Review



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# Pre-operative and post-operative atrial fibrillation in patients undergoing SAVR/TAVR

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# Abstract

Atrial fibrillation (AF) is a common preoperative comorbidity and post-operative complication associated with cardiac surgery and is recognized as a significant predictor of adverse clinical outcomes. This review aims to highlight the current literature regarding the incidence, risk factors, and outcomes of atrial fibrillation in patients undergoing surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR) procedures. A literature search of relevant articles was conducted via PubMed, Medline, and EMBASE. Pre-existing AF is seen in 6.3%-35.2% of SAVR patients and 15.7%-48.9% of TAVR patients and is associated with increased risk of mortality (OR = 2.2) and stroke (OR = 5.9). Postoperative AF (POAF) is more common after SAVR and in patients with hemodynamic instability. The rates for POAF range from 11.1%-84% following SAVR and range from 3.0%-55.6% following TAVR. In-hospital mortality (7.8% vs. 3.4%; P < 0.01) and stroke (4.7% vs. 2.0%; P < 0.01) are higher in the POAF group. POAF can be prevented via prophylactic antiarrhythmic medications and atrial pacing. Therapeutic anticoagulation is recommended as it reduces the risk of thrombotic complications following SAVR and TAVR procedures in the setting of POAF. Compared to those not on anticoagulant therapies, patients on anticoagulation have decreased rates of stroke (1.7% vs. 5.5%) and fewer 30-day thrombotic complications (3% vs. 40%). These preventive measures are essential as POAF is associated with more thromboembolic events, longer hospital stays, and higher overall morbidity and mortality rates.



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Keywords: SAVR, TAVR, atrial fibrillation

# INTRODUCTION

Atrial fibrillation (AF) is a common comorbidity among patients undergoing cardiac surgery. In patients with aortic stenosis (AS), pre-existing AF is noted to be associated with an increased risk of heart failure, mortality, and stroke<sup>[1]</sup>. Symptomatic AS can further contribute to hemodynamic complications and can be fatal despite medical management as the 5-year mortality rate is 50%-60%, and the 10-year mortality rate is 90%<sup>[2,3]</sup>. Procedures such as surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR) can treat aortic stenosis. However, these procedures are associated with high rates of pre-operative and post-operative atrial fibrillation (POAF). AF is among the most common post-operative outcomes following cardiac surgery (10%-40%) and is recognized to be a significant predictor of adverse clinical outcomes. In this review, we highlight the relevant literature regarding incidence rates, predictors, management, and prevention of preoperative and postoperative AF following SAVR/TAVR procedures.

# **METHODS**

A literature search of relevant articles was conducted via the following PubMed, Medline, and EMBASE search: "SAVR" OR "surgical aortic valve replacement" OR "TAVR" or "transcatheter aortic valve replacement" AND "atrial fibrillation" OR [atrial fibrillation (MeSH Terms)]. Further, a Web of Science backward literature search was conducted to identify relevant literature.

# **PREOP AF RISKS**

# Etiology

Atrial fibrillation is commonly associated with aortic stenosis. While the exact pathophysiological mechanism behind the etiology of atrial fibrillation in aortic stenosis is unclear, one leading theory involves the left ventricular (LV) response. It is believed that aortic stenosis leads to LV outflow obstruction, which results in left atrial and LV pressure overload. The pressure overload, in turn, leads to myocardial fibrosis and LV hypertrophy, in addition to increased diastolic filling pressure, impaired relaxation, and left atrial dilation. These changes lead to increased left atrial pressure and further systolic and diastolic dysfunction, ultimately resulting in atrial fibrillation<sup>[1,4]</sup>.

# Predictors

The exact predictors of pre-existing atrial fibrillation in SAVR patients are unknown. However, some predictors of pre-existing atrial fibrillation in TAVR patients include the presence of moderate to severe mitral regurgitation, moderate to severe tricuspid regurgitation, and pulmonary hypertension<sup>[5]</sup>. Other predictors of TAVR with atrial fibrillation include older age, female gender, and comorbidities such as diabetes, chronic lung disease, congestive heart failure, chronic renal disease, anemia, arthritis, hypothyroidism, and peripheral vascular disease<sup>[6]</sup>.

# PREOP AF RATES

#### SAVR

The association between atrial fibrillation and aortic valve replacement has been studied in the literature, and there seems to be a correlation between pre-existing atrial fibrillation and subsequent aortic valve replacement. Regarding SAVR particularly, atrial fibrillation has been seen in 6.3%-35.2% of patients prior to surgery [Table 1].

Ref.	SAVR sample size (n)	Preoperative SAVR AF (%)	
Jørgensen et al. <sup>[7]</sup> 2017	38	8 (21.1)	
Leon <i>et al.<sup>[8]</sup></i> 2016	1021	359 (35.2)	
Mack et al. <sup>[9]</sup> 2019	454	85 (18.8)	
Smith <i>et al.</i> <sup>[10]</sup> 2011	351	30 days: 56 (16.0) 1 year: 60 (17.1)	
Takahashi et al. <sup>[11]</sup> 2014	63	4 (6.3)	
Bowdish <i>et al.</i> <sup>[12]</sup> 2016 *Not specific to AS	492	53 (10.8)	
Shahim et al. <sup>[13]</sup> 2021	452	88 (19.5)	
Reardon et al. <sup>[14]</sup> 2017	796	211 (26.5)	

Table 1. Preoperative atrial fibrillation rates for surgical aortic valve replacement

Comparison of preoperative SAVR AF rates. SAVR: Surgical aortic valve replacement; AF: atrial fibrillation; AS: aortic stenosis.

#### **TAVR**

Pre-existing atrial fibrillation has been reported in 15.7%-48.9% of patients undergoing TAVR [Table 2]. Furthermore, Tarantini *et al.*<sup>[5]</sup> reported that pre-existing atrial fibrillation has a significantly higher prevalence in TAVR patients treated using the transapical approach than those treated using the transfemoral approach (41.8% *vs.* 32.7%, P < 0.01). The higher rates of preoperative atrial fibrillation in TAVR compared to SAVR can be attributed to more comorbidities and a worse clinical profile among TAVR patients<sup>[21]</sup>.

#### **Cardiac diseases**

While atrial fibrillation in patients undergoing aortic valve replacement is fairly common, it is essential to know the prevalence of atrial fibrillation in aortic stenosis and compare this prevalence with the prevalence of atrial fibrillation in other similar conditions, such as aortic regurgitation, mitral stenosis, and coronary artery disease (CAD), above the normal increase due to aging. Pre-existing atrial fibrillation is seen in 5.0% of aortic stenosis patients and a similar 5.8% in aortic regurgitation<sup>[22]</sup>. Pre-existing atrial fibrillation has been seen in 33.9% of patients with mitral valve stenosis, significantly higher than the prevalence rates seen in aortic stenosis<sup>[22]</sup>. While the prevalence of CAD in atrial fibrillation patients is quite high, the rate of atrial fibrillation in CAD patients is only around 0.2% to 5%<sup>[23]</sup>. These low rates are also seen in normal aging, with a prevalence of atrial fibrillation of 2.3% among people over 40 years and 5.9% among people over 65 years<sup>[24]</sup>.

# PREOP AF OUTCOMES

#### SAVR

A significant proportion of patients receiving aortic valve replacement have pre-existing atrial fibrillation. Shahim *et al.*<sup>[13]</sup> studied the impact of pre-existing atrial fibrillation on outcomes after aortic valve replacement surgery. They found that atrial fibrillation was significantly associated with non-cardiac-related death and major complications. Death, stroke, or rehospitalization at 2 years occurred in 24.6% of SAVR patients with preexisting atrial fibrillation but only occurred in 15.8% of SAVR patients without preoperative AF (OR = 2.22; 95%CI: 1.19-4.13). Further studies are needed to truly understand the impact of pre-existing atrial fibrillation in the SAVR specific population.

#### TAVR

Given the prevalence of preoperative atrial fibrillation, several studies have tried to determine the impact of baseline atrial fibrillation on post-TAVR outcomes. Short-term 30-day, adverse outcomes like mortality, stroke, vascular complications, and repeat hospitalization have been significantly higher in patients with

Ref.	TAVR sample size (n)	Preoperative TAVR AF (%)	
Jørgensen et al. <sup>[7]</sup> 2017	40	12 (30)	
Leon et al. <sup>[8]</sup> 2016	1011	313 (31.0)	
Mack et al. <sup>[9]</sup> 2019	496	78 (15.7)	
Yankelson <i>et al.</i> <sup>[16]</sup> 2014	380	118 (31.1)	
Maan et al. <sup>[17]</sup> 2015	137	67 (48.9)	
Sannino et al. <sup>[18]</sup> 2016	708	219 (30.9)	
Zweiker <i>et al.<sup>[19]</sup></i> 2017 *Not specific to AS	398	172 (43.2)	
Biviano et al. <sup>[20]</sup> 2016	1879	504 (26.8)	
Tarantini <i>et al.<sup>[5]</sup></i> 2016	1925	685 (35.6)	
Mentias <i>et al.</i> <sup>[15]</sup> 2019 *Not specific to AS	72660	29,563 (40.7)	
Shahim et al. <sup>[13]</sup> 2021	496	80 (16.1)	
Reardon <i>et al.</i> <sup>[14]</sup> 2017	864	243 (28.1)	
Sannino et al. <sup>[18]</sup> 2016	708	219 (30.9)	

Comparison of preoperative TAVR AF rates. TAVR: Transcatheter aortic valve replacement; AF: atrial fibrillation; AS: aortic stenosis.

baseline AF is receiving TAVR<sup>[17]</sup>. Beyond 30 days, preexisting AF has been an independent predictor of major late bleeding complications, cardiovascular events, and mortality. Yankelson*et al.*<sup>[16]</sup>, studied 380 consecutive patients undergoing transcatheter aortic valve implantation, 118 of whom had baseline atrial fibrillation, and found that baseline AF was a significant predictor of stroke and mortality. Previous AF has been shown to be associated with an increased risk for stroke at 30 days (OR = 8.7; P = 0.058) and at 1 year after the TAVR procedure (OR = 5.9; P = 0.015). Mortality rates at 1 year were significantly higher in patients with previous AF at baseline than those without AF prior to TAVR (34.9% *vs.* 8.2%; P < 0.01). Multivariate adjusted Cox proportional hazard analysis conducted by Yankelson *et al.*<sup>[16]</sup> found that previous AF (OR = 2.2; 95%CI: 1.3-3.8) was the most significant predictor of mortality throughout the follow-up period after the TAVR procedure. Several other studies have shown baseline AF to be significantly associated with higher 1-year mortality or predicting 1-year mortality<sup>[5,18,19,20,25]</sup>.

# **NEW-ONSET POAF RISKS**

#### SAVR

One major postprocedural complication of SAVR is new-onset POAF. A possible explanation for the development of POAF after SAVR can be attributed to inflammation caused by surgical trauma. SAVR is associated with several adverse surgical-related factors such as right atrium incisions for venous cannulation, pericardiectomy, aortic cross-clamping, and cardiopulmonary bypass<sup>[26]</sup>. This inflammation theory is similar to the explanation of POAF development following coronary artery bypass graft surgery. The reason why SAVR is more likely to cause POAF than TAVR can also be linked to surgical complications<sup>[21]</sup>.

Several risk factors have been reported in the literature to predict the development of postoperative atrial fibrillation following SAVR and TAVR procedures. Predictive risk factors of POAF following SAVR include a preoperative age  $\geq$  of 70 years, low body mass index, a history of heart failure, a maximum transvalvular gradient  $\geq$  of 85 mmHg, end-systolic interventricular septum thickness  $\geq$  1.8 cm, and preoperative and early postoperative left ventricular ejection fraction  $\leq$  50%<sup>[26]</sup>. Independent predictors of prolonged POAF after SAVR include old age and left atrial enlargement<sup>[27]</sup>. In addition, inflammatory responses from surgical trauma and an accompanying coronary artery bypass graft (CABG) surgery have also been shown to be

linked with POAF<sup>[26]</sup>.

#### TAVR

Similar to the explanation of POAF after SAVR procedures, a systemic inflammatory response is considered why atrial fibrillation develops following TAVR procedures. Inflammation and atrial oxidative stress lead to slower atrial conduction and shorter refractoriness. These changes induce re-entry and ectopic activity, which lead to atrial remodeling and tissue fibrosis, which ultimately result in atrial fibrillation development<sup>[28]</sup>.

In predicting POAF following TAVR, key risk factors include hemodynamic instability, atrial size, and procedural access site. Hemodynamic instability during the procedure has been shown to be one of the strongest predictors, with a ninefold increase in the risk of POAF (OR = 9.3; 95%CI: 1.5-59)<sup>[25]</sup>. A left atrial size  $\ge 27 \text{ mm/m}^2$  on echocardiography has shown the highest sensitivity (67%) and specificity (61%) for predicting POAF in patients following TAVR<sup>[29]</sup>. Transapical access TAVR has been associated with a fivefold increase in POAF risk compared to a transfermoral approach (OR = 4.96; 95%CI: 1.9-13.2)<sup>[25]</sup>. While the patients undergoing transapical TAVR generally have more pre-existing comorbidities than those undergoing transfemoral TAVR, the increased incidence of POAF with the transapical approach may be attributed to epicardial and pericardial injury caused by the procedure approach<sup>[28,30]</sup>. In comparison to transfemoral procedures, transapical procedures are more associated with systemic inflammatory responses, similar to those seen after SAVR. In addition, the onset of a majority of POAF episodes occurs during the first 48 to 96 postprocedural hours, which matches the timing of peak inflammatory responses<sup>[30]</sup>. Not only does transapical TAVR increase POAF risk, but transaortic TAVR also increases the risk of POAF in comparison with a transfemoral approach. While subclavian TAVR is associated with a slightly higher risk of POAF than transfemoral TAVR, it is not statistically significant<sup>[31]</sup>. Other risk factors of POAF following TAVR include age, low left ventricular ejection fraction, previous cerebrovascular events, worse functional status (New York Heart Association classes III or IV), chronic lung disease, balloon aortic valvuloplasty, and periprocedural complications such as cardiac tamponade<sup>[30]</sup>.

Similarities in POAF risk factors following SAVR and TAVR include age, low left ventricular ejection fraction, increased left atrial size, and inflammatory responses. However, TAVR POAF is associated with many more studies examining predictive risk factors. In addition, multiple diagnostic approaches using anatomical or electrocardiograph parameters to predict POAF following TAVR are currently being investigated<sup>[28]</sup>. Given the scarcity of articles on the predictive risk factors of POAF following SAVR, compared to the list of studies on the risk factors of TAVR POAF, there should also be more exploration into the prediction of POAF after SAVR. It is essential to effectively predict the risk of POAF after SAVR or TAVR so that patients can be better protected and managed.

# **NEW-ONSET POAF RATES**

#### SAVR and TAVR

New-onset postoperative atrial fibrillation is a known complication of various cardiac procedures, with overall incidence usually ranging from 20%-50%. Specifically focusing on SAVR and TAVR, new-onset atrial fibrillation is a significant postoperative complication and has been shown to impact both short-term and long-term outcomes dramatically. The incidence rates of SAVR and TAVR differ based upon both follow-up time and type of procedure. Despite this, several studies have indicated significantly increased rates of POAF following SAVR when compared to TAVR. The rates for POAF following SAVR procedures have been noted to range from 11.1%-84% [Table 3]; the rates for POAF following TAVR procedures range from 3.0% to 55.6% [Table 4]. Further, Tanawuttiwat *et al.*<sup>[32]</sup> reported the incidence of new-onset atrial

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#### Table 3. Postoperative atrial fibrillation rates for surgical aortic valve replacement

Ref.	Pre-SAVR no AF sample size or overall sample size used for POAF calculation	POAF post-SAVR (%)	Concomitant procedure with SAVR (Y/N)
Jørgensen <i>et al.</i> <sup>[7]</sup> 2017	25	2 weeks: 21 (84%) Noted significant decrease to 50% at 8-10 weeks	Y (Implantation of Medtronic Reveal XT 9529™ ILR cardiac monitor)
Conte et al. <sup>[33]</sup> 2017	0-3 days: 359 4-30 days: 354	0-3 days: 67 (18.7) 4-30 days: 45 (12.7)	Ν
Leon <i>et al.<sup>[8]</sup></i> 2016	1021	30 days: 265 (26.4) 1 year: 272 (27.2) 2 years: 273 (27.3)	Y (9.1% of patients had concomitant surgery including aortic endarterectomy, aortic-root enlargement or replacement, and mitral or tricuspid valve repair/replacement)
Mack et al. <sup>[9]</sup> 2019	369	30 days: 145 (39.5)	Y (26.4% had concomitant coronary revascularization or other procedure)
Smith et al. <sup>[10]</sup> 2011	351	30 days: 56 (16.0) 1 year: 60 (17.1)	Ν
Tanawuttiwat <i>et al.</i> <sup>[32]</sup> 2014	35	21 (60)	Ν
Waksman et al. <sup>[34]</sup> 2018	719	293 (40.8)	Y (concomitant procedure other than coronary artery bypass graft surgery)
Thourani <i>et al.</i> <sup>[35]</sup> 2018	458	51 (11.1)	Y (CABG, aortic root enlargement or replacement, aortic endarterectomy, mitral or tricuspid valve surgery, and an ablation procedure for atrial fibrillation
Madhu Reddy et al. <sup>[36]</sup> 2010	139	69 (44)	Y (concomitant coronary bypass surgery)
lmanishi et al. <sup>[37]</sup> 2014	27	15 (56)	Ν
Hu et al. <sup>[38]</sup> 2015	107	37 (34.6)	Ν
Saxena <i>et al.<sup>[39]</sup></i> 2013 *Not specific to AS	2065	725 (35.1)	Ν
Cameli <i>et al</i> . <sup>[40]</sup> 2014	76	15 (19.7)	Ν
Girerd et al. <sup>[41]</sup> 2011 *Not specific to AS	2287	951 (41.6)	Y (concomitant CABG)
Pivatto <i>et al.</i> <sup>[42]</sup> 2014	348	114 (32.8)	Ν
Dandale <i>et al.<sup>[43]</sup></i> 2014	830	316 (38)	Y (concomitant CABG and mitral valve surgery)
Takahashi et al. <sup>[11]</sup> 2014	63	44 (65)	Ν
Swinkels <i>et al.</i> <sup>[44]</sup> 2017 *Not specific to AS	569	241 (42.4)	Y (concomitant CABG)
Bowdish et al. <sup>[12]</sup> 2016	493 *Used overall population in POAF calculation	143 (29)	Ν

#### Tummala et al. Vessel Plus 2022;6:17 | https://dx.doi.org/10.20517/2574-1209.2021.114

Filardo et al. <sup>[45]</sup> 2010 1039	380 (37)	Y (concomitant CABG)
*Not specific to AS		

Comparison of postoperative SAVR AF rates. SAVR: Surgical aortic valve replacement; AF: atrial fibrillation; AS: aortic stenosis; POAF: postoperative atrial fibrillation; CABG: coronary artery bypass graft; Y/N: yes/no.

fibrillation in patients stratified by type of TAVR procedure. They identified that new-onset AF was most commonly found in the transapical TAVR (53%) subgroup, which was significantly greater than the transaortic TAVR (33%) and transfermoral TAVR (14%) subgroups.

#### SAVR sternotomy vs. mini SAVR

Over the past two decades, minimally invasive cardiac surgical procedures have started to replace traditional sternotomy to reduce surgical complications. Given that new-onset POAF is one of the major complications following cardiac surgery, it is essential to see how minimally invasive surgical procedures impact POAF development. While minimally invasive mitral valve surgery has been shown to be associated with lower rates of POAF than conventional full sternotomy, the data is less clear in terms of surgical aortic valve replacement. Some studies have shown significantly lower rates of POAF in the mini SAVR procedures in comparison to traditional sternotomy (10.2% *vs.* 30.6%; P < 0.05)<sup>[48]</sup>. However, numerous other studies have shown no significant difference in POAF incidence between minimally invasive and full sternotomy surgical approaches<sup>[49]</sup>. Given the conflicting data, more research is needed into the safety and efficacy of minimally invasive SAVR procedures.

#### **NEW-ONSET POAF OUTCOMES**

Atrial fibrillation is a common postoperative outcome after aortic valve replacement in both surgical and transcatheter approaches. As many as 64% of patients experience new-onset of atrial fibrillation after SAVR and 32% experience new-onset after TAVR<sup>[26]</sup>. Given the high incidence of POAF, several studies have looked at the associations and the predictive value of POAF for other adverse outcomes. These studies have shown that POAF is a severe postoperative outcome associated with more cardiovascular events, a longer length of hospital stay, and an overall higher morbidity and mortality rate. These effects will be discussed in the following paragraphs.

#### Short-term

#### SAVR outcomes

Although no association has been found between POAF and increased in-hospital or 30-day mortality compared to no new AF (1.5% *vs.* 1.0%; P = 0.48), POAF has been significantly associated with other short-term adverse outcomes<sup>[39,44,50,43]</sup>.

The risk of stroke for patients with POAF is higher when compared to patients who remain in sinus rhythm  $(8.5\% vs. 0.0\%)^{[50]}$ . POAF has also been associated with a longer and more tenuous length of stay than no postoperative AF (9 days vs. 6 days;  $P < 0.01)^{[32]}$ . This same outcome has been seen by other

Ref.	Pre-TAVR no AF sample size	POAF post-TAVR (%)
Jørgensen et al. <sup>[7]</sup> 2017	27	2 weeks: 15 (55.6) Remained stable at 8-10 weeks
Amat-Santos et al. <sup>[29]</sup> 2012	138	30 days: 44 (31.9)
Conte et al. <sup>[33]</sup> 2017	0-3 days: 391 4-30 days: 384	0-3 days 33 (8.4) 4-30 days: 16 (4.2)
Leon <i>et al.</i> <sup>[8]</sup> 2016	1011	30 days: 91 (9.1) 1 year: 100 (10.1) 2 years: 110 (11.3)
Mack et al. <sup>[9]</sup> 2019	417	30 days: 21 (5.0)
Smith <i>et al.</i> <sup>[10]</sup> 2011	348	30 days: 30 (8.6) 1 year: 42 (12.1)
Tanawuttiwat et al. <sup>[32]</sup> 2014	88	31 (35)
Waksman et al. <sup>[34]</sup> 2018	200	6 (3.0)
Yankelson et al. <sup>[16]</sup> 2014	262	31 (11.8)
Maan et al. <sup>[17]</sup> 2015	70	21 (30)
Furuta et al. <sup>[46]</sup> 2016 *Not specific to AS	1959	149 (7.6)
Sannino <i>et al.</i> <sup>[18]</sup> 2016	708	66 (9.3)
Zweiker et al. <sup>[19]</sup> 2017	226	16 (7)
Yoon et al. <sup>[47]</sup> 2019 *Not specific to AS	297	31 (10.4)
Biviano et al. <sup>[20]</sup> 2016	1375	113 (8.2)

Table 4. Postoperative atrial fibrillation rates for transcatheter aortic valve replacement

Comparison of postoperative TAVR AF rates. TAVR: Transcatheter aortic valve replacement; AF: atrial fibrillation; AS: aortic stenosis; POAF: postoperative atrial fibrillation.

researchers<sup>[39,43]</sup>. The trend of POAF associated with a longer stay can also be seen in ICU length of stay, not just hospital length of stay, where a patient with POAF is more likely to have a significantly longer ICU stay than if the patient was in sinus rhythm (7.0 ± 1.8 days *vs.*  $3.5 \pm 0.3$  days; P < 0.05)<sup>[50]</sup>. These patients are also more likely to have new renal failure, gastrointestinal problems such as pancreatitis and cholecystitis, and 30-day readmission<sup>[39]</sup>.

#### TAVR outcomes

Researchers have studied the impact of POAF on in-hospital and 30-day outcomes after TAVR. Biviano *et al.*<sup>[20]</sup> analyzed the data from the PARTNER trial and found that 30-day mortality was higher amongst those who developed POAF rather than those who stayed in sinus rhythm. Chopard *et al.*<sup>[51]</sup> defined a combined safety endpoint encompassing all-cause mortality, stroke, life-threatening bleeding, acute kidney injury, stage 2 or 3 (including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication, or valve-related dysfunction requiring repeat intervention (i.e., TAVI, SAVR, balloon aortic valvuloplasty) and found that it was significantly higher in those who developed POAF. Vora *et al.*<sup>[52]</sup> identified 1138 patients who developed new atrial fibrillation, when compared with those who did not develop POAF, in-hospital mortality (7.8% *vs.* 3.4%; *P* < 0.01) and stroke (4.7% *vs.* 2.0%; *P* < 0.01) were higher in the POAF group.

Studies have looked at whether there is an association between POAF and cerebrovascular events. Like Vora *et al.*<sup>[52]</sup>, they have found that POAF significantly increases the risk of cerebrovascular events after TAVR. Amat-Santos *et al.*<sup>[29]</sup> and Yoon *et al.*<sup>[47]</sup> independently found that POAF was significantly associated with an increased rate of combined stroke and embolism after TAVR. A study done by Nuis *et al.*<sup>[53]</sup> found that those who developed POAF after TAVR had a 4.4-fold greater risk of stroke.

POAF has also been associated with longer length of stay after TAVR than no new AF  $(10.6 \pm 8.1 \text{ days } vs. 6.3 \pm 5.0 \text{ days}; P = 0.001)^{[25]}$ . Like hospital length of stay, patients with POAF are also more likely to have longer stays in the ICU.

Other adverse outcomes like acute kidney injury (25.0% *vs.* 7.7%), postprocedural heart failure (44% *vs.* 15%), new pacemaker implantation (6.5% *vs.* 1.7%), myocardial infarction, and cardiac arrest have also been significantly higher with POAF after TAVR than no AF after TAVR<sup>[20,25,52]</sup>.

#### Long-term

#### SAVR outcomes

Studies looking at the long-term impact of atrial fibrillation in patients undergoing SAVR have shown conflicting results. Saxena *et al.*<sup>[39]</sup>, found that POAF had no impact on 7-year survival in patients compared to no new AF SAVR patients (78% *vs.* 83%; P = 0.63). Similarly, Swinkels *et al.*<sup>[44]</sup> found that at 20 years, the survival between patients with POAF and those without are similar. Filardo *et al.*<sup>[45]</sup>, however, found that for patients undergoing aortic valve replacement surgery, or aortic valve replacement surgery with coronary artery bypass surgery, those who developed POAF had a 48% higher 10-year risk of mortality after propensity matching baseline risk factors.

#### TAVR Outcomes

Researchers have looked at the long-term impact of POAF on a patient's health, given the association of POAF with serious short-term outcomes after TAVR. Like short-term outcomes, POAF has been significantly linked to increased rates of adverse events at 1 year. Rates of rehospitalization at 1 year are higher in patients diagnosed with POAF after their TAVR surgery than those with no new AF (62.5% *vs.* 34.8%; P = 0.004)<sup>[19]</sup>. Similarly, Vora *et al.*<sup>[52]</sup> found that the risk of rehospitalization due to a bleeding event at 1 year was significantly higher in patients with POAF in comparison to those without POAF (31.7% *vs.* 23.0%; OR = 1.24; 95%CI: 1.10-1.40).

Similar to short-term mortality, long-term mortality has been linked to POAF after TAVR. Amat-Santos *et al.*<sup>[29]</sup>, found that the development of AF by discharge (SR/AF) was a significant predictor of 1-year mortality in patients. The mortality rate at 1 year is higher in patients with POAF after TAVR than those with no AF development (30.1% *vs.* 16.1%; OR = 1.37; 95%CI: 1.19-1.59)<sup>[52]</sup>. This increased mortality risk at 1 year has been independently seen in several other studies<sup>[20,18,28,51,52]</sup>.

The rates of cerebrovascular events at 1 year are higher in TAVR patients who develop POAF than those who do not (7.2% *vs.* 3.8%; OR = 1.50; 95%CI: 1.14-1.98)<sup>[52]</sup>. Yoon *et al.*<sup>[47]</sup> found that the development of POAF was a predictor of the combined endpoint of stroke or embolism. This was also seen by Amat-Santos *et al.*<sup>[29]</sup>, who found that the cumulative incidence of stroke or embolism was significantly higher in patients with POAF. Tarantini *et al.*<sup>[28]</sup>, found that POAF was an independent predictor of stroke at 2 years.

Other adverse outcomes like renal failure and new pacemaker implantation have been linked to POAF after TAVR<sup>[20]</sup>. A study done by Tarantini *et al.*<sup>[28]</sup> found that rates of renal failure were higher amongst POAF patients than those with sinus rhythm (32.5% *vs.* 14.2%, P < 0.0001). Chopard *et al.*<sup>[51]</sup> found that POAF was an independent predictor of renal failure at 1 year.

# **NEW-ONSET POAF PREVENTION**

The onset of atrial fibrillation after a SAVR and TAVR procedure is an adverse outcome that can be prevented with proper medical management. Unfortunately, there is limited literature on how to give prophylaxis best to prevent new-onset POAF. Like a clinical case with pre-existing non-surgical atrial fibrillation, patients undergoing SAVR and TAVR procedures can receive antiarrhythmics peri-operatively to decrease the likelihood of new-onset atrial fibrillation. The most commonly used medications for prophylaxis include amiodarone and sotalol. Another management option that can be performed post-operatively would be prophylactic atrial pacing for at least 24  $h^{[s2]}$ .

# NEW-ONSET POAF ANTICOAGULATION AND TREATMENT

# SAVR

New-onset atrial fibrillation following SAVR and TAVR has been shown to be an independent predictor of mortality and thrombotic events, such as stroke<sup>[45,54]</sup>. The current recommendations for antiplatelet and anticoagulant therapy following aortic valve replacement come from the American Heart Association/American College of Cardiology (AHA/ACC) and the European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS). Following SAVR, the AHA/ACC recommends lifelong daily aspirin 75-100 mg for all bioprosthetic valve patients and daily aspirin 75-100 mg only for mechanical valve patients with antiplatelet indications. The AHA/ACC also recommends a vitamin K antagonist for 3 to 6 months in bioprosthetic valve patients with a low risk of bleeding. The ESC/EACTS recommends aspirin 75-100 mg/day and an oral anticoagulant for the first 3 months following the procedure in all patients, and lifelong oral anticoagulation in patients with indications for it, such as a hypercoagulable state, venous thromboembolism, and atrial fibrillation<sup>[55]</sup>.

Given the association between POAF and thrombosis, clinical trials have examined the impact of anticoagulation treatment following aortic valve replacement. However, very few studies have examined the role of antithrombotic treatment after SAVR. One study to do so is a 2019 paper by Chakravarty *et al.*<sup>[56]</sup>, which found that a greater proportion of patients after SAVR, in comparison to TAVR patients, were discharged home on anticoagulant and antiplatelet therapy. The study found no difference in aortic valve mean gradient or area, major or minor bleeding, rehospitalization, aortic valve intervention, or death between SAVR patients discharged with or without anticoagulant treatment. However, the one major difference was that patients discharged with anticoagulant therapy had significantly decreased stroke rates compared to those not on anticoagulant treatments (1.7% *vs.* 5.5%). Given the improvement in stroke risk and lack of increased bleeding risk, the study found it safe and beneficial to initiate anticoagulation therapy in patients following SAVR. While this study does not specifically examine SAVR in the setting of atrial fibrillation, lifelong anticoagulant therapy is indicated after SAVR if POAF develops<sup>[57]</sup>. Discontinuing anticoagulant therapy within the first 3 to 6 months after surgery has been associated with an increased risk of stroke and cardiovascular events in patients with unknown atrial fibrillation status<sup>[58]</sup>.

# TAVR

Following TAVR, the AHA/ACC recommends lifelong aspirin 75-100 mg/day, clopidogrel 75/day for 6 months, and a vitamin K antagonist for at least 3 months if there is a low bleeding risk. In addition, the 2017 ESC/EACTS guidelines recommend dual antiplatelet therapy for the first 3 to 6 months, followed by single platelet therapy. For patients with indications for anticoagulation, including atrial fibrillation, the guidelines recommend lifelong oral anticoagulation<sup>[55]</sup>.

Numerous studies have examined the impact of anticoagulation treatment on patients after TAVR procedures. A study by Amat-Santos *et al.*<sup>[29]</sup> found that 40% of TAVR patients with POAF who did not

receive anticoagulant therapy developed thromboembolism complications within 30 days, whereas only 3% of TAVR patients with POAF who received anticoagulant treatments had similar complications. Anticoagulation was also associated with lower rates of bioprosthetic valve dysfunction in the setting of POAF after TAVR<sup>[59]</sup>.

In terms of specific anticoagulant treatment, there is a lack of established consistency in clinical studies. Some studies recommend the use of a combination of an oral anticoagulant like warfarin and an antiplatelet drug such as aspirin or clopidogrel<sup>[26,60]</sup>. However, other studies have shown oral anticoagulant monotherapy to be safe with a lower risk of major bleeding complications than a combined therapy of an oral anticoagulant and an antiplatelet drug<sup>[61]</sup>. In terms of oral anticoagulants used in TAVR patients with atrial fibrillation, vitamin K antagonists seem to be the first-line choice<sup>[30]</sup>. However, non-vitamin K oral anticoagulants appear to be equally effective with lower intracranial hemorrhage, ischemic stroke, and mortality rates than vitamin K antagonists<sup>[30,62]</sup>. An alternative to oral anticoagulation in TAVR patients with atrial fibrillation is left atrial appendage occlusion. While relatively new, the surgical procedure has been shown to be safe, effective, and associated with reduced bleeding compared to traditional anticoagulant therapy<sup>[27,30]</sup>. In summary, there are various therapeutic approaches to prevent strokes in TAVR patients who develop POAF.

# Treatment and follow-up

Anticoagulation in the new-onset atrial fibrillation has been endorsed by the major cardiac societal guidelines; however, it is still a topic of major debate among many physicians, especially regarding their efficacy in real-life practice. The common practice is to treat it with rate and rhythm control medications. Gillinov *et al.*<sup>[63]</sup> found that 89.9% of POAF patients treated with rate-control therapy and 93.5% of patients treated with rhythm-control therapy had a stable, sustained heart rhythm without AF at the time of discharge (P = 0.14). More specifically, B-blockade and amiodarone have had the most conclusive studies affirming their efficacy. Another drug that has recently emerged as a potential preventative option for post-operative atrial fibrillation is colchicine<sup>[64]</sup>.

It would also be optimal to have the patients under cardiac monitoring surveillance with continuous electrocardiographic telemetry monitoring until hospital discharge. If an abnormal rhythm were to be noted on the cardiac monitoring device, the medical team could manage it within an inpatient setting prior to discharge to prevent future complications. Anticoagulation should be used with caution to prevent excess bleeding<sup>[32]</sup>.

# CONCLUSION

Atrial fibrillation is associated with detrimental preoperative and postoperative outcomes regarding surgical and transcatheter aortic valve replacement. Pre-existing atrial fibrillation has been seen in 6.3% to 35.2% of SAVR patients and 15.7% to 48.9% of patients undergoing TAVR and has a higher prevalence in patients with moderate to severe mitral regurgitation, moderate to severe tricuspid regurgitation, and pulmonary hypertension.

Patients with pre-existing AF who undergo aortic valve replacement (AVR) have a greater risk of mortality and major complications following the procedure than patients without AF. The risk of complications is much greater in patients undergoing TAVR as SAVR has a 2-year mortality and major complication rate of 24.6%, while TAVR has a 1-year mortality rate of 34.9%, not even accounting for complications. The higher prevalence of baseline comorbidities, including AF, among TAVR patients most likely explains the increase in complications compared to SAVR. The risks of untreated aortic stenosis, especially severe symptomatic

aortic stenosis, are also extremely detrimental, with a 5-year mortality rate of 50% and 10-year mortality of 90%. However, there is no data on mortality rates among untreated aortic stenosis patients with AF. More importantly, SAVR and TAVR procedures without complications can curtail the progression of aortic stenosis and improve the quality of life for many patients. However, a thorough examination of comorbidities in patients with AF is beneficial prior to AVR, especially TAVR, given the high rates of mortality which are comparable with untreated aortic stenosis.

In terms of POAF, it was more common after SAVR and in patients with old age, low body mass index, a history of heart failure, hemodynamic instability, left atrial enlargement, and preoperative and early postoperative left ventricular ejection fraction  $\leq$  50%. The rates for POAF following SAVR procedures have been noted to range from 11.1% to 84%, while the rates for POAF following TAVR procedures range from 3.0% to 55.6%. Of note, POAF rates following TAVR were significantly greater in the transapical TAVR subgroup (53%) in comparison to the transaortic TAVR subgroup (33%) and the transfemoral TAVR subgroup (14%). Therefore, the risk of POAF can be lowered by choosing a transfemoral or transaortic approach over a transapical approach. POAF can be prevented in high-risk patients via prophylactic antiarrhythmic medications and atrial pacing for 24 h to several days. Prophylactic anticoagulants should also be provided as they reduce the risk of thrombotic complications following SAVR and TAVR procedures in the setting of POAF. These preventive measures are essential as POAF is associated with higher mortality, cardiovascular events, a longer length of hospital stay, and an overall higher rate of morbidity/mortality.

POAF after SAVR, in comparison to no AF development, is associated with increased stroke rates (8.5% *vs.* 0.0%) and longer hospital stays (9 days *vs.* 6 days). Given conflicting data, mortality may or may not be higher among POAF patients, but 7-year mortality rates after SAVR are as high as 83% in non-AF and 78% in POAF groups. Similarly, POAF after TAVR, compared to no AF development, is associated with increased stroke rates (4.7% *vs.* 2.0% at 30 days and 7.2% *vs.* 3.8% at 1 year) and longer hospital stays (10.6 days *vs.* 6.3 days). POAF after TAVR is also associated with 1-year rehospitalizations (62.5% *vs.* 34.8%) and major bleeding (31.7% *vs.* 23.0%). Notably, POAF after TAVR is associated with increased mortality rates (7.8% *vs.* 3.4% at 30 days and 30.1% *vs.* 16.1% at 1 year). In both SAVR and TAVR, the development of POAF seems to increase the risk of complications by around 1.5-fold, and prophylactic treatment should be given in patients to prevent the development of POAF. Between the SAVR and TAVR procedures, TAVR seems to be the preferred approach in terms of AF, given the lower risk of POAF development. However, the risk of complications following AVR does not seem to improve expected survival compared to untreated aortic stenosis drastically and should be prioritized in patients with severe aortic stenosis.

# Limitations

While most articles referenced were specific to aortic valve replacement in aortic stenosis patients, a few articles did not specifically limit studied patients to those with underlying aortic stenosis or aortic regurgitation. In addition, the articles do not mention if the patients studied had concomitant mitral regurgitation. Finally, the articles do not differentiate between bioprosthetic and mechanical/metallic valves; however, the usage of mechanical valves in AVR has significantly decreased from 59.5% usage in 2008 to 29.2% usage in 2017 due to the rise in popularity of the bioprosthetic valve<sup>[65]</sup>.

# DECLARATIONS

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#### Authors' contributions

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Provided significant administrative, technical, and material support in addition to writing feedback and suggestions: Bilfinger T, Shroyer AL

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All authors declared that there are no conflicts of interest.

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