Real-life practice in the management of new-onset postoperative atrial fibrillation early after cardiac surgery

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OBJECTIVES: To investigate the real-world pharmacological management of postoperative atrial fibrillation (POAF) in patients undergoing cardiac surgery.

METHODS: A retrospective cohort analysis consisting of adult patients who underwent coronary artery bypass grafting, valve or combined surgery from January to December 2011 was performed using a clinical registry. The peri- and postoperative pharmacological management (rate control, rhythm control, anticoagulant therapy) of POAF was evaluated. Stepwise multivariate regression analyses were used to identify determinants for medication use at discharge.

RESULTS: The cohort consisted of 1145 patients, of whom 377 (32.9%) developed POAF and 271 (23.7%) were included. At discharge, 251 patients (92.6%) received β-blocker therapy and 122 (45.0%) received antiarrhythmic therapy. Two hundred sixty-one (96.3%) received rate- and/or rhythm-control therapy. Forty-eight (17.7%) patients received warfarin on discharge, although 38 had an additional indication. Men and urgent inpatients were less likely to be discharged on warfarin. Among 145 patients discharged on antiarrhythmic and/or anticoagulant therapy, 121 (83.4%) attended follow-up. Only 28.1% (34 of 121) had an electrocardiogram or Holter monitoring performed; despite this, antiarrhythmic medications were either continued or not addressed in 47.7% (51 of 107) of patients discharged on therapy.

CONCLUSIONS: Treatment of POAF with rate- and/or rhythm-control medications was consistent with current national guideline recommendations. However, anticoagulant therapy use was low and appeared to be limited to patients with another indication. Assessment of POAF medications and rhythm status at postoperative follow-up visit was inconsistent. Thus, efforts to improve the management of POAF should focus on appropriately discontinuing unnecessary medications at postoperative follow-up to minimize the risk of adverse effects.

Key Words: *ACE inhibitors; Amiodarone; Antiarrhythmics; Anticoagulants; Atrial fibrillation; Beta-blockers; Coronary artery bypass graft surgery; Health outcomes research; Nondihydropyridine calcium channel blockers; Rate control; Rhythm control; Warfarin*

Postoperative atrial fibrillation (POAF) is a frequent complication of cardiac surgery (1-3). Although the majority of new-onset cases are self-limiting, POAF has been associated with an increased risk for hemodynamic deterioration, thromboembolic events and cognitive impairment (3-6). It has also been shown to prolong length of hospital stay and increase health care costs (1,2). The incidence of POAF after cardiac surgery ranges from 30% to 50% and varies according to the type of surgery (eg, coronary artery bypass grafting [CABG], valve replacement/repair), with the highest incidence occurring in patients who undergo concurrent CABG and valve surgeries (3,7). Patient characteristics associated with an increased risk for developing POAF include advanced age (>70 years), male sex, history of hypertension, history of preoperative atrial fibrillation (AF), need for intraoperative balloon pump and prolonged postoperative ventilation (>24 h) (1-4).

Recent guidelines from the Canadian Cardiovascular Society recommend strategies for the prevention and treatment of POAF (8). These include controlling ventricular response rate with β-blockers, nondihydropyridine calcium channel blockers or amiodarone; preventing cardioembolic stroke with anticoagulant medications; and converting patients to normal sinus rhythm. Pharmacological therapy for maintenance of sinus rhythm is preferred over isolated direct current cardioversion in this setting due to the high risk for early AF recurrence (8).

The Mazankowski Alberta Heart Institute (MAHI) is a quaternary care referral centre in Edmonton, Alberta, where approximately 1200 cardiac surgeries are performed annually. The local practice patterns and concordance with national guidelines at our institution are currently unknown. Optimal application of evidence-based pharmacotherapy and appropriate follow-up are essential to minimize the risks associated with treatment. The objective of the present study was to compare the pharmacological management of POAF in cardiac surgery patients at our institution with national guidelines, and identify determinants for use of rate-control, rhythm-control and anticoagulant medications.

METHODS

A single-centre retrospective cohort analysis was performed. The cohort consisted of consecutive patients who underwent cardiac surgery at the MAHI over a 12-month period (January 1 to December 31, 2011). Data regarding the peri- and postoperative management of patients who developed POAF were collected using the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) database, a clinical registry that prospectively collects information on all patients who undergo cardiac surgery in Alberta (9). Follow-up data on patients discharged from hospital on an antiarrhythmic and/or anticoagulant medication were collected from outpatient records. Included were patients ≥18 years of age who had undergone CABG and/or a valve replacement/repair surgery and developed new-onset POAF. The prespecified definition of POAF was the occurrence of AF requiring treatment (eg, pharmacological therapy, direct current cardioversion) post-cardiac surgery in patients who did not have preoperative AF. Patients with a history of a preoperative atrial or ventricular arrhythmia, atrial ablation, Cox maze procedure, or who had a cardiac pacemaker or automated implantable cardioverter

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TABLE 1
Baseline cohort characteristics (n=271)

Age, years, mean ± SD	68.3±9.7
Male sex	217 (80.1)
Postoperative length of stay, days, mean ± SD	9.1±4.8
Comorbidities	
Hypertension	229 (84.5)
Previous myocardial infarction	107 (39.5)
Chronic obstructive pulmonary disease	106 (39.1)
Heart failure	40 (14.8)
Previous percutaneous coronary intervention	37 (13.7)
Previous coronary artery bypass graft	6 (2.2)
Extent of coronary artery disease	
Three-vessel disease	100 (36.9)
Left main disease	73 (26.9)
One- or two-vessel disease	38 (14.0)
Normal/data missing	60 (22.1)
Left ventricular ejection fraction	
≥35%	104 (38.4)
<35%	11 (4.1)
Data missing	156 (57.6)
Preoperative medications	
Acetylsalicylic acid	151 (55.7)
β-blocker	188 (69.4)
Angiotensin-converting enzyme inhibitor	104 (38.4)
Thienopyridine (clopidogrel or ticlopidine)	27 (10.0)
Warfarin	1 (0.4)
Type of surgery	
Coronary artery bypass graft	156 (57.6)
Valve	65 (24.0)
Combined coronary artery bypass graft and valve	50 (18.4)
Valve procedure performed*	
Aortic valve repair	5 (1.8)
Aortic valve replacement (bioprosthetic)	75 (27.7)
Aortic valve replacement (mechanical)	8 (3.0)
Mitral valve repair	18 (6.6)
Mitral valve replacement (bioprosthetic)	12 (4.4)
Mitral valve replacement (mechanical)	0 (0.0)
Priority of surgery	
Low risk	22 (8.1)
Urgent outpatient	154 (56.8)
Urgent inpatient	85 (31.4)
Emergency	10 (3.7)

*Data presented as n (%) unless otherwise indicated. *Three patients under went >1 valve procedure*

defibrillator were excluded. As well, patients taking antiarrhythmic medications on admission or who had a postoperative length of stay >28 days or died during their index hospitalization were also excluded. The present study was approved by the Health Research Ethics Board at the University of Alberta (Edmonton, Alberta).

The primary outcome was the proportion of patients discharged from hospital on β-blocker therapy. Prespecified secondary outcomes included percentage of patients discharged on an antiarrhythmic or anticoagulant medication, percentage of patients discharged on a rate- versus rhythm-control strategy, determinants of a rate-control, rhythm-control or anticoagulant therapy at discharge, percentage of patients who continued on an antiarrhythmic or anticoagulant medication at postoperative follow-up and percentage of patients who had an objective measure of heart rhythm (eg, electrocardiogram, Holter monitor) at follow-up.

Data analysis was completed using SPSS version 21.0 (IBM Corporation, USA). Descriptive statistics were used for baseline

TABLE 2
Pharmacological therapy on discharge (n=271)

β-blocker therapy	251 (92.6)
Preoperative β-blocker continued	178 (65.7)
β-blocker initiated perioperatively	73 (26.9)
Antiarrhythmic therapy	122 (45.0)
Amiodarone	121 (44.6)
Other	1 (0.4)
Rate- and/or rhythm-control therapy	261 (96.3)
Rate- and rhythm-control therapy	114 (42.1)
Anticoagulant therapy (warfarin)	48 (17.7)

Data presented as n (%)

TABLE 3
Determinants for use of anticoagulant medication at discharge

Variable	OR	95% CI	P
Male sex	0.33	0.13–0.89	0.028
Urgent inpatient surgery	0.14	0.03–0.72	0.019
Valvular surgery	8.80	1.20–64.40	0.032
Combined CABG and valve surgery	6.98	2.03–24.02	0.002

CABG Coronary artery bypass graft

demographic and clinical characteristics, as well as the proportional primary and secondary outcomes. A stepwise multivariate logistic regression was completed to identify determinants for use of rate-control, rhythm-control and anticoagulant medications at discharge. Each analysis was adjusted for age, sex and any variable that demonstrated significant predictive value (P<0.10) for the dependent outcome based on the univariate analysis. P<0.05 was considered to be statistically significant.

RESULTS

The cohort consisted of 1145 patients. Of these patients, 377 (32.9%) developed POAF and 271 (23.7%) met the inclusion criteria. The most common reasons for exclusion included a preoperative arrhythmia or antiarrhythmic medication (81 of 106 [76.4%]), postoperative length of stay >28 days (26 of 106 [24.5%]) and mortality during index hospitalization (15 of 106 [14.2%]). Patient baseline demographic and clinical characteristics are included in Table 1.

The primary outcome occurred in 92.6% (251 of 271) of patients (Table 2). One hundred twenty-two patients (122 of 271 [45.0%]) were discharged on an antiarrhythmic medication and 48 (48 of 271 [17.7%]) were discharged on an anticoagulant medication (warfarin). Two hundred sixty-one patients (261 of 271 [96.3%]) were discharged on either rate- or rhythm-control therapy. One hundred thirty-seven (137 of 271 [50.6%]) were discharged on a rate-control strategy only (β-blocker or nondihydropyridine calcium channel blockers) and 10 patients (10 of 271 [3.7%]) were discharged on a rhythm-control strategy only. One hundred fourteen patients (114 of 271 [42.1%]) were discharged on both a rate- and rhythm-control agent.

The multivariate analysis identified no independent predictors for use of rate- or rhythm-control medications at discharge. However, male sex, urgent inpatient surgery, isolated valve surgery and combined CABG/valve surgery were independent predictors for use of an anticoagulant medication at discharge (Table 3).

One hundred forty-five (145 of 271 [53.5%]) patients were discharged on an antiarrhythmic and/or anticoagulant medication (Table 4). Only 121 (121 of 145 [83.4%]) attended postoperative follow-up with a cardiac surgeon (mean 59 days postoperatively). Of these patients, 107 patients (107 of 121 [88.4%]) were discharged on an antiarrhythmic medication (amiodarone). In 56 patients (56 of 107 [52.3%]), amiodarone was discontinued either

before or at follow-up. Amiodarone was continued in 18 patients (18 of 107 [16.8%]) and not assessed in 33 patients (33 of 107 [30.8%]) at follow-up. Only 34 patients that attended follow-up (34 of 121 [28.1%]) had an electrocardiogram or Holter monitoring performed at the follow-up appointment. Thirty-seven patients that attended follow-up (37 of 121 [30.6%]) were discharged on warfarin, which was continued in 23 patients (23 of 37 [62.2%]) and discontinued in eight of 37 (21.6%) patients. Warfarin was not addressed in six of 37 (16.2%) patients at follow-up.

DISCUSSION

POAF is a common complication of cardiac surgery and has been associated with adverse patient outcomes (1-6). The annual incidence of new-onset POAF in patients who underwent CABG and/or valve surgery at the MAHI in 2011 was approximately 33%, which is consistent with the published literature (3,7). Data regarding risk factors for POAF were not collected because they are already well defined in the literature (1-4).

While POAF is frequently self-limiting, the goals of therapy are parallel to those for AF in other clinical settings. In the absence of conclusive evidence comparing a rate- versus rhythm-control strategy in patients with POAF, guidelines suggest that either may be appropriate (8). It is also recommended that anticoagulation be considered in patients who remain in AF for >72 h. The use of rate- and rhythm-control medications for the treatment of POAF at the MAHI was predominantly consistent with current national guidelines; approximately 96% of patients received a rate-control and/or antiarrhythmic medication. However, surprisingly few patients (48 of 271 [17.7%]) were recommended warfarin therapy on discharge, the majority of whom (38 of 48 [79.2%]) had another compelling indication (eg, mechanical valve or mitral valve repair/replacement). The reason for the low utilization of warfarin on discharge is not clear; however, it may be reflective of most patients having a short duration of AF (<72 h) or concern regarding increased risk for bleeding in the early postoperative period.

Multivariate regression analyses did not identify any independent determinants for use of rate- or rhythm-control medications at discharge, which may be the result of the small sample size. However, multiple determinants for anticoagulant therapy were identified. Men were less likely to be discharged on warfarin, which may be secondary to the small number of women included in the cohort (approximately 20%). Patients who underwent urgent inpatient surgery were also less likely to be on warfarin at discharge. This may be related to the increased acuity and comorbid disease burden associated with urgent surgical candidates, which often equates to an increased risk for bleeding. Patients who underwent any type of valvular surgery were more likely to be discharged on warfarin compared with patients who underwent isolated CABG surgery; this likely demonstrates the appropriate use of anticoagulant therapy in patients with valvular heart disease.

In most patients, POAF will resolve within six to 12 weeks postoperatively (10,11). Accordingly, medications for POAF should be recommended for a defined period of time or reassessed at postoperative follow-up to eliminate unnecessary medications and minimize the risk for adverse effects (8,12-14). In this cohort, postoperative follow-up was lower than expected (approximately 83%), but was within the recommended timeframe (mean 8.4 weeks) (8). Warfarin was discontinued in only one-fifth of patients discharged on therapy because most patients had an additional indication for prolonged treatment (eg, mechanical valve, mitral valve replacement/repair). Unexpectedly, less than one-third of patients received an objective measure of heart rhythm assessment at follow-up, despite a high percentage of patients being discharged on a rhythm-control medication. Regardless, antiarrhythmic therapy was either continued or not addressed in almost one-half of patients. While a rhythm-control strategy is recommended in the immediate postoperative period to prevent early recurrence, converting to a rate-control strategy is typically preferred for patients who remain in AF six to 12 weeks postoperatively due to a lack of benefit and increased adverse effects with antiarrhythmics compared with negative chronotropic agents (8,13,15,16).

TABLE 4
Follow-up cohort baseline characteristics (n=145)

Age, years, mean ± SD	67.4±9.6
Male sex	116 (80.0)
Postoperative length of stay, days, mean ± SD	8.9±4.3
Comorbidities	
Hypertension	122 (84.1)
Previous myocardial infarction	52 (35.9)
Chronic obstructive pulmonary disease	24 (16.6)
Heart failure	3 (2.1)
Previous percutaneous coronary intervention	26 (17.9)
Previous coronary artery bypass graft	58 (40.0)
Extent of coronary artery disease	
Three-vessel disease	53 (36.6)
Left main disease	30 (20.7)
One- or two-vessel disease	30 (20.7)
Normal/data missing	32 (22.1)
Left ventricular ejection fraction	
≥35%	52 (35.9)
<35%	3 (2.1)
Data missing	90 (62.0)
Preoperative medications	
Acetylsalicylic acid	75 (51.7)
β-blocker	94 (64.8)
Angiotensin-converting enzyme inhibitor	49 (33.8)
Thienopyridine (clopidogrel or ticlopidine)	17 (11.7)
Warfarin	1 (0.7)
Type of surgery	
Coronary artery bypass graft	71 (49.0)
Valve	40 (27.6)
Combined coronary artery bypass graft and valve	34 (23.4)
Valve procedure performed*	
Aortic valve repair	5 (3.4)
Aortic valve replacement (bioprosthetic)	39 (26.9)
Aortic valve replacement (mechanical)	8 (5.5)
Mitral valve repair	15 (10.3)
Mitral valve replacement (bioprosthetic)	9 (6.2)
Mitral valve replacement (mechanical)	0 (0.0)
Priority of surgery	
Low risk	14 (9.7)
Urgent outpatient	88 (60.7)
Urgent inpatient	34 (23.4)
Emergency	9 (6.2)

*Data presented as n (%) unless otherwise indicated. *Two patients underwent >1 valve procedure*

The present study has several limitations that warrant discussion. Although data in the APPROACH registry are collected prospectively, the registry is limited by a finite number of characteristics and outcome measures. The perioperative sequence of events was not captured, making it difficult to assess the proportion of patients who experienced additional complications secondary to POAF and whether more than one treatment intervention was required. The registry captures medications at the time of admission and discharge, but does not include inpatient medication use. As a result, it was not possible to evaluate how POAF therapy was selected, and the temporal relationship between the development of POAF and initiation of pharmacotherapy. The registry also does not capture whether patients remained in AF for >72 h; thus, it was not possible to evaluate the appropriateness of anticoagulant medications at discharge. Moreover, patients who had an indication other than POAF for long-term anticoagulation were not differentiated in the analysis. Follow-up data were limited by the completeness of documentation in the outpatient records.

In addition, follow-up from other providers (eg, cardiologists, general practitioners) was not consistently documented.

CONCLUSIONS

Initiation of rate- and rhythm-control medications at discharge for the treatment of POAF in cardiac surgery patients at the MAHI was consistent with current national guideline recommendations. However, the use of anticoagulant therapy on discharge was low and appeared to be limited to patients with another indication (eg, mechanical valve, mitral valve replacement/repair). Assessment of POAF medications and rhythm status at the six- to 12-week postoperative follow-up visit was inconsistent. Antiarrhythmic medication was either continued or not addressed in almost one-half of the cohort, and less than one-third of patients underwent an objective investigation of rhythm status. Thus, efforts to improve the management of POAF should focus on a systematic approach to the assessment and appropriate discontinuation of unnecessary medications at postoperative follow-up to minimize the risk for adverse effects.

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