Review Article

Postoperative atrial fibrillation (POAF) after cardiac surgery: clinical practice review

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Abstract: Postoperative atrial fibrillation (POAF) after cardiac surgery is associated with elevated morbidity and mortality. Although current prediction models have limited efficacy, several perioperative interventions can reduce patients' risk of POAF. These begin with preoperative medications, including beta-blockers and amiodarone. Moreover, patients should be screened for preexisting atrial fibrillation (AF) so that concomitant surgical ablation and left atrial appendage occlusion can be performed in appropriate candidates. Intraoperative interventions such as posterior pericardiectomy can reduce mediastinal fluid accumulation, which is a trigger for POAF. Furthermore, many preventive strategies for POAF are implemented in the immediate postoperative period. Initiating beta-blockers, amiodarone, or both is reasonable for most patients. Overdrive atrial pacing, colchicine, and steroids have been used by some, although the evidence base is less robust. For patients with POAF, rate-control and rhythm-control strategies have comparable outcomes. Decision-making regarding anticoagulation should recognize that the stroke risk associated with POAF appears to be lower than that for general nonvalvular AF. The evidence that oral anticoagulation reduces stroke risk is less clear for POAF patients than for patients with general nonvalvular AF. Given that POAF tends to be shorter-lived and is associated with greater bleeding risks in the perioperative period, decisions regarding anticoagulation should be individualized. Finally, wearable technology and machine learning algorithms for better predicting and managing POAF appear to be coming soon. These technologies and a comprehensive clinical program could meaningfully reduce the incidence of this common complication.

Keywords: Postoperative atrial fibrillation (POAF); cardiac surgery; cardiac arrhythmia prevention; rate control; rhythm control

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Introduction

Background

Postoperative atrial fibrillation (POAF) is the most common complication after cardiac surgery and is associated with early and late morbidity and mortality (1,2).

Rationale

The Society of Thoracic Surgeons defines POAF as new-onset post-surgical AF that lasts for more than 1 hour and/or requires treatment (3).

Knowledge gap

Because there is wide variation in practice patterns, taking a comprehensive approach to POAF in the perioperative period offers opportunities to reduce the incidence of and the risks associated with POAF. Surgeons, anesthesiologists, cardiologists, intensivists, and the multidisciplinary care team should emphasize POAF prevention in perioperative care.

Objective

In this clinical practice review, we focus on preventive and treatment strategies for POAF in all three phases of perioperative care. These strategies include using preoperative medications prophylactically, intraoperative techniques to reduce POAF, and postoperative prevention and management. Lastly, we examine future directions of integrating clinical knowledge, informatics, and machine learning (ML) for continued improvement in care.

Epidemiology of POAF

Incidence

Patients undergoing cardiac surgery have a high POAF risk ranging from 15% to 50%. Rates are lowest after isolated coronary artery bypass grafting (CABG), higher after isolated valve surgery, and highest after combined valve/CABG procedures (4,5). The incidence of POAF after proximal aortic surgery is similarly high (30–50%), indicating that POAF is common after nearly any cardiac surgical procedure (6,7).

Adverse outcomes

In a systematic review and meta-analysis of 57 studies and 246,340 patients, Caldonazo and colleagues found a strong association between POAF and adverse outcomes (1). POAF was associated with perioperative mortality [odds ratio (OR) =1.92, 95% confidence interval (CI): 1.58–2.33], stroke (OR =2.17, 95% CI: 1.90–2.49), myocardial infarction (OR =1.28, 95% CI: 1.06–1.54), and acute renal failure (OR =2.74, 95% CI: 2.42–3.11). However, patients developing POAF are generally older with more comorbidities; consequently, it is difficult to attribute the patients' greater morbidity to patient risk or to POAF. Moreover, most studies treat POAF as a binary (yes/no) complication; details on the duration of POAF or its presence or absence at discharge are often omitted.

A closer examination using number needed to harm/treat (NNH/NNT) analysis provides a better perspective. The differences between patients developing POAF and no-POAF were as follows: perioperative mortality (3.37% *vs.* 1.64%, NNH =58), stroke (2.67% *vs.* 1.22%, NNH =69), myocardial infarction (2.45% *vs.* 1.59%, NNH =111), and acute renal failure (7.53% *vs.* 2.60%, NNH =20) (1). Thus, POAF is associated with elevated risk of mortality and adverse events; understanding the degree of risk is important when considering additional therapeutic interventions or potential bleeding from anticoagulation.

The long-term stroke risk was examined by Wang *et al.* in a systematic review and meta-analysis of 55 studies and 540,209 patients who underwent cardiac surgery. The overall risk of late stroke in the POAF group was 1.06% per 100 patient-years, compared with 0.88% per 100 patient-years (relative risk increase of 20%) (2). In addition, paroxysmal AF progresses to permanent AF in an estimated 25% of patients over 5–10 years; patients who develop POAF have a 5-fold greater risk of long-term AF than no-POAF patients (8). Furthermore, in a multivariable analysis, POAF was associated with both all-cause and heart failure readmission (1), creating a major cost burden on our healthcare system.

Risk factors for development of POAF

Age is a significant independent risk factor for POAF. Shen *et al.* observed that the incidence of POAF was 25% at age 60, 40% at age 70, and 50% at age 80 (9). Other clinical risk factors for POAF after cardiac surgery include male gender, obesity, prior paroxysmal AF, left atrial enlargement, decreased left ventricular systolic function, chronic pulmonary obstructive disease, chronic renal failure, diabetes mellitus, rheumatic heart disease, and perioperative withdrawal from beta-blockers (10). In a multicenter international trial conducted in patients undergoing cardiac surgery, Akintoye *et al.* found that several surgical and patient characteristics were associated with adverse outcomes, including POAF (4), observing progressively greater risk across categories of cardiac surgical procedures. Compared with CABG alone, isolated valve surgery was associated with higher POAF risk (OR =1.4, 95% CI: 1.1–1.9), especially when valvular surgery was combined with other procedures. The use of cardiopulmonary bypass (OR =2.4; 95% CI: 1.7–3.5) and cardioplegia (OR =1.7, 95% CI: 1.2–2.5) were significant intraoperative risk factors (4).

Multiple POAF score algorithms have been developed that use many of these risk factors (11). The POAF score incorporates renal function, preoperative intra-aortic balloon pump, chronic obstructive pulmonary disease, emergency surgery, valve surgery, and left ventricular ejection fraction <30%. In one study, patients with a score of zero had a POAF rate of approximately 12%, whereas those with a score ≥3 had a rate of 42% (12). Yin *et al.* found that the $CHADS_2$ (cardiac failure, hypertension, age, diabetes, stroke (doubled)) and CHA_2DS_2-VASc scores (congestive heart failure, hypertension, age 75 (doubled), diabetes, stroke (doubled), vascular disease, age 65–74, and sex category (female)) were significantly higher in patients with POAF (P<0.001) (13). Also, on univariate and multivariate regression, both scores were significant and comparable predictors of POAF (P<0.001). However, when Fleet *et al.* evaluated a dozen different scoring systems for POAF prediction, none was a better predictor than patient age alone (14).

Pathogenesis

The pathogenesis of POAF is multifactorial and includes atrial structural deterioration from hypertension, myocardial ischemia, and valvular pathologies. The pulmonary veins are the most frequent triggering focus, followed by the coronary sinus, ligament of Marshall, and posterior wall of the left atrium. Circulating catecholamines, cardiopulmonary bypass, and inotrope administration have all been implicated in POAF (15).

Surgical insults such as pericardiotomy and atriotomy create a proinflammatory state. Inflammation decreases the effective refractory period of a myocyte, thereby decreasing production of the protein sarcolipin, which normally inhibits the sarcoplasmic endoplasmic reticulum Ca-ATPase (SERCA) protein. This inhibition increases myocardial calcium levels, which can trigger AF (16). Oxidative stress with increased circulation of reactive oxygen species has also been implicated in the development of POAF through several mechanisms (17). There is still much to be learned about POAF pathophysiology that could potentially offer insights into prevention, treatment, and avoiding recurrence.

Summary of major societal guidelines

A comparison of AF guidelines and consensus statements from American (18,19), European (20), Canadian (21), and anesthesiology societies (22) shows considerable overlap, reflecting the quality of the evidence (*Table 1*) (18,21-24). There are small differences among them, most of which are of minor significance.

Preoperative prevention strategies

Beta-blockers have been extensively studied and widely used for POAF prevention. Since 2007, beta-blocker administration within 24 hours of CABG has been a quality recommendation by the National Quality Forum for reducing POAF (25). Although studies have shown that perioperative beta-blocker use reduces POAF risk, meta-analyses have grouped preoperative, intraoperative, and postoperative beta-blocker use together, making the precise contribution of preoperative use unclear (26). A Cochrane database review of 63 studies and 7,768 patients associated perioperative beta-blocker use with a reduction in POAF from 327 to 164 per 1,000, yielding a risk reduction (RR) of 0.50 (95% CI: 0.42–0.59) and an NNT of 6 (27). A high proportion of patients undergoing cardiac surgery are already on beta-blockers; the general recommendation is to continue use until surgery. The evidence base is less clear on whether beta-blockers should be prescribed preoperatively to patients not already taking them and without contraindications to their use (28,29).

Amiodarone is a potent class III antiarrhythmic drug in the Vaughn-Williams classification, commonly used for both prevention and treatment of AF. Its half-life is 40–55 days, and its side effect profile includes bradycardia, heart block, and pulmonary, hepatic, and thyroid toxicity.

In the Prophylactic Amiodarone for the Prevention of

Table 1 Comparison of guidelines for postoperative atrial fibrillation after cardiac surgery

Phase of care	Treatment/intervention	Guidelines			
		2014 ACC/AHA/HRS Atrial Fibrillation Guidelines (18); 2019 ACC/AHA/HRS Focused Update to Atrial Fibrillation Guidelines (23); 2023 ACC/AHA/HRS Atrial Fibrillation Guidelines (19)	2016 ESC/EACTS Atrial Fibrillation Guidelines (24)	2019 SCA/EACTA Practice Advisory (22)	Canadian Cardiovascular Society/Canadian Heart Rhythm Society (2020) (21)
Preoperative	Oral BB for prevention	IIA (B-NR)	I (B)	I (A/B)	Strong, high-quality (for patients on preoperative BB) Weak, low-quality for patients not on preoperative BB
	Preoperative amiodarone for prevention			IIA (A)	
	Perioperative amiodarone to prevent POAF	IIA (B-NR)	IIA (A)	IIA (A/B)	
Intraoperative	Posterior pericardiotomy in patients undergoing CABG, AVR, or ascending aortic aneurysm surgery at high risk for POAF	IIA (B-NR) in 2023			
	Surgical occlusion of the LAA may be considered in patients with preexisting AF undergoing cardiac surgery as part of the overall heart team approach	IIB (B-NR) in 2019; I (A) in 2023	IIB (B)		
Postoperative	BB for rate control	I (A)		I (B)	
	Nondihydropyridine calcium channel blocker for rate control	I (B-R)		IIA/NC (B/low)	
	Restoration of sinus rhythm by electrical cardioversion for hemodynamic instability	I (B-R)	I (C)	I (C)	
	Asymptomatic AF initially managed with rate control and anticoagulation	B/low	IIA (A)	IIA/NC	
	Long-term anticoagulation should be considered in patients with POAF, considering individual stroke and bleeding risk	IIA (B-NR)	IIA (B)	IIA (B/C)	Consider withholding anticoagulation for the first 72 h postoperatively Weak, low-quality evidence When anticoagulation is started, reconsider its continuation after 6–12 weeks. Strong- to moderate-quality evidence

Table 1 (*continued*)

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Phase of care	Treatment/intervention	Guidelines			
		2014 ACC/AHA/HRS Atrial Fibrillation Guidelines (18); 2019 ACC/AHA/HRS Focused Update to Atrial Fibrillation Guidelines (23); 2023 ACC/AHA/HRS Atrial Fibrillation Guidelines (19)	2016 ESC/EACTS Atrial Fibrillation Guidelines (24)	2019 SCA/EACTA Practice Advisory (22)	Canadian Cardiovascular Society/Canadian Heart Rhythm Society (2020) (21)
	Antiarrhythmic drugs or cardioversion for symptomatic POAF to restore NSR	IIA (C-LD)	IIA (C)	IIA (B/C)	
	Prophylactic sotalol to prevent POAF after cardiac surgery	IIB (B)			
	Colchicine to reduce POAF	IIB (B)		IIB (B)	

Class of recommendation: I, recommended; IIA, is reasonable; IIB, may be reasonable; III, not recommended. Level of evidence (LOE): A, data derived from multiple randomized trials or meta-analyses; B, data derived from a single randomized trial or large randomized studies; C, consensus opinion of experts and/or small studies, retrospective studies, registries; NC, no classification; NR, nonrandomized; R, randomized; LD, limited data. ACC, American College of Cardiology; AHA, American Heart Association; HRS, Heart Rhythm Society; ESC, European Society of Cardiology; EACTS, European Association of Cardio-Thoracic Surgery; SCA, Society of Cardiovascular Anesthesiologists; EACTA, European Association of Cardiothoracic Anaesthesiology; BB, beta-blocker; POAF, postoperative atrial fibrillation; LAA, left atrial appendage; AF, atrial fibrillation; NSR, normal sinus rhythm.

Arrhythmias that Begin Early After Revascularization, Valve Replacement, or Repair (PAPABEAR) randomized trial, 601 patients received either high-dose oral amiodarone (10 mg/kg daily) or placebo, commencing 6 days preoperatively through 6 days postoperatively (30). The amiodarone group had a significantly lower rate of POAF [16.1% *vs.* 29.5%, hazard ratio (HR) 0.52 (0.34–0.69), P<0.005, NNT =7]. Hillis *et al.* found no difference in proarrhythmic or bradycardic events between patients given preoperative amiodarone or placebo. The suggested protocol was 400 mg of oral amiodarone daily for three days before surgery, followed by 200 mg daily for ten days afterward (31). Waterford and Ad posit that preoperative oral amiodarone is the single most powerful preoperative intervention to reduce POAF risk (32).

A 2013 Cochrane meta-analysis identified randomized controlled trials (RCTs) of amiodarone, beta-blockers, sotalol, and magnesium for preventing POAF in patients undergoing cardiac surgery (33). Thirty-three studies in 4,698 patients evaluated beta - blockers for preventing POAF and supraventricular tachycardia, with varied dosing regimens through oral and parenteral routes. The beta - blocker recipients had less POAF than the control group (16.3% *vs.* 31.7%, OR =0.33, 95% CI: 0.26–0.43, I^2=55%, NNT =6). Thirty-three studies involving 5,402 participants evaluated amiodarone for preventing POAF and supraventricular tachycardia. The relative reduction in POAF in the amiodarone group compared with the no-amiodarone group was similar to that seen with beta-blockers (19.4% *vs.* 33.3%, OR =0.43, 95% CI: 0.34–0.54, I^2=63%, NNT =7) (33). Dosing regimens, including loading doses and infusion rates, varied among studies, and drugs were delivered both orally and intravenously. Approximately half of the studies began amiodarone administration preoperatively and half immediately postoperatively.

Other strategies such as correcting electrolyte abnormalities and using fish oil and different drugs like sotalol, steroids, statins, and nonsteroidal anti-inflammatory medications have shown variable degrees of effectiveness as prophylaxis against POAF. A lack of consistent benefit and concern for adverse effects have prevented the widespread use of these drugs; routine use cannot be recommended at this time. Preoperative prevention strategies are summarized in *Figure 1*.

Intraoperative strategies

While our focus is POAF prevention, patients with

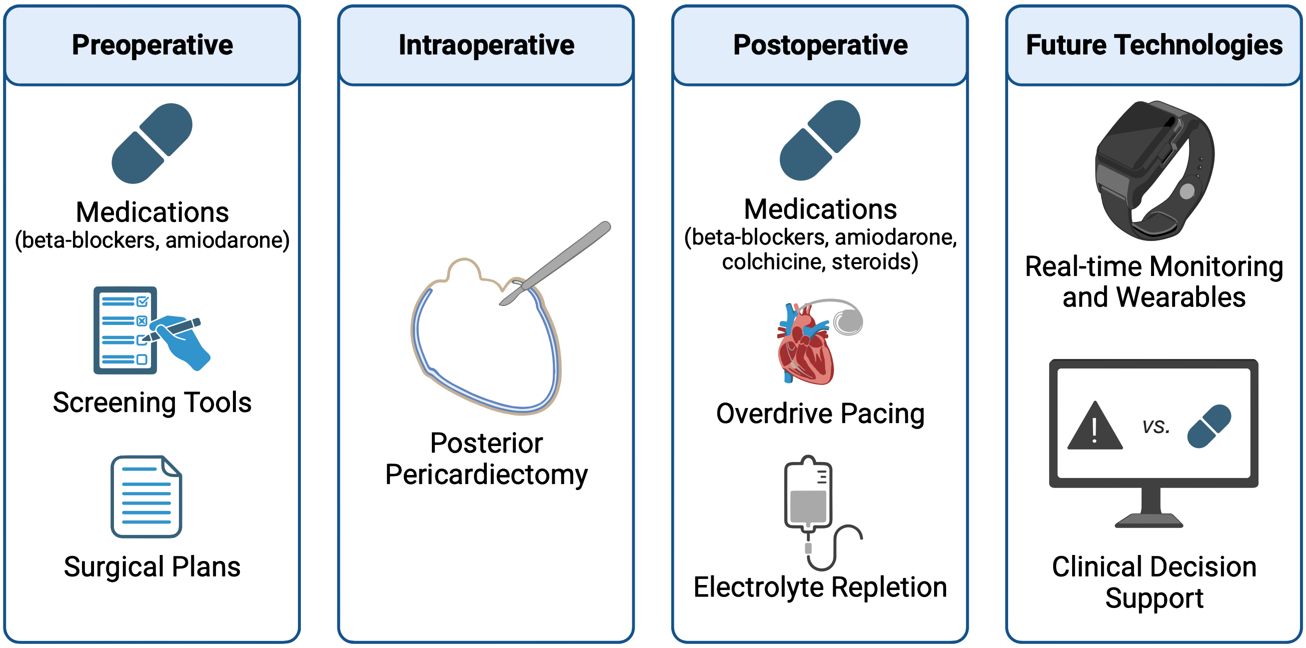

Figure 1 Summary of preoperative, intraoperative, and postoperative phases of care along with future technologies for preventing and treating postoperative atrial fibrillation after cardiac surgery.

preexisting AF are candidates for operative intervention. Concomitant surgical ablation and left atrial appendage occlusion (LAAO) are a Class I recommendation in clinical practice guidelines of both the Society of Thoracic Surgeons (STS) (34) and the American Association for Thoracic Surgery (AATS) (35). Patients should be screened preoperatively for AF; appropriate candidates should be offered concomitant surgical ablation, particularly those having first-time cardiac surgery. Recent data from the STS Adult Cardiac Surgery Database show that concomitant surgical ablation is underused (48%); it is used more often in mitral valve surgery (68%) and far less often during aortic valve replacement (39%) and CABG (33%) (36).

Several intraoperative interventions have been evaluated as preventive measures against POAF. Posterior pericardiotomy (PP) is the most well-studied intervention and aims to prevent proinflammatory postoperative pericardial effusions (37). The procedure is simple, quick, and without cost, requiring only a 4- to 5-cm vertical incision posterior to the phrenic nerve from the left inferior pulmonary vein to the diaphragm (37). This reduces pericardial blood accumulation by allowing drainage into the left pleural space, minimizing epicardial inflammation. The PALACS (The Effect of Posterior Pericardiotomy on the Incidence of Atrial Fibrillation After Cardiac Surgery) trial was a randomized study of PP in 420 patients who underwent CABG, aortic valve, or aortic procedures (38). Patients who had PP had significantly less POAF than patients who did not (17% *vs.* 32%, P=0.0007, NNT =7, OR =0.44, 95% CI: 0.27–0.70, P=0.0005). Moreover, the PP group had fewer pericardial effusions (12% *vs.* 21%, RR =0.58, 95% CI: 0.37–0.91) and comparable left pleural effusions (30% *vs.* 32%, RR =0.95, 95% CI: 0.71–1.26), with only 1% of pleural effusions needing drainage.

Two separate systematic reviews and meta-analyses confirm the findings of the PALACS trial. Xiong *et al.* (39) focused on the effectiveness of PP in preventing POAF after CABG in 1829 patients from ten studies and showed significantly less POAF in the PP group (10% *vs.* 26%, NNT =7, RR =0.45, 95% CI: 0.29–0.64, P<0.0001). Soletti and colleagues broadened the population even further with a meta-analysis (18 RCTs, n=3,531 patients) that included valvular procedures and found significantly lower risk of POAF (OR =0.45, 95% CI: 0.32–0.64, P<0.0001) in the PP cohort. They reported a higher incidence of radiographic pleural effusions (OR =1.42, 95% CI: 1.06–1.90, P=0.02) but not pulmonary complications (mechanical ventilation >24 hours, pneumonia, pulmonary embolism, and pleural effusion requiring drainage) in the PP group (40).

PP is currently included as a recommendation with limited evidence in both American (41) and European (42) guidelines. However, these recent trials demonstrating a benefit in reducing POAF have led the authors of the 2023 American guidelines to make PP a Class IIA (B-R) recommendation for patients undergoing CABG, aortic valve replacement, or ascending aortic replacement surgery (19). Given the ease with which it can be performed, PP is reasonable when feasible. Intraoperative prevention strategies are summarized in *Figure 1*.

Autonomic dysregulation has been established as a primary POAF cause (43). Not surprisingly, inflammatory signaling molecules are increased in the pericardial fluid after cardiac surgery (44), altering autonomic signaling of the atria (43). The four major atrial ganglionic plexi found in the epicardial fat pads act as the primary source of autonomic innervation (45). Botulinum toxin injected into the epicardial fat pads reduces POAF risk for as long as 36 months (46). The Prevention Atrial Fibrillation by BOTulinum Toxin Injections (BOTAF) study (NCT04075981) and the Botulinum Toxin Type A for the Prevention of Post-operative Atrial Fibrillation in Patients Undergoing Open-chest Cardiac Surgery (NOVA) (NCT03779841) are both ongoing RCTs designed to test the effectiveness of this operative adjunct; results are expected by 2024. Intraoperative interventions that modulate autonomic responses to cardiac surgery are promising, having a favorable risk-benefit ratio in preliminary studies. As more robust clinical data become available, adoption may widen.

The central role of the LAA in cardioembolic strokes associated with AF has led to the development of multiple surgical and percutaneous LAAO techniques (47). Surgical LAAO does not prevent POAF but does offer some protection from stroke (LAAO =7.0% *vs.* No-LAAO =4.8%; OR =0.67, 95% CI: 0.53–0.85, NNT =45 at 5-year follow-up) in patients with preexisting AF undergoing concomitant surgery, as seen in The Left Atrial Appendage Occlusion Study III (LAAOS III) (48). However, two previous studies of prophylactic LAAO in patients without AF did not show a benefit in stroke prevention while, paradoxically, showing an increase in POAF (49,50). Notably, in the LAAOS III trial, the late benefit in stroke reduction was only seen in patients with preexisting AF. Although it is not possible to recommend routine prophylactic LAAO at this time, identifying subgroups (e.g., patients with high CHA_2DS_2-VASc score or left atrial enlargement) at higher risk who could benefit from prophylactic LAAO is worthwhile.

Prevention of POAF in the postoperative period

In the immediate perioperative period, attention is focused on ensuring hemodynamic stability, adequate cardiac output, and routine postoperative care, of which POAF prevention is an important aspect. A single-center analysis by Melby *et al.* found that the risk for POAF after cardiac surgery is highest immediately postoperatively (phase I) and at 48 hours (phase II) (51). The peak risk in phase I gradually declined to zero by the 18th postoperative hour; the peak risk in phase II slowly declined to zero over the next 4 to 7 days. Thus, postoperative POAF reduction measures should be started early. Postoperative prevention and treatment strategies are briefly outlined in *Figure 1*.

Beta-blockers

Beta-blocker use after cardiac surgery is the most widely studied POAF preventive strategy. A meta-analysis that excluded studies potentially confounded by non-study beta-blocker withdrawal in the control group found that among 1,163 patients, beta-blockers still reduced POAF (OR =0.69, 95% CI: 0.54–0.87, P=0.002) (52). Although differences among specific beta-blocker types are not well established, in a subgroup analysis from another meta-analysis of 10 RCTs, carvedilol was superior to metoprolol in POAF prevention after CABG (53). Carvedilol is especially attractive for patients with hypertension or reduced ejection fraction. In addition to reducing POAF rates, perioperative beta blockade has been associated with reduction in ventricular arrhythmias, with no significant differences from placebo in 30-day all-cause mortality, myocardial infarction, cerebrovascular events, hypotension, or bradycardia (27). The 2021 ACC/AHA guidelines and 2020 ESC/EACTS guidelines issued Class 1 recommendations for beta-blockers for POAF prevention after cardiac surgery (20,54).

Amiodarone

Although amiodarone is approved by the US Food and Drug Administration (FDA) for use in life-threatening ventricular arrhythmias, it is used off-label for managing AF in both inpatient and outpatient settings. A Cochrane meta-analysis of 33 RCTs similarly showed that perioperative amiodarone significantly reduces POAF incidence after cardiac surgery compared with placebo (19.4% *vs.* 33.3%, OR =0.43, 95% CI: 0.34–0.54) (4). No significant differences were observed when amiodarone therapy was initiated preoperatively, on the day of surgery, or the day after surgery. Although oral and intravenous amiodarone regimens similarly reduce POAF risk, the enteral-exclusive regimens have been associated with less bradycardia, hypotension, or QT prolongation (55). A meta-analysis comparing POAF incidences between patients receiving prophylactic beta-blocker or amiodarone therapy found no significant difference (56). Another meta-analysis found that amiodarone was the only intervention independently associated with a reduction in stroke rate (2.4% *vs.* 1.2%, OR =0.54, 95% CI: 0.30–0.95, NNT =83) (52). Therefore, ACC/AHA guidelines do not comment on amiodarone for POAF prevention, whereas the ESC/EACTS guidelines recommendations are Class I for amiodarone or beta-blockers for POAF prevention.

Alternative strategies for prevention of POAF

Sotalol is a class III antiarrhythmic with simultaneous beta-blocking effects. Although sotalol is less widely used than other beta-blockers and amiodarone, a 2011 meta-analysis of 15 studies that compared sotalol with different controls found a significant reduction in POAF with sotalol compared with placebo (23% *vs.* 42%, RR =0.55, 95% CI: 0.45–0.67, P<0.001), no treatment (12% *vs.* 39%, RR =0.33, 95% CI: 0.24–0.46, P<0.001), and beta-blockers (14% *vs.* 23%, RR =0.64, 95% CI: 0.50–0.84, P<0.001), but no significant difference in comparison with amiodarone or magnesium (57). Despite its apparent effectiveness in the reduction of POAF, sotalol is not considered first-line therapy because of the risk of torsades de pointes, bradycardia, and QT prolongation. Only the American guidelines issue even a weak (Class IIB) recommendation for sotalol.

The rationale for using corticosteroids to prevent POAF arises from the theory that the postoperative inflammatory response contributes to POAF. A Cochrane meta-analysis showed that prophylactic corticosteroids reduced POAF compared with placebo (25% *vs.* 35%, RR =0.74, 95% CI: 0.63–0.86, P<0.01) regardless of dose given, with no additional benefit seen from hydrocortisone doses greater than 1,000 mg (58). Subsequent large, double-blinded, placebo-controlled RCTs such as the Steroids in Cardiac Surgery (SIRS) trial of methylprednisolone and the Dexamethasone for Cardiac Surgery (DECS) trial of high-dose dexamethasone found no difference in POAF incidence (59,60). Given the elevated risk of hyperglycemia, impaired wound healing, and infection from perioperative glucocorticoid administration without demonstrated benefit in preventing POAF, routine use is not recommended.

Colchicine is an anti-inflammatory alkaloid, predominantly used for gout, that prevents migration of neutrophils to sites of inflammation. The COlchicine for the Prevention of the Post-pericardiotomy Syndrome (COPPS) trial, a double-blinded, placebo-controlled RCT of colchicine for preventing postcardiotomy pericarditis and pericardial effusion, showed that colchicine significantly reduced the incidence of postpericardiotomy syndrome (61). Because postoperative pericardial effusion and the resultant inflammation on the epicardial surface have been implicated in POAF, a subsequent COPPS substudy analysis showed that compared with placebo, colchicine administered on postoperative day 3 and continuing for one month also significantly reduced POAF by reducing pericardial effusion (12.0% *vs.* 22.0%, P=0.021, relative RR =0.45, NNT =11) (62). Approximately 10% of patients in the colchicine group withdrew because of gastrointestinal side effects. However, although the subsequent, placebo-controlled COPPS-2 trial confirmed that colchicine reduces postpericardiotomy syndrome (10% *vs.* 29%, 95% CI: 1–19%, NNT =10), it did not significantly reduce POAF (34% *vs.* 42%, 95% CI: −2–18%) (63). Moreover, 20% of the colchicine group withdrew because of gastrointestinal side effects. Currently, aside from a weak recommendation by American guidelines, routine use of colchicine for POAF prevention is not recommended.

Overdrive atrial pacing is thought to reduce AF by preventing bradycardia and subsequent ectopic atrial beats. A Cochrane review meta-analysis showed a significant reduction of POAF after cardiac surgery with overdrive atrial pacing versus no pacing (18.7% *vs.* 32.8%, OR =0.47, 95% CI: 0.36–0.61) (4). However, the meta-analysis was limited by significant heterogeneity among studies in concomitant pharmacological therapy and pacing duration, site, mode, and rate. A subsequent meta-analysis, which similarly found POAF reduction with overdrive pacing compared with control (34.8% *vs.* 24.6%), further compared results by type of pacing and found that biatrial pacing yielded the greatest effect size, reducing the POAF rate from 35.3% to 17.7% in the paced group (OR =0.44, 95% CI: 0.31–0.64) (52). Given that biatrial wires are not commonly placed at the time of cardiac surgery, this strategy would probably not become widely adopted.

In preventing POAF, amiodarone has been shown to be superior to both atrial septal pacing (AFIST II trial) (64) and biatrial pacing (65). Furthermore, the addition of overdrive pacing to amiodarone does not reduce POAF rates further (66). Therefore, overdrive pacing is not first-line treatment for POAF after cardiac surgery and is only recommended for patients with beta-blocker and amiodarone intolerance (16,21).

Hypomagnesemia increases patients' risk of POAF, probably by modulating potassium and calcium channel function (67). In a meta-analysis of 22 trials and 2,896 patients, postoperative intravenous magnesium administration significantly reduced POAF (OR =0.57, 95% CI: 0.42–0.77, P=0.007); however, these findings were limited by significant heterogeneity among studies with respect to dose, timing of delivery, and concomitant use of beta-blockers (52). Another meta-analysis of 1,028 patients in seven double-blinded, randomized, placebo-controlled trials found that intravenous magnesium reduced the incidence of POAF by 36% (RR =0.64, 95% CI: 0.50–0.83, P=0.001, NNT =13), with no reported heterogeneity among the trials (68). Administering doses of up to 60 mmol for at least 24 hours and up to 5 days postoperatively can reduce the incidence of POAF after cardiac surgery (69). Other investigators have also paradoxically found that higher potassium and magnesium levels were associated with more POAF; prospective trials are necessary to find optimal levels of these electrolytes (70).

Management of postoperative AF

Initial assessment of any new-onset AF mandates an assessment of hemodynamics; POAF associated with hemodynamic instability should be treated with prompt cardioversion consistent with resuscitation algorithms. As with any new-onset AF, the initial management of POAF should include correcting reversible causative factors such as electrolyte abnormalities—namely hypokalemia and hypomagnesemia—hypoxemia, hypercapnia, hypotension, metabolic acidosis, and atrial myocardial ischemia. Excessive sympathetic stimulation, potentially indicating inadequate sedation and analgesia, and excessive inotrope support may contribute to POAF risk, so dosing adjustments may be necessary.

While any predisposing factors are being corrected, subsequent medical management—pharmacological or electrical—of POAF is required. Historically, rhythm control has been the initial approach for managing POAF, as promptly restoring sinus rhythm avoided the need for postoperative anticoagulation. Additionally, immediate postoperative patients requiring inotrope or significant vasopressor administration may not tolerate rate-controlling medications because of the negative inotropic component. The PREVENT-IV trial substudy—derived from the PREVENT-IV randomized, double-blind, placebo-controlled trial of *ex vivo* treatment of autologous vein grafts with edifoligide in patients undergoing CABG surgery—specifically evaluated practice patterns for managing post-CABG POAF. Of the 24% of patients who developed POAF, 81% received a rhythm-control strategy as primary management, whereas only 23% received anticoagulation with warfarin (71). This study was notably limited by significant heterogeneity among centers in preoperative beta-blocker administration, use of warfarin for anticoagulation for POAF, and POAF management, highlighting the need for further RCTs.

Advocates for initially using rate control to manage POAF after cardiac surgery cite the generally short, self-limited course of POAF as a reason to avoid antiarrhythmic medications and their associated adverse effects. In the CTSNet trial, Gillinov *et al.* addressed the discrepancy in practice through a large, multicenter trial in which 523 post–cardiac surgery patients were randomly assigned to the rate-control group, with a target resting heart rate <100 bpm, or the rhythm-control group, in which patients received amiodarone and possible cardioversion for POAF persisting more than 24 to 48 hours (72). The two groups did not differ significantly in the primary outcome of total hospital days or in mortality or serious adverse events, including thromboembolic and bleeding events. Notably, freedom from POAF did not differ significantly between the rate-control and rhythm-control groups at discharge (89.9% *vs.* 93.5%, P=0.14) and through 60 days (84.2% *vs.* 86.9%, P=0.41) (72). However, this study was limited by approximately 25% crossover between groups due to drug ineffectiveness (rate control) or adverse drug reactions (rhythm control).

The findings of the CTSNet trial are further confirmed by a systematic review by Ahmed *et al.* of eight RCTs and 990 patients that compared rate versus rhythm control. The review found no clear advantage to a rate- or a rhythm-control strategy (73). A survey of American (n=262) and European (n=379) anesthesiologists found certain differences in their use of different drugs for POAF prophylaxis, specifically beta-blockers (American 60% *vs.* European 53%), amiodarone (39% *vs.* 34%), and

Table 2 Comparison of efficacy of various postoperative atrial fibrillation interventions

Treatment/intervention	NNT for POAF prevention	NNT for stroke/adverse event prevention	Reference(s)
Perioperative beta-blocker	6		(27,33)
Preoperative amiodarone	7		(30)
Postoperative amiodarone	7	83 (stroke)	(33,52)
Surgical left atrial appendage occlusion		45 (late stroke)	(48)
Posterior pericardiectomy	7		(38,39)
Colchicine	10–11		(62,63)
Magnesium supplementation	12		(68)
Oral anticoagulation		125 (early stroke)	(75)
Direct oral anticoagulant *vs.* vitamin K antagonists		204 (prevent stroke) 143 (prevent bleeding)	(76)

Early stroke defined as occurring within 30 days of surgery. Late stroke defined as occurring more than 30 days after surgery. NNT, number needed to treat; POAF, postoperative atrial fibrillation.

supplemental magnesium (37% *vs.* 65%) (74).

The recommendations found in various national and international societal guidelines echo the discrepancies in practice for POAF management, emphasizing the importance of an individualized approach for each patient. Whereas the ESC/EACTS guidelines (20) recommend a rate-control approach in asymptomatic POAF patients, the Canadian Cardiovascular Society (CCS) (21) recommends POAF treatment with either a rate-control or a rhythm-control approach, and the ACC/AHA guidelines do not specifically address the topic. The efficacy of various interventions is summarized in *Table 2* (19,27,30,33,38,39,48,52,62,63,68,75,76).

Rate control

Beta-blockers are the standard first-line medications for rate control in POAF because they mitigate the postoperative hyperadrenergic state. Although an optimal target heart rate has not been established, studies of permanent AF have shown no significant difference between lenient rate control (resting heart rate <110 bpm) and strict rate control (resting heart rate <80 bpm) with respect to death from cardiovascular causes, hospitalization for heart failure, stroke, systemic embolism, bleeding, and life-threatening arrhythmic events (77). Subsequent trials specifically addressing POAF management have employed a target resting heart rate less than 100 bpm (72), coinciding with the recommendations from the 2020 ESC/EACTS guidelines (20).

Routine use of calcium channel blockers (CCBs) or digoxin for POAF prophylaxis is not recommended by societal guidelines because of limited data supporting these drugs' effectiveness. However, in patients with preserved EF and either contraindications to or ineffective rate control from beta-blockers, CCBs and digoxin can be used in addition or as alternatives. In patients with reduced EF, beta-blockers and digoxin are preferred (20). For patients in whom rate control is difficult to achieve with any these pharmacologic agents, amiodarone can be used because it possesses both antiarrhythmic and beta-blocking properties (21).

Rhythm control

Rhythm control for POAF can be achieved through pharmacological or electrical cardioversion. As previously mentioned, historically rhythm control was the primary treatment modality for POAF. Despite the recent trend toward rate control as the initial approach, in specific subsets of patients the restoration of sinus rhythm remains paramount.

Synchronized electrical cardioversion should be employed for all hemodynamically unstable patients with POAF. Because of the risk of thromboembolism during the procedure, the patient should ideally be on anticoagulation for 3–4 weeks before the procedure, or preprocedural transesophageal echocardiography should be used to rule out the presence of thrombus in the left atrium or ventricle. Subsequent administration of antiarrhythmic medication is preferred because of the high early risk of recurrent POAF with isolated direct current cardioversion (DCCV) (9,16). In asymptomatic patients who have POAF shortly before hospital discharge or whose POAF persists for more than 24–48 hours, DCCV can be used to restore sinus rhythm (77).

Rhythm control is also recommended in symptomatic but otherwise hemodynamically stable patients, through either electrical or pharmacological cardioversion. Class IA, IC, and III antiarrhythmics are recommended for patients with normal EF and have shown similar efficacy to that of a rate-control approach (9,40,41). In patients with reduced EF, amiodarone is recommended. Because POAF is typically self-limited, antiarrhythmic therapy is unlikely to exceed 6-12 weeks; however, the decision to terminate treatment should include outpatient cardiac rhythm evaluation (9,16,37).

Approach to anticoagulation

The benefit of anticoagulation for AF is an approximately two-thirds reduction in stroke risk; initiating oral anticoagulation (OAC) is generally recommended at a CHA_2DS_2-VASc score ≥1 for men and 2 for women (18,20,78). The main differences between POAF and general nonvalvular AF are that most cases of POAF resolve spontaneously and that bleeding risk from recent surgery is higher in POAF cases. Avoiding stroke and thromboembolism from POAF while not increasing bleeding complications from OAC requires an individualized approach.

In a systematic review and meta-analysis of nine observational trials and 254,200 patients, Wang and colleagues found that the short-term absolute risk (AR) reduction for thromboembolism was 0.8% (95% CI: 0.4–1.4, NNT =125), with a long-term AR reduction of two events per 1,000 person-years (75). Patients on OAC were three times more likely to have a bleeding event (RR =3.22). The short-term AR increase for bleeding was 0.5% (95% CI: 0.4–0.6, NNH =200), with a long-term increased bleeding risk of 42 events per 1,000 patient-years.

In POAF, stroke risk appears to increase when the CHA_2DS_2-VASc score is ≥4. In an analysis of 6,368 patients in Sweden who developed POAF after CABG, Taha *et al.* found that the risk for ischemic stroke at 1 year was very low for patients with a CHA_2DS_2-VASc score of ≤3 (79). In the 10-year follow-up to the Arterial Revascularization (ART) Trial, Benedetto *et al.* found that among the 3,102 patients who developed POAF, the stroke risk increased with a CHA_2DS_2-VASc score ≥4 (80). An analysis of 166,747 patients who underwent isolated CABG from the Society of Thoracic Surgeons Adult Cardiac Surgery Database (STS-ACSD) found that 26% of patients who developed POAF were discharged with OAC (3). The use of OAC was 17% in low-stroke-risk patients with a CHA_2DS_2-VASc score of zero and was 30% in the high-risk group (CHA_2DS_2-VASc score ≥5). The OAC and no-OAC groups did not differ in stroke readmission rate (adjusted OR =0.87, 95% CI: 0.65–1.16, P=0.35); however, at 30 days, the OAC cohort had higher mortality (adjusted OR =1.20, 95% CI: 1.02–1.40, P=0.02) and more frequent readmission for bleeding (adjusted OR =4.30, 95% CI: 3.69–5.03, P<0.001) than those not receiving anticoagulation.

A systematic review analyzed 12 studies comparing direct oral anticoagulants (DOACs; n=8,587) with vitamin K antagonists (VKAs; n=8,315) for POAF: five RCTs (n=1,435; 8.5% of the overall sample) and seven observational studies (n=15,467; 91.5% of the overall sample) (76). The major neurological event (stroke) rate for DOACs was 0.9%, compared with 1.4% for warfarin, yielding a 37% relative RR (0.63, 95% CI: 0.48–0.83, P=0.01) and a 0.5% AR reduction (NNT =204). Pooled mortality was 1.7% (95% CI: 0.7–4.2%) for patients receiving DOACs, with no difference in mortality between patients treated with DOACs versus warfarin (RR =1.02, 95% CI: 0.77–1.35, P=0.9). The bleeding rate was 2.1% in the DOAC group and 2.8% in the warfarin group, for a 26% relative RR (0.74, 95% CI: 0.62–0.89, P=0.01) and a 0.7% AR reduction favoring DOACs (NNT =143).

Increasing data suggest that our current approach to anticoagulation may be overly aggressive (81). Indeed, we may be too aggressive with anticoagulation for lower-risk patients and not aggressive enough in higher-risk patients. The traditional criteria for anticoagulation may need to be revised for POAF patients. Practical recommendations are summarized by phase of care in *Table 3*.

Out-of-hospital considerations

Patients with POAF are at elevated risk for recurrent, paroxysmal, or permanent AF (82,83). Data from the SWEDEHEART (Swedish Web System for Enhancement and Development of Evidence‑based Care in Heart Disease Evaluated According to Recommended Therapies)

Table 3 Summary of practical recommendations and appropriate candidates

Phase of care	Treatment/intervention	POAF prevention	AF/POAF treatment	Stroke prevention
Preoperative	Oral beta-blocker	XX		
	Preoperative amiodarone in patients at high risk of POAF	XX		
	Perioperative amiodarone	XX		
Intraoperative	Posterior pericardiotomy	XX		
	Surgical ablation for atrial fibrillation		XX	XX
	Surgical occlusion of the LAA may be considered in patients with AF undergoing cardiac surgery as part of the overall heart team approach			XX
Postoperative	Beta-blocker for rate control		XX	
	Nondihydropyridine calcium channel blocker for rate control		XX	
	Restoration of sinus rhythm by electrical cardioversion of antiarrhythmic drugs recommended for POAF with hemodynamic instability		XX	
	Asymptomatic AF initially managed with rate control and anticoagulation		XX	
	Long-term anticoagulation should be considered in patients with POAF, considering individual stroke and bleeding risk			XX
	Antiarrhythmic drugs or cardioversion for symptomatic POAF to restore NSR		XX	
	Prophylactic sotalol to prevent POAF after cardiac surgery	XX		
	Colchicine to reduce POAF	XX		

XX indicates that the guidelines include this recommendation. POAF, postoperative atrial fibrillation; AF, atrial fibrillation; LAA, left atrial appendage; NSR, normal sinus rhythm.

study showed that the rate of late recurrent AF in the POAF cohort was 4 per 100 patient-years [adjusted HR 4.16 (3.76–4.60)] (84). A systematic review of eight studies and 1,157 patients found among patients developing POAF but discharged in sinus rhythm, 28% had recurrent POAF within 30 days (85). The Apple and Fitbit Heart Studies (N=419,297 and N=455,699) demonstrated the feasibility of relatively inexpensive preliminary data collection in large cohorts (86,87). With positive predictive values of 84% and 97%, these technologies offer an efficient method of screening POAF patients for recurrence. These methods may better identify patients at higher risk of recurrence and stroke and potentially guide patient selection for anticoagulation.

Future directions: artificial intelligence (AI) in POAF prediction and management

The integration of informatics into cardiac care has continuously evolved from simple data collection and storage to predictive modeling, real-time monitoring, and decision support (88) (*Figure 1*). ML, a subset of AI, has emerged as a promising tool in POAF prediction. Several studies have developed ML-based models incorporating support vector machines (89), gradient-boosted trees (90), and random forests algorithms (91) to predict POAF with accuracy (area under the receiver-operator characteristics curve) ranging from 0.70 to 0.78. Notably, the strength of ML is that in large datasets, it can recognize patterns often imperceptible to humans. Specifically, researchers have assessed the utility of deep learning, a subset of ML that uses layered neural networks, on only preoperative ECGs to effectively predict POAF (92).

ML augmented with real-time monitoring systems can provide additional advantages. Wearable technologies and continuous monitoring devices provide a platform for AI-driven tools for early POAF detection by pattern recognition. Immediate alerts to healthcare professionals can facilitate early intervention, potentially preventing POAF or mitigating its severity (93). Additionally, wearable technologies like smartwatches and adhesive patches have been employed to detect early signs of POAF after hospital discharge. A pilot clinical trial involving 330 participants observed that continuous ECG monitoring with CardioSTAT wearable patches improved the 30-day detection of POAF by 17% (94).

AI has also extended into the domain of clinical decision support (CDS). QRhythm, an AI-driven CDS system using supervised and reinforcement learning, tailors rhythm-management strategies according to patient characteristics (95). Future directions in POAF prevention are summarized in *Figure 1*.

The use of ML-based technologies in healthcare is evolving, enabling them to play an increasing role in pattern recognition, early identification, and decision support. However, AI tools are adjuncts to clinical judgment, not replacements for it, complementing but not supplanting human expertise.

Strengths and limitations of the review

The strength of this review is its thorough, evidence-based discussion of POAF after cardiac surgery with the use of landmark randomized trials, systematic reviews, and societal guidelines. In addition, the multispecialty background of the authors (cardiac surgery, anesthesiology, cardiology, and critical care) provides a broad perspective. The limitations include the broad scope of the review, which did not allow deeper investigation into potentially important areas.

Conclusions

POAF is the most common complication after cardiac surgery. Specific interventions in the preoperative, intraoperative, and postoperative phases of care can provide an opportunity for reducing the incidence of this complication. Most promising are those interventions that have been shown in randomized trials to have a number NNT of fewer than eight patients, indicating an especially high-yield intervention. A comprehensive approach to POAF prevention would incorporate preoperative amiodarone, perioperative beta-blockers or amiodarone, and posterior pericardiectomy at the time of surgery. Randomized, multicenter trials of this combination approach should be considered in the near future.

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Footnote

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