Atrial Fibrillation Following Coronary Artery Bypass Surgery in Medical Center Manila

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Abstract

BACKGROUND: Atrial fibrillation (AF) after coronary artery bypass graft (CABG) surgery may lead to prolonged hospital stay and increased morbidity and mortality. Identifying people at risk may help in the management and improve the outcome of patients undergoing this procedure.

OBJECTIVES: The aims of this were to determine the incidence of AF in patients who underwent CABG surgery in ManilaMed–Medical Center Manila and whether certain factors were associated with developing AF in patients who underwent the procedure.

METHODS: This was a single-center, retrospective, cross-sectional study wherein adult patients who underwent CABG, without previous AF, were included.

RESULTS: Among patients included in the study, 29 developed AF, with an incidence of 27.62%. Patients who had AF after CABG were, on average, older (65.79 vs 59.29 years, $P = 0.002$); had dyslipidemia (72% vs 47%, $P = 0.021$), a higher average left atrial volume index (LAVI) (26.72 vs. 23.45, $P = 0.038$), an LAVI greater than 34 mL/m^2 (24% vs 3%, $P = 0.002$), and an episode of previous stroke (28% vs 11%, $P = 0.038$); and had been taking diuretics (28% vs 9%, $P = 0.027$) but had a lower prevalence of having diabetes (41% vs 66%, $P = 0.023$).

CONCLUSION: Atrial fibrillation remains to be a frequent arrhythmia after CABG occurring in 28% of patients who had CABG. It may occur in older patients, patients with dyslipidemia, patients with a large left atrium, patients who had a previous stroke, and patients taking diuretics. On the other hand, the odds of a diabetic patient developing AF after CABG are low.

KEYWORDS: Cardiac Biomarkers, Chest CT, COVID-19, CT Severity, NT-proBNP, Troponin I

INTRODUCTION

According to the Philippine Statistics Authority, ischemic heart disease was the leading cause of death in the Philippines in 2016, comprising 12.7% of all causes of death. It is the leading cause of death in men and the second leading cause of death in women.[1] In 2017, the World Health Organization's latest data showed that coronary heart disease death reached 19.86% of total deaths in the Philippines.[2]

Coronary artery bypass graft (CABG) surgery is a common procedure and has been successfully performed in numerous patients with coronary artery disease (CAD). It has been shown to prolong survival in patients with multivessel CAD, patients with left ventricular systolic dysfunction, and those with severe symptoms with high-risk criteria on noninvasive testing.

The most common arrhythmia following CABG is atrial fibrillation (AF). In a prospective study by Thorén et al[3] performed at Uppsala University Hospital in Sweden, 19 of the 67 patients (28%) developed postoperative AF. Thirty percent of the 67 patients who underwent CABG later developed AF after discharge. Postoperative AF had a higher incidence of postdischarge AF compared with nonpostoperative AF patients with an odds ratio (OR) of 6 (95% confidence interval [CI], 1.9–19; $P = 0.002$).[3]

A retrospective study performed by Tadic et al[4] in 2011 showed that the incidence of AF among 322 patients who underwent first CABG was 22.4%. Using logistic regression analysis identified the following independent clinical variables as predictors of AF: age 65 years or older (OR, 1.78; 95% CI, 1.06–2.76; $P = 0.043$), hypertension (OR, 1.97; 95% CI, 1.15–3.21; $P = 0.018$), diabetes mellitus (OR, 2.09; 95% CI, 1.31–5.33; $P = 0.010$), obesity (OR, 1.51; 95% CI, 1.03–3.87; $P = 0.031$), and hypercholesterolemia (OR, 2.17; 95% CI, 1.05–4.25; $P = 0.027$).[4]

In a study performed by Gorczyca et al[5] at the Swietokrzyskie Center of Cardiology in Poland, 166 of the patients (21%) developed postoperative AF; 76.5% developed AF during the first 3 days after surgery. They also identified age older than 69 years (hazard ratio [HR], 2.3; 95% CI for HR, 1.6136–3.3316; $P < 0.0001$), low cardiac output syndrome after CABG (HR, 1.8; 95% CI for HR, 1.0935–3.1117; $P=0.0217$), and stable angina (HR, 1.7; 95% CI for HR, 1.1185–2.7312; $P=0.0142$) as predictors of postoperative AF.[5]

Patients who develop AF postoperatively had a higher prevalence of complications that is, stroke, pneumonia, and a longer hospital stay. Atrial fibrillation post-CABG surgery is also associated with higher mortality rates in the short and long term. This was evident in a multicenter observational prospective study performed by Almassi et al,[6] where both in-hospital mortality (5.95%, $P < 0.002$) and mortality at 6 months (9.36%, $P < 0.001$) were significantly higher in patients with postoperative AF. The study also identified 10 independent factors as predictors of postoperative AF such as increasing age (OR, 1.6; 95% CI, 1.48–1.75; $P < 0.0001$), chronic obstructive pulmonary disease (COPD) (OR, 1.37; 95% CI, 1.12–1.66; $P < 0.001$), and digoxin use (OR, 1.37; 95% CI, 1.10–1.70; $P < 0.003$), among others.[6]

Coronary artery bypass graft surgery is on the rise in ManilaMed–Medical Center Manila (MCM). Since the first CABG surgery in MCM, there has been no study to show the incidence of AF postoperatively. The knowledge on the clinicodemographic profile and perioperative variables of patients who underwent CABG can be used to develop a statistical model to help predict and stratify patients at risk of developing AF.

OBJECTIVES

The aims of this study were to determine the incidence of AF in patients who underwent CABG surgery in MCM and whether certain factors, such as age older than 65 years, male sex, diabetes, obesity, dyslipidemia, COPD, left atrial volume index (LAVI) greater than 34 mL/m^2, and ejection fraction (EF) of less than 40%, were associated with developing AF in postoperative patients who underwent bypass surgery.

METHODS

This was a single-center, retrospective, cross-sectional study conducted in MCM. Patients at least 19 years old who underwent CABG surgery in MCM from 2015 to 2020 with sinus rhythm preoperatively were included. Meanwhile, patients who had AF prior to surgery, patients with chronic kidney disease (CKD), and those with electrolyte imbalance were excluded.

The sample size was derived from one of the significant independent variables gathered from the review of related literature, in this case, diabetes with an OR of 2.09%. Using Epi Info version 7, the computed sample size was 124 patients.

Charts of patients who were admitted at MCM who underwent CABG were collected and reviewed. The patient's baseline clinicodemographic profile, that is, age, sex, presence of hypertension, diabetes, obesity, and dyslipidemia, was tabulated in Microsoft Excel (Microsoft Inc, Redmond, Washington, USA). The presence of AF was confirmed by 12-lead electrocardiogram postoperatively. Clinical postoperative data, such as number of vessels grafted, bypass time, cross-clamp time, duration of hospitalization, and any postoperative complications, were noted.

Data were encoded using Microsoft Excel worksheet and checked for completeness, correctness, and consistency prior to analysis. Descriptive analysis was used to determine the profile of the subjects. Measures of central tendency and variation (mean ± standard deviation and range) were used for quantitative variables and frequency distribution for categorical variables. The incidence of AF was computed by dividing the number of subjects who experienced AF after CABG by the total number of subjects for the duration of the study. The 95% CI of the incidence was also determined. Inferential analysis consisted of crude analysis (independent t test, Fisher exact test, and χ^2 test) and multiple logistic regression utilizing a direct (or standard) model to determine what variables are independently associated with AF at 5% level of significance. All analyses were performed using SPSS version 21 (SPSS Inc, Chicago, Illinois, USA).

The investigators gathered data from the patients' charts; hence, the proposal was submitted to the ethics review board of the center for approval. Once approved, a letter to the records section asking permission to review the patients' charts was submitted. Information was gathered using the data collection form. Each patient was assigned a number, and no personal information was collected. The files were kept in a cabinet secured with a lock located at the heart station on the fifth floor of MCM, and the data were encoded in the personal computer of the investigator with a password. Only the principal investigator and the research adviser had access to the data collected. Strict compliance to the Data Privacy Act of 2012 was enforced.

RESULTS

Demographic Characteristics

Of the computed sample size, the investigators were able to gather only 105 subjects. All the 105 subjects who underwent CABG were included in the study, and their demographic profile is presented in Table 1. Average age (± standard deviation) was 61.09 years with the youngest at 37 years and the oldest at 85 years old. Most of the subjects were male (87%).

Incidence of AF

Among the 105 subjects, 29 developed AF after CABG, giving an incidence of 27.62% over 6 years (2015–2020) with a 95% CI of 19.97% to 36.85%. This means that there is 95% certainty that the true incidence is between 19.96% and 36.85% over a period of 6 years.

Demographic and Clinical Profile of the AF Group

To determine the factors associated with AF after CABG, subjects were classified into two groups, namely, those "with AF" (AF group, 29 subjects) and those "without AF" (no AF or NAF group, 76 subjects), and these two groups were compared in terms of their characteristics. The comparison of their demographic and clinical characteristics is presented in Table 2.

In terms of demographic characteristics, the AF group was significantly older on average than the NAF group (65.79 vs 59.29 years, *P* = 0.002). Although there was a descriptively higher proportion of subjects 65 years or older in the AF group compared with the NAF group, this did not achieve statistical significance (45% vs 32%, *P* = 0.204). Also, there is a descriptively smaller proportion of males in the AF group compared with the NAF group (76% vs 91%), which was close to but did not achieve statistical significance (76% vs 91%, *P* = 0.057).

Table 1. Demographic Profile of Patients Who Underwent CABG

Demographic Characteristics	Value or Frequency, %
Age, y	
Mean ± SD	61.09 ± 9.72
Range	37–85
Gender	
Male	91 (87)
Female	14 (13)

In terms of clinical characteristics, the AF group significantly differed from the NAF group in terms of having

1. a higher prevalence of dyslipidemia (72% vs 47%, *P* = 0.021),
2. a lower prevalence of diabetes (41% vs 66%, *P* = 0.023),
3. a higher average LAVI (26.72 vs 23.45, *P* = 0.038) as well as a higher prevalence of LAVI of greater than 34 mL/m^2 (24% vs 3%, *P* = 0.002),
4. a higher prevalence of previous stroke (28% vs 11%, *P* = 0.038), and
5. a higher prevalence of diuretic use (28% vs 9%, *P* = 0.027).

The other clinical characteristics did not differ significantly between the AF Group and the NAF group (*P* > 0.05). Details of these comparisons are also presented in Table 2.

Variables Independently Associated With AF

A direct (or standard) model for logistic regression was predefined based on variables associated with AF in literature including age older than 65 years; male sex; and presence of obesity, COPD, diabetes mellitus, dyslipidemia, elevated LAVI (>34 mL/m^2), and depressed EF (<40%). Results of the multiple logistic regression analysis are presented in Table 3.

Among the subject characteristics in the multiple logistic regression model, only diabetes was independently associated with AF. The likelihood that those with diabetes would have AF is approximately only a quarter compared with those without diabetes (OR, 0.26; *P* = 0.020). The other factors (age >65 years; male sex; and presence of obesity, COPD, dyslipidemia, elevated LAVI, and depressed EF) did not have enough evidence of an independent association with AF (*P* > 0.05). However, two of these variables (presence of dyslipidemia and elevated LAVI) had *P* values that are fairly small (both 0.101 and very close to 10%). In such cases, it is possible that these variables are independently associated with AF, but the deficient number of subjects gathered in this study is inadequate to detect an association, and a larger sample size (corresponding to higher study power) may be needed to confirm it.

DISCUSSION

Our finding of 27.62% incidence of AF after CABG mirrors the finding from other studies wherein AF after CABG ranges from 21% to 28%.[3–5] This, however, was lower as compared with the study by Dr Malinis,[7] conducted from 1994 to 1998 at Cebu Heart Institute Perpetual Succor Hospital, which showed 46% incidence of AF after CABG and higher as compared with the study by Dr Garcia at the Philippine Heart Center in 2018, where the incidence was 18%.[8]

As the patient's age increases, there is loss of myocardial fibers and increase in fibrosis and collagen deposition in the atria. Patients with advanced age were consistently found to develop AF after cardiac surgery.[4,5,9,10] This was also the case in our study, but it was not an independent predictor from the multiple logistic regression analysis, similar to a few studies that did not report

Table 2. Demographic and Clinical Profile of Patients Undergoing CABG With and Without Atrial Fibrillation Postoperatively

Characteristics	With AF or AF Group (n = 29)	Without AF or NAF Group (n = 76)	P Value
Age, mean ± SD, range, y	65.79 ± 8.36, 52–85	59.29 ± 9.65, 37–76	0.002[a]
Age ≥65 y	13 (45)	24 (32)	0.204[b]
Male	22 (76)	69 (91)	0.057[c]
Hypertension	28 (97)	68 (90)	0.439[c]
BMI, mean ± SD, range, kg/m^2	26.72 ± 5.13, 16–38	27.07 ± 4.31, 19–46	0.731[a]
Obesity (BMI >27.5 kg/m^2)	11 (38)	30 (40)	0.885[a]
Creatinine, mean ± SD, range, mg/dL	1.28 ± 0.91, 0.53–5.70	1.04 ± 0.56, 0.50–4.97	0.206[a]
eGFR ≤30 mL/min	0 (0)	5 (7)	0.319[c]
Smoking	15 (52)	45 (59)	0.488[b]
COPD	3 (10)	7 (9)	1.000[c]
Dyslipidemia	21 (72)	36 (47)	0.021[b]
Diabetes mellitus	12 (41)	50 (66)	0.023[b]
Left main artery involvement	11 (38)	26 (34)	1.000[c]
Three-vessel CAD	26 (90)	65 (86)	0.753[c]
NYHA class I II III IV	 0 22 (76) 7 (24) 0	 0 66 (87) 10 (13) 0	0.235[c]
NYHA classes III–IV	7 (24)	10 (13)	0.235[c]
EF, mean ± SD, range, %	53.59 ± 13.09, 31–84	54.78 ± 13.45, 23–77	0.684[a]
Depressed EF (<40%)	4 (14)	10 (13)	0.319[c]
LAVI, mean ± SD, range	26.72 ± 8.60, 12–47	23.45 ± 6.50, 10–38	0.038[a]
LAVI >34 mL/m^2	7 (24)	2 (3)	0.002[c]
Left ventricular mass index	110.34 ± 40.91, 67–216	104.46 ± 25.98, 62–196	0.475[a]
Diastolic dysfunction	22 (76)	44 (58)	0.115[c]
Previous MI	9 (31)	25 (33)	1.000[b]
Previous stroke	8 (28)	8 (11)	0.038[c]
Statin	23 (79)	60 (79)	0.967[b]
β-Blocker	19 (66)	40 (53)	0.234[b]
Amiodarone	1 (3)	4 (5)	1.000[c]
ACE inhibitor	23 (79)	60 (79)	0.967[c]
Aspirin	16 (55)	42 (55)	0.993[c]
Calcium-channel blocker	12 (41)	23 (30)	0.280[c]
Diuretic use	8 (28)	7 (9)	0.027[b]

[a]Independent t test used.
[b]Two-sided Fisher exact test used.
[c]Two-sided χ^2 test used.
ACE=angiotensin-converting enzyme; BMI, body mass index; CAD=coronary artery disease; COPD=chronic obstructive pulmonary disease; EF=ejection fraction; eGFR=estimated glomerular filtration rate; LAVI=Left atrial volume index; MI=myocardial infarction; NYHA=New York Heart Association; SD=standard deviation.

Table 3. Multiple Logistic Regression Analysis Results on Association of Subject Characteristics With Atrial Fibrillation

Characteristics	OR	95% CI	*P* Value
Age >65 y	1.39	0.50–3.92	0.529
Male sex	0.31	0.07–1.33	0.115
Obesity	1.59	0.56–4.54	0.383
COPD	0.97	0.19–5.13	0.975
Diabetes	0.26	0.08–0.81	0.020
Dyslipidemia	2.44	0.84–7.08	0.101
Elevated LAVI (>34 mL/m^2)	4.68	0.74–29.57	0.101
Depressed EF (<40%)	1.53	0.28–8.37	0.621

CI=confidence interval; COPD=chronic obstructive pulmonary disease; EF=ejection fraction; LAVI=left atrial volume index; OR=odds ratio.

age as an independent variable.[11,12]

Male sex was another independent predictor of post-CABG AF.[12,13] Mathew et al[14] noted the odds of developing postoperative AF were increased by 41% in men, brought about by sex-based difference in the expression of ion channels, hormonal effects on autonomic tone, and difference in the myocardial architecture and fiber orientation. Male sex, however, did not show a statistically significant relationship to AF after CABG in our study.

Obesity, another independent predictor of post-CABG AF,[4,15] causes AF from increased preload, leading to left ventricular diastolic dysfunction, hypertrophy, and left atrial remodeling.[16] This, together with postoperative volume overload, induces left atrial enlargement, leading to more AF as confirmed in the study by Tadic et al.[4] In this study, no association was noted on logistic regression analysis.

In the study by Almassi et al,[6] COPD proved to be a predictor of postoperative AF. Ventilation perfusion mismatch and hypoxia were aggravated by poor ventilator mechanics and atelectasis in the perioperative period. Furthermore, hypoxia, together with COPD, predisposes patients to developing premature atrial contractions that may lead to AF.[6] The study was also not able to show an association.

An EF of less than 40% was also noted by some studies to be an independent predictor of post-CABG AF,[10,11] as well as an LAVI of greater than 34 mL/m^2.[11] An enlarged left atrium produces disorganization of the atrial muscle bundles, leading to disparate conduction velocities and inhomogeneous refractory periods. Our study did not show lower EF of less than 40% having more incidence of post-CABG AF; however, we noted more patients with higher-than-average LAVI and LAVI greater than 34 mL/m^2 developing AF after CABG. These findings, however, were not significantly associated with AF post-CABG.

Histologic changes brought about by lipid deposits, atrial dilation, and increasing age produce nonuniform anisotropic conduction within the atria, resulting in slow electrical conduction, which provides a substrate for arrhythmia formation.[17] Patients with dyslipidemia were noted to develop AF after CABG in our study, but it was not an independent predictor of post-CABG AF as compared with a previous study by Tadic et al.[4]

Diabetes was a strong independent predictor of AF in the study by Tadic et al,[4] whereas some did not show that diabetes was associated with postoperative AF.[9,10] The enhanced oxidative stress, together with high free fatty acids and chronic inflammation, in patients with diabetes leads to left ventricular dysfunction, which affects the left atrial structure and electrophysiology. This was a counterintuitive finding in our study where patients with diabetes were less likely to develop postoperative AF.

The exact pathophysiologic mechanism of AF after cardiac surgery has yet to be determined, but from the earlier findings, the cause must be multifactorial. These factors may be the reason why the results of different studies, including our own, varied. Moreover, the manner used to detect AF, the perioperative care that the patients receive, the surgical approach used, and the wide variability in the baseline characteristics all together contribute to the diverse findings.

Aside from the limitations of a retrospective study, other limitations of our study may be due to the small sample size we were able to gather during the study period. There is also the possibility of underestimating patients who developed AF because AF may develop even after only the first few days postsurgery. We were also limited to the sexual variability because most of our study subjects were male. Finally, we recommend doing a multicenter, multiracial study to strengthen the applicability of the study.

CONCLUSION

Atrial fibrillation remains to be a frequent arrhythmia after CABG, occurring in 28% of patients who had CABG. It may occur in older patients, patients with dyslipidemia, patients with large left atrium, patients who had previous stroke, and patients taking diuretics. On the other hand, the odds of a diabetic patient developing AF after CABG are low.

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