



Sleep disorders and acute myocardial infarction: overview of systematic reviews

Distúrbios do sono e infarto agudo do miocárdio: overview de revisões sistemáticas

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ABSTRACT

Background: Sleep disorders (SD) comprise various clinical conditions that can negatively interfere with organs and physiological systems, especially the cardiovascular system. **Objective:** To synthesize the clinical evidence on the association between SD and acute myocardial infarction (AMI). **Design and Settings:** This is an overview conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses reporting standards, using population, intervention, comparison, and outcome (PICO) strategies. **Methods:** This is an overview of systematic reviews conducted on the IBECS, WPRIM, LILACS, BDNPAR, BINACIS, CUMED, EMBASE, PubMed and Cochrane Review databases. The studies were searched in databases based on eligibility criteria for systematic reviews, addressing sleep disorders and ischemic events, published up to September 2024. This study has been registered with the *Open Science Framework* under the domain osf.io/gvsyu/. **Results:** 5 SRs met the inclusion criteria, involving 16,561 participants. There is a significant correlation between patients previously diagnosed with coronary artery disease and the influence of obstructive sleep apnea (OSA) on worsening the clinical picture, which may be one of the reasons for instability and may act as a trigger for nocturnal myocardial ischemia. Systematic reviews indicate a significant association between OSA and cardiovascular events. **Conclusion:** Patients with OSA and acute coronary syndrome have a higher rate of restenosis after percutaneous coronary intervention, which may suggest that OSA contributes as a

RESUMO

Introdução: Os distúrbios do sono (DS) compreendem várias condições clínicas que podem interferir negativamente em órgãos e sistemas fisiológicos, especialmente o sistema cardiovascular. **Objetivo:** Sintetizar as evidências clínicas sobre a associação entre DS e infarto agudo do miocárdio (IAM). **Métodos:** Esta é uma visão geral conduzida de acordo com os Itens de Relatório Preferenciais para Padrões de Relatórios de Revisões Sistemáticas e Meta-Análises, usando estratégias de população, intervenção, comparação e resultado (PICO). **Métodos:** Esta é uma visão geral de revisões sistemáticas conduzidas nas bases de dados IBECS, WPRIM, LILACS, BDNPAR, BINACIS, CUMED, EMBASE, PubMed e Cochrane Review. Os estudos foram pesquisados em bases de dados com base em critérios de elegibilidade para revisões sistemáticas, abordando distúrbios do sono e eventos isquêmicos, publicados até setembro de 2024. Este estudo foi registrado no *Open Science Framework* sob o domínio osf.io/gvsyu/. **Resultados:** 5 RS preencheram os critérios de inclusão, envolvendo 16.561 participantes. Há uma correlação significativa entre pacientes previamente diagnosticados com doença arterial coronária e a influência da apneia obstrutiva do sono (AOS) na piora do quadro clínico, o que pode ser uma das razões para a instabilidade e pode atuar como um gatilho para isquemia miocárdica noturna. Revisões sistemáticas indicam uma associação significativa entre AOS e eventos cardiovasculares. **Conclusão:** Pacientes com AOS e síndrome coronariana aguda têm uma taxa maior de reestenose após intervenção coronária

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pathophysiological worsening mechanism for these patients. Furthermore, no systematic review has demonstrated strong evidence for the use of CPAP in patients with OSA in cardiac ischemic events. **Mesh Terms.** Sleep. Sleep Medicina Specialty. Sleep Apnea Syndromes. Myocardial Ischemia.

Keywords: Sleep Disorders. Acute Myocardial Infarction. Quality of life. Sleep-Wake Disorders.

percutânea, o que pode sugerir que a AOS contribui como um mecanismo de piora fisiopatológica para esses pacientes. Além disso, nenhuma revisão sistemática demonstrou fortes evidências para o uso de CPAP em pacientes com AOS em eventos isquêmicos cardíacos. **Descritores DeCS:** Sono. Especialidade em medicina do sono. Síndromes de apneia do sono. Isquemia miocárdica

Descritores: Distúrbios do sono. Infarto agudo do miocárdio. Qualidade de vida. Distúrbios do sono-vigília.

INTRODUCTION

Sleep disorders (SD) comprise various clinical conditions that can negatively interfere with organs and physiological systems, especially the cardiovascular system. The consequences vary and are not limited to the impaired sleep phase; they also affect wakefulness, compromise quality of life, and contribute to the onset of various diseases¹.

Despite the growing recognition that respiratory disorders, particularly obstructive sleep apnea (OSA), are relatively common conditions, their incidence has increased. When associated with cardiovascular diseases, OSA ranges from 30 to 56% in people with systemic arterial hypertension and 38 to 87% in people with coronary artery disease. In addition, it is estimated that the prevalence in patients with atrial fibrillation ranges from 32 to 82%^{2,3}.

Although the association between sleep disorders and cardiovascular alterations is still controversial, there is a need to study the ability of these disorders to predict cardiovascular events, especially acute myocardial infarction (AMI). Results suggest that intermittent hypoxia could function as a protective factor for ischemic events. This phenomenon has been observed in apneic patients who developed less severe heart damage than patients without OSA after an AMI^{1,3}.

To date, randomized clinical trials (RCTs) and observational studies have investigated the correlation between sleep disorders and acute myocardial infarction; however, the body of evidence has never summarized the primary clinical and epidemiological evidence. This overview of systematic reviews (SRs) aims to synthesize the primary clinical evidence on the association between these two conditions, facilitating decision-making and promoting evidence-based practice in sleep medicine and cardiology.

METHODOLOGY

Type of study

This is an overview of a systematic review conducted according to the methods described in the Cochrane Handbook for Systematic Reviews. The review was completed following the Brazilian Guidelines on Systematic Reviews. The stages were drafting the research question, defining the inclusion criteria, locating and selecting the SRs, extracting the data, assessing the quality and risk of bias of the SRs included, and analyzing and presenting the results⁴.

This overview was prepared according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). The study protocol was then submitted to the *Open Science Framework* under the *osf.io/gvsyu/* domain.

To carry out the research, the Population, Intervention, Comparison, Outcome, and Type of Study (PICOS) strategy was used, where a) Population (Patients with a diagnosis of sleep disorder and acute myocardial infarction); b) Intervention (any intervention or combination of interventions that helps with quality of life and improves the prognosis for patients with SD and AMI); c) Comparison (any other intervention or no intervention); d) Outcome (worsening of the clinical condition of AMI in untreated individuals with SD); e) Types of study (systematic review of randomized controlled clinical trials, quasi-randomized or cluster-randomized, with no time cut-off). Thus, the following guiding question was defined: "What is the evidence from systematic reviews about the association between sleep disorders and acute myocardial infarction, compared to each other or no intervention, in the adult population?"

Inclusion and exclusion criteria

Cochrane SRs and non-Cochrane SRs that met the criteria were included: SRs of randomized, quasi-

randomized, or cluster-randomized controlled clinical trials of any intervention involving patients over 18 years of age who have a diagnosis of any sleep disorder (central apnea, mixed apnea, obstructive sleep apnea, and hypopnea) and who have developed some ischemic cardiac involvement.

Studies that discussed, in addition to the outcome of interest, the association of SD with AMI, such as clinical condition, new cardiovascular events, and worsening quality of life, were also included and presented. There were no restrictions on language, year of publication, or place of clinical care. We excluded SRs that did not address the topic described, as well as preprints and productions titled as SRs without methodological rigor.

Location and selection

The electronic search was conducted in July 2024 for all the databases consulted. Among the databases used were those associated with the Virtual Health Library such as Índice Bibliográfico Español en Ciencias de la Salud (IBECS), Index Medicus para el Pacífico Occidental (WPRIM), Literatura Latino-Americana y Caribe en Ciencias de la Salud (LILACS), Base de Datos Nacional del Paraguay (BDNPAR), Bibliografía Nacional en Ciencias de la Salud Argentina (BINACIS), Centro Nacional de Información de Ciencias Médicas (CUMED). Searches were also conducted in Cochrane Review, Excerpta Medica Database (EMBASE), and Medical Literature Analysis and Retrieval System Online (MEDLINE/PUBMED).

The search strategies were meticulously crafted, utilizing the official terms and their synonyms from the Medical Subject Headings (MESH) and the Embase Subject Headings (EMTREE). Repositories and websites of SR registries were also consulted on the PROSPERO platform. Chart 1 shows the search strategy adopted in PubMed and Embase, adapted for the other analyzed databases.

Two reviewers selected The SRs independently based on the inclusion/exclusion criteria previously established. The same pair of reviewers took part in reading the titles and abstracts and the full texts. In both selection stages, disagreements were discussed by a third reviewer.

Data collection

For data extraction, the authors' pre-defined instrument was used. This instrument included data regarding the review's identification, authors, objectives, intervention studied, inclusion and exclusion criteria, number of populations included, number of Randomized Clinical Trials (RCTs) included, number of Observational

Studies included, results reported, and how the risk of bias/methodological quality was assessed.

Evaluation of methodological quality

In addition, the AMSTAR-2 (Assessment of Multiple Systematic Reviews) instrument was used to assess the methodological quality of systematic reviews⁵. AMSTAR 2 uses a classification system based on seven critical and nine non-critical domains. In this way, it assesses overall quality based on performance in the crucial and non-critical domains, assigning different weights in the classification rules. Two independent reviewers made reliability judgments independently and duplicated for each review sample. Discrepancies were defined by consensus or recourse to a third author.

Chart 1. PubMed and Embase database search strategy - Rio de Janeiro, RJ, Brazil, 2024.

Database	Search strategy
PubMed	((((((Sleep Apnea, Obstructive) OR (Sleep Apnea Syndromes)) OR (Sleep Apnea, Central)) AND (myocardial infarction)) OR (ST Elevation Myocardial Infarction)) OR (Non-ST Elevated Myocardial Infarction)) OR (Anterior Wall Myocardial Infarction)
Embase	((('obstructive sleep apnea'/exp OR 'obstructive sleep apnea' OR (obstructive AND ('sleep'/exp OR sleep) AND ('apnea'/exp OR apnea)) OR 'sleep apnea syndromes'/exp OR 'sleep apnea syndromes' OR (('sleep'/exp OR sleep) AND ('apnea'/exp OR apnea) AND syndromes) OR 'central sleep apnea syndrome'/exp OR 'central sleep apnea syndrome' OR (('central'/exp OR central) AND ('sleep'/exp OR sleep) AND ('apnea'/exp OR apnea) AND ('syndrome'/exp OR syndrome))) AND ('heart infarction'/exp OR 'heart infarction' OR (('heart'/exp OR heart) AND ('infarction'/exp OR infarction))) OR 'st segment elevation myocardial infarction'/exp OR 'st segment elevation myocardial infarction' OR (('st'/exp OR st) AND segment AND ('elevation'/exp OR elevation) AND myocardial AND ('infarction'/exp OR infarction)) OR 'non st segment elevation myocardial infarction'/exp OR 'non st segment elevation myocardial infarction' OR (non AND ('st'/exp OR st) AND segment AND ('elevation'/exp OR elevation) AND myocardial AND ('infarction'/exp OR infarction)) OR 'anterior myocardial infarction'/exp OR 'anterior myocardial infarction' OR (anterior AND myocardial AND ('infarction'/exp OR infarction))) AND [systematic review]/lim

Source: Authorial.

The assessment domains include 1) research questions and inclusion criteria for the review including the PICO components; 2) a priori design; 3) justifications for selecting the study design; 4) search strategies; 5) duplicate study selection; 6) extraction of duplicate data; 7) reference to excluded studies; 8) characteristics of the included studies; 9) technique for assessing the risk of bias of the included studies; 10) reporting of the source of funding for the included studies; 11) methods for analyzing results; 12) evaluation of the impact of the risk of bias on the results of the meta-analysis; 13) consideration of the risk of bias in the interpretation and discussion of the results; 14) discussion and explanation of heterogeneity; 15) investigation of publication bias; 16) reporting of the conflict of interest of the authors of the review.

Domains 1, 4, 7, 9, 11, 13, and 15 are considered critical by the AMSTAR-2 tool. Each domain was assessed by two independent authors, who classified each item as entirely adequate (“yes”), partially adequate (“partially yes”), inadequate (“no”), or not applicable. After all the evaluations, the AMSTAR-2 platform was used to assess

overall confidence in the results, following the checklist available on the AMSTAR-2 website (http://amstar.ca/Amstar_Checklist.php). According to AMSTAR-2 recommendations, overall confidence in the results was classified into four categories: critically low, low, moderate, and high.

In addition, the risk of bias assessments will not be repeated or updated; the assessment contained in the included systematic reviews will be reported.

RESULTS

Identification and selection of studies

The review brought together 846 studies using the search strategy used in the databases. Notably, 119 were found to be repeated in more than one source and were therefore excluded. After selection, 5 systematic reviews met the inclusion criteria, totaling 37 randomized clinical trials, 15 cohort studies, and 1 review. The total number of participants in the study was 16,561. Figure 1 below shows the selection process according to the PRISMA protocol.

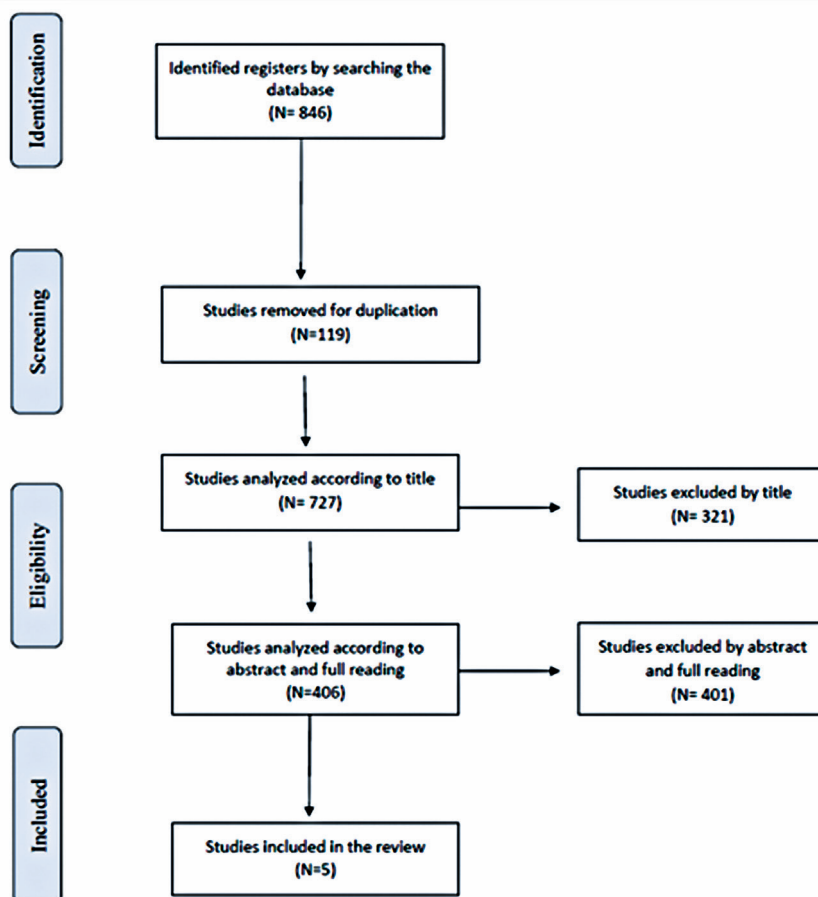


Figure 1. Article selection process according to the *Preferred Reporting Items for Systematic Reviews and Meta-Analysis*. Source: Authorial (2024).

Methodological evaluation of the studies

Table 1 shows the results of the judgments of the AMSTAR-2 items. Overall confidence in the results of the included SRs was classified as high at 60% (3/5) and moderate at 40% (2/5).

Characteristics of the included reviews

Data analysis reveals that the year with the highest prevalence of publications was 2018 (n=2/40%), followed by 2020, 2021, and 2022, with one publication in the following years. In addition, the country of origin of the publications was China (n=3/60%), followed by Chile (n=1/20%) and Brazil (n=1/20%).

Of the five studies evaluated, 3, SR 2, SR 3, and SR 4 (60%) included RCTs^{6,7,8}, considered the gold standard in clinical research. SR 1 and SR 5, on the other hand, focused solely on cohort studies (n=2/30%)^{9,10}.

The central theme of the five reviews was convergence about the association of sleep disorders with cardiovascular events. It was noted that in some patients with OSA, myocardial damage occurs in subclinical form. Only SR 5¹⁰ focused primarily on the association between OSA and MI; the other reviews assessed MI as a secondary event. Only SR 3⁷ and SR 4⁸ aimed to evaluate Continuous Positive Airway Pressure (CPAP) as a protective factor for cardiovascular events.

The same two reviews, SR 2⁷ and SR 4⁸, discussed that using CPAP, compared to usual care, is associated with reduced risks of cardiovascular outcomes or death in patients with OSA and coronary artery disease and that it is possible to improve cardiovascular outcomes. SR 1⁹ was the only review to address the percutaneous coronary intervention procedure for patients with AMI and concluded that the presence of OSA is associated with a higher risk of recurrent adverse cardiovascular events, all-cause death, cardiovascular death, and repeat revascularization.

In addition, it should be noted that SR 2⁶ was the only study to consider the laboratory values of troponin, creatine kinase (CK), and CK-MB when assessing

patients with OSA; however, no significant differences were observed between the peaks of these biomarkers when there was an acute cardiovascular event.

DISCUSSION

OSA is directly linked to various pathophysiological mechanisms triggered by hypoxia^{11,12,13} and sleep fragmentation^{11,14,15}, including sympathetic activation, inflammation, endothelial dysfunction, altered coagulability, and others. These mechanisms can be common pathways to other cardiovascular consequences, such as hypertension, arrhythmias, metabolic syndromes, acute myocardial infarction, and heart failure¹.

It is generally accepted that any factors that reduce the caliber of the airways, the tone of the muscles involved in respiratory function, or lead to an increase in inspiratory pressure are predisposing factors for the development of OSA. Airway collapsibility, identified as the main factor in the etiopathogenesis of apneas, is influenced by anatomical anomalies that reduce airway space and airflow volume¹⁶.

During an obstructive respiratory event, hemodynamic variables and autonomic activity oscillate between periods of normal ventilation and obstruction^{17,18}. Heart rate and blood pressure increase 10 seconds after apnea, coinciding with micro-awakening, peak ventilation, and saturation nadir. Parasympathetic stimulation occurs when an increase in the heart rate cycle is observed, and bradyarrhythmia occurs. The heart rate rises after the airway is opened due to vagus inhibition and micro-awakening^{1,19}.

Ineffective inspiratory ventilatory efforts lead to a reduction in intrathoracic pressure with an increase in left ventricle (LV) transmural pressure and afterload^{1,20}. In addition, changes in intrathoracic pressure seem to intensify mitral regurgitation in patients who already have this condition, which is a possible mechanism for worsening HF(heart failure). At the same time, there is an increase in venous return to the right ventricle

Table 1. AMSTAR-2 items for methodological evaluation.

SR	AMSTAR-2 Items																General confidence
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
SR 1	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	NA	Y	Y	NA	Y	Moderate confidence
SR 2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High confidence
SR 3	Y	Y	Y	PY	Y	Y	PY	PY	NA	N	Y	Y	Y	Y	Y	Y	High confidence
SR 4	N	Y	Y	Y	Y	Y	NA	Y	Y	NA	Y	Y	Y	Y	Y	Y	High confidence
SR 5	Y	PY	Y	PY	Y	Y	N	Y	N	N	NA	NA	Y	Y	NA	Y	Moderate confidence

Source: Authorial (2024).
Key: Y - Yes; N - No; NA - Not Applicable; PY- Partially Yes.

Chart 2. Characteristics of the included studies and their main results.

Author/Year	Sample/ Country	Objective/Intervention	Results	Conclusion
Wang et al., 2018 ⁹ (SR 1)	Cohort: 9 Population: 2,755 Country: China	To assess the impact of obstructive sleep apnea on subsequent cardiovascular outcomes after percutaneous coronary intervention	The study showed that OSA increases the risk of cardiovascular events after PCI by about two times. In one of the studies analyzed, with 798 patients, only 12% had been suspected or diagnosed with OSA before being hospitalized for AMI. The mortality rate related to the study population was not different from that expected in the general population with coronary artery disease. In one of the studies, it was found that although treatment for patients diagnosed with OSA using CPAP therapy and CAD did not interfere with new cardiovascular events, the outcomes of these events were better compared to those who had not adhered to the treatment.	In patients undergoing PCI, the presence of OSA is associated with a higher risk of recurrent adverse cardiovascular events, all-cause death, cardiovascular death, and repeat revascularization. It has not been proven whether treating OSA prevents subsequent cardiovascular events.
Xie et al., 2022 ⁶ (SR 2)	RCT: 26 Population: 4,217 Country: China	To assess the impact of sleep apnea and hypopnea syndrome on cardiovascular events.	Patients with OSA have higher levels of troponin, CK, and CK-MB. However, no significant differences were observed between the peaks of these biomarkers when there was an acute cardiovascular event. A higher incidence of acute coronary syndrome was observed in those patients diagnosed with OSA. It was also noted that in some patients with OSA, myocardial injury occurs subclinical, and more significant development of collateral vessels was observed, which can contribute to myocardial tissue ischemia.	Patients with OSA have higher levels of troponin, CK, and CK-MB. Still, no significant differences were observed between the peaks of these biomarkers during an acute cardiovascular event. Myocardial cells may have accommodated intermittent hypoxia early and suffered less damage from abrupt ischemia through preconditioning.
Labarca et al., 2020 ⁷ (SR 3)	RCT: 8 Population: 5,817 Country: Chile	To analyze the current evidence on the efficacy of using CPAP to prevent cardiovascular events in patients with OSA, focusing on primary and secondary prevention.	Although the use of CPAP is linked to better health outcomes for patients diagnosed with OSA, the study designs analyzed do not provide sufficient evidence to support the theory that there are benefits to using CPAP to prevent cardiovascular events.	Although there is no evidence that CPAP therapy improves cardiovascular outcomes in patients with moderate to severe OSA, it is necessary to develop new studies with a lower risk of bias to truly understand the benefits of using CPAP to prevent cardiovascular events.
Chen et al., 2021 ⁸ (SR 4)	Cohort: 6 RCT: 3 literary review: 1 Population: 2,590 Country: China	To determine and explore the exact association of CPAP use with cardiovascular risks and mortality in patients diagnosed with OSA and CAD.	There was a 37% reduction in the risk of MACE associated with using CPAP compared to the control population using usual care to treat OSA. There was a more significant benefit among patients who used CPAP for at least 4 hours a night, especially those with fewer than 30 apnea and hypopnea events per hour. However, the analysis showed no MI, stroke, or repeat revascularization results.	The use of CPAP, when compared to usual care, is associated with reduced risks of cardiovascular outcomes or death in patients with OSA and CAD.
Porto, Sakamoto, Salles, 2018 ¹⁰ (SR 5)	Cohort: 3 Population: 5,067 Country: Brazil	Checking the association between OSA and MI	All the patients underwent nocturnal polysomnography, and all the studies found an association between OSA and fatal and non-fatal cardiovascular outcomes. It was observed that 644 (12.7%) of the 5,067 patients suffered a myocardial infarction (MI) or CVA or required a revascularization procedure, and 25.6% of these cardiovascular events were fatal.	MI was responsible for 29.5% of the 644 outcomes analyzed. In males, there is an association between OSA and MI, with the apnea and hypopnea index being one of the most reliable markers.

Source: Authorial (2024). Key: OSA - Obstructive Sleep Apnea, MI - Myocardial Infarction, PCI - Percutaneous Coronary Intervention, CAD - Coronary Artery Disease, CK - Creatine kinase, CVA - Cerebral Vascular Accident, CPAP - Continuous Positive Airway Pressure.

(RV), compromising its relaxation and shifting the interventricular septum to the left²¹, impairing left ventricular filling. Figure 2 below elucidates the pathophysiological process of the influence of OSA and myocardial damage due to hypoxia.

Some studies have shown an association between AMI and OSA^{8, 22, 23}. (2012)²⁴ showed that OSA increases the risk of AMI, revascularization procedures, and cardiovascular death. However, the study did not exclude patients who received treatment for OSA over 2.9 years of follow-up. It should also be mentioned that the same survey infers that CPAP reduces the risk of fatal and nonfatal cardiovascular events.

On the other hand, Kendzerska et al., (2014)²⁵ in a study aimed at determining whether OSA independently increases the risk of coronary events, concluded that the apnea and hypopnea index was associated with composite cardiovascular outcomes in the univariate analysis, but this association was not maintained in the multivariate analysis. The result was based on the fact that studies with large population samples may not include important predictors related to OSA or may selectively report the conclusions of subgroup analyses.

Patients who required medical treatment were not excluded from the study based on the justification that using CPAP was unrelated to the risk of an event. In the analysis of patients who did not receive treatment, compared to the total sample, all the predictors continued to be significantly associated with the outcome, except daytime sleepiness²⁵.

There is evidence to support that CPAP does not reduce the incidence of SAH or cardiovascular events. Studies have not shown the benefit of CPAP in preventing cardiovascular events in patients with OSA. An analysis of primary prevention subgroups reported a non-significant reduction in arrhythmic or ischemic events⁷.

In the multicenter Sleep Apnea Cardiovascular Endpoints study, the use of CPAP failed to reduce cardiovascular events in patients with moderate to severe OSA and established cardiovascular disease after an average follow-up period of 3.7 years²². In another randomized trial, the Intervention With CPAP in Coronary Artery Disease and Sleep Apnea, 224 patients with OSA and CAD who had undergone revascularization were included. The results showed that there was no

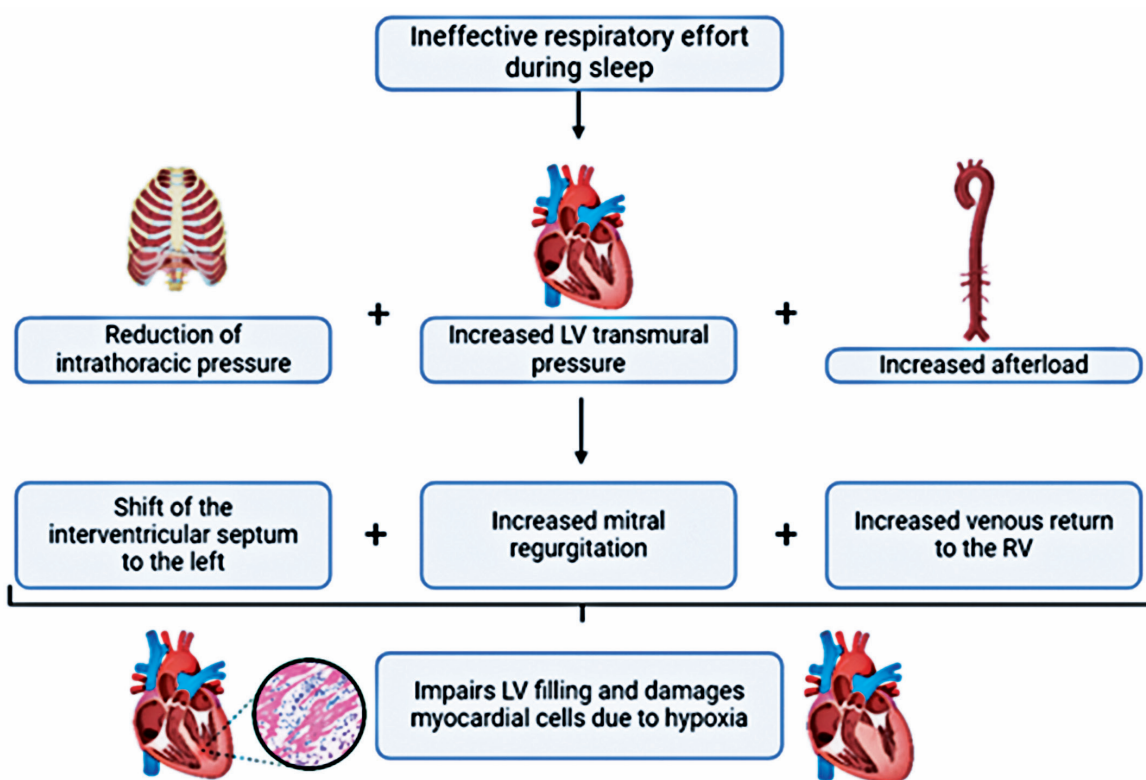


Figure 2. Pathophysiological mechanism of OSA in developing ischemic heart disease. Source: Produced at BioRender.com. Author (2024). Key: LV - Left ventricle; RV - Right ventricle.

significant difference in the composite outcome of repeat revascularization, myocardial infarction, stroke, or cardiovascular death between patients treated with CPAP and those who did not receive the therapy²⁶.

However, an adjusted analysis of patients under treatment indicated better results for treating OSA among those who used CPAP for at least 4 hours a night. Although the benefits of the intervention for OSA are still controversial, large-scale randomized trials are still needed to investigate further the effects of CPAP treatment in high-risk groups with homogeneous CAD populations, such as MI or percutaneous coronary intervention²⁶.

When evaluating OSA with cardiovascular outcomes after percutaneous coronary intervention, the primary outcome was major adverse cardiovascular events, which included death from any cardiovascular cause such as myocardial infarction, stroke, repeat revascularization, or heart failure. The analysis showed that OSA is associated with an increased risk of MACE after PCI, with a combined relative risk of 1.96. In addition, the presence of OSA significantly increased the incidence of all-cause death, cardiovascular death, and repeat revascularization in patients undergoing PCI. However, it also suggests that the sample size and quality of the studies included may influence the heterogeneity of the results⁹.

About confounding factors such as SAH, diabetes mellitus, and dyslipidemia, the treatment of these pathologies has a significant impact on AMI outcomes^{27,28}. These comorbidities corroborate the metabolic syndrome, which represents a significant risk factor for the development of CAD²⁹.

Studies have shown the prevalence of type 2 DM in the apneic population. Elevated catecholamines combined with sleep deprivation are associated with insulin resistance. There are data suggesting an association between OSA and glucose intolerance. Chen et al., (2014)⁸ concluded in their meta-analysis that treatment with CPAP, although it does not alter glycated hemoglobin levels, improves insulin resistance, impacting on DM symptoms.

Understanding the effects of OSA may suggest explanations for its association with AMI. The prevalence of sleep disorders in patients with CAD is up to twice as high as in individuals without CAD²³. Bhama et al. (2006) reported a prevalence of up to 30% of apnea among patients with CAD.

Pathophysiological mechanisms point to the contribution of OSA in the origin and progression of CAD, one of the etiologies of AMI. These include intermittent hypoxemia, acidosis, elevated blood pressure,

sympathetic vasoconstriction, and changes in cardiac structure, as mentioned above. In chronic form, the mechanisms of heart and vascular disease, including endothelial dysfunction and systemic inflammation, cause damage to the vasculature of the coronary arteries^{23,7}. It has been noted that in patients without CAD and with OSA, there is significant calcification in the coronary arteries³¹.

Defining the relationship between CAD and OSA means clarifying precautions to prevent AMI in the apneic population. Making sleep apnea a marker of heart disease implies early screening of these patients and public encouragement of treatment and prevention of cardiovascular disease. Endothelial, neurohormonal, and metabolic alterations should not be neglected, as this is the only way to intervene in the development and worsening of CAD²³.

Recurrent cycles of hypoxia with reoxygenation promote oxidative stress, sympathetic activation, and inflammatory responses, leading to endothelial dysfunction and reduced repair capacity, which are responsible for the onset and progression of atherosclerosis^{32,33}. By intravascular ultrasound assessment for symptomatic CAD, patients with OSA had greater total atheroma volume than those without, even after adjusting for traditional risk factors^{9,34,26}.

In patients with acute coronary syndrome, the presence of OSA was associated with a higher rate of restenosis after PCI within six months. There is also an increased risk of repeat revascularization after PCI in patients with OSA, supporting the current evidence. OSA can also trigger nocturnal myocardial ischemia^{9,34,26}.

In patients presenting with myocardial infarction, this could exert a continuous effect and result in less myocardial preservation and impaired cardiac function, even after successful PCI. In addition, patients with OSA have increased platelet activation and aggregation and reduced fibrinolytic capacity^{35,36,37}.

Furthermore, when assessing myocardial damage via biomarkers in patients with sleep apnea-hypopnea syndrome (SAHS), there was no significant difference between the groups when assessing CK and CK-MB⁶. The hypothesis that intermittent hypoxemia in SAHS may induce a protective effect, reducing the severity of cardiovascular events, was considered. However, patients with SAHS showed more severe coronary lesions, suggesting that although SAHS may have some protective effect in terms of biomarkers, it is still associated with a worse condition of the coronary arteries^{6,38}.

CONCLUSION

OSA and AMI have significant correlations triggered by pathophysiological mechanisms such as intermittent hypoxia and sleep fragmentation, which in turn induce exacerbated sympathetic activation, systemic inflammation, endothelial dysfunction, coagulability changes, and fatigue. There is an essential correlation between patients previously diagnosed with CAD and the influence of OSA on worsening the clinical picture, which may be one of the reasons for instability and may act as a trigger for nocturnal myocardial ischemia.

To date, no systematic review has shown strong evidence for the use of CPAP in patients with OSA to prevent cardiac ischemic events and other major cardiovascular events. However, using CPAP may be beneficial for improved sleep comfort in patients diagnosed with OSA.

In addition, it was noted that patients with OSA and acute coronary syndrome have a higher rate of restenosis after percutaneous coronary intervention, which may suggest that OSA contributes as a pathophysiological worsening mechanism for these patients.

However, further research, with a more extended follow-up period for patients diagnosed with OSA, is still needed to understand and describe the epidemiology of AMI and OSA.

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