Strategy and Data Sources

This narrative review was based on a literature search of PubMed and Google Scholar for studies published up to 1 March 2026. The literature search was initiated in October 2025 and completed in early 2026. The search strategy combined Medical Subject Headings (MeSH) and free-text terms using Boolean operators (AND, OR). Key terms included “sleep fragmentation” or “arousal index” combined with “obstructive sleep apnea (OSA)” or related metrics (AHI, TST90), and cardiovascular or autonomic outcomes such as “heart rate variability (HRV)”, “sympathetic overactivity”, “hypertension”. Searches were limited to English and Polish publications. As this was a narrative review, no formal risk-of-bias assessment was performed.

2.2. Eligibility Criteria

Predefined inclusion and exclusion criteria were applied. Priority was given to studies published between 2014 and 2026, with selected earlier landmark studies included for background context. Eligible studies involved adult populations (≥18 years) and included randomized controlled trials, cohort studies, systematic reviews, meta-analyses, and international clinical guidelines examining associations between sleep fragmentation, OSA, and autonomic or cardiovascular outcomes. Pediatric studies, animal or in vitro research, case reports, non-peer-reviewed publications, editorials, conference abstracts without full text, and studies lacking defined autonomic or cardiovascular endpoints were excluded.

2.3. Study Selection and Data Extraction

Titles and abstracts were screened for relevance, followed by full-text evaluation according to predefined criteria. Emphasis was placed on recent high-quality evidence and seminal studies describing key pathophysiological mechanisms. Data extraction focused on autonomic markers (e.g., HRV, MSNA), pathophysiological pathways, and clinical cardiovascular outcomes. In total, approximately 78 records were identified through database and supplementary searches. After removal of duplicates and exclusion of clearly irrelevant records, 34 full-text publications were assessed for eligibility, and 20 sources were included in the final narrative synthesis.

3. Results

3.1. Pathophysiology and mechanisms

Sleep fragmentation

Sleep fragmentation resulting from recurrent episodes of upper airway obstruction leads to numerous micro-arousals that correlate with heart rate variability (HRV) [6]. A higher arousal index was positively associated with HRV [6]. Sleep fragmentation also promotes the development of sympathetic overdrive, leading to dominance of the sympathetic nervous system [6,7]. Shift of autonomic activity toward sympathetic predominance translates into cardiac manifestations among patients experiencing sleep fragmentation. The observed changes in sympathetic activity are primarily attributable to sleep fragmentation rather than to systemic hypoxia [6]. The peak intensity of sympathetic markers during sleep is estimated to occur around 4:00 a.m., when levels of adrenaline, noradrenaline, and cortisol are highest [7]. Sleep fragmentation causes an increase in both nocturnal and daytime blood pressure values and results in loss of the physiological nocturnal blood-pressure dip [6,7]. This leads to impairment of both baroreceptor and chemoreceptor function [6]. The pressure-related changes induced by sleep fragmentation are associated with increased susceptibility to morning cardiovascular events [7]. Adverse effects of sleep fragmentation are also evident in the heart's pump function. As a result of autonomic changes, there is reduced myocardial contractility, reflected by decreased stroke volume and cardiac index, as well as prolongation of the pre-ejection period and left ventricular ejection time [7]. Further changes include reduction in cardiac output and decreased left ventricular performance index [7]. Sleep fragmentation also induces hemodynamic alterations, including vasoconstriction and enhanced prothrombotic response [6].

Obstructive sleep apnea

Obstructive sleep apnea represents a chronic model of repeated exposure of the organism to cycles of hypoxia and reoxygenation [2,8], resembling an ischemia-reperfusion-like mechanism [8]. The characteristic intermittent hypoxia of OSA leads to increased production of reactive oxygen and nitrogen species (ROS/RNS), initiating oxidative stress and activating numerous redox-sensitive signaling pathways, including HIF-1α, NF-κB, AP-1, and Nrf2 [8]. Recurrent episodes of hypoxia and reperfusion activate leukocytes, platelets, and endothelial cells and induce the production of pro-inflammatory cytokines, resulting in a sustained, systemic inflammatory state [8]. Endothelial dysfunction is also a key component of the pathophysiology, arising from an imbalance between nitric oxide (NO) and the superoxide anion radical (O_2^-) [8]. OSA may also substantially disturb the function of the hypothalamic-pituitary-adrenal (HPA) axis [9]. The HPA axis regulates the body's response to stress and maintains metabolic and hormonal homeostasis, and it is under tight circadian control [10]. In OSA, the organism is exposed to repeated stimuli acting as recurrent stressors, leading to activation of the autonomic nervous system and pulsatile release of HPA-axis hormones. This results in neuroendocrine dysregulation, including alterations in ACTH and cortisol secretion and impairment of glucocorticoid-mediated feedback mechanisms [9].

3.2. Autonomic dysfunction and the cardiovascular system

Chronic adrenergic stimulation leads to impaired myocardial relaxation, clinically manifested as development of left ventricular diastolic dysfunction and, in parallel, to fixation of structural changes in the myocardium, including progressive cardiomyocyte hypertrophy, increased interstitial fibrosis, and reduced ventricular wall compliance [11]. Over time, diastolic filling capacity of the ventricle deteriorates and hemodynamic instability further worsens, both mechanisms mutually reinforce each other, facilitating disease progression [11]. Sympathetic overactivity, observed across all major phenotypes of heart failure, underscores the universal nature of this pathophysiological mechanism and its key role in initiating and sustaining heart failure [11,14]. It also induces a range of functional and structural alterations in the vasculature, including gradual increase in vascular wall stiffness and concomitant reduction in vessel distensibility [12]. These changes are driven by sympathetic-dependent increases in heart rate and by neurotransmitters released from sympathetic nerve endings that promote smooth-muscle contraction, thereby raising the elastic modulus of the vessel wall and limiting its ability to undergo passive distension [12]. At the same time, excessive adrenergic activation favors endothelial dysfunction-characterized by reduced nitric oxide bioavailability and heightened oxidative stress-whereas the endothelium, through secretion of vasoconstrictive factors such as endothelin-1, further amplifies sympathetic activity, creating a vicious cycle that deteriorates vascular function [12]. High local and systemic levels of neurotransmitters play a fundamental role in the pathogenesis of cardiac arrhythmias, particularly in mechanisms associated with myocardial ischemia and reperfusion [13,14]. It has been shown that isolated premature beats or induced episodes of tachycardia can trigger generalized,

pathological adrenergic activation in the post-extrasystolic period, which coincides with a phase of heightened electrical instability of cardiomyocytes, thereby promoting initiation of malignant ventricular arrhythmias [13]. Chronic exposure to elevated noradrenaline concentrations and disturbances in local sympathetic regulation constitute an independent risk factor for ventricular tachycardia, ventricular fibrillation, and sudden cardiac death [14].

3.3. Clinical implications

Chronic oxidative stress and the accompanying inflammatory response play a central role in the development of end-organ complications in patients with OSA, particularly within the cardiovascular system. Excessive ROS production leads to endothelial dysfunction, impaired NO-dependent vasodilation, and increased vascular tone, thereby promoting the development of arterial hypertension [8]. At the same time, activation of inflammatory cells and upregulation of adhesion molecules enhance leukocyte-endothelial interactions and contribute to progression of atherosclerotic lesions, as a result, OSA is recognized as a significant risk factor for coronary artery disease, myocardial infarction, heart failure, and cardiac arrhythmias [8]. Oxidative damage to lipids, proteins, and DNA further destabilizes atherosclerotic plaques and worsens vascular function [8]. Moreover, oxidative stress closely interacts with other cardiovascular-metabolic risk factors, such as obesity, insulin resistance, type 2 diabetes, and dyslipidemia, creating a self-perpetuating mechanism that amplifies injury to vessels and myocardium [8]. Chronic activation of the stress-response system favors the development of multiple metabolic and cardiovascular complications [9]. Sympathetic activation increases vascular tone and sustains hemodynamic hyperstimulation, which in turn promotes a persistent inflammatory response with immune-system activation and development of neuroinflammation that disrupts neurotransmission and function of brain structures crucial for emotional regulation [15]. Dysregulation of the HPA axis may therefore represent one of the key mechanisms linking obstructive sleep apnea to increased risk of cardiovascular diseases. OSA substantially increases the risk of developing heart failure, which occurs in approximately 30-60% of patients with established heart disease [16]. OSA is also associated with elevated risk of cardiac arrhythmias, including atrial fibrillation, with a 2- to 5-fold higher probability of arrhythmia occurrence, particularly during nighttime hours, the highest risk of arrhythmic episodes is observed within about 90 seconds after an apneic event [16]. In addition, OSA raises the risk of stroke, coronary artery disease, and cardiovascular mortality, with particularly poor survival among patients with severe OSA (AHI >30), and a peak incidence of sudden cardiac death between midnight and 6:00 a.m. [16]. In patients who already have heart failure, OSA worsens prognosis by increasing the risk of post-discharge mortality and recurrent hospitalizations [16]. Of note, in women, the presence of OSA shows a stronger association with left ventricular hypertrophy [16]. An important clinical aspect of obstructive sleep apnea is also its association with a distinct pattern of arterial hypertension. In OSA patients, nocturnal hypertension and loss of the physiological nocturnal blood-pressure dip (non-dipper pattern) are common, resulting from recurrent episodes of hypoxia, micro-arousals, and sympathetic activation, which trigger transient blood-pressure surges during apneas [17]. This abnormal hemodynamic profile leads to sustained elevation of nocturnal blood pressure, increases the risk of cardiovascular complications-including left ventricular hypertrophy, vascular damage, and stroke and frequently coexists with treatment-resistant hypertension [17]. It is estimated that obstructive sleep apnea may occur in up to 70-80% of patients with treatment-resistant hypertension, underscoring the need to routinely consider this disorder when evaluating secondary causes of hypertension [17]. Obstructive sleep apnea triggers a cascade of pathophysiological processes-oxidative stress, endothelial dysfunction, and persistent sympathetic overactivity-that contribute to cardiovascular autonomic dysfunction (Figure 1).

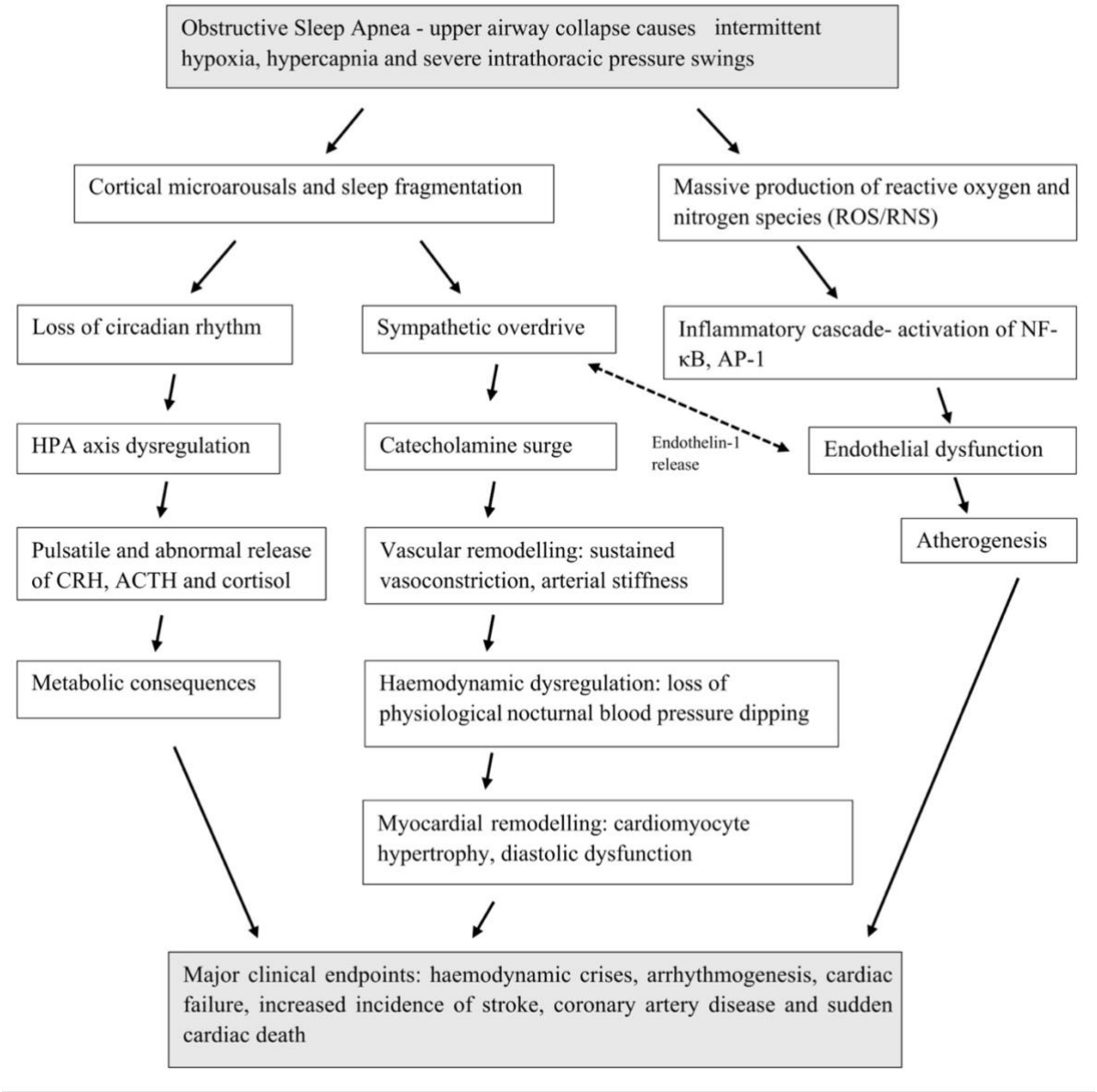

Fig. 1. *Pathophysiological cascade from obstructive sleep apnea to cardiovascular autonomic dysfunction*

3.4. Diagnosis of OSA

Diagnosis of obstructive sleep apnea is primarily based on polysomnography (PSG), which is considered the gold-standard diagnostic method. This examination allows comprehensive assessment of breathing during sleep through simultaneous recording of multiple physiological parameters [2]. The diagnosis is established by evaluating the number of respiratory-disturbance episodes per hour of sleep, expressed as the apnea-hypopnea index (AHI) or the respiratory disturbance index (RDI), OSA is typically diagnosed when the value is ≥15 episodes/h or ≥5 episodes/h in the presence of characteristic clinical symptoms [2]. In selected cases, diagnosis can be performed using portable sleep-monitoring devices (portable monitoring, PM), which record basic respiratory parameters and are recommended in patients with moderate or high pretest probability of OSA and without significant comorbid conditions [2]. When PM yields a negative result but clinical suspicion remains high, full polysomnography is indicated [2]. Clinical evaluation and the use of standardized screening questionnaires, such as the Epworth Sleepiness Scale (ESS) and the STOP-BANG questionnaire, support the diagnostic process by helping estimate the risk of disease and the severity of symptoms [2]. The most precise method for assessing sympathetic nervous system (SNS) activity is microneurography, which enables direct measurement of sympathetic nerve discharges in awake individuals, including muscle sympathetic nerve activity (MSNA) recorded from nerves innervating skeletal muscle [11]. Direct assessment of sympathetic

activity by MSNA allows clinicians to link the degree of SNS hyperactivity with the severity of hypertension, including resistant or nondipping forms, and is regarded in the literature as the "gold-standard" technique for evaluating sympathetic outflow [11].

3.5. Treatment of OSA

Management of OSA is undergoing substantial evolution-from a traditional "one-size-fits-all" approach toward strategies grounded in precision and individualized medicine [18]. Because OSA is a highly heterogeneous disorder, optimal treatment selection requires identification of the predominant pathophysiological mechanisms in each patient, such as increased collapsibility of the upper airways [18]. The cornerstone of therapy for obstructive sleep apnea remains continuous positive airway pressure (PAP) treatment [19]. An alternative for selected patients is oral appliance therapy (OAT), particularly mandibular advancement devices (MAD), while surgical procedures such as uvulopalatopharyngoplasty or bilateral maxillomandibular advancement are considered in patients who are insufficiently controlled by conservative measures [18]. Behavioral interventions remain an essential component of therapy, including weight reduction and positional therapy [18]. These strategies may be supplemented by orofacial myofunctional therapy, and in recent years there has been growing interest in neuromodulation techniques. Hypoglossal nerve stimulation represents a modern therapeutic option for patients who cannot tolerate PAP [18]. In parallel, novel therapeutic approaches are being developed, including pharmacologic interventions such as incretin-based agents or SGLT2 inhibitors, which may indirectly influence the course of OSA [19]. Research is also ongoing on additional treatment modalities, including other pharmacologic strategies. The development of next-generation oral appliances, based on digital dental scans and computer-guided mandibular advancement, allows a high degree of personalization and more precise optimization of upper-airway patency [20]. A summary of available OSA treatment options, including their underlying mechanisms and limitations, is presented in Table 1.

Table 1. Therapeutic Options and Precision Treatment Strategies for Obstructive Sleep Apnea

Therapeutic Method	Pathophysiological Mechanism of Action	Main Indications and Clinical Limitations
Positive Airway Pressure therapy- PAP	Acts as a pneumatic splint maintaining upper airway patency, eliminating hypoxemia and sleep fragmentation	Gold standard for moderate to severe OSA Primary barrier is low adherence due to aerophagia, mucosal dryness, and claustrophobia
Intraoral Appliances	Mechanical forward mandibular advancement and tongue base repositioning	Effective PAP alternative, modern splints designed precisely from digital dental scans
Neuromodulation	Inspiration-synchronized hypoglossal nerve electrical stimulation preventing tongue base collapse	For PAP-intolerant patients, requires strict qualification via drug-induced sleep endoscopy
Surgical Interventions	Increases upper airway skeletal space	Option for conservative treatment failures; demands careful selection due to high invasiveness
Behavioral Interventions & OMT	Reduces airway compression from neck adipose tissue and strengthens pharyngeal muscle tone	Weight loss, positional therapy, and orofacial myofunctional therapy (OMT) as universal adjuncts
Experimental Pharmacotherapy	GLP-1 agonists (obesity reduction) and central neuromuscular control modulation	Emerging approach targeting obesity and pharyngeal dilator muscle hypotonia directly

4. Discussion

This review demonstrates that obstructive sleep apnea and sleep fragmentation exert multilevel pathophysiological effects on the cardiovascular system. A paramount insight from the analyzed data is sleep fragmentation's capacity to induce autonomic dysfunction independent of hypoxic episodes. Traditionally, OSA pathogenesis emphasized sequelae of recurrent desaturations and reperfusion; however, mounting evidence implicates sleep continuity disruption alone in initiating clinically significant neurohumoral cascades. Notably, arousal index correlations with heart rate variability parameters suggest microarousals as potent sympathetic triggers. This disrupts nocturnal sympathovagal balance and circadian cardiovascular regulation, with profound clinical ramifications. Conventional OSA severity metrics like AHI or hypoxemia duration may thus incompletely capture total pathophysiological burden from sleep disturbances. Sleep fragmentation merits

recognition not merely as an apnea byproduct but as an independent autonomic mediator. Recurrent microarousals engender cyclic autonomic fluctuations destabilizing hemodynamics and perpetuating chronic sympathetic overactivity. Prolonged cardiovascular exposure erodes physiologic nocturnal blood pressure dipping. Absent this protective mechanism, vascular and myocardial wall stress mounts, fostering hypertension, cardiac remodeling, and vascular progression. The delineated mechanisms support a unified pathophysiological model wherein sleep fragmentation initiates progressive cardiovascular injury. Microarousals activate the autonomic nervous system, provoking acute sympathetic surges, heart rate lability, and blood pressure swings. Sustained nocturnal hyperactivity abolishes dipping, heightening arterial stiffness and endothelial dysfunction. Vasodilator-vasoconstrictor imbalance curtails nitric oxide bioavailability while amplifying pro-inflammatory and vasoconstrictive mediators, driving atherogenesis and myocardial remodeling. This process is self-perpetuating: endothelial dysfunction fuels further sympathetic activation, while chronic adrenergic stimulation exacerbates vascular injury and hemodynamic derangements. The resultant vicious feedback loop contributes to hypertension progression, left ventricular hypertrophy, and amplified cardiovascular risk. Obstructive sleep apnea must thus be viewed as a systemic disorder wherein respiratory, neurohormonal, metabolic, and inflammatory mechanisms converge. Intermittent hypoxia remains a cornerstone, intensifying oxidative stress through recurrent oxygen desaturation-reoxygenation cycles that boost reactive oxygen and nitrogen species production, activating inflammatory signaling cascades. This precipitates endothelial dysfunction and accelerated atherogenesis. Concomitantly, hypothalamic-pituitary-adrenal axis dysregulation ensues, with chronic activation elevating cortisol secretion to promote insulin resistance and visceral adiposity. OSA thereby integrates into a broader cardiometabolic spectrum encompassing obesity, metabolic syndrome, and type 2 diabetes. No less critical is chronic sympathetic overactivity; sustained adrenergic stimulation induces structural cardiovascular changes - including cardiomyocyte hypertrophy, interstitial fibrosis, and vascular stiffening - that impair left ventricular diastolic function and heighten arrhythmogenic susceptibility. Patients with OSA consequently face markedly elevated risks of arrhythmias, heart failure, and sudden cardiac death. From a clinical standpoint, the robust OSA - atrial fibrillation association merits emphasis. Underlying mechanisms span atrial structural remodeling and autonomic dysregulation. Post-apneic sympathetic surges may trigger arrhythmias in vulnerable electrophysiologic substrates, while chronic myocardial remodeling and fibrosis sustain rhythm disturbances. OSA also heightens sudden cardiac death risk, distinguished by a nocturnal peak - contrasting the general population’s morning predominance likely reflecting cumulative hypoxia, sleep fragmentation, and abrupt autonomic shifts during apneas. Enhanced OSA pathophysiology comprehension has prompted a therapeutic paradigm shift in recent years. Traditional approaches prioritized airway obstruction alleviation via positive airway pressure therapy. Although supremely effective at reducing apneic events, clinical implementation is hampered by tolerability issues and suboptimal long-term adherence. Consequently, emphasis has pivoted to disease mechanistic heterogeneity. The OSA endotype concept posits patient-specific pathophysiological dominance - e.g., upper airway collapsibility, respiratory control derangements, or aberrant arousal thresholds - enabling precision therapy matching. This elevates alternatives including mandibular advancement devices, hypoglossal nerve stimulation, behavioral interventions, and select surgeries, potentially enhancing efficacy and patient acceptance. Future diagnostics and therapy may leverage expanded autonomic markers for risk stratification. Metrics like heart rate variability, blood pressure variability, and arterial stiffness offer insights into cardiovascular burden in OSA. Integrating these with conventional diagnostics could yield comprehensive risk assessment and refined personalization. Interpreting these findings requires acknowledging limitations. Much evidence derives from observational studies, precluding definitive causality attribution. Methodologic heterogeneity and population disparities impede comparability. A key knowledge gap persists in interventional trials evaluating selective sleep fragmentation mitigation on long-term cardiovascular outcomes. Future investigations should prioritize patient phenotyping wherein fragmentation predominates pathophysiologically, alongside novel biomarkers for early high-risk identification. Long-term prospective trials evaluating diverse therapeutic strategies against hard endpoints - such as myocardial infarction, stroke, or cardiovascular mortality - will prove pivotal for field advancement. In summary, obstructive sleep apnea constitutes a multifaceted systemic disorder with profound cardiovascular implications. Sleep fragmentation assumes a far greater role than hitherto recognized, functioning as an independent autonomic dysfunction driver. Elucidating these mechanisms holds clinical import, underscoring the need for holistic OSA patient evaluation and therapies targeting not only apneic reduction but also sleep quality and continuity enhancement. Integrating cardiology, pulmonology, and sleep medicine expertise remains essential for effective cardiovascular complication prevention in this population.

5. Conclusions

Obstructive sleep apnea is a multifaceted disorder with widespread cardiovascular effects. Mechanisms include intermittent hypoxia, sleep fragmentation and chronic neurohormonal activation. Sleep fragmentation independently drives cardiovascular injury, with recurrent microarousals causing sustained sympathetic overactivity, loss of nocturnal blood pressure dipping, and increased hemodynamic variability. Interactions among hypoxia, oxidative stress, endothelial dysfunction, and hyperactive sympathetic and HPA axes lead to cardiovascular remodeling, including vascular stiffening, cardiomyocyte hypertrophy, and interstitial fibrosis. Chronic catecholamine exposure increases arrhythmia risk, including ventricular arrhythmias, atrial fibrillation, and sudden cardiac death. Effective management requires precision medicine: identifying patient-specific endotypes to guide tailored therapies, combining positive airway pressure with targeted alternatives to improve efficacy and reduce long-term cardiovascular complications.

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