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Taking on the elephant in the room-postoperative atrial fibrillation: a clinical program management perspective

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Abstract
Postoperative atrial fibrillation (POAF) is the most common complication after cardiac surgery, yet there is no consistent cardiothoracic professional society-based definition of new-onset POAF, nor a broadly accepted consensus on how to prevent or treat it. Importantly, there is an ever-growing body of evidence that new-onset POAF is associated with worse patient outcomes. Given the lack of evidence-based guidelines, detection and treatment of POAF, in addition to understanding how POAF is related to these worse outcomes, represents an unaddressed quality of care concern. In the United States, the annual cardiac surgical POAF patient costs are estimated at ~$1 billion. The entire US Medicare annual budget has been reported at ~$141.2 billion for all hospital-related care; thus, the administrative challenges uniquely posed by POAF have been exposed for the first time. Mapping future tactics, this Vessel Plus special atrial fibrillation publication, swings the pendulum from impromptu observations towards action. A new strategic framework is proposed to begin the tedious but necessary task of taking on this elephant in the room. With ideal collaboration between clinical providers, health care systems, professional societies and insurers, a five-step approach is proposed to overcome these POAF patient care challenges.

Keywords: Postoperative atrial fibrillation, cardiac surgery, atrial fibrillation, administration management, quality of health care, administrative efficiency

INTRODUCTION

Postoperative atrial fibrillation (POAF) is one of the most prevalent complications after cardiac surgery, reported by the Society of Thoracic Surgeons (STS) as occurring in 20%-50% of cardiac surgical patients[1,2]. With over 300,000 cardiac operations performed annually in the United States, there are estimated to be 60,000 to 120,000 cardiac patients with new-onset POAF occurring per year[3]. Once thought to be an inconsequential postoperative clinical nuisance, there is mounting evidence of an association of any POAF with worse short- and long-term outcomes[4,5]; thus, POAF represents a complication and phenotype in need of serious attention. Despite the consistently high reported rates of the incidence of POAF, astoundingly little is known about the "who", "what", "when", "where", "why" and "how" of cardiac surgical POAF[5].

Across all cardiothoracic programs, POAF is arguably the largest "elephant in the room". Unfortunately, the published literature and professional society guidelines do not currently utilize a consistent definition of postoperative atrial fibrillation, and nor is there a broadly followed consensus on how to prevent, treat or manage POAF either in the hospital or after index cardiac surgical discharge[6]. Furthermore, there is no clear understanding of how POAF, regardless of rate- or rhythm-control strategies and resolution in the perioperative period, is related to worse short- and long-term outcomes[2]. Reviewing the POAF patient care and management challenges posed herein, a strategic planning framework has been proposed to overcome these POAF challenges.

Define POAF? the devil is in the details

Based on the literature review summarized by Pardo and colleagues, the atrial fibrillation (AF) and POAF definitions used by clinical care providers are varied[6]. These POAF definitions have specified the inclusion of atrial fibrillation lasting more than 30 s, 60 s, 15 min, 30 min, 1 h, or the presence of any atrial fibrillation at all. The published literature has specified the inclusion of atrial fibrillation requiring any treatment, occurring within 7 days of surgery, or occurring within 10 days of surgery[3-8]. Furthermore, conditions for POAF detection have fluctuated between studies; these detection methods ranged from identifying new-onset POAF using postoperative telemetry for 48 h, 72 h, until hospital discharge or no systematic detection method was reported at all[3].

A case in point is the STS Adult Cardiac Surgery Database (ACSD) definition of POAF. As the largest United States-based cardiothoracic surgery database, the STS ACSD monitors POAF as a postoperative adverse outcome. The most recent STS ACSD definition of POAF is "atrial fibrillation/flutter (AF) after operating room exit that: (1) lasts longer than 1 h; or (2) lasts less than 1 h but requires medical or procedural intervention, excluding patients who were in atrial fibrillation at the start of surgery (entry into operating room)"[9].

Several recent studies have advocated for a broader-based, more inclusive definition of POAF to better capture adverse outcomes in patients excluded by the more restrictive POAF definitions. Two multicenter studies of POAF in post-CABG patients compared the number of patients with an episode of atrial fibrillation or flutter detected via continuous telemetry to the number of patients who were captured by the more restrictive STS definition of AF lasting longer than 1 h or requiring treatment[10,11]. In Filardo's recent analysis of over 7000 isolated CABG patients with no prior history of AF, 2263 (31.8%) experienced POAF, including 422 patients (18.5%) missed by the current STS POAF definition[11]. For reference, the incidence of STS-defined POAF post-CABG across STS participating centers was reported as 26.3%[12]. Although not risk-adjusted, the group of patients with POAF based on the more inclusive definition (and missed by the STS definition) had a significantly greater risk of 30-day mortality compared to the STS POAF group (OR: 2.08; 95%CI: 1.17 to 3.69, $P = 0.02$)[10].

A POAF consensus definition appears urgently needed. Specifically, the POAF consensus definition will be highly consequential to define "at-risk" patients, identify differential detection rates, and evaluate POAF treatment impacts for mortality and other adverse outcome rates (e.g., stroke). Though the STS POAF definition is historically considered the "gold standard", this most recent analysis by Filardo *et al.*[10] highlights the significant limitations of using this more restrictive STS definition; it is now time to build upon the STS definition and expand this construct towards the goal of improving all POAF patients' quality of care and clinical outcomes.

Consequential outcomes after POAF

Mortality

The above multicenter analyses demonstrate a clear association of any POAF with increased 2-year mortality. Earlier this year, Eikelboom *et al.*[3] summarized data from 32 studies including over 155,000 patients [Table 1]. The incidence of POAF was 23.7% in patients after cardiac surgery; this POAF patient cohort had increased mortality rates at 1, 5 and 10 years[3].

Stroke

Stroke is a well-documented complication of atrial fibrillation. Part of the presumption that POAF was an inconsequential perioperative complication was based on an unfounded premise that POAF that resolved in the early postoperative weeks carried a lower stroke risk. Lin *et al.*[13] recently performed a meta-analysis of 35 cohort studies with more than 2.4 million participants; their research team observed that patients with new-onset POAF had 62% higher odds of early stroke and 44% higher odds of mortality compared with those without POAF[13]. In this study, patients with new-onset POAF had a 37% higher risk of long-term stroke and 37% higher risk of long-term mortality compared with those without POAF. The hazard ratio for stroke in the setting of POAF after cardiac surgery was 1.2, 95%CI: 1.1-1.3. The hazard ratio for mortality in the setting of POAF after cardiac surgery was 1.4, 95%CI: 1.3-1.5. Although risk differences may exist, this meta-analysis demonstrates a significantly increased stroke risk in patients with POAF after cardiac surgery. Though it remains unclear whether these strokes are all attributable to POAF, if these two outcomes are independent, or more likely, somewhere in between, this association has been corroborated by several other studies[3,4,14,15].

Increased LOS and cost

During the index cardiac surgical hospitalization, a significantly increased length of stay (LOS) has been repeatedly associated with POAF[7,13,15,16]. With POAF, both the ICU and floor LOS are increased (5.7 *vs.* 3.4 days; $P = 0.0001$ and 10.9 *vs.* 7.5 days; $P = 0.0001$, respectively)[15]. In turn, health care costs also rise. POAF associated with an increased LOS of 4.9 days, was associated with extra charges of $10,055-$11,500 per patient[16].

In the Department of Veterans Affairs ROOBY Trial sub-analyses, POAF patients had higher index hospitalization costs (adjusted mean cost difference of $13,993, $P < 0.001$) and 1-year cumulative costs (adjusted mean cost difference of $15,593, $P < 0.001$) as compared to non-POAF patients[7]. Comparing non-POAF to POAF patients, this cost difference (estimated at $10,000 per patient for over 100,000 POAF

Table 1. Mortality after cardiac surgery with and without postoperative atrial fibrillation, adapted from Eikelboom *et al.*[3]

Years after cardiac surgery	% Mortality with POAF	% Mortality with no POAF	Odds ratio mortality with POAF (95%CI)	*P* value
1	6%	4%	1.7 (1.1-2.6)	$P = 0.02$
5	15%	10%	1.6 (1.5-1.7)	$P < 0.0001$
10	29%	23%	1.5 (1.4-1.6)	$P < 0.0001$

cardiac surgical patients per year) results in over $1 billion per year of increased cardiac surgical hospitalization-related costs alone, not to mention the additional costs associated with medical treatments (e.g., anticoagulation) and post-discharge monitoring. In 2020, the Medicare total expenditures for all hospital care were reported at $141.2 billion[17]. Not directly reimbursed by Medicare, these POAF "unpaid" costs are born by health care providers. As a gigantic elephant in the room, this $1 billion for estimated post-cardiac surgical atrial fibrillation cost represents a significant (potentially preventable) burden that has not been-as of yet-directly raised for discussion by professional societies or hospital providers.

POAF prophylaxis

Although various pharmacologic and non-pharmacologic interventions have been promoted to prevent POAF, POAF still remains the most common complication after cardiac surgery.

Pharmacologic prophylaxis

Since 2007, the STS ACSD has incorporated a National Quality Forum endorsed quality measure for isolated CABG related to preoperative beta-blocker administration: "Indicate whether or not the patient received beta-blockers within 24 h preceding incision time, or if beta-blocker was contraindicated"[7]. Although the dose details (e.g., 12.5 mg of metoprolol within 24 h) were not required to be documented, this quality metric was added due to evidence that beta-blockers may reduce the incidence of POAF[18-20]. Despite the very high (90.3%) level of preoperative beta-blocker administration compliance across STS participating centers, the incidence of STS-defined POAF remains at 26.3%[12]. If one assumes that a large proportion of patients are excluded by the more restrictive STS definition per the analysis by Filardo *et al.*[10], then the POAF rate of 26.3% represents an underestimation.

In addition to beta blockade, preoperative amiodarone (Class IIa, level of evidence A), prophylactic sotalol (Class IIb, level of evidence B) and prophylactic postoperative colchicine (Class IIb, level of evidence B) are also recommended as pharmacologic interventions that can be considered to reduce POAF[21,22].

Non-pharmacologic prophylaxis

Non-pharmacologic interventions that can be considered to reduce the incidence of POAF include atrial pacing and posterior pericardiotomy. Gaudino *et al.*[23] recently published a single-center randomized controlled trial examining the effect of posterior pericardiotomy on the incidence of POAF in patients undergoing coronary, aortic valve and or aortic surgery. POAF was significantly lower in the left pericardiotomy group, 17% *vs.* 32%, $P = 0.0007$. Lower incidence of POAF was associated with a lower incidence of pericardial effusion, 12% *vs.* 21%, relative risk 0.58 (95%CI: 0.37-0.91)[23].

A Cochrane systematic review evaluated randomized controlled trials of pharmacologic and non-pharmacologic interventions and efficacy in preventing POAF or supraventricular tachycardia after cardiac surgery[14]. The pharmacologic interventions included in the review were amiodarone, beta-blockers, sotalol and magnesium. The non-pharmacologic interventions included atrial pacing and posterior pericardiotomy. Reviewing 118 studies that included 17,364 patients, all of these interventions were found to significantly reduce the rate of POAF after cardiac surgery compared with a placebo control [Table 2]. Beta-blockers and sotalol were documented to have similar efficacy. In six trials, amiodarone, atrial pacing and posterior pericardiotomy were also found to be effective for POAF reduction. In this analysis, magnesium was shown to prevent POAF; however, the impact of magnesium may be slightly less than that of the other pharmacological agents. Importantly, the additional investigation could establish more extensive professional society-based recommendations for POAF interventions.

POAF treatment

When POAF is encountered postoperatively, beta blockade (Class I level of evidence A), nondihydropyridine calcium channel blockers (Class I level of evidence B), and antiarrhythmic agents (Class II, level of evidence B) are recommended to convert POAF to sinus rhythm and/or rate control in atrial fibrillation. Guidelines also recommend it is reasonable to restore sinus rhythm with direct-current cardioversion in patients with POAF (Class IIa, level of evidence B)[21]. In addition to rhythm and rate control, guidelines support anticoagulation in patients with POAF (Class IIa, level of evidence B)[21,22].

Contemporary practice patterns of cardiac surgeons were recently examined; based on these findings, postoperative care teams appeared to aim to achieve rhythm control and avoid anticoagulation. Matos *et al.*[24] used STS ACSD data from 2011-2018 to evaluate discharge medications in patients receiving an isolated CABG who experienced POAF. Anticoagulation for post-CABG AF had a greater than 4-fold increase in the risk of major bleeding. Only 26% of those with POAF were discharged on anticoagulation despite a mean CHA2DS2-VASc score of 3.2. In addition, more than three-quarters of patients with post-CABG AF were discharged on amiodarone, and 57% of the total population received amiodarone without concomitant anticoagulation. The manuscript does not report the duration of POAF nor whether left atrial appendage occlusion was performed. Compared to the number of patients discharged on amiodarone, cardiac surgeons did not start anticoagulation for atrial fibrillation in at least 1 out of 4 postoperative patients. The randomized control trial by Gillinov *et al.*[2] comparing rate- *vs.* rhythm-control in cardiac surgery patients with POAF showed, in intention-to-treat analysis, no difference between groups in days of hospitalization, thromboembolic or bleeding events in the first 60 days[2]. Patients who remained in AF or had recurrent AF were "recommended" to be anticoagulated with warfarin. Anticoagulation with warfarin was higher in this trial (43%) compared to what Matos *et al.*[24] reported (26%) but still, not even the majority of patients were anticoagulated, and no CHA2DS2-VASc scores were reported. With limited randomized controlled trial data on rate- *vs.* rhythm-control and the benefit of anticoagulation, surgeon-based patterns appear to favor early rhythm control for new-onset POAF patients in a presumed attempt to avoid the bleeding risk associated with anticoagulation, even with side effects from antiarrhythmic medication occurring in as many as 15% of patients[2]. Given this controversy, additional research appears warranted to identify the risks and benefits associated with POAF management in cardiac surgery patients[2,25-27]. Pending additional data-driven findings, future clinical POAF practices may be better aligned with professional society guidelines.

POAF and the role of the left atrial appendage

Left atrial appendage (LAA) closure is a non-pharmacologic strategy for stroke prevention; historically, LAA has been identified as the main source of cardiac thrombi leading to arterial embolization and stroke[24]. The recent meta-analysis by Martín *et al.*[28] reported that a preoperative atrial fibrillation burden greater than 70% benefits from LAA closure during cardiac surgery, although across these studies, the LAA closure methods used were highly variable. In this meta-analysis, overall, there was minimal use of epicardial occlusion-which has been documented as the most durable obliteration method[28]. In a meta-

Table 2. Pharmacologic and non-pharmacologic interventions studied regarding their efficacy in preventing postoperative atrial fibrillation or supraventricular tachycardia, adapted from Arsenault *et al.*[14]

Intervention	Treatment arm events/total	Control arm events/total	Odds ratio of POAF (95%CI)
Amiodarone	19.4% (n = 505/2603)	33.3% (n = 932/2799)	0.43 (0.34-0.54)
Beta blocker	16.3% (n = 375/2294)	31.7% (n = 762/2404)	0.33 (0.26-0.43)
Sotalol	18.1% (n = 145/799)	40.0% (n = 324/810)	0.34 (0.26-0.43)
Magnesium	16.5% (n = 258/1567)	26.2% (n = 373/1421)	0.55 (0.41-0.73)
Atrial pacing	18.7% (n = 270/1446)	32.8% (n = 487/1487)	0.47 (0.36-0.61)
Posterior pericardiotomy	14.0% (n = 53/379)	33.1% (n = 127/384)	0.35 (0.18-0.67)

analysis of two randomized clinical trials looking at high-risk patients with nonvalvular AF, LAA closure was shown to be non-inferior to anticoagulation with warfarin for a composite endpoint including stroke[29]. All patients were candidates for chronic anticoagulation, but patients with LAA closure had improved rates of hemorrhagic stroke, death and nonprocedural bleeding compared to warfarin. One of the most frequently accepted indications for LAA closure is high stroke risk with contraindications to anticoagulation treatment[30]. Given the significant risk of bleeding while on anticoagulation in the immediate postoperative period, LAA closure for high-risk POAF non-surgical candidates may reduce their risk of stroke[31]. Interestingly, some data suggest incomplete surgical LAA closure may be thrombogenic and arrhythmogenic. Although the costs of prophylactic POAF procedures may be prohibitive, further study of surgical LAA closure techniques and outcomes appears to be warranted[30,31].

Improving our POAF perspective

Given the high prevalence, impact on mortality outcomes, and high costs associated with POAF, the time for action is at hand. To reject the current status quo, cardiac surgeons and cardiothoracic professional societies must work together to address this daunting POAF challenge. As noted by Dr. Ernest Amory Codman, "To effect improvement, the first step is to admit and record the lack of perfection. The next step is to analyze the causes of failure and to determine whether these causes are controllable"[32].

This review highlights the tremendous burden of POAF due to the annual, colossal $1 billion strain on the United States healthcare system. This clinically significant and costly problem represents an opportunity for the quality improvement initiatives such as the STS ACSD, the American Association for Thoracic Surgery (AATS) Quality Gateway, as well as large healthcare systems such as the Veterans Health Administration (VHA)[33,34]. There are 42 cardiac surgery programs serving veterans in the VHA system, and the VHA Surgical Quality Improvement Program along with the STS ACSD and the AATS Quality Gateway, could make a big impact by first adopting a uniform POAF definition. Uniform definitions, consistent monitoring and standardized reporting of POAF, prophylaxis and treatment is the first step to improving quality and ultimately reducing the incidence of POAF. Given the compelling data advocating for an inclusive POAF definition, a new POAF definition is recommended-that is, to identify any new atrial fibrillation event occurring after cardiac surgery and before discharge. Using this approach, the largest POAF patient population might be identified; thus, these POAF patients may potentially benefit from any intervention to prevent or more effectively treat POAF[10,11]. Additional details regarding POAF duration, treatment and discharge medications must also be collected and reported; these should be compared to literature-based standards. To facilitate future research, this broader-based, more inclusive POAF definition will ensure that all patients that may potentially benefit from treatment will also be included.

To facilitate clinical practice management improvements, the second step to improve POAF patients' quality of care will be to establish a uniform approach for early POAF detection; thus, standard operating procedures should ensure consistent postoperative telemetry monitoring occurs post-surgery during the index hospitalization. By requiring postoperative telemetry monitoring to identify new-onset POAF patients, variation in POAF detection approaches would be minimized and POAF reporting consistency ensured.

For clinicians, hospitals, professional societies, and insurers, the third step will be to work collaboratively in a multidisciplinary manner to expand consensus guidelines for the interim management of POAF. An appropriate level of evidence recommendations should incorporate contemporary surgeon concerns and practice including a consensus on the specifics regarding initiation of amiodarone and anticoagulation as well as recommendations on termination of these agents after a reasonable postoperative period[24]. As management of the atrial appendage evolves, guidelines for management for POAF should include recommendations in the setting of an obliterated appendage.

The fourth step in this strategic framework will be to measure, record, and compare provider adherence to these new guidelines by expanding the POAF-related data elements contained in the current adult cardiac surgery databases. Using these data-driven reports, risk-adjusted provider and POAF sub-group comparisons may be facilitated. Combining all adult cardiac surgical databases' de-identified patient data records together, individual patient data-driven pooled analyses should be used to identify opportunities to improve POAF care.

As the fifth step in this strategic framework, future research projects must be coordinated. Based on these preliminary, database-driven, observational studies' findings, new clinical trials may be designed and implemented. These new clinical trials must not only compare treatment-specific outcomes, but also evaluate combinations of POAF therapies to reflect the most common approaches used in clinical practice management. Beyond an overall focus on all POAF patients, additional investigations should target "high-risk" POAF patients-that is, patient subpopulations with preoperative AF and those subpopulations known to have increased risk of POAF-associated strokes or mortality. The proposed framework can facilitate the study of preoperative identification of patients with subclinical atrial fibrillation, genetic and epidemiologic factors that increase POAF risk, computer-assisted pattern recognition to identify those at risk for POAF, existing and new pharmacologic strategies and ablation interventions for prevention and management of POAF, left atrial appendage management strategies, at-home rhythm monitoring before surgery and after discharge, and most importantly, longitudinal POAF monitoring and reporting of longer-term outcomes (e.g., 5-10 year survival); additionally, it would be imperative to evaluate the most common clinical practice-based approaches.

The time has come to address this elephant in the room-to create uniform POAF definitions, standardize POAF detection, and expand POAF data collection to include approaches for prophylaxis and treatment. The momentum is building to define, measure and unpack the phenotype of POAF that is associated with worse short- and long-term outcomes. At this convergence of technology, economics and multidisciplinary collaborations, a change in perspective is warranted to improve POAF patients' quality of care and reduce the burden and negative consequences of this most common post-cardiac surgical complication-POAF.

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