

Incidence of Atrial Fibrillation after Cardiac Surgery and its Pharmacological Management

Persis Ann George, Anila Varkey, Adithya Nandan, Uday Venkat Mateti, Mundayat Gopalakrishnan¹, Rovin Mathew Theempalangad

Department of Pharmacy Practice, NGSIM Institute of Pharmaceutical Sciences, Nitte (Deemed to be University), ¹Department of Cardiothoracic Surgery, K.S. Hegde Medical Academy, Nitte (Deemed to be University), Mangalore, Karnataka, India

Abstract

Aim: Postoperative atrial fibrillation (POAF) is one of the most commonly occurring complications after cardiac surgery. The study aims to determine the incidence of POAF and to analyze its pharmacological management in patients scheduled for cardiac surgery. **Methodology:** A prospective observational study was carried out for 6 months (October 2016 to March 2017) in cardiothoracic surgery. Drug therapy details by medication chart review and clinical review in patients who underwent coronary artery bypass graft, mitral valve replacement (MVR), and aortic valve replacement was carried out and analyzed for the incidence of POAF. The statistical analysis was performed using SPSS. **Results:** A total of 83 patients were recruited for this study. The POAF incidence was 18.07% with the highest incidence on the 2nd postoperative day. The mean age of patients with POAF was 49.40 ± 12.77 years. Rheumatic heart disease and alcohol were identified as the predisposing factors of POAF. The incidence of POAF was the highest following MVR (80%) than other cardiac surgeries. Patients who developed POAF had a longer length of hospitalization (median 9 vs. 7 days). Amiodarone, metoprolol, verapamil, atorvastatin, clopidogrel, and aspirin were the most frequently prescribed drugs for the management of POAF. Administration of metoprolol, nebivolol, atorvastatin, bisoprolol, metoprolol + atorvastatin + aspirin, and other combinations before cardiac surgery reduced the risk of developing POAF. **Conclusion:** The overall incidence of POAF was 18.07%. Amiodarone (13.3%), metoprolol (40%), verapamil (66.7%), aspirin (26.7%), clopidogrel (13.3%), and atorvastatin (20%) were found to be safe and effective in the treatment of POAF patients.

Keywords: Atrial fibrillation, cardiac surgery, pharmacological, postoperative

INTRODUCTION

Every year more than 750,000 coronary artery bypass graft or heart valve surgeries are performed globally.^[1] Postoperative atrial fibrillation (POAF) is the most common complication after cardiac surgery, and its onset is usually between the 2nd and 4th day following the procedure with the peak incidence on the postoperative day 2.^[2] AF is distinguished by unorganized rapid and irregular atrial activation with the loss of atrial contraction and with an irregular ventricular rate that is diagnosed by AV nodal conduction. The ventricular rate also tends to be rapid and variable, in an untreated patient, between 120 and 160 beats/min, and in some patients, it may exceed 200 beats/min.^[3] Although the basic mechanism involved in the development of POAF is unknown, it may be related to atrial dilation from volume overload, sympathetic activation, or pericarditis or inflammation.^[1]

Different predisposing factors such as advanced age, previous history of AF, male gender, reduced left ventricular ejection

fraction (LVEF), valvular heart surgery, chronic obstructive pulmonary disease (COPD), chronic renal failure, diabetes mellitus, and rheumatic heart disease (RHD), associated with the development of POAF have been identified.^[4] In a study conducted by Tsai *et al.*, similar risk factors have been recognized along with dyslipidemia, smoking, and increased serum electrolytes.^[5] The possible risk factor for POAF also attributes to preoperative increase in P wave duration on the surface (>116 ms) or on signal-averaged (>140 ms) electrocardiography (ECG).^[6] Obese patients older than 50 years are also at a higher risk for the development of

Address for correspondence: Dr. Uday Venkat Mateti, Head, Department of Pharmacy Practice, NGSIM Institute of Pharmaceutical Sciences, Nitte (Deemed to be University), Paneer, Deralakatte, Mangalore - 575 018, Karnataka, India. E-mail: udayvenkatmateti@gmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: George PA, Varkey A, Nandan A, Mateti UV, Gopalakrishnan M, Theempalangad RM. Incidence of atrial fibrillation after cardiac surgery and its pharmacological management. Acta Med Int 2018;5:58-62.

Access this article online

Quick Response Code:



Website:
www.actamedicainternational.com

DOI:
10.4103/ami.ami_88_17

AF after isolated coronary artery bypass graft (CABG) surgery.^[7]

The reported incidence of POAF varies between 20% and 50%.^[6] It is approximately 30% after isolated CABG surgery, 40% following valve replacements and increases to approximately 50% after combined procedures.^[4] POAF is often associated with rapid ventricular rates, and the onset is frequently symptomatic. In the majority of cases, the diagnosis of POAF is based on 12-lead ECG findings. Patients with AF presents with an abrupt change in rhythm with the loss of P waves. The diagnosis can be confirmed by using atrial electrograms that are mostly used at the time of cardiac surgery.^[6]

POAF can result in higher risk of stroke and a longer duration of hospitalization, although it usually transforms spontaneously.^[1] The consequences of POAF include increased morbidity and mortality, prolonged length of hospital stay, and increased healthcare costs. Therefore, it remains as a significant challenge for patients, physicians, and healthcare policymakers due to its increasing prevalence, numerous complications, and large costs.^[8] A review study reported that to attain rhythm control in patients with POAF, drugs prescribed are amiodarone, sotalol, ibutilide, and procainamide, whereas, for rate control, drugs include digoxin, beta-blockers and calcium channel blockers in addition to anticoagulants for the prevention of stroke.^[4]

Over the past decades, the incidence of POAF has increased continuously. The incidence of AF is age-dependent, and due to the increasing proportions of elderly cardiac surgical patients, it is expected that the POAF incidence will rise in the future.^[7] Hence, this study was conducted to determine the incidence of POAF and to analyze its pharmacological management in patients scheduled for CABG, mitral valve replacement (MVR), and aortic valve replacement (AVR).

METHODOLOGY

Study design

A prospective observational study was carried out for 6 months between October 2016 and March 2017 among patients who underwent cardiac surgeries that includes CABG, mitral valve replacement (MVR), and aortic valve replacement (AVR).

Ethics

This study (REF: INST.EC/EC/106/2016–2017) was approved by the Institutional Ethics Committee, KS Hegde Medical Academy, Mangaluru. Informed consent was obtained from all individual participants included in the study.

Sample size

The sample size was calculated using below mentioned formula:

$$n = \frac{Z_{1-\alpha/2}^2 P(1 - P)}{d^2}$$

Where $Z_{1-\alpha/2} = 1.96$ (5%),

P (expected proportion) = 0.3,

d (precision) = 0.1,

The minimum sample required for conducting this study is 80.

Selection and description of participants

Inpatients of either gender, aged 18 years and above scheduled for CABG, valve surgery or mixed were included whereas, patients with severe congestive heart failure and those not willing to participate in the study were excluded from the study. A purposive sampling method was adopted for choosing patients.

A suitable data collection form was designed to collect and document the required data, which includes patient demographics, laboratory parameters, and prescription details from the patient's case notes, treatment charts, and relevant laboratory investigations. Demographic details such as patient's age, gender, date of admission, date of discharge, complaints on admission, past medical history, social habits, diagnosis, and a number of medication per prescription were collected. The vital signs, ECG, echo, and chest X-ray findings were noted. The medical records were thoroughly analyzed to assess the postoperative complication. Patients who underwent cardiac surgery were assessed for the incidence of POAF. All the prescriptions of the study population had been screened to analyze the prophylactic therapy and the treatment options for the management of POAF. The pharmacological interventions for POAF include amiodarone, metoprolol, verapamil, atorvastatin, clopidogrel aspirin, nebivolol, and bisoprolol. Medication and their dose, frequency, and route of administration taken by the patients during the study were also noted.

Statistical analysis

The incidence of AF after cardiac surgery and medications prescribed (yes/no) were documented in frequency and percentage. Descriptive statistics (mean \pm standard deviation and median) were used to describe continuous variables. Associations of categorical variables were tested using Chi-square/Fischer's exact test with $P < 0.05$ was considered as statistically significant. The statistical analysis was performed using SPSS software version 16.0 (IBM Corp., Armonk, NY, United States of America).

RESULTS

A total of 83 patients were enrolled based on the study criteria. Out of 83 patients, 15 patients developed POAF, and the incidence was 18.07%. The incidence was greater in patients who underwent MVR (80%) than after CABG (20%). POAF did not develop in any patients who underwent AVR. MVR is significantly associated with the development of POAF with $P = 0.000$. In the present study, the majority of the patients who experienced POAF belongs to the age group 40–60 (60%) followed by age groups <40 (20%) and >60 (20%). The mean age of patients with POAF is 49.40 ± 12.77 years. There is a significant difference in the mean age between the patients with and without POAF with a value of $P = 0.028$. Among the patients who experienced POAF, females (66.66%) were

found to have an increased incidence than males (33.33%). Female (66.66%) gender is significantly associated with the development of POAF than males (33.33%) with $P = 0.0001$.

The patients who developed POAF had RHD (53.33%), HTN (40%), diabetes (20%), and COPD (6.66%) as comorbidities. RHD is significantly associated with the development of POAF with $P = 0.000$. Out of 83 patients, 9.63% of patients had social habits. Out of 15 POAF patients, 6.66% of patients were smoker, 6.66% were alcoholic, and 6.66% patients had substance abuse. Alcohol is significantly associated with the development of POAF with $P = 0.032$. The incidence of POAF ranges between 1 and 8 postoperative days with the peak incidence on the postoperative day 2. The median onset of POAF was 2 days [Figure 1]. Patients who developed AF postoperatively had a longer length of hospital stay than those who did not develop AF (median 9 vs. 7 days) [Figure 2]. The clinical characteristics of patients are presented in Table 1.

Preoperative administration of metoprolol, nebivolol, atorvastatin, bisoprolol, metoprolol + atorvastatin + aspirin, metoprolol + aspirin, atorvastatin + aspirin, metoprolol + rosuvastatin, metoprolol + rosuvastatin + aspirin and amiodarone + atorvastatin + aspirin reduced the risk of developing AF after cardiac surgery whereas, patients who received propranolol, amiodarone, bisoprolol, diltiazem, aspirin, atorvastatin, and metoprolol + atorvastatin preoperatively, developed POAF. The most frequently used prophylactic drugs for patients scheduled for cardiac surgery is depicted in Table 2. The most commonly prescribed drugs for the management of POAF includes amiodarone (13.3%), metoprolol (40%), verapamil (66.7%), aspirin (26.7%), clopidogrel (13.3%), and atorvastatin (20%) [Figure 3].

Table 1: Clinical characteristics of patients with and without atrial fibrillation after cardiac surgery

Variables	AF (n=15)	Non-AF (n=68)	P
Age (years), mean±SD	49.40±12.77	56.72±11.21	0.028*
Sex (%)			
Male	5 (33.33)	59 (86.76)	0.000***
Female	10 (66.66)	9 (13.23)	
DM (%)	3 (20)	26 (38.23)	0.180
HTN (%)	6 (40)	38 (55.88)	0.265
COPD (%)	1 (6.66)	3 (4.41)	0.712
RHD (%)	8 (53.33)	6 (8.82)	0.000***
Dyslipidemia (%)	-	2 (2.95)	0.501
Renal dysfunction (%)	-	3 (4.41)	0.407
Smoking (%)	1 (6.66)	4 (5.88)	0.908
Alcoholic (%)	1 (6.66)	-	0.032*
Substance abuse (%)	1 (6.66)	1 (1.47)	0.235
CABG (%)	3 (20)	55 (80.88)	0.000***
MVR (%)	12 (80)	7 (10.29)	
AVR (%)	-	6 (8.82)	

DM: Diabetes mellitus, HTN: Hypertension, COPD: Chronic obstructive pulmonary disease, RHD: Rheumatic heart disease, CABG: Coronary artery bypass graft, MVR: Mitral valve replacement, AVR: Aortic valve replacement, AF: Atrial fibrillation, SD: Standard deviation. *P is significant at the 0.05 level; ***P is significant at the 0.001 level

DISCUSSION

AF is one of the most common complications occurring after cardiac surgery. It may be associated with atrial dilation from volume overload, sympathetic activation, or any inflammation. This complication can result in increased morbidity and mortality, longer length of hospitalization and increased health care costs.

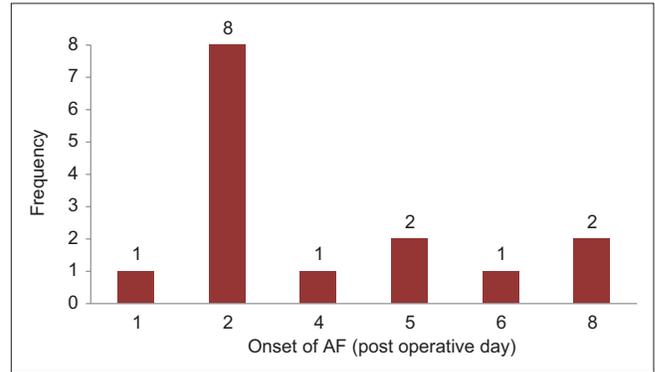


Figure 1: Incidence of atrial fibrillation in days after the procedure

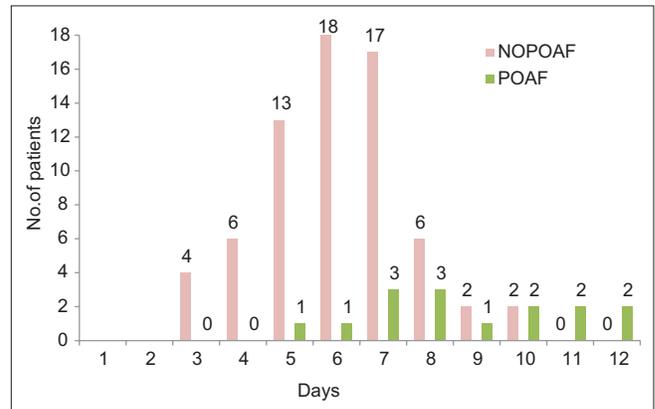


Figure 2: Length of hospital stay in patients with and without postoperative atrial fibrillation

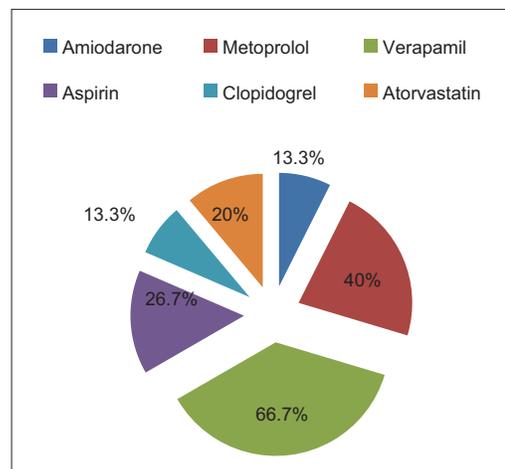


Figure 3: Patterns of commonly prescribed drugs in the management of postoperative atrial fibrillation

Table 2: Prophylactic drugs for patients with and without postoperative atrial fibrillation

Drugs used preoperatively	AF (n=15), Non-AF (n=68),		P
	n (%)	n (%)	
Amiodarone	3 (3.61)	2 (2.40)	0.002***
Metoprolol	3 (3.61)	16 (19.27)	0.682
Propranolol	1 (1.20)	-	0.032**
Nebivololol	-	1 (1.20)	0.637
Bisoprolol	-	1 (1.20)	0.637
Aspirin	1 (1.20)	3 (3.61)	0.712
Diltiazem	1 (1.20)	-	0.032**
Atorvastatin	-	2 (2.40)	0.501
MAA	-	13 (15.66)	0.065
MA	2 (2.40)	6 (7.22)	0.592
MAs	1 (1.20)	7 (8.43)	0.667
AA	-	3 (3.61)	0.407
MR	-	1 (1.20)	0.637
MRAs	-	1 (1.20)	0.637
AAA	-	1 (1.20)	0.637

MAA: Metoprolol + atorvastatin + aspirin, MA: Metoprolol + atorvastatin, MAs: Metoprolol + aspirin, AA: Atorvastatin + aspirin, MR: Metoprolol + rosuvastatin, MRAs: Metoprolol + rosuvastatin+aspirin, AAA: Amiodarone+atorvastatin + aspirin, AF: Atrial fibrillation. **P is significant at the 0.01 level, ***P is significant at the 0.001 level

In the present study, middle-aged patients of the age group 40–60 (60%) had an increased incidence of POAF when compared to advanced age, i.e., >60 (20%) and age below 40 (20%). However, contradictory results were shown by a study where the patients who developed POAF were greater than 75 years of age.^[9] Another study reported an 18% incidence of POAF in patients <60 years and 52% for those aged >80 years.^[10]

Female patients (66.66%) were found to have an increased incidence of POAF than males (33.33%). Similar results were shown by a study where female gender (16.7%) was associated with the development of POAF.^[11] This result is in contrast to a study wherein their study, the incidence of POAF was more in males (30.2%) than in females (27.4%).^[12] In this study, RHD and alcohol were identified as the risk factors for the development of POAF. These results are similar to a study where RHD was identified as the risk factor for POAF development in addition to diabetes, COPD, decreased LVEF and impaired renal function.^[4]

The overall incidence of POAF was found to be 18.07%. The peak incidence was found in patients who underwent MVR (80%), followed by CABG (20%). None of the patients developed POAF after AVR. Similar results were shown by a study where, the incidence of POAF was greater for MVR (48.8%), followed by AVR (32.9%) and CABG (27.6%).^[13]

The prophylactic drugs (that includes metoprolol, nebivolol, atorvastatin, bisoprolol, metoprolol + atorvastatin + aspirin, metoprolol + aspirin, atorvastatin + aspirin, metoprolol + rosuvastatin, metoprolol + rosuvastatin + aspirin and amiodarone + atorvastatin + aspirin given to the patients scheduled for cardiac surgery reduced the risk for developing

POAF. This result was similar to a study where amiodarone and beta-blockers (BBs) given as prophylaxis were found to be effective in preventing POAF.^[14] A study was conducted on the role of prophylactic statins in POAF patients and found that it was effective for the same.^[15]

In this study, the most commonly prescribed drugs for the management of POAF were amiodarone (13.3%), metoprolol (40%), atorvastatin (20%), verapamil (66.7%), clopidogrel (13.3%), and aspirin (26.7%). Similar results have been shown in a study where rhythm control was attained with Amiodarone and rate control with BBs, calcium channel blockers, or digoxin.^[16] The results are also supported by another study where they identified that statins can decrease the risk of cardiovascular events that includes myocardial infarction, stroke and death.^[17] In the present study, the onset of POAF was between the days 1 and 8 with the highest incidence on second postoperative day. This result is supported by a study where the patients included in their study developed POAF with the higher incidence between the 1st and 4th postoperative day.^[18] A retrospective study also showed similar results where the majority of patients in their study developed POAF within 3 days following surgery with the 2nd day being the most common.^[19] The length of hospital stay was increased in patients who developed POAF compared to patients who did not have POAF (median 9 vs. 7 days). Similar results were shown by a study where, for patients with POAF, the length of hospitalization was more than patients without POAF.^[20]

Study limitations

In this study, the study duration was less and a bigger sample size may give much better results. Furthermore, it was difficult to assess the patient's condition after discharge.

CONCLUSION

In this study, the incidence of AF in patients who underwent cardiac surgery was 18.07%. The incidence was higher in patients following MVR (80%) than after CABG (20%), whereas patients who underwent AVR did not experience POAF. The median onset of POAF was 2 days. The predisposing factors for the development of POAF include RHD and alcohol. POAF patients had a longer length of hospital stay when compared to patients without POAF (median 9 vs. 7 days). Amiodarone, metoprolol, verapamil, aspirin, clopidogrel, and atorvastatin were found to be safe and effective in the treatment of POAF patients. Metoprolol, nebivolol, atorvastatin, bisoprolol, metoprolol + atorvastatin + aspirin, metoprolol + aspirin, atorvastatin + aspirin, metoprolol + rosuvastatin, metoprolol + rosuvastatin + aspirin and amiodarone + atorvastatin + aspirin reduced the risk of developing POAF in patients undergoing cardiac surgery.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. White CM, Song JC, Kalus JS. Cardiac arrhythmias. In: Alldredge BK, Corelli RL, Ernst ME, Guglielmo BJ, Jacobson PA, Kradjan WA, editors. *Koda-Kimble & Young's Applied Therapeutics: The Clinical Use of Drugs*. 10th ed. United States of America: Lippincott Williams & Wilkin; 2013. p. 489-519.
2. Nair SG. Atrial fibrillation after cardiac surgery. *Ann Card Anaesth* 2010;13:196-205.
3. Michaud GF, Stevenson WG. Supraventricular tachyarrhythmias. In: Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J, editors. *Harrison's Principles of Internal Medicine*. 19th ed. United States of America: McGraw-Hill Education; 2015. p. 1485-6.
4. Alqahtani AA. Atrial fibrillation post cardiac surgery trends toward management. *Heart Views* 2010;11:57-63.
5. Tsai YT, Lai CH, Loh SH, Lin CY, Lin YC, Lee CY, *et al.* Assessment of the risk factors and outcomes for postoperative atrial fibrillation patients undergoing isolated coronary artery bypass grafting. *Acta Cardiol Sin* 2015;31:436-43.
6. Peretto G, Durante A, Limite LR, Cianflone D. Postoperative arrhythmias after cardiac surgery: Incidence, risk factors, and therapeutic management. *Cardiol Res Pract* 2014;2014:615987.
7. Echahidi N, Pibarot P, O'Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. *J Am Coll Cardiol* 2008;51:793-801.
8. Maddox TM, Nash IS, Fuster V. Economic costs associated with atrial fibrillation. *Contemporary cardiology*. In: Natale A, Jalife J, eds. *Atrial Fibrillation, From Bench to Bedside*. Totowa, NJ: Humana Press; 2008. p. 13-26.
9. Zaman AG, Archbold RA, Helft G, Paul EA, Curzen NP, Mills PG, *et al.* Atrial fibrillation after coronary artery bypass surgery: A model for preoperative risk stratification. *Circulation* 2000;101:1403-8.
10. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, *et al.* Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. *Circulation* 1996;94:390-7.
11. Perrier S, Meyer N, Hoang Minh T, Announe T, Bentz J, Billaud P, *et al.* Predictors of atrial fibrillation after coronary artery bypass grafting: A Bayesian analysis. *Ann Thorac Surg* 2017;103:92-7.
12. Filardo G, Ailawadi G, Pollock BD, da Graca B, Sass DM, Phan TK, *et al.* Sex differences in the epidemiology of new-onset in-hospital post-coronary artery bypass graft surgery atrial fibrillation: A large multicenter study. *Circ Cardiovasc Qual Outcomes* 2016;9:723-30.
13. Almassi GH, Schowalter T, Nicolosi AC, Aggarwal A, Moritz TE, Henderson WG, *et al.* Atrial fibrillation after cardiac surgery: A major morbid event? *Ann Surg* 1997;226:501-11.
14. Arsenault KA, Yusuf AM, Crystal E, Healey JS, Morillo CA, Nair GM, *et al.* Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. *Cochrane Database Syst Rev* 2013;1:CD003611.
15. Bockeria OL, Shvartz VA, Akhobekov AA, Kiselev AR, Prokhorov MD, Golukhova EZ, *et al.* Statin therapy in the primary prevention of early atrial fibrillation after coronary artery bypass grafting. *Indian Heart J* 2016;68:792-7.
16. Gillinov AM, Bagiella E, Moskowitz AJ, Raiten JM, Groh MA, Bowdish ME, *et al.* Rate control versus rhythm control for atrial fibrillation after cardiac surgery. *N Engl J Med* 2016;374:1911-21.
17. Fedoruk LM, Wang H, Conaway MR, Kron IL, Johnston KC. Statin therapy improves outcomes after valvular heart surgery. *Ann Thorac Surg* 2008;85:1521-5.
18. Rostagno C, La Meir M, Gelsomino S, Ghilli L, Rossi A, Carone E, *et al.* Atrial fibrillation after cardiac surgery: Incidence, risk factors, and economic burden. *J Cardiothorac Vasc Anesth* 2010;24:952-8.
19. Musa AF, Quan CZ, Xin LZ, Soni T, Dillon J, Hay YK, *et al.* A retrospective study on atrial fibrillation after coronary artery bypass grafting surgery at The National Heart Institute, Kuala Lumpur. *F1000Res* 2018;7:164.
20. Steinberg BA, Zhao Y, He X, Hernandez AF, Fullerton DA, Thomas KL, *et al.* Management of postoperative atrial fibrillation and subsequent outcomes in contemporary patients undergoing cardiac surgery: Insights from the society of thoracic surgeons CAPS-care atrial fibrillation registry. *Clin Cardiol* 2014;37:7-13.