

Original Research Article

Post-operative atrial fibrillation in off pump coronary artery bypass graft: association with medication

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Received: 20 September 2021

Revised: 04 October 2021

Accepted: 05 October 2021

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ABSTRACT

Background: Post-operative atrial fibrillation is a common post-operative complication and has significant morbidity and mortality. This study was done with an objective to determine the association of various medication use in patients undergoing coronary artery bypass graft (CABG) with post-operative atrial fibrillation (POAF).

Methods: This was a prospective observational study done in the department of cardiovascular and thoracic surgery of GMC Kottayam from December 2019 to December 2020 after obtaining institutional review board clearance. A sample size of 334 was fixed and patients undergoing off pump (OP) CABG were consecutively recruited in the study. The association of intraoperative and postoperative medication use with occurrence of POAF were analysed using the univariate analysis with a $p < 0.05$ using the SPSS 16 software.

Results: Peri-operative inotrope use was found to be significantly associated with post operative atrial fibrillation odds ratio 1.08 (95% CI 1.02-1.13). We could not find any association with preoperative use of beta blockers/agonist, antidiabetics, levothyroxine, ACE inhibitors or antiplatelet drugs. All the patients 60 (18%) who developed POAF were given amiodarone as per protocol.

Conclusions: Perioperative inotrope use was found to have significant association with the development of post operative atrial fibrillation following OPCABG. More multi-institutional studies with determination of association with individual drugs and doses with POAF need to be conducted in future.

Keywords: POAF, OPCABG, Inotrope use, Medication

INTRODUCTION

Off pump (OP) CABG has become the main approach in surgical revascularization of the heart over the past few decades. POAF is one of the most common postoperative complication following cardiac surgical procedures with an incidence of 10% to 40%.¹ Atrial fibrillation is an important cause of stroke, heart failure and death.² Several studies have been conducted to identify the predictors of atrial fibrillation in which high CHA₂DS₂-VASc (Congestive heart failure, hypertension, age >75 years, diabetes mellitus, prior stroke, transient ischemic

attack, thromboembolism, vascular disease), smoking, left ventricular ejection fraction, left atrial size have been found to be independent predictors or associated with POAF.^{1,3} The association of preoperative and perioperative medication like beta blocker use, preoperative antiplatelet therapy, nitrates, perioperative inotropes use have been assessed in some studies.^{1,4,5} However, the literature on medication use in patients developing POAF is sparse. This study was done with an objective to determine the association of various medication use in patients undergoing CABG with postoperative atrial fibrillation.

METHODS

This was a prospective observational study done in the department of cardiovascular and thoracic surgery of a government tertiary care centre, GMC Kottayam for a period of one year (December 2019-December 2020). In the study by Arribas-Leal et al, the incidence of postoperative AF following CABG was 23%, so sample size of 334 was fixed.³ All patients undergoing elective OPCABG surgery were consecutively included in the study after obtaining informed consent. Those with recent ischemic attack and chronic renal failure were excluded from the study.

Atrial fibrillation was defined to be sustained if persisting >10 minutes and such AF occurring until 7th post-operative day were recorded in a structured proforma in this study. For the purpose of analysis, only a first event was recorded. Approval was obtained from the institutional review board (IRB No. 103/2018 dated 28.02.2019). Statistical analysis was done using SPSS version 16.0. Descriptive data were expressed using mean or percentages and frequencies. The association of intraoperative and pre-operative medication use with occurrence of POAF were analysed using the univariate analysis with a p<0.05.

RESULTS

Three hundred and thirty-four patients who underwent OPCABG were consecutively recruited for this study. The proportion of patients who developed post operative atrial fibrillation was 60 (18%) of which 6 (10%) were females and 54 (90%) were males as shown in Figure 1.

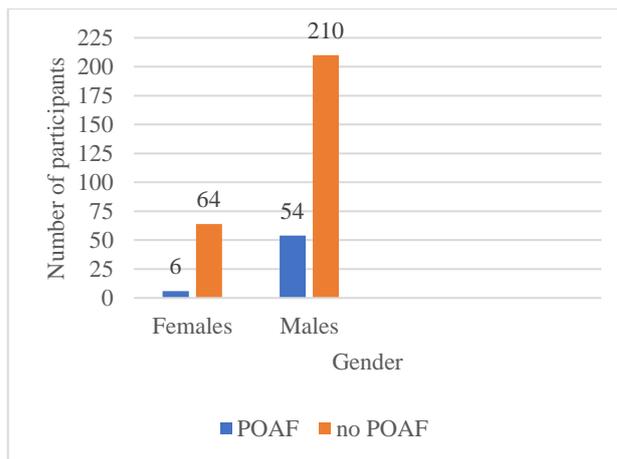


Figure 1: Gender-wise distribution of participants.

The mean age of patients who developed POAF was 61.38±7.63 years and that of patients who did not develop POAF was 58.43±8.11years.

POAF occurred the most on third postoperative day 33 (9.9%), 20 (6%) developed it on the second, four (1.2%) developed AF on the first and 3 (0.9%) developed it on the fourth post operative day.

The non-AF and AF group were compared in terms of use of medications like preoperative beta blockers, angiotensin converting enzyme inhibitors (ACEI), antiplatelet use, levothyroxine use, beta agonist use and perioperative inotrope use. Chi square test was done to evaluate binary variables.

Table 1: Association of medication use with POAF.

Variables	AF group, (n=60) (%)	Non-AF group, (n=274) (%)	P value	OR (95% CI)
Pre-operative				
Beta blocker	36 (60)	149 (54.4)	0.43	1.21 (0.76-1.93)
Antidiabetic medication	39 (65)	176 (64.2)	0.91	1.03 (0.64-1.67)
Levothyroxine	4 (6.7)	13 (4.7)	0.54	1.33 (0.55-3.25)
Beta agonist	1 (1.7)	1 (0.4)	0.23	0.24 (0.03-1.76)
Angiotensin converting enzyme inhibitors	9 (15)	56 (20.4)	0.34	0.73 (0.27-1.41)
Antiplatelet	14 (23.3)	72 (26.3)	0.64	0.88 (0.51-1.52)
Peri-operative inotrope use	59 (98.3)	250 (91.2)	0.05	1.08 (1.02-1.13)

As shown in Table 1, peri-operative inotrope use was found to be significantly associated with post operative atrial fibrillation (p=0.05, OR 1.08 (1.02-1.13). We could not find any association with pre-operative use of beta blockers/agonist, antidiabetics, levothyroxine, ACE inhibitors or antiplatelet drugs shown in Table 1 by p>0.05.

All the patients 60 (18%) who developed POAF were given injection amiodarone 150 mg IV bolus. If the arrhythmia was not reverted a second dose of 150 mg was repeated after one hour. This was followed by 900 mg IV

infusion over next 24 hours. Then the patient would be started on tablet amiodarone 200 mg in deescalating doses of thrice daily for a week, twice daily for a week and then once daily for a week.

DISCUSSION

This was a high-volume single center study where a total of 1198 cardiac cases are done of which 857 are CABG surgeries amongst which 731 are OPCABG. We recruited 334 consecutive patients who underwent OPCABG for this study. Atrial fibrillation is an arrhythmia

characterized by 350 to 600 atrial depolarization per minute without effective atrial contractions.⁷ It is one of the commonest encountered arrhythmias following CABG and the incidence of the same amongst ONCABG and OPCABG has been found to be comparable.⁸ Despite the benign course the propensity to increase the morbidity and mortality associated with POAF necessitates its prompt identification and management. Even though there are several studies which look into the predictors of POAF none have specifically evaluated the association of medication use of the patient with the development of the same.

We observed that there was a significant association of POAF with the use of perioperative inotrope use-odds ratio 1.08 (1.02-1.13) and postoperative inotrope use 3.81 (1.65-8.76) and the risk of developing POAF was higher in them. In a study evaluating the health outcomes with and without inotrope use in cardiac surgery by Nielsen et al the absolute event rate of arrhythmia was 35%.⁶ In our study, amongst the 309 patients who received perioperative inotrope 59 (19.1%) developed POAF. The use of Phosphodiesterase inhibitors and dobutamine carry a significant risk of arrhythmia related to the increase in intracellular calcium levels.^{9,10} In this institution noradrenaline and dobutamine were the routinely used inotropes. The clinical recovery after OPCABG is enhanced by improving the cardiac output and vascular tone when inotropes are used.¹¹ Various studies show that, several risk factors like advancing age, reduced ejection fraction, cardiomegaly, history of congestive cardiac failure, left main coronary artery disease and three vessel coronary artery disease are associated with need for inotropes.¹²⁻¹⁴ Inotropes are used to augment cardiac output, increase renal perfusion and stabilize hemodynamics in patients during and immediately following CABG surgery, however it has been associated with AF especially with a racial predilection for the black patients.^{5,15} This racial difference in POAF has been linked to genetic polymorphism in the Beta adrenergic signaling pathway which changes the β receptor sensitivity and density thus increasing the risk of developing POAF in patients receiving inotropes.^{16,17}

We could not find any statistically significant association of POAF with preoperative beta blockers, angiotensin converting enzyme inhibitors (ACEI), antiplatelet use, levothyroxine use, antidiabetic medication and beta agonist use. B blockers, which receive a class I recommendation from multiple societies for AF prophylaxis have been extensively used for the prevention of POAF after cardiac surgery. They cause decrease in sympathetic tone which increases atrial refractoriness and decreases the initiation of arrhythmias.¹⁸⁻²⁰ Even though metoprolol and esmolol are the commonly used drugs antioxidant property of carvedilol makes it a better drug than Metoprolol or esmolol.²¹ However, several studies have found that preoperative beta blocker is a risk factor of POAF.^{1,22,23} This might be attributed to the β blocker rebound

phenomenon occurring after temporary discontinuation for a few days from the day of operation. In this study out of the 185 patients on Beta blockers only 36 developed POAF.

Antiplatelet therapy was found to be an independent predictor of POAF in some studies.^{1,4} Perrier et al stated that interaction between the risk factors of antiplatelet treatment and atherosclerosis could act as a confounder.¹ Efirid et al., stated that in the presence of antiplatelets agents, the use of preoperative nitrates increased the POAF. They proposed that co-administration of nitrates with antiplatelet agents reduce the conversion rate of cyclic guanosine monophosphate to guanosine monophosphate and increase concentration of free radicals and catecholamines which predispose to POAF.⁴ It might also be due to the release of some proarrhythmic platelet activation compounds.²⁴ In this study amongst 86 patients on antiplatelet therapy 14 developed POAF.

Beta adrenoreceptor agonists used for bronchial dilation owing to β_2 receptor stimulation can increase heart rate due to β_1 receptor agonist activity and may precipitate arrhythmias depending on the difference in β receptor selectivity to inhalants among individuals.²⁵ A meta-analysis found that the initiation of treatment with β adrenoreceptor agonists increases heart rate and reduces potassium concentrations which can precipitate arrhythmias.²⁶ In this study only 2 patients were on β adrenoreceptor agonists of which one developed POAF and the other did not.

A study by Gong et al stated that among older persons treated with levothyroxine, levothyroxine at doses 75 microgram/day was associated with an increased risk of AF compared to lower exposure.²⁷ Levothyroxine can stimulate the pacemaker-related genes through transcription as well as the beta-adrenergic system in cardiomyocytes because of which heart rate increase.²⁸ In this study out of the 17 patients who were on levothyroxine only 4 developed POAF.

The protective effects of angiotensin blockade with ACE inhibitors or ARBs by direct action on the structural and electrical properties of the atria, as well as the indirect influence of improved control of heart failure and hypertension decreases the incidence of AF.²⁹ Reduction in atrial stretch due to increased left atrial (LA) pressure can affect the refractory period and conduction properties of atrial myocardium which triggers initiation and perpetuation of AF.³⁰ Of the 65 patients who received ACE inhibitors only 9 developed POAF.

All the patients who developed POAF received amiodarone. Amiodarone has been approved as an effective rhythm control agent that also has rate control therapy and there is level 1 evidence that perioperative use reduces the incidence of AF and is useful in patients with high risk.¹⁸

Limitations of study are that it was a single institution study. Since our study was observational unmeasured confounders could have influenced our findings. The doses and effects of individual medications were not assessed.

CONCLUSION

Perioperative inotrope use was found to have significant association with the development of post operative atrial fibrillation following OPCABG. We could not determine any association of medications like beta blockers/agonists, ACE inhibitors, antiplatelets or levothyroxine with the development of POAF. More multi-institutional studies with determination of association with individual drugs and doses with POAF need to be conducted in future.

ACKNOWLEDGEMENTS

Author would like to thank all the faculty and staff of dept. of CTVS of the institution. Also, thank SBMR for funding this research project.

Funding: Funding sources by State board of medical research, government of Kerala through government medical college, Kottayam

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Chooriyil N, Jayakumar TKN, Palappallil DS. Post-operative atrial fibrillation in off pump coronary artery bypass graft: association with medication. *Int J Res Med Sci* 2021;9:3319-23.