Prophylaxis for postoperative atrial fibrillation: Impact of the implementation of a medication bundle protocol

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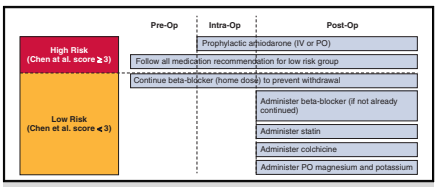

Postoperative atrial fibrillation protocol.

CENTRAL MESSAGE

At our institution, a POAF prevention medication protocol was created for patients undergoing cardiac surgery that includes beta blockers, amiodarone, statins, colchicine, and scheduled electrolytes.

Postoperative atrial fibrillation (POAF) is the most common arrhythmic complication following cardiac surgery.[1] Although typically transient, it is associated with increased mortality, length of stay (LOS), and recurrent AF.[2] Several strategies have aimed to identify high-risk patients and prevent POAF. Chen and colleagues[3] created a scoring system to stratify POAF risk for patients undergoing coronary artery bypass graft (CABG).[3] Risk factors in this score include age older than 65 years, hypertension, heart failure, and myocardial infarction. A score $\geq$3 indicates high POAF risk. This scoring system has been adopted by our institution for patients undergoing cardiac surgery due to simplicity of use at bedside.

Several medications have been studied to prevent POAF, with amiodarone, beta blockers, statins, colchicine, and electrolyte replacement showing the most benefit.[4] Although they have shown individual benefit, their combined efficacy has not been established. Chatterjee and colleagues[5] recently highlighted the development of a POAF prevention and management turnkey order set. At our institution, a POAF prevention medication protocol that is similar to the order set of Chatterjee and colleagues[5] was created for patients undergoing cardiac surgery. We sought to demonstrate the influence of our protocol by exploring the efficacy and safety of pre- and postprotocol cohorts.

METHODS

This was a retrospective, pre/post cohort study of adult patients who underwent CABG, surgical valve replacement, ascending/transverse aortic artery repair or replacement (or any combination) from March 3, 2021, through December 22, 2022. The institutional review board of our institution did not approve this study because they deemed it exempt (23-1342 – 6/12/2023). Patient written consent was not received due to the retrospective nature of the study. Eligible patients received the appropriate protocol medications within 48 hours (24 hours for amiodarone) of the conclusion of their surgery (postprotocol cohort only). Key exclusion criteria included postoperative mechanical circulatory support, history of AF or atrial flutter, presurgical sinus bradycardia, ventricular pacing >48 hours postoperatively, or corrected QT $\geq$500 milliseconds.

A summary of our protocol is found in Figure 1. The statin, colchicine, amiodarone, and electrolytes are continued through postoperative day 4, at which time continuation is reassessed. The beta blocker medications are continued through (and after) discharge.

The primary outcome was the incidence of POAF (AF lasting for $\geq$5 minutes on telemetry) by postoperative day 7 or discharge (whichever was sooner). Secondary outcomes included hospital LOS, intensive care unit LOS, hospital mortality, ventricular arrhythmias ($\geq$30 beats of ventricular fibrillation or tachycardia), ischemic stroke or transient ischemic attack (TIA), and oral anticoagulation initiation. Key safety outcomes included bradycardia requiring beta-blocker dose reduction/discontinuation, new thyroid abnormalities requiring amiodarone discontinuation, liver function tests >3 times the upper limit of normal requiring amiodarone or statin discontinuation, and/or gastrointestinal toxicity requiring dose reduction/discontinuation of amiodarone or colchicine.

Based on an estimated reduction in POAF of 20% in the postprotocol cohort, a sample size of 164 patients was required to meet 80% power to detect a statistically significant difference with an alpha of 0.05. Data analysis included the Kruskal-Wallis test and Fisher exact test for continuous and categorical data, respectively.

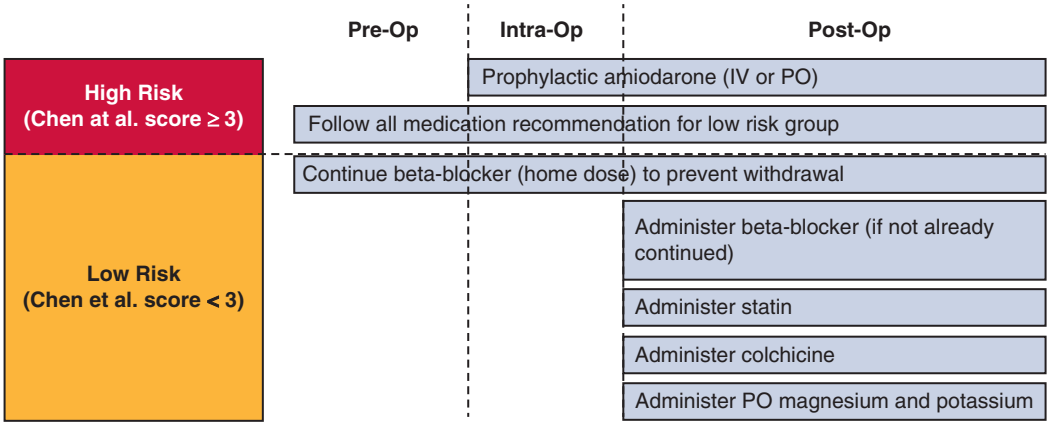

FIGURE 1. Postoperative atrial fibrillation prophylaxis protocol.

RESULTS

A total of 413 patients were screened for inclusion in this study with 245 patients excluded, most commonly due to protocol nonadherence (n = 157), history of AF or atrial flutter (n = 47), and/or mechanical circulatory support (n = 20). There were 168 patients included, 84 in the preprotocol cohort and 84 in the postprotocol cohort. Overall, baseline characteristics were mostly similar between groups; however, weight, history of stroke/TIA, history of heart failure, and postoperative epinephrine use were all higher in the preprotocol cohort ($P < .05$ for all). CABG was performed in 53.6% compared with 60.7% ($P = .4358$) and valve replacement was performed in 29.8% compared with 16.7% ($P = .0668$) of preprotocol and postprotocol patients, respectively. Chen score was 2.11 for preprotocol and 1.65 for postprotocol patients ($P = .027$).

The primary outcome was observed in 24 (28.6%) patients in the preprotocol cohort and 15 (17.9%) patients in the postprotocol cohort ($P = .143$). Hospital LOS was 11.76 days in the preprotocol cohort compared with 9.85 days in the postprotocol cohort ($P = .033$). There was a significant increase in beta blocker, statin, colchicine, potassium, and magnesium use in the postprotocol cohort ($P < .001$). There was no statistically significant difference

TABLE 1. Primary and secondary outcomes

Outcomes	Preprotocol (n = 84)	Postprotocol (n = 84)	*P* value
POAF	24 (28.6)	15 (17.9)	.143
Hospital LOS (d)	11.76 ± 8.11	9.85 ± 8.11	.033
ICU LOS (d)	3.94 ± 3.52	3.42 ± 2.23	.346
In-hospital death	2 (2.4)	1 (1.2)	1.000
Ventricular arrhythmia	4 (4.8)	4 (4.8)	1.000
Ischemic stroke or TIA	1 (1.2)	0 (0.0)	1.000
Systemic anticoagulation initiation	9 (10.7)	6 (7.1)	.590
Beta blocker initiation	37 (44.0)	84 (100.0)	<.001
Amiodarone initiation	23 (27.4)	34 (41.0)	.074
Statin initiation	65 (77.4)	84 (100.0)	<.001
Colchicine initiation	15 (17.9)	84 (100.0)	<.001
Scheduled potassium initiation	6 (7.1)	84 (100.0)	<.001
Scheduled magnesium initiation	20 (23.8)	84 (100.0)	<.001
Bradycardia	3 (3.6)	4 (4.8)	1.000
Thyroid abnormalities	0 (0.0)	0 (0.0)	1.000
AST/ALT elevations	2 (2.4)	3 (3.6)	1.000
GI toxicity	0 (0.0)	0 (0.0)	1.000

Values are presented as n (%) or mean ± SD. *PAOF*, Postoperative atrial fibrillation; *LOS*, length of stay; *ICU*, intensive care unit; *TIA*, transient ischemic attack; *AST/ALT*, aspartate transaminase/alanine transaminase; *GI*, gastrointestinal.

found in any other secondary or safety outcomes. A full description of outcomes is found in Table 1.

DISCUSSION

In our study of the influence of a POAF prevention protocol, we did not find a statistically significant reduction in POAF. However, we found a >10% absolute risk reduction, suggestive of a clinically meaningful benefit. Our study also found an increase in the use of POAF prophylactic therapies with no detectable harm, representing significant improvement in the delivery of care. Additionally, we found a statistically significant reduction in hospital LOS with the use of the protocol, likely leading to decreases in healthcare costs. POAF has shown to increase LOS; therefore, it is possible the larger percentage of patients with POAF in the preprotocol cohort led to a prolonged LOS. Given pressures to discharge patients in a timely fashion, adoption of this protocol should be considered by any cardiac surgery program.

None of the safety end points showed any signal of harm. One possible concern upon implementation of our protocol was the risk for postoperative bradycardia; however, this occurred in <5% of patients in both groups.

Our study has several limitations. The retrospective nature allows for selection bias. The pre-protocol group had a higher incidence of stroke/TIA, heart failure, higher Chen score, and higher use of postoperative epinephrine, likely increasing surgical and POAF risk. Also, a significant number of patients were excluded in the postprotocol group due to protocol nonadherence, most commonly due to lack of beta blocker initiation. Additionally, we are likely underestimating the incidence of gastrointestinal toxicity from colchicine due to lack of documentation in the medical record.

CONCLUSIONS

A POAF prophylaxis protocol that includes beta blockers, statins, colchicine, electrolytes, and selective amiodarone resulted in a statistically nonsignificant but clinically relevant 10% absolute risk reduction in POAF compared with a preprotocol cohort. This protocol increased the use of POAF prophylactic therapies and resulted in a statistically significant reduction in hospital LOS.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. Patti G, Pasceri V, Colonna G, et al. Atorvastatin pretreatment improves outcomes in patients with acute coronary syndromes undergoing early percutaneous coronary intervention: results of the ARMYDA-ACS randomized trial. *J Am Coll Cardiol*. 2007;49(12):1272-1278.
2. Frendl G, Sodickson AC, Chung MK, et al. 2014 AATS guidelines for the prevention and management of perioperative atrial fibrillation and flutter for thoracic surgical procedures. *J Thorac Cardiovasc Surg*. 2014;148(3):e153-e193.
3. Chen L, Du X, Dong J, Ma CS. Performance and validation of a simplified postoperative atrial fibrillation risk score. *Pacing Clin Electrophysiol*. 2018;41(9):1136-1142.
4. Dobrev D, Aguilar M, Heijman J, Guichard J, Nattel S. Postoperative atrial fibrillation: mechanism, manifestations and management. *Nat Rev Cardiol*. 2019;16(7):417-436.
5. Chatterjee S, Cangut B, Rea A, et al. ERAS Cardiac Society turnkey order set for prevention and management of postoperative atrial fibrillation after cardiac surgery: proceedings from the AATS ERAS Conclave 2023. *J Thorac Cardiovasc Surg Open*. 2024;18:118-122.