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Original Article

Novel Predictor of the AF Development in Patients with OSAS: Importance of Visceral Adipose Index

OSAS'li Hastalarda AF Gelişiminin Yeni Bir Belirleyicisi: Visseral Adipozite İndeksinin Önemi

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ABSTRACT

Objective: Obstructive sleep apnea syndrome (OSAS) is a sleep disorder whose frequency is increasing daily due to modern lifestyle. Patients with atrial fibrillation (AF), which has the same predisposing factors, frequently visit the outpatient clinic with complaints of palpitation. Existing symptoms are often associated with the course of OSAS, and the development of AF, a disease with high morbidity and mortality, cannot be detected. In our study, we investigated the relationship between the visceral adiposity index (VAI) and AF development in these patients.

Methods: We retrospectively analyzed 207 patients with OSAS who visited the cardiology outpatient clinic. The data of 44 patients with AF and 163 patients without AF were compared.

Results: Demographic characteristics and clinical risk factors were similar between the groups (p>0.05). VAI, apnea-hypopnea index, and inflammatory markers were higher in the AF group, and these risk factors were significant in the multivariate analysis (p<0.05).

Conclusions: Our study is important in terms of showing VAI as one of the most important predictors of AF, which has an impact on mortality and morbidity in patients with OSAS, whose frequency is increasing daily. Further prospective studies are required to confirm our observations and determine their clinical applicability.

Keywords: Apnea-hypopnea index, obstructive sleep apnea syndrome, visceral adiposity index

ÖZ

Amaç: Obstrüktif uyku apne sendromu (OSAS) modern yaşam tarzı nedeniyle sıklığı her geçen gün artan bir uyku bozukluğudur. Atrial fibrilasyon (AF) ile aynı predispozan faktörlere sahip olan hastalıkta hastalar çok sık çarpıntı şikayeti ile polikliniğe başvurmaktadır. Mevcut semptomlar sıklıkla OSAS hastalığın seyrine bağlanmakta ve morbiditesi ve mortalitesi yüksek bir hastalık olan AF'nin gelişimi yakalanamamaktadır. Çalışmamızda bu hastalardaki visseral adipozite indeksi (VAI) ile AF gelişimi arasındaki ilişkiyi araştırmayı amaçladık.

Yöntemler: Çalışmamızda kardiyoloji polikliniğine başvuran 207 hastanın verileri retrospektif olarak analiz edildi. AF gelişen 44 ve gelişmeyen 163 hastanın verileri karşılaştırıldı.

Bulgular: Gruplar arası demografik özellikler ve klinik risk faktörleri benzerdi (p>0,05). AF gelişen grupta VAI, apne-hipopne indeksi ve enflamatuvar markerların daha yüksek olduğu saptandı ve multivariate analizde bu risk faktörlerinin anlamlı olduğu tespit edildi (p<0,05).

Sonuçlar: Çalışmamız sıklığı her geçen gün artan OSAS'li hastalarda mortalite ve morbidite üzerinde etkisi olan AF'nin en önemli prediktörlerinden birisi olarak VAI'yı göstermesi bakımından önemli olduğunu saptadık. Gözlemlerimizi doğrulamak ve klinik uygulanabilirliğini belirlemek için daha ileri prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Apne-hipopne indeksi, obstrüktif uyku apne sendromu, visseral adipozite indeksi

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS), an epidemic health problem, is a common sleep-disordered breathing disorder that affects approximately 25% of men and 10% of women worldwide[1,2]. Its prevalence is increasing daily because of increasing obesity, sedentary lifestyle, prolonged life expectancy, and deterioration of sleep quality due to modern lifestyle[3]. The disease is characterized by repeating episodes of total or partial upper airway collapse while sleeping, leading to fragmentation of sleep patterns and recurrent episodes of desaturation. This intermittent state of hypoxia and hypercapnia leads to structural and functional remodeling of the body, which correlates with disease progression[4]. The severity of the disease is measured by the apnea-hypopnea index (AHI) (mild OSAS:

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5-15, moderate OSAS: 15-30, severe OSAS: >30) and causes various metabolic complications and functional pathologies in the body[5]. One such complication is atrial fibrillation (AF), a condition characterized by irregular and often rapid heartbeats, leading to increased morbidity and mortality, including thromboembolism and heart failure[6,7].

The visceral adiposity index (VAI) is a relatively new gender-specific anthropometric measure used to assess the distribution of visceral adipose tissue in the body and lipotoxicity[8]. It is calculated using waist circumference, body mass index (BMI), and lipid profile, which are strongly associated with obesity, metabolic disorders, and cardiovascular risk factors[9]. Its superiority in assessing lipotoxicity has made it a more functional parameter in the assessment of cardiovascular disease (CVD), metabolic syndrome, diabetes, insulin resistance, and chronic slow inflammation than traditional BMI, a measure of weight relative to height[8].

OSAS is a complex sleep disorder with a multifactorial etiology involving multiple risk factors. In addition to anatomical and genetic factors, its etiology includes clinical risk factors such as heart failure, advanced age, obesity, diabetes, alcohol consumption, hypertension, and smoking. These clinical factors also contribute to AF etiology. These two diseases are closely related because they have similar etiologic risk factors and common pathophysiological processes, including inflammation, oxidative cellular damage, and autonomic nervous system dysregulation. Several cross-sectional studies have confirmed this relationship[7]. On the other hand, the presence of OSAS is an important predictor of AF[10]. Despite this strong association and similar etiological parameters, the incidence of AF in patients with OSAS has been reported to be between 7.6% and 20%[11].

In this study, we investigated whether VAI is a predictor of AF development in patients with OSAS.

MATERIALS and METHODS

This study was a retrospective analysis of the data of 207 patients who applied to the cardiology outpatient clinic between January 1, 2018, and January 1, 2023 and were diagnosed with OSAS before admission. Patients with an ejection fraction <50%, moderate to severe mitral stenosis and severe mitral regurgitation, congenital structural heart disease, left atrium >45 mm, chronic metabolic inflammatory disorders, immunosuppressive or chronic anti-inflammatory drug use, unreperfused coronary artery disease or AF in the setting of acute ischemic heart disease, and C-reactive protein values >5 mm/dL or active infection were excluded. The flowchart of the patients included in the study is shown in Figure 1.

Data regarding the patient's complaints at admission, medical history, echocardiographic parameters indicating cardiac function and valvular heart disease status, apnea-hypopnea status, electrocardiogram (ECG)/ECG Holter results at admission, and laboratory parameters were obtained from their medical records. Conventional echocardiographic assessments were performed following the recommendations of the guidelines[12]. AF was diagnosed according to the guidelines and recommendations of the European Society of Cardiology and the European Heart Rhythm Association[13].

The systemic immune inflammation index (SII), which is considered an indicator of the balance between immune response and inflammation, was calculated using the formula [neutrophil count (Neu)×PLT count/ lymphocyte count (Lym)][14].

The BMI is defined as the body mass in kilograms divided by the square of the height in meters[15].

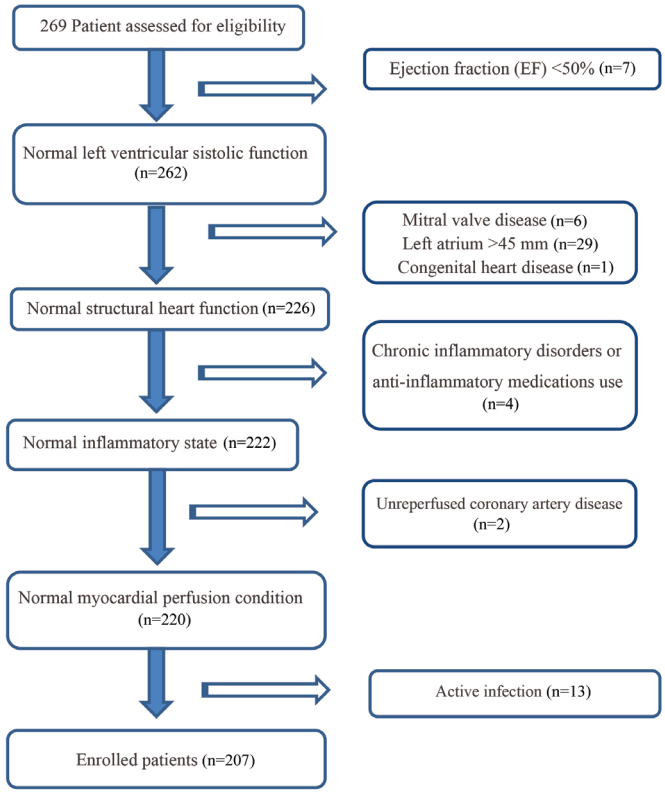

Figure 1. Flow chart of patient inclusion.

VAI values are calculated using the following formulas[16]:

Males: VAI={WC/(39.68+[1.88×BMI])}×(TG/1.03)×(1.31/HDL)

Females: VAI={WC/(36.58+[1.89×BMI])}×(TG/0.81)×(1.52/HDL)

Our study was approved by the Trakya University Faculty of Medicine Non-invasive Scientific Research Ethics Committee (decision no: 08/23, date: 08.05.2023) and complied with the Declaration of Helsinki.

Statistical Analysis

Data analysis was performed using Version 26.0 of the Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, Illinois, USA). The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. Descriptive statistics are given, presenting mean ± standard deviation or median (minimum-maximum) values based on the distribution's normality. For comparisons of normally distributed continuous variables, an independent-sample t-test was employed, whereas non-normally distributed continuous variables were assessed using the Mann-Whitney U test. Categorical data were compared using the chi-square test. Binary logistic regression analysis was used for univariate and multivariate analyses. All statistical tests were performed at a predetermined level of significance set at $p<0.05$. The receiver operating characteristic (ROC) curve was used to calculate the area under the curve for AF estimation.

RESULTS

Data from 207 patients with OSAS who met the inclusion criteria were analyzed. The mean age was 49.9±4.06 years, and 80.1% of the participants were male (n=166). Patients admitted with palpitations were categorized into the AF or normal sinus rhythm (NSR) groups according to the ECG or ECG Holter results at admission (patients with sinus rhythm at admission were monitored with ECG Holter for diagnostic purposes). The demographic data and laboratory parameters of the groups are shown in Table 1.

When the groups were compared in terms of their demographic data, the two groups were found to be similar. AHI values, inflammatory parameters, SII, and VAI were higher in the group that developed AF. The results of the univariate and multivariate analyses of the predictors of AF development are presented in Tables 2 and 3.

When the results of the multivariate analysis were analyzed, it was found that the increases in AHI, SII, and VAI values, BMI values, and PAP height were significantly correlated with the development of AF.

In the ROC analysis, it was not found that the cut-off value of 25.5 in AHI could predict AF development with 66.7% sensitivity and 68.5% specificity, and the cut-off value of 7.53 in VAI could predict AF development with 68.6% sensitivity and 68% specificity. Figure 2 shows the ROC curve and values.

DISCUSSION

The most important finding of this study is that VAI is a strong predictor of AF development in patients with OSAS. VAI has been associated with cardiometabolic diseases, slow, low-grade chronic inflammation, metabolic syndrome, and diabetes[8,17-19]. To the best of our knowledge, this is the first study to demonstrate the association between VAI and AF development.

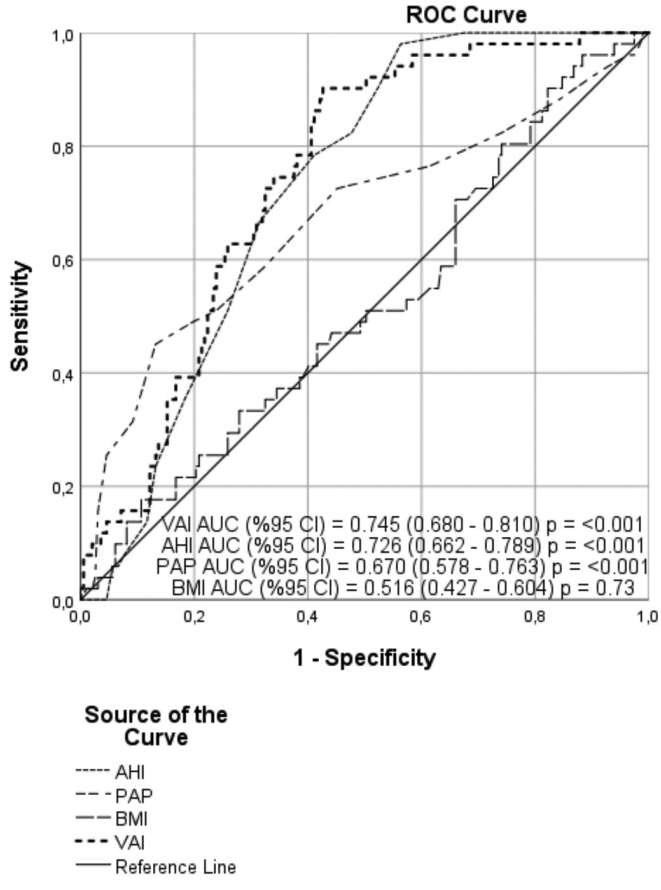

Figure 2. ROC curve and analysis results.

AHI: Apnea hypopnea index, BMI: Body mass index, PAP: Pulmonary artery pressure, VAI: Visceral adipose index, ROC: Receiver operating characteristic, AUC: Area under the curve

OSAS accelerates the progression of CVD by causing CVD in patients without traditional risk factors and can lead to fatal cardiovascular events when not effectively treated[20,21]. Hypoxia and reoxygenation episodes during the disease course lead to increased production of free oxygen radicals and impaired antioxidant balance. Oxidative stress leads to endothelial dysfunction, decreased nitric oxide bioavailability, and increased inflammatory mediator levels. In addition, metabolic dysfunction in patients with OSAS leads to increased insulin resistance and dyslipidemia[22]. Autonomic dysfunction, increased afterload, and ventricular remodeling cause diastolic dysfunction in these patients, leading to a decrease in exertional capacity and making them more symptomatic[23].

VAI is calculated using anthropometric measurements and laboratory parameters and provides a detailed evaluation of visceral adipocytes[16]. Excessive adiposity in visceral tissues leads to the production and release of proinflammatory cytokines called adipokines (IL-6, TNF-α, etc.)[24]. These cytokines cause low-grade chronic inflammation. These cytokines also cause adipocyte cell dysfunction and increase the release of free fatty acids and adipokines[25]. Moreover, these inflammatory cytokines cause fibrosis and structural remodeling of the atrial tissue[26]. Although many risk factors for the development of AF have been identified, recent studies have shown that the major substrate is the structural and electrical remodeling of the atrial tissue[27,28]. In contrast, several studies have shown that the extent of fibrosis in the atrial tissue affects the development, recurrence, and persistence of AF[29]. Another clinical significance of excess adiposity in visceral tissue is its role in the development of clinical risk factors such as insulin resistance, CVDs,

Table 1. Demographic characteristics, laboratory findings, and echocardiographic characteristics of the study populations.

	AF (n=44)	NSR (n=163)	p
Age, median (min-max)	49 (39-57)	50 (40-64)	0.08
Gender (male) n(%)	37 (72.5)	129 (65.5)	0.33
Hypertansion n(%)	22 (43.1)	71 (36)	0.35
Dyslipidemia n(%)	22 (43.1)	74 (37.6)	0.28
Smoking n(%)	11 (21.6)	48 (24.4)	0.81
Diabetes Mellitus n(%)	13 (25.5)	38 (19.3)	0.43
Drinking n(%)	5 (9.8)	9 (4.6)	0.14
Previous CVD n(%)	10 (19.6)	40 (20.3)	0.91
AHI	27 (21-33)	23 (8-36)	**<0.001**
HDL-C (mg/dL)	39 (30-45)	41 (28-53)	**0.003**
Triglyceride	213 (174-267)	197 (144-255)	**0.001**
Total cholesterol	213.5±32.8	216.6±26.5	0.53
LDL-C (mg/dL)	143.5±17.8	152.3±14.9	**<0.001**
Creatinine	1.1±0.2	1±0.2	**0.02**
ALT	23 (16-34)	23 (13-31)	0.36
AST	23.6±5.7	26.1±4.6	0.06
Hb	13.6±1.9	13.2±1.6	0.15
PLT	232.7±32.3	211.2±31.4	**<0.001**
WBC	8.9 (5.9-13.4)	9.6 (5.2-13.2)	0.24
Lym	1.8 (1.3-2.3)	2.2 (1.3-3.1)	**<0.001**
Neu	5±1	5.4±1.5	**0.03**
EF	58 (51-69)	57 (50-65)	**0.013**
PAP	38 (27-46)	35 (24-46)	**<0.001**
BMI	33.4±4.9	32.9±4.9	0.55
VAI	8 (5.3-15.5)	6.7 (3.8-14.6)	**<0.001**
SII	624.4 (284.5-950.6)	539.4 (238.7-1131.0)	**<0.001**

AHI: Apnea hypopnea index, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, EF: Ejection fraction, Hb: Hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, Lym: Lymphocyte, Neu: Neutrophil, PAP: Pulmonary artery pressure, SII: Systemic inflammatory index, VAI: Visceral adipose index, WBC: White blood count, NSR: Normal sinus rhythm

metabolic syndrome, and type 2 diabetes, which are associated with the development of AF[30]. In our study, VAI was significantly higher in patients with OSAS who developed AF.

SII is a systemic marker that indicates the balance between systemic immune status and inflammatory responses in the body. Recent studies have shown that it can be used to analyze the inflammatory status in the

Table 2. Univariate analysis results of predictors of AF development in patients with OSAS.

Univariate			
	OR	**(95% CI)**	**p**
Age	0.92	(0.851-0.995)	0.037
Hypertansion	1.346	(0.72-2.517)	0.352
Dyslipidemia	1.261	(0.675-2.355)	0.467
Smoking	0.854	(0.406-1.793)	0.676
Diabetes mellitus	1.431	(0.695-2.948)	0.33
Drinking	2.271	(0.726-7.098)	0.159
Previous CVD	0.957	(0.442-2.075)	0.912
AHI	1.16	(1.082-1.243)	**<0.001**
HDL-C (mg/dL)	0.899	(0.836-0.966)	**0.004**
Triglyceride	1.067	(1.044-1.092)	**<0.001**
Total cholesterol	0.996	(0.985-1.007)	0.483
LDL-C (mg/dL)	0.965	(0.945-0.985)	**0.001**
EF	1.151	(1.05-1.262)	**0.003**
PAP	1.175	(1.079-1.279)	**<0.001**
BMI	1.019	(0.958-1.084)	0.553
VAI	1.471	(1.244-1.741)	<0.001
SII	1.003	(1.001-1.004)	**0.002**

AHI: Apnea hypopnea index, BMI: Body mass index, EF: Ejection fraction, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, PAP: Pulmonary artery pressure, SII: Systemic inflammatory index, VAI: Visceral adipose index

Table 3. Multivariate analysis of predictors of AF development in patients with OSAS.

Multivariate			
	OR	**(95% CI)**	**p**
Age	0.959	(0.865-1.064)	0.434
Hypertansion	1.462	(0.635-3.366)	0.372
Dyslipidemia	0.99	(0.428-2.291)	0.982
Smoking	1.18	(0.436-3.197)	0.744
Diabetes mellitus	1.178	(0.412-3.365)	0.76
Drinking	2.893	(0.66-12.675)	0.159
Previous CVD	0.882	(0.307-2.532)	0.815
AHI	1.22	(1.109-1.342)	**<0.001**
Total cholesterol	0.996	(0.982-1.01)	0.592
LDL-C (mg/dL)	0.951	(0.926-0.976)	**<0.001**
PAP	1.188	(1.064-1.327)	**0.002**
BMI	1.135	(1.035-1.245)	**0.007**
VAI	1.81	(1.399-2.341)	**<0.001**
SII	1.003	(1.001-1.005)	**0.004**

AHI: Apnea hypopnea index, BMI: Body mass index, LDL: Low-density lipoprotein, PAP: Pulmonary artery pressure, SII: Systemic inflammatory index, VAI: Visceral adipose index

body and related diseases[31,32]. Electrical and structural remodeling of the atrial tissue, which underlies the etiology of AF, develops against a background of inflammation, and SII is one of the best indicators of this[33]. In the literature, an association between high SII values and AF development has been reported[34,35]. In our study, SII values were significantly higher in patients with AF.

AHI is a polysomnographic parameter used in the diagnosis and assessment of OSAS severity. In their study, Kawakami et al.[36] showed that AF development increased as AHI increased. Recent studies have shown that this may be due to 1) fragmentation of the sleep cycle causing activation of the sympathetic nervous system; 2) intermittent hypoxia causing oxidative stress and inflammation after reoxygenation; and 3) structural and electrical remodeling due to atrial enlargement and fibrosis. In our study, AHI was significantly higher in OSAS patients with AF.

Lipotoxicity is the excessive accumulation of free fatty acids and triglycerides in non-adipose tissues, including the heart. Studies have shown that this condition is closely associated with metabolic syndrome, inflammation, and insulin resistance and may affect the development of cardiac arrhythmia in cardiolipotoxicity[37]. Studies have shown that an increase in epicardial adipose tissue, which is an important indicator of cardiolipotoxicity, predisposes patients to AF development[38]. Li et al.[39] showed that high triglyceride and low high-density lipoprotein levels affect the development of AF. A lipidogram study by Harrison et al.[40] showed that high low-density lipoprotein (LDL) levels may protect against the development of AF. In our study, we obtained results that coincided with the data from these studies.

When the results of the multivariate analysis were analyzed, it was observed that in addition to VAI, high AHI and low LDL values were the most important factors for AF development. In this patient group, BMI and high PAP were found to significantly affect the development of AF. In the ROC analysis, the highest predictive values were found for VAI and high AHI.

The most important limitation of our study is that it was a single-center retrospective study with a limited patient population. In addition, because the patient population describing palpitations was included in the study, it may not reflect the general patient population.

CONCLUSION

Our study is important in terms of showing VAI as one of the most important predictors of AF, which has an effect on mortality and morbidity in patients with OSAS, the frequency of which is increasing daily. This patient group applied to cardiology outpatient clinics with considerable palpitations in clinical practice. In the absence of pathology on the surface and/or ECG holter follow-ups, palpitations are considered to be predictors of OSAS. Our study suggests that patients with OSAS and high VAI are at a higher risk for AF development and that longer rhythm monitoring should be performed in these patients. Therefore, we believe that long-term rhythm holter follow-up should be performed in this patient group in cases of frequent palpitations, or devices such as smartwatches with rhythm monitoring may be recommended.

Ethics

Ethics Committee Approval: Trakya University Faculty of Medicine Ethics Committee (protocol code TUTF-GOBAEK 2023/172 and date of approval 08 May 2023 (decision no: 08/23).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Author Contributions

Surgical and Medical Practices: U.O., M.G., Concept: U.O., M.G., Design: U.O., M.G., Data Collection and/or Processing: U.O., M.G., Analysis and/or Interpretation: U.O., M.G., Investigation: U.O., M.G., Methodology: U.O., M.G., Project Administration: U.O., M.G., Resources: U.O., M.G., Supervision: U.O., M.G., Literature Search: U.O., M.G., Writing: U.O., M.G.

Conflict of Interest: The authors have no conflict of interest to declare.

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REFERENCES

1. Senaratna CV, Perret JL, Lodge CJ, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev. 2017;34:70-81.
2. Abumuamar AM, Dorian P, Newman D, Shapiro CM. The prevalence of obstructive sleep apnea in patients with atrial fibrillation. Clin Cardiol. 2018;41:601-7.
3. Lv R, Liu X, Zhang Y, et al. Pathophysiological mechanisms and therapeutic approaches in obstructive sleep apnea syndrome. Signal Transduct Target Ther. 2023;8:218.
4. Di Bello F, Napolitano L, Abate M, et al. Nocturia and obstructive sleep apnea syndrome: A systematic review. Sleep Med Rev. 2023;69:101787.
5. Hudgel DW. Sleep Apnea Severity Classification - Revisited. Sleep. 2016;39:1165-6.

6. Holmqvist F, Guan N, Zhu Z, et al. Impact of obstructive sleep apnea and continuous positive airway pressure therapy on outcomes in patients with atrial fibrillation-Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). Am Heart J. 2015;169:647-54.
7. Gami AS, Pressman G, Caples SM, et al. Association of atrial fibrillation and obstructive sleep apnea. Circulation. 2004;110:364-7.
8. Amato MC, Giordano C. Visceral adiposity index: an indicator of adipose tissue dysfunction. Int J Endocrinol. 2014;2014:730827.
9. Nusrianto R, Tahapary DL, Soewondo P. Visceral adiposity index as a predictor for type 2 diabetes mellitus in Asian population: A systematic review. Diabetes Metab Syndr. 2019;13:1231-5.
10. Abumuamar AM, Mollayeva T, Sandor P, Newman D, Nanthakumar K, Shapiro CM. Efficacy of Continuous Positive Airway Pressure Treatment in Patients with Cardiac Arrhythmia and Obstructive Sleep Apnea: What is the Evidence? Clin Med Insights Ther. 2017;9:1-10.
11. Gami AS, Hodge DO, Herges RM, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. J Am Coll Cardiol. 2007;49:565-71.
12. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28:1-39.
13. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42:4194.
14. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res. 2014;20:6212-22.
15. Nuttall FQ. Body Mass Index: Obesity, BMI, and Health: A Critical Review. Nutr Today. 2015;50:117-28.
16. Leite NN, Cota BC, Gotine AREM, Rocha DMUP, Pereira PF, Hermsdorff HHM. Visceral adiposity index is positively associated with blood pressure: A systematic review. Obes Res Clin Pract. 2021;15:546-56.
17. Jayedi A, Soltani S, Motlagh SZ, et al. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516.
18. Rana MN, Neeland IJ. Adipose Tissue Inflammation and Cardiovascular Disease: An Update. Curr Diab Rep. 2022;22:27-37.
19. Vizzuso S, Del Torto A, Dilillo D, et al. Visceral Adiposity Index (VAI) in Children and Adolescents with Obesity: No Association with Daily Energy Intake but Promising Tool to Identify Metabolic Syndrome (MetS). Nutrients. 2021;13:413.
20. Bouloukaki I, Mermigkis C, Kallergis EM, Moniaki V, Mauroudi E, Schiza SE. Obstructive sleep apnea syndrome and cardiovascular disease: The influence of C-reactive protein. World J Exp Med. 2015;5:77-83.
21. Baratta F, Pastori D, Fabiani M, et al. Severity of OSAS, CPAP and cardiovascular events: A follow-up study. Eur J Clin Invest. 2018;48:e12908.
22. Voulgaris A, Archontogeorgis K, Papanas N, et al. Increased risk for cardiovascular disease in patients with obstructive sleep apnoea syndrome-chronic obstructive pulmonary disease (overlap syndrome). Clin Respir J. 2019;13:708-15.
23. Bodez D, Lang S, Meuleman C, et al. Left ventricular diastolic dysfunction in obstructive sleep apnoea syndrome by an echocardiographic standardized approach: An observational study. Arch Cardiovasc Dis. 2015;108:480-90.
24. Borges MD, Franca EL, Fujimori M, et al. Relationship between Proinflammatory Cytokines/Chemokines and Adipokines in Serum of Young Adults with Obesity. Endocr Metab Immune Disord Drug Targets. 2018;8:260-7.
25. Unamuno X, Gómez-Ambrosi J, Rodríguez A, Becerril S, Frühbeck G, Catalán V. Adipokine dysregulation and adipose tissue inflammation in human obesity. Eur J Clin Invest. 2018;48:e12997.
26. Agbaedeng TA, Zacharia AL, Iroga PE, et al. Associations between adipokines and atrial fibrillation: A systematic review and meta-analysis. Nutr Metab Cardiovasc Dis. 2022;32:853-62.
27. Harada M, Nattel S. Implications of Inflammation and Fibrosis in Atrial Fibrillation Pathophysiology. Card Electrophysiol Clin. 2021;13:25-35.
28. Sohns C, Marrouche NF. Atrial fibrillation and cardiac fibrosis. Eur Heart J. 2020;41:1123-31.
29. Platonov PG. Atrial fibrosis: an obligatory component of arrhythmia mechanisms in atrial fibrillation? J Geriatr Cardiol. 2017;14:233-37.
30. Neeland IJ, Ross R, Després JP, et al. Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. Lancet Diabetes Endocrinol. 2019;7:715-25.
31. Xia Y, Xia C, Wu L, Li Z, Li H, Zhang J. Systemic Immune Inflammation Index (SII), System Inflammation Response Index (SIRI) and Risk of All-Cause Mortality and Cardiovascular Mortality: A 20-Year Follow-Up Cohort Study of 42,875 US Adults. J Clin Med. 2023;12:1128.
32. Yilmaz Y, Kelesoglu S, Elcik D, Ozmen R, Kalay N. Predictive Values of Systemic Immune-Inflammation Index in New-Onset Atrial Fibrillation Following Coronary Artery Bypass Grafting. Braz J Cardiovasc Surg. 2023;38:96-103.
33. Kaplan E, Ekızler FA, Saribaş H, et al. Effectiveness of the systemic immune inflammation index to predict atrial fibrillation recurrence after cryoablation. Biomark Med. 2023;17:101-9.
34. Wang J, Hu S, Liang C, Ling Y. The association between systemic inflammatory response index and new-onset atrial fibrillation in patients with ST-elevated myocardial infarction treated with percutaneous coronary intervention. BMC Cardiovasc Disord. 2022;22:525.
35. Lin KB, Fan FH, Cai MQ, et al. Systemic immune inflammation index and system inflammation response index are potential biomarkers of atrial fibrillation among the patients presenting with ischemic stroke. Eur J Med Res. 2022;27:106.
36. Kawakami H, Nagai T, Fujii A, et al. Apnea-hypopnea index as a predictor of atrial fibrillation recurrence following initial pulmonary vein isolation: usefulness of type-3 portable monitor for sleep-disordered breathing. J Interv Card Electrophysiol. 2016;47:237-44.
37. Alí A, Boutjdir M, Aromolaran AS. Cardiolipotoxicity, Inflammation, and Arrhythmias: Role for Interleukin-6 Molecular Mechanisms. Front Physiol. 2018;9:1866.

38. Conte M, Petraglia L, Cabaro S, et al. Epicardial Adipose Tissue and Cardiac Arrhythmias: Focus on Atrial Fibrillation. Front Cardiovasc Med. 2022;9:932262.

39. Li ZZ, Du X, Guo XY, et al. Association Between Blood Lipid Profiles and Atrial Fibrillation: A Case-Control Study. Med Sci Monit. 2018;24:3903-8.

40. Harrison S, Lip GYH, Lane DA, et al. The cholesterol paradox in atrial fibrillation: results from the LIPIDOGRAM 2015 study. Eur Heart J. 2020;41(Suppl 2):451.