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ASSOCIATION BETWEEN OBSTRUCTIVE SLEEP APNEA SYNDROME AND ATRIAL REMODELING IN PATIENTS WITH ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW

ASSOCIAÇÃO ENTRE A SÍNDROME DA APNEIA OBSTRUTIVA DO SONO E O REMODELAMENTO ATRIAL EM PACIENTES COM FIBRILAÇÃO ATRIAL: UMA REVISÃO SISTEMÁTICA

ASOCIACIÓN ENTRE EL SÍNDROME DE APNEA OBSTRUCTIVA DEL SUEÑO Y EL REMODELADO AURICULAR EN PACIENTES CON FIBRILACIÓN AURICULAR: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia, and its pathophysiology is closely linked to atrial remodeling, characterized by structural and electrophysiological alterations of the left atrium. Obstructive sleep apnea syndrome (OSAS) has been increasingly recognized as an important risk factor and potentially modifiable condition associated with AF. Contemporary guidelines emphasize the relevance of OSAS in the integrated management of atrial fibrillation. The aim of this systematic review was to evaluate the association between obstructive sleep apnea syndrome and atrial remodeling in patients with atrial fibrillation. This systematic review was conducted in accordance with PRISMA 2020 recommendations, with searches performed in PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library. The included studies demonstrated a consistent association between OSAS and

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alterations in the atrial substrate, particularly evidenced by electroanatomical remodeling, reduced atrial voltage, increased low-voltage areas, and structural and functional changes of the left atrium. In conclusion, OSAS is associated with a greater degree of atrial remodeling in patients with atrial fibrillation, reinforcing its role as a clinically relevant and potentially modifiable factor in arrhythmia management.

Keywords: Atrial Fibrillation. Obstructive Sleep Apnea. Atrial Remodeling. Left Atrium.

RESUMO

A fibrilação atrial (FA) é a arritmia cardíaca sustentada mais prevalente, e sua fisiopatologia está intimamente relacionada ao remodelamento atrial, caracterizado por alterações estruturais e eletrofisiológicas do átrio esquerdo. A síndrome da apneia obstrutiva do sono (SAOS) tem sido cada vez mais reconhecida como um importante fator de risco e uma condição potencialmente modificável associada à FA, sendo destacada por diretrizes contemporâneas como relevante no manejo integrado da fibrilação atrial. O objetivo desta revisão sistemática foi avaliar a associação entre a síndrome da apneia obstrutiva do sono e o remodelamento atrial em pacientes com fibrilação atrial. Esta revisão sistemática foi conduzida de acordo com as recomendações do PRISMA 2020, com buscas realizadas nas bases de dados PubMed/MEDLINE, Embase, Scopus, Web of Science e Cochrane Library. Os estudos incluídos demonstraram uma associação consistente entre a SAOS e alterações no substrato atrial, particularmente evidenciadas por remodelamento eletroanatômico, redução da voltagem atrial, aumento de áreas de baixa voltagem e alterações estruturais e funcionais do átrio esquerdo. Conclui-se que a SAOS está associada a um maior grau de remodelamento atrial em pacientes com fibrilação atrial, reforçando seu papel como um fator clinicamente relevante e potencialmente modificável no manejo das arritmias. Palavras

Palavras-chave: Fibrilação Atrial. Apneia Obstrutiva do Sono. Remodelamento Atrial. Átrio Esquerdo.

RESUMEN

La fibrilación auricular (FA) es la arritmia cardíaca sostenida más prevalente, y su fisiopatología está estrechamente vinculada al remodelado auricular, caracterizado por alteraciones estructurales y electrofisiológicas de la aurícula izquierda. El síndrome de apnea obstructiva del sueño (SAOS) ha sido reconocido de forma creciente como un importante factor de riesgo y una condición potencialmente modificable asociada a la FA, siendo destacado por las guías clínicas contemporáneas en el manejo integral de la fibrilación auricular. El objetivo de esta revisión sistemática fue evaluar la asociación entre el síndrome de apnea obstructiva del sueño y el remodelado auricular en pacientes con fibrilación auricular. Esta revisión sistemática se realizó de acuerdo con las recomendaciones PRISMA 2020, con búsquedas efectuadas en PubMed/MEDLINE, Embase, Scopus, Web of Science y la Biblioteca Cochrane. Los estudios incluidos demostraron una asociación consistente entre el SAOS y alteraciones del sustrato auricular, evidenciadas especialmente por remodelado electroanatómico, reducción del voltaje auricular, aumento de áreas de bajo voltaje y cambios estructurales y funcionales de la aurícula izquierda. En conclusión, el SAOS se asocia con un mayor grado de remodelado auricular en pacientes con fibrilación auricular, lo que refuerza su papel como un factor clínicamente relevante y potencialmente modificable en el manejo de las arritmias.

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Palabras clave: Fibrilación Auricular. Apnea Obstructiva del Sueño. Remodelado Auricular. Aurícula Izquierda.

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1 INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with an increased risk of stroke, heart failure, recurrent hospitalizations, and cardiovascular mortality (Hindricks *et al*., 2020). The development and perpetuation of AF are strongly related to atrial remodeling, a progressive process involving left atrial dilation, myocardial fibrosis, electrical conduction heterogeneity, and impaired atrial mechanical function.

In this context, obstructive sleep apnea syndrome (OSAS) has emerged as a highly prevalent comorbidity among patients with AF. OSAS is characterized by recurrent episodes of upper airway obstruction during sleep, resulting in intermittent hypoxia, sleep fragmentation, intrathoracic pressure swings, and chronic sympathetic nervous system activation (Brasca *et al*., 2024).

Pathophysiological studies suggest that these mechanisms contribute to systemic inflammation, oxidative stress, and activation of profibrotic pathways in the atrial myocardium, thereby promoting both structural and electrical atrial remodeling (Dimitri *et al*., 2012). Consequently, OSAS may act as a facilitator of AF initiation and maintenance.

Despite strong biological plausibility and a growing number of observational studies, findings regarding the association between OSAS and atrial remodeling in patients with AF remain heterogeneous. Therefore, a systematic synthesis of the available evidence focusing specifically on atrial remodeling is warranted.

2 OBJECTIVE

To evaluate, through a systematic review of the literature, the association between obstructive sleep apnea syndrome and atrial remodeling in patients with atrial fibrillation.

3 METHODS

3.1 STUDY DESIGN AND METHODOLOGICAL GUIDELINES

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines, ensuring methodological rigor, transparency, and reproducibility (Page *et al*., 2021).

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3.2 RESEARCH QUESTION AND PICO STRATEGY

The research question was structured using the PICO framework: adult patients with atrial fibrillation (P), presence of obstructive sleep apnea syndrome (I), absence of OSAS (C), and objective parameters of atrial remodeling, including structural and/or functional measures, as outcomes (O).

3.3 SEARCH STRATEGY AND INFORMATION SOURCES

A systematic search was planned in PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library using controlled vocabulary and free-text terms related to atrial fibrillation, obstructive sleep apnea, and atrial remodeling. The complete search strategies for each database should be provided as supplementary material, according to journal requirements.

3.4 ELIGIBILITY CRITERIA

Eligible studies included observational studies and clinical trials involving adult patients with documented atrial fibrillation, OSAS diagnosed by polysomnography or validated criteria, and objective assessment of atrial remodeling. Exclusion criteria comprised case reports, narrative reviews, editorials, pediatric studies, and publications lacking objective atrial measurements.

3.5 STUDY SELECTION AND DATA EXTRACTION

Study selection was performed in two stages-title/abstract screening followed by full-text review-by independent reviewers. Extracted data included sample characteristics, diagnostic methods, atrial remodeling parameters, and main outcomes.

3.6 METHODOLOGICAL QUALITY ASSESSMENT

The methodological quality of observational studies was assessed using the Newcastle–Ottawa Scale (Stang, 2010).

4 RESULTS

4.1 STUDY SELECTION

The study selection process is summarized in the PRISMA 2020 flow diagram (Figure 1). A total of 822 records were identified across five databases. After removal of 291

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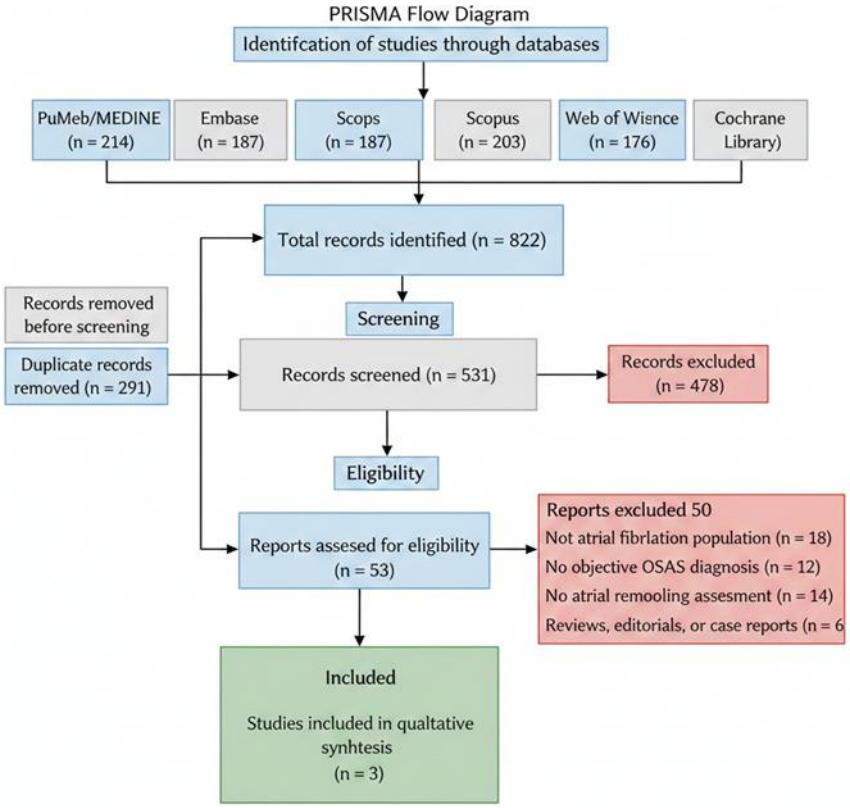
duplicate records, 531 studies were screened based on titles and abstracts, of which 478 were excluded. Fifty-three full-text articles were assessed for eligibility, and 50 were excluded for predefined reasons. Ultimately, three studies met the inclusion criteria and were included in the qualitative synthesis.

Figure 1

Flow diagram of study selection according to PRISMA 2020



Source: Authors, adapted from the PRISMA 2020 Statement (Page *et al*., 2021).

4.2 ELECTROANATOMICAL ATRIAL REMODELING

Dimitri *et al*. (2012), in a study of patients with paroxysmal AF undergoing catheter ablation, demonstrated that individuals with OSAS exhibited significantly reduced atrial voltage, conduction slowing, and increased electrogram complexity, indicating more pronounced electrical remodeling compared with patients without OSAS.

More recently, Takada *et al*. (2024) evaluated patients with AF undergoing ablation and found that the severity of intermittent hypoxia, measured by the oxygen desaturation index, was significantly associated with the extent of left atrial low-voltage areas, even in the absence of significant left atrial enlargement, suggesting early electroanatomical remodeling.

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4.3 STRUCTURAL AND FUNCTIONAL ATRIAL REMODELING

Echocardiographic studies have shown that patients with OSAS present increased left atrial volume and impaired atrial function, assessed by two-dimensional, three-dimensional, and strain echocardiography techniques (Oliveira *et al*., 2008; Kim *et al*., 2012). These findings support the biological plausibility that OSAS contributes to left atrial structural and functional remodeling.

In the specific context of AF, Hunt *et al*. (2024), in a randomized clinical trial, evaluated the impact of continuous positive airway pressure (CPAP) therapy on atrial remodeling in patients with paroxysmal AF and OSAS and found no significant reversal of left atrial volume or function after 12 months of treatment.

Table 1

Main characteristics of studies included in the systematic review

Author (Year)	Country	Study design	Sample size (n)	AF population	OSAS diagnosis	Atrial remodeling assessment	Main findings
Dimitri *et al*. (2012)	Australia	Observational comparative study	40 (20 OSAS / 20 controls)	Paroxysmal AF undergoing catheter ablation	Polysomnography (AHI ≥15 events/h)	Electrophysiological study and atrial voltage mapping	Patients with OSAS exhibited reduced atrial voltage, increased electrogram complexity, and conduction slowing, indicating more pronounced electrical atrial remodeling
Takada *et al*. (2024)	Japan	Cross-sectional observational study	83 (49 OSAS / 34 controls)	AF undergoing catheter ablation	Polysomnography and oxygen desaturation index (ODI)	3D electroanatomical mapping (low-voltage areas)	Intermittent hypoxia severity was significantly

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							associated with the extent of left atrial low-voltage areas, even in the absence of left atrial enlargement
Hunt *et al.* (2024)	United Kingdom	Randomized controlled trial	109	Paroxysmal AF with OSAS	Polysomnography (AHI ≥15 events/h)	Advanced echocardiography (left atrial volume and strain)	Twelve months of CPAP therapy did not result in significant reverse remodeling of left atrial structure or function

Abbreviations: AF = atrial fibrillation; OSAS = obstructive sleep apnea syndrome; AHI = apnea–hypopnea index; ODI = oxygen desaturation index; CPAP = continuous positive airway pressure.

5 DISCUSSION

The findings of this systematic review indicate that obstructive sleep apnea syndrome is associated with a greater degree of atrial remodeling in patients with atrial fibrillation. Evidence from electrophysiological and electroanatomical studies suggests that OSAS contributes to early alterations of the atrial substrate, including reduced atrial voltage and expansion of low-voltage areas (Dimitri *et al*., 2012; Takada *et al*., 2024).

From a pathophysiological perspective, intermittent hypoxia characteristic of OSAS promotes systemic inflammation, oxidative stress, and profibrotic signaling, thereby facilitating both electrical and structural remodeling of the left atrium (Brasca *et al*., 2024). Chronic sympathetic activation further contributes to atrial electrical instability, favoring AF persistence.

Although treatment of OSAS with CPAP has been associated with reduced AF recurrence in observational studies and meta-analyses (Shukla *et al*., 2015), evidence regarding reversal of atrial structural remodeling remains inconclusive. The randomized trial

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by Hunt *et al*. (2024) suggests that atrial reverse remodeling may not occur over short-term follow-up, even with adequate OSAS treatment, highlighting the importance of early identification and comprehensive risk factor management.

Beyond the pathophysiological implications, the findings of this systematic review have direct clinical relevance for the contemporary management of atrial fibrillation. The identification of obstructive sleep apnea syndrome as a condition associated with atrial remodeling reinforces the need for an integrated and multidisciplinary approach to patients with AF, extending beyond isolated pharmacological or interventional strategies. Systematic screening for OSAS, particularly in patients with arrhythmia recurrence or suboptimal response to catheter ablation, may contribute to improved risk stratification and therapeutic individualization. Moreover, evidence suggesting that electroanatomical alterations may precede measurable structural changes supports the concept that early intervention targeting intermittent hypoxia-related mechanisms could have a greater impact when implemented in the initial stages of the natural history of AF.

In this context, future studies should prioritize prospective designs with longitudinal assessment of atrial remodeling using combined methodologies, such as advanced echocardiography and electroanatomical mapping, and investigate whether multimodal interventions, including OSAS treatment alongside intensive management of cardiometabolic risk factors, can sustainably modify the atrial substrate and improve long-term clinical outcomes.

6 CONCLUSION

Obstructive sleep apnea syndrome is associated with more pronounced atrial remodeling in patients with atrial fibrillation, particularly with respect to electroanatomical substrate alterations and structural and functional changes of the left atrium. These findings reinforce the importance of identifying and managing OSAS as an integral component of atrial fibrillation care. Furthermore, the evidence that atrial electrical and electroanatomical changes may precede overt structural remodeling highlights the potential value of early detection and intervention. Integrating OSAS assessment and treatment into comprehensive risk factor management strategies may contribute to modifying the atrial substrate and improving long-term outcomes in patients with atrial fibrillation.

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