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| RESEARCH ARTICLE

Association Between Obesity and Postoperative Atrial Fibrillation in Patients Undergoing Cardiac Surgery: An Updated Systematic Review

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| ABSTRACT

Postoperative atrial fibrillation (POAF) is a frequent and severe complication following cardiac surgery. While obesity is established as a risk factor for atrial fibrillation (AF) in non-surgical settings, its role in the postoperative period is still debated. This systematic review aims to assess the relationship between obesity and POAF in patients undergoing cardiac surgery. A comprehensive literature search was conducted in PubMed, Embase, Web of Science, and Cochrane Library, focusing on randomized controlled trials (RCTs) published until June 2023. Data were extracted independently by two authors and assessed using the Cochrane Risk of Bias Tool (RoB2). From an initial search of 1,284 articles, 11 studies met the inclusion criteria, with a range of sample sizes between 300 and 5,000 patients. The incidence of POAF in obese patients ranged from 30% to 54%, compared to 20% to 46% in non-obese patients. Five studies concluded that obesity was a significant risk factor for POAF, whereas four found no statistically significant relationship, and two reported an "obesity paradox," where obesity appeared protective or neutral regarding POAF risk. Our review provides evidence regarding obesity developing POAF after cardiac surgery.

| KEYWORDS

Categories: Cardiac/Thoracic/Vascular Surgery, Cardiology, Endocrinology/Diabetes/Metabolism

Keywords: heart rhythm, systematic review, cardiac surgery, postoperative atrial fibrillation, obesity

| ARTICLE INFORMATION

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1. Introduction and Background

Atrial fibrillation (AF) is a supraventricular arrhythmia defined by very rapid and uncoordinated activity of the atria [1]. Postoperative atrial fibrillation (POAF) refers to new-onset atrial fibrillation that occurs immediately after surgery and is the most important type of secondary AF. It is typically brief, transient, asymptomatic, and frequently recurrent (especially within the first week) with the highest incidence between the 2nd to 4th day post-surgery [2]. POAF is one of the most prevalent complications

after cardiac surgery and occurs in up to 30-50% of patients [3,4]. Most of the studies have found POAF rates after coronary artery bypass grafting (CABG) to be around 20-40%, 40-50% after valvular surgery, up to 60% after combined CABG and valvular surgery and 80% post multiple valvular surgery [5-7]. It is associated with longer hospital and ICU stays increased in-hospital mortality as well as mid-term and long-term mortality rates, higher risk of stroke, higher hospital expenses and an eight-times increased risk of development of atrial fibrillation again later in life [5]. Understanding the factors contributing to POAF is important for risk stratification, preventive strategies, and effective patient management. Several risk factors predispose to POAF for example advanced age, obesity, hypertension, metabolic syndrome, diabetes, diastolic dysfunction, left atrial enlargement, left ventricular hypertrophy and genetic predisposition [4]. Among these factors, obesity stands prominent due to its rising prevalence worldwide [8]. Obesity, defined by a body mass index (BMI) of 30 kg/m2 or higher, is a known risk factor for AF in the population [9]. AF in obese patients is caused by three main mechanisms, namely inflammation, increased oxidative stress and atrial remodelling. Obesity being a constant state of low-grade inflammation, has an increased expression of pro- inflammatory cytokines. These cytokines cause changes in cardiomyocyte excitability. Obesity also

increases oxidative stress in cardiomyocytes due to an increased production of reactive oxygen species (ROS) as well as a decrease in ROS-scavenging enzymes. Furthermore, atrial remodeling which includes fibrosis, fatty infiltration, and atrial enlargement interrupts conduction. These changes combine to increase the susceptibility of the heart to develop AF [10]. Obesity's role in postoperative settings, particularly after cardiac surgery, remains ambiguous with conflicting results reported in existing literature [11,12].

AF is the most common arrhythmia affecting an estimated 33 million people worldwide [13]. Generally, the incidence rises after cardiac surgical procedures, often leading to adverse outcomes such as stroke, heart failure, and even death [14]. A particular study has identified factors such as advanced age, male gender, and a history of AF as predictors for POAF [15], the association between obesity and POAF is still under investigation. It is widely established that obesity increases the chances of AF [16], however, the impact after surgery remains complex and not completely clear. Some studies indicate that obesity may elevate the risk of POAF, with factors such as increased inflammation and oxidative stress [17,18]. Other studies have reported an "obesity paradox," where obese patients have a similar or even lower risk of developing POAF [19,20]. This systematic review aims to evaluate the association between obesity and POAF in patients undergoing cardiac surgery, proposing to elucidate whether obesity serves as an independent risk factor for POAF, which could impact preoperative risk assessments and the postoperative management of patients undergoing cardiac surgery.

2. Review

2.1 Methods/Search Strategy

A systematic search was conducted with PubMed, Embase, Web of Science, and Cochrane Library databases. The search was performed using the terms "obesity," "atrial fibrillation," "postoperative," and "cardiac surgery". The search period was limited to articles published from inception through June 2023 [21].

2.1 Inclusion and Exclusion Criteria

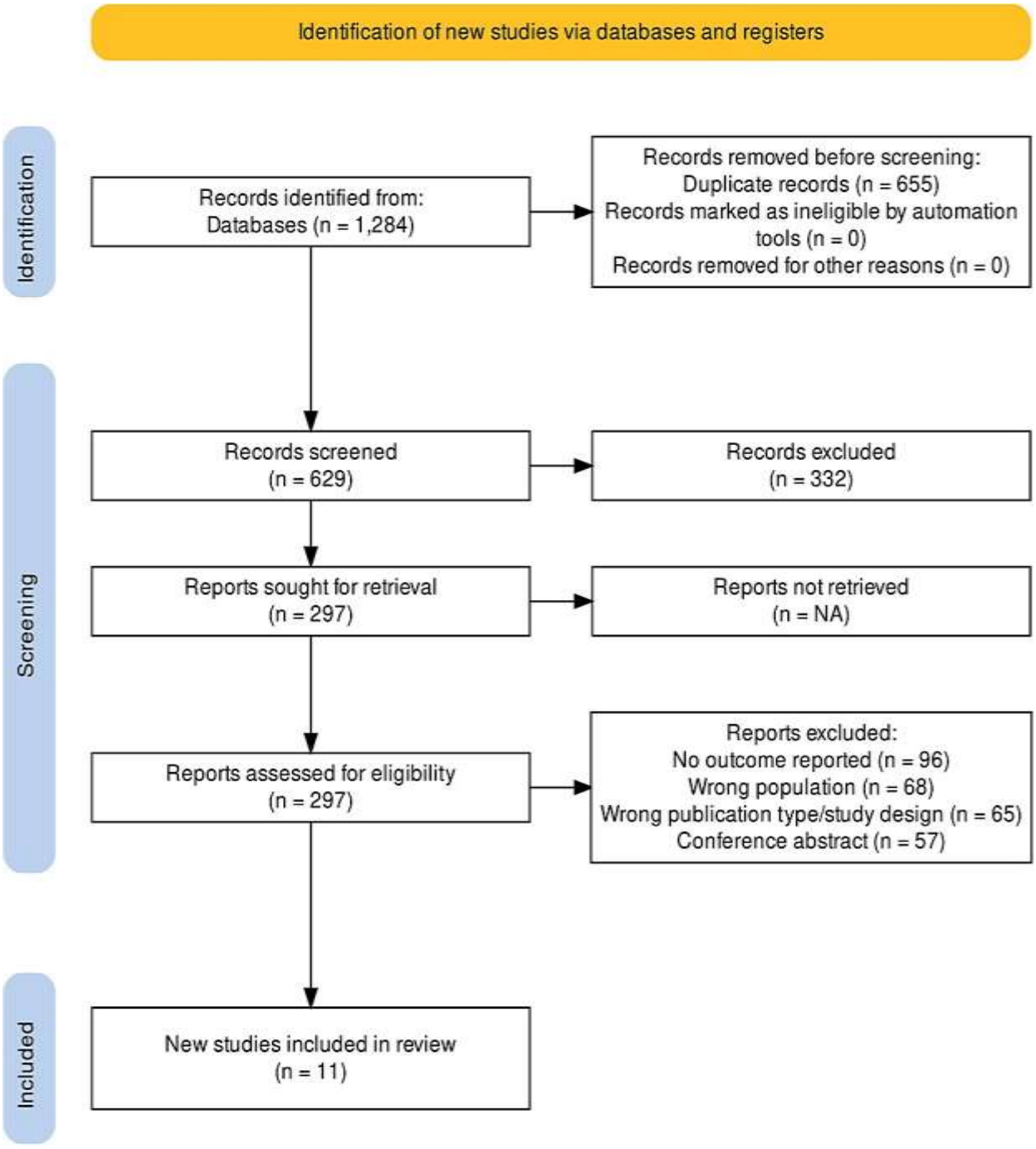
Studies were included if they were only RCTs, between obesity and POAF in patients who had undergone cardiac surgery. Studies that did not report outcomes between obesity and postoperative atrial fibrillation, non-RCTs or those with insufficient data, were excluded [22].

2.1 Data Extraction and Quality Assessment

Data were independently extracted by two authors and double-checked to minimize errors, disagreements were resolved by a third reviewer and consensus-based discussion. The quality of the studies was assessed using the RoB2 [23].

3. Results

After identifying a total of 1,284 articles, we screened them based on their titles and abstracts, narrowing down to 297 potential articles. After full-text review, we did the final selection of 11 articles that met the inclusion and exclusion criteria [24]. The sample sizes ranged from 300 to 5,000 patients, and the studies themselves spanned across diverse geographical regions, including North America, Europe, and Asia (Figure 1) [25].



3. Effect of POAF on coronary heart disease

The EPIC (European Prospective Investigation Into Cancer and Nutrition) study conducted by Arsenault et al. on 21,448 residents of Norfolk, United Kingdom, found that 1,310 out of 9,348 men and 776 out of 12,100 women developed coronary heart disease (CHD) in the follow-up period of 11 years. The average baseline waist circumference of men who developed CHD was 98 +/- 10 cm and that of women who developed CHD was 86 +/- 11 cm. This was significantly different from the average baseline waist circumference of participants who did not develop CHD, which was 95 +/- 9 cm in men and 81 +/- 10 cm in women who did not develop CHD. The study found that among participants with low low-density lipoprotein cholesterol (LDL-C) levels (<100 mg/dl), those with high non-high-density lipoprotein cholesterol (non-HDL-C) levels (>130 mg/dl) had a hazard ratio (HR) for future CHD of 1.84, compared to those with low non-HDL-C levels (<130 mg/dl) [26]. Furthermore, among participants with low LDL-C levels, those with high triglyceride (TG)

levels (>150 mg/dl) had an HR of 1.63 compared to those with low TG levels (<150 mg/dl) and those with high TC/HDL-C ratio (>5) had a HR of 2.19 compared to those with low total cholesterol (TC)/HDL-C ratio (<5) [26]. According to a practice guideline published by Poirier P et al. in 2009, obesity rarely leads to severe arrhythmias but may lead to arrhythmias due to sleep apnea (most common), idiopathic atrial fibrillation, atrial flutter, bradyarrhythmia due to sinus node dysfunction and ventricular tachycardia. 10 years of severe obesity (body size ≥75 of ideal body weight or BMI ≥40 kg/ m2) may significantly increase the risk of obesity cardiomyopathy, which may cause diastolic and/or systolic heart dysfunction [27]. A 7-year follow-up study conducted by McTigue et al with 90,185 women found obesity to be a risk factor for CHD mortality. With increasing weight, CHD incidence also increased. They found that most of this obesity-related risk was mediated by diabetes, hypertension, and hyperlipidemia [27,28]. Patients with massive obesity may have increased right ventricular filling pressures or increased abdominal pressure which may be the cause of pedal edema in these patients. A study conducted with data from the Rochester Epidemiology Project found an increased rate of cardiac complications among overweight and obese patients undergoing urgent hip fracture repair [27,29]. BMI≥50 kg/m2 increases the risk of complications in bariatric surgery. The Obesity Surgery Mortality Risk Score (OS-MRS) includes BMI≥50 kg/m2 as one of the five risk factors to assess the mortality risk in bariatric surgery [27,30]. Intraoperatively, an increased incidence of pulmonary hypertension and right sided heart failure is seen among patients with obesity-hyperventilation syndrome. In general, patients having severe obesity-related complications have an increased risk of intraoperative complications.

However, these complications are infrequent if the surgeries are performed by experienced surgeons at good well-resourced hospitals. In the practice guideline, Poirier P et al. said that a 12-lead ECG and chest X-ray should be obtained in all severely obese patients as pre-operative evaluation. Among these patients, additional non-invasive investigations should be considered in those who have >3 coronary heart disease (CHD) risk factors or diagnosed CHD, if the tests are believed to affect the management plan [27].

4. Effect of polyunsaturated fatty acids

A study conducted by Calo et al. in 2005 involving 160 patients undergoing CABG, found that 2g/day n-3 polyunsaturated fatty acids (PUFAs) given at least 5 days prior to CABG surgery caused a significant reduction in the incidence of POAF (caused POAF in 12 patients compared to placebo, which led to POAF in 27 patients). PUFA also significantly reduced the length of hospital stay. It didn't have any effect on the incidence of nonfatal postoperative complications and postoperative mortality [31].

5. Effect of obesity

Patients undergoing cardiac surgery who have an excessive BMI are at greater risk of additionally having the five diseases associated with obesity, including type II DM, hypertension, hyperlipidemia, stroke, and coronary artery disease (CAD) [32]. Obesity, as evaluated by Metropolitan Relative Weight, has been demonstrated to be a crucial independent predictor of cardiovascular disease (CVD) in long-term follow-up of the original Framingham cohort [33]. It has been noted that having an excessive BMI has a direct correlation with diastolic dysfunction and systolic impairment. When compared to the non-obese patients, Wigfield et al. observed a rise in certain morbidities after cardiac surgery in the extremely obese patient group, including prolonged ventilation (39% vs. 23.5%; p = 0.01), incidence of renal failure (14.3% vs. 5.0%; p

= 0.01), and length of hospital stay (11.4 vs. 9.6; p = 0.001) [34]. Obesity has been linked to left atrial dilatation, diastolic dysfunction, and ERP shortening in the left atria, all of which increase the likelihood of AF [35]. It is plausible that post-operatively, various factors cause AF to persist in different patients which is made apparent by the fact that only some patients benefit from preventive and therapeutic treatments in the initial phase following heart surgery. POAF may develop not only in the first post-operative phase but also

in the days and weeks that follow in patients with severely damaged atrial tissue, such as those caused by chronic atrial strain or advanced age. In fact, the growing data on late POAF suggests that there might be a need for continued observation in high-risk patients [36]. Filardo et al. evaluated the relationship between BMI and in-hospital mortality following coronary artery bypass graft (CABG) surgery in 5,762 patients who underwent isolated CABG classified the patients' body mass indices (BMI) into weight classes. BMI (modeled with a restricted cubic spline) was found to have a highly significant (P=0.003) correlation with mortality. In comparison to patients with BMIs in the mid-20s or higher than 40 kg/m2, individuals with BMIs in the low- 30s had a lower risk of in-hospital death. However, results were discordant when BMI was examined using the numerous classification schemes cited in the literature, showing that categorization has a significant impact on study outcomes. Thus, it seems that the way BMI is stated in a multivariable model is crucial to the model's efficacy and could contribute to clarifying the contradictory and mixed

results that have been reported in the literature, with some studies finding no relationship between obesity and mortality [37-39] and others finding an increased risk of mortality in patients who are obese, severely obese or underweight [40-42]

6. Discussion

Approximately 5 out of the 11 studies included in our review explicitly identified obesity as a significant predictor of POAF. This substantiates previous research suggesting that obesity, with its attendant metabolic and structural changes, can significantly impact cardiac function [44,45]. Elevated inflammatory markers altered autonomic tone, and structural changes in the atria were some of the mechanisms postulated in the literature to explain this association [46,47]. Our review also found a smaller number of studies reporting the "obesity paradox," some phenomenon wherein obese patients seem to have a similar or even lower risk of POAF. This paradox has been previously observed in cardiovascular diseases and has led to debates within the academic community [43]. While the preponderance of evidence leans toward obesity being a risk factor for POAF, it's essential to consider the heterogeneity among the studies. Factors such as different definitions of obesity, variations in surgical procedures, and inconsistent reporting of POAF could contribute to the observed discrepancies [48].

7. Conclusion

Our study review points toward an association between obesity and an increased incidence of POAF in patients undergoing cardiac surgery but with some conflicting evidence. Future research should aim to resolve these contradictions and examine the underlying mechanisms, which could have significant implications for preoperative risk assessment and the management of obese patients undergoing cardiac procedures.

Additional Information

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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