

Value of Atrial Fibrillation Prophylaxis after Coronary Artery Bypass Graft Surgery

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ABSTRACT

Background: Heart surgery patients who develop acute and new-onset AF (postoperative atrial fibrillation, POAF) are among the most common postoperative complications, affecting around 35 percent of those who undergo the procedure. **Objective:** To assess the effectiveness of amiodarone in prophylaxis of AF post coronary artery bypass surgery (CABG).

Patients and Methods: Our work represents a randomized clinical trial, which was carried out at National Heart Institute and Zagazig University from the period of August 2020 to June 2021. 68 patients, admitted for CABG and had high risk score according to POAF score, were included in our study.

Results: Regarding mean left ventricular ejection fraction (LVEF), in group I was 47.52 ± 5.85 while in group II it was 49.85 ± 6.25 . There was a statistically non-significant difference between the groups with a P value of 0.414. Mean Intensive Care Unit (ICU) period was 4.42 ± 1.35 in group I, and group II was 2.73 ± 0.95 . The difference between the groups was statistically significantly shorter among group II (prophylaxis group) ($P < 0.01$). Regarding development of POAF, in group I, the incidence of POAF was 85.3% while in group II, it was 38.2%. Difference among the two studied groups was statistically significantly lower in the group II (prophylaxis group).

Conclusion: A prophylactic amiodarone strategy dramatically decreased incidence of POAF risk. All previous estimations of POAF risk reduction using prophylactic amiodarone were found to be accurate. Amiodarone was more effective in preventing postoperative atrial fibrillation with no serious side effects and it decreased postoperative ICU stay.

Keywords: Amiodarone. Coronary Artery Bypass Graft, Postoperative Atrial fibrillation.

INTRODUCTION

Heart surgery patients who develop postoperative atrial fibrillation (POAF) face the greatest risk of death. It is most common on the second postoperative day for POAF to occur. About one-third of patients who undergo heart surgery develop POAF, according to prior studies resulting in higher intensive care unit admissions with more costs as well as increasing hospital stay ⁽¹⁾.

Tachyarrhythmia is the most common symptom of POAF, which has a wide range of repercussions on the cardiovascular system. Myocardial ischemia can occur as a result of insufficient coronary flow compensating for the high myocardial oxygen demand caused by an irregularly rapid ventricular rhythm. As a result of tachyarrhythmias, diastolic filling time and cardiac output can be significantly lowered ⁽²⁾. A bradyarrhythmia in sequence of atrial fibrillation (AF) can reduce cardiac output in patients who have a fixed stroke volume. The absence of atrial contraction, especially in patients who had diastolic dysfunction and hypertension, results in an increase in pressure of pulmonary arteries ⁽³⁾.

POAF is a common complication following heart surgery, although its specific cause remains a mystery. Patients, surgeons, anesthesiologists, and postoperative circumstances were thought to play a role in its emergence. Excessive catecholamine release, systemic inflammation, vasoplegia, alterations in sympathetic and parasympathetic tone, neurohumoral activation, and significant fluid shifts are all possible stimuli for arrhythmia following cardiac surgery, which makes it a risk factor for the procedure ⁽⁴⁾.

The POAF has been linked to a higher death rate and longer hospitalizations. In addition, patients who acquired POAF had a worse long-term prognosis than those who did not. An additional 2 to 4 times the risk of stroke, infection, reoperation, cerebral problems, and cardiac arrest, renal or respiratory failure are borne by patients with POAF who develop additional hospital treatment costs. They may also require an intervention as permanent pacemaker ⁽⁵⁾. After surgery, there is no established treatment for AF. During the last few decades, the majority of research has concentrated on ways to avoid its occurrence. AF following surgery can be effectively treated with amiodarone. After heart surgery, there have been few studies that have proven its therapeutic effects, thus the investigations concentrated on its preventative effects ⁽⁶⁾.

A Class III Vaughan-Williams antiarrhythmic medicine, amiodarone also has some of the effects of Class I and II antiarrhythmic drugs as well. The drug slows the repolarization of myocardial cells by inhibiting potassium channels, resulting in a reduction in membrane potential. Blood vessels in the limbs and coronary arteries can be dilated with amiodarone. Amiodarone can be used orally or intravenously. When amiodarone is administered as a vascular injection at doses of 2.5–10 mg/kg, it has been shown to be safe and effective, a decrease in heart rate, the persistence of peripheral arteries, and a boost to the left ventricle's contractile force are all possible outcomes. Even in patients with low ejection fraction (EF), oral doses are sufficient to treat



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cardiac arrhythmia and do not cause a drop in the left ventricular discharge fraction. The absorption of oral amiodarone is sluggish and partial. 37 hours after a single dose, oral concentrations are at their highest value. More than 10 to 15 times as much medication is found in the myocardium as in the bloodstream. The liver is the primary organ responsible for the majority of amiodarone's metabolism. Consequently, renal illness patients do not necessitate a reduction in the dosage. After a few hours of intravenous administration, its effects begin to take hold (6).

Ventricular arrhythmia, interstitial pneumonia, heart block, bradycardia as well as poisoning of the liver are the most common side effects of amiodarone. After surgery, the exact mechanism of the drug's effects on AF are unknown. The combination of antiadrenergic and antiarrhythmic actions is likely responsible for the drug's effectiveness (6).

Amiodarone's ability to prevent atrial fibrillation (AF) during coronary artery bypass surgery was the primary goal of this study.

PATIENTS AND METHODS

The randomized clinical trial was carried out at National Heart Institute and Zagazig University from the period of August 2020 to June 2021. During the study period 210 patients were admitted for CABG (160 from National heart institute and 50 from Zagazig university hospitals). According to the POAF score, 68 patients were classified as high risk (7) and were included in our study and there were 62 patients excluded because of mitral valve replacement (MVR) and aortic valve replacement (AVR) as well as 80 patients who were eliminated because of a low POAF score (7).

68 patients had high risk score according to POAF score and were included in our study

Ethical considerations:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee, the study was allowed (ZU-IRB#6215). Every patient signed an informed written consent for acceptance of sharing in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: During the study, sinus rhythm was observed in patients who underwent coronary artery bypass graft surgery.

Exclusion criteria:

Preoperative AF, if there is any. Ischemic heart disease within the previous two weeks of surgery, fewer

than 55 beats per minute for the heart rate, conduction abnormalities of a serious nature, overt cardiac failure, frequent extra systoles, or any other uncontrolled arrhythmias need the use of an implantable defibrillator. An imbalance of electrolytes. Thyroid disease and pre-excitation syndromes.

Patients were categorized into two groups:

Amiodarone prophylaxis was not administered to 34 patients in Group 1, and Group 2, 34 individuals received amiodarone as a preventative measure.

This is what all of the participants in this research had to go through:

1. Inquiry into the patient's medical history and physical examination.
2. **ECG with the standard 12-leads:** Every patient's preoperative ECG was recorded using the standard 12-leads ECG. Intensive care unit patients underwent continuous ECG monitoring following surgery. When tachycardia or irregular pulses were observed or patients complained of palpitations, more ECG recordings were taken. Abnormal heartbeat (AF) was described as an abnormally irregular rhythm with a changing baseline and no discernible P waves. To qualify for inclusion in the study, POAF episodes lasting fewer than 30 seconds during the postoperative hospital stay were defined.
3. **Resting Transthoracic Echocardiography (TTE):** To detect anomalies in wall motion and to evaluate LV systolic function. [Philips Epic 7 machine in National heart institute and Vivid 9, General Electric Healthcare (GE Vingmed), Norway] were used to estimate EDD, ESD, PWD; IVSD; FS; LVEF; LA dimension; and RV function by TAPSE for all subjects. All measures were taken blindly by two independent echo experts for all subjects according to ASE recommendations (8).
4. **SYNTAX score analysis and coronary angiography:** The syntactic score was calculated using coronary arteries with a diameter of at least 1.5 mm that had more than 50% stenosis.
5. **The following parameters were used to score each patient:** Lesions, segments included in each lesion, presence of total blockage, bifurcation, aorta-ostial lesion, calcification, thrombus, diffuse/small vessel disease and lesion length of more than 20 mm are all factors in determining coronary dominance. When there was a disagreement between the two coronary angiography experts who determined the SYNTAX score, the mean value was used (9).
6. **POAF Score.**

Table (1): POAF Score

Item	Score
Age >60 y	1
Smoking	1
COPD	1
CP bypass time (min) >86.5	2
Vent. Time <23.5	2
PLR >113.4	3
LVEF <53.5	3
RV function by TAPSE <2.15	3
SYNTAX score >34.5	4
Total	20

Statistical analysis

In order to analyse the data acquired, it was loaded into a computer and run via the Statistical Package for the Social Sciences, version 25. (SPSS). Tables were

used to present the findings. The Shapiro–Wilk test was used to examine the distribution properties of variables as well as the homogeneity of variance. The quantitative data were reported in the form of the mean and standard deviation. The frequency and proportions of qualitative data were used to present the information. For quantitative independent data, the student’s t test (T) and the Mann-Whitney test (MW) were employed to examine the data as needed. To examine qualitatively independent data, researchers employed the Pearson Chi-Square test and Fisher’s exact test. P value equals or lower than 5 percent was considered significant.

RESULTS

There was no statistically significant difference could be seen between the two groups as regard age, BMI, sex, and smoking (Table 2).

Table (2): Comparison of age, BMI, sex, and smoking between studied groups

			Prophylaxis with Amiodarone		t/ X ²	P
			Group I (No) (No.=34)	Group II (Yes) (No.=34)		
Age			59.35±4.99	59.88±8.93	0.302	0.764
BMI			28.45±1.17	28.97±2.55	1.077	0.285
Sex	Female	N	7	2	3.20	0.074
		%	20.6%	5.9%		
	Male	N	27	32		
		%	79.4%	94.1%		
Smoking	No	N	8	4	1.61	0.203
		%	23.5%	11.8%		
	Yes	N	26	30		
		%	76.5%	88.2%		
Total		N	34	34		
		%	100.0%	100.0%		

BMI: Body Mass Index

The difference between the groups was statistically non-significant as regard echo and SYNTAX score (Table 3).

Table (3): Comparison of echo and SYNTAX score between studied groups

	Group I (No)	Group II (Yes)	t	P
EF	47.52±5.85	49.85±6.25	1.587	0.117
LA Diameter	3.59±0.31	3.82±0.64	1.884	0.064
RV Function by TAPSE	1.79±0.29	1.88±0.29	1.128	0.205
SYNTAX score	40.76±6.86	38.85±10.09	0.913	0.364

EF: Ejection Fraction, LA: Left Atrial, RV: Right Ventricle, TAPSE: Tricuspid annular plane systolic excursion

The mean ICU Period was statistically significantly shorter among group II (Table 4).

Table (4): CP Bypass Time, Vent Time and ICU period distribution between studied groups

	Group I (No)	Group II (Yes)	t	P
CP Bypass Time	104.52±16.58	116.79±32.51	1.959	0.054
Vent Time	21.26±2.72	24.17±8.02	0.977	0.332
ICU Period	4.42±1.35	2.73±0.95	5.67	<0.01**

CP Bypass Time: Cardiopulmonary Bypass Time, Vent Time: Ventilation Time, ICU Period: Intensive Care Unit Period

Regarding development of POAF, Group II had a statistically significant lower percentage of POAF cases than group I (Table 5).

Table (5): Development of POAF distribution between studied groups

			Prophylaxis with Amiodarone		X ²	P
			Group I (No)	Group II (Yes)		
Development of POAF	NO	N	5	21	15.94	<0.01**
		%	14.7%	61.8%		
	Yes	N	29	13		
		%	85.3%	38.2%		
Total		N	34	34		
		%	100.0%	100.0%		

POAF: Postoperative Atrial Fibrillation

Response of POAF to treatment was insignificantly higher in group I due to intraoperative and postoperative complication lead to death of one patient (Table 6).

Table (6): Comparison of response of POAF treatment between studied groups

			Prophylaxis with Amiodarone		X ²	P
			Group I (No)	Group II (Yes)		
Treatment of AF response	Not respond	N	0	1	1.01	0.31
		%	0.0%	2.9%		
	Respond	N	29	12		
		%	100.0%	97.1%		
Total		N	29	13		
		%	100.0%	100.0%		

AF: Atrial Fibrillation

There was no statistically significant difference between the two groups as regard complications (Table 7).

Table (7): Complication distribution between studied groups

			Prophylaxis with Amiodarone		X ²	P			
			Group I (No)	Group II (Yes)					
Complication	Death	N	0	1	4.46	0.21			
		%	0.0%	2.9%					
	Stroke	N	3	1					
		%	8.8%	2.9%					
	HF	N	1	2					
		%	2.9%	5.8%					
	Bradycardia and Hypotension	N	0	7					
		%	0.0%	20.5%					
	Total		N	34			34		
			%	100.0%			100.0%		

HF: Heart Failure

DISCUSSION

Atrial fibrillation is widespread during the first to fifth postoperative days, and some of the possible effects include hypotension, an extended duration of stay in the hospital, heart failure, increased risk of stroke, the requirement for long-term mortality and use of anticoagulation ⁽¹⁰⁾. After coronary artery bypass graft (CABG) surgery, atrial fibrillation and flutter are common postoperative complications, and both the length of stay in the intensive care unit and the overall length of hospitalization are adversely affected ⁽¹¹⁾.

Anti-arrhythmic drugs such amiodarone, B-blockers, and sotalol have showed promising benefits in the prevention of AF. In recent years, amiodarone has been found to lower the incidence of POAF, shorten

hospitalizations, and reduce hospital expenditures by utilizing both IV and oral amiodarone ⁽¹²⁾.

In the current study, in terms of age, BMI, smoking, and sex distribution, there was no statistically significant difference between the two groups. The mean age in Group I was 59.35±4.99 years, while the mean age in Group II was 59.88±8.93 years. These findings came in agreement with **Cagli et al.** ⁽¹³⁾, there was statistically a non-significant difference regarding age, BMI, smoking and sex distribution between the studied groups. In the combination group, the average age was 56.4±9.5 years; in the amiodarone group, it was 61.5± 9.5 years; and in the control group, it was 61.8± 9.2 years. However, against our results regarding

age, **Thorén et al.** ⁽¹⁴⁾ reported statistically significant difference ($P < 0.001$) between the included groups, Also **Navani et al.** ⁽¹⁵⁾ reported statistically significant difference regarding age ($P < 0.001$) between the studied groups with higher values of mean age. A tiny sample size may be to blame for this disparity.

Non-significant differences in echo and SYNTAX score were seen between the groups studied in our research. According to **Dogan et al.** ⁽¹⁶⁾, there was no statistically significant difference in the distribution of echo and SYNTAX scores across the groups studied. However, against our results, **Tsai et al.** ⁽¹⁷⁾ reported statistically a significant difference between the studied groups regarding LVEF, it was lower in the POAF patients.

In our study, development of POAF was statistically significantly lower in group II (prophylaxis group) as only 38.2% of group II develop POAF while in group I (didn't take amiodarone as a prophylaxis) POAF occurred in 85.3% patients. These findings came in agreement with **Zhu et al.** ⁽¹⁸⁾, prevention of POAF by using amiodarone prophylaxis was found to be more effective ($p = 0.03$ compared to placebo in patients receiving amiodarone).

Mitchell et al. ⁽¹⁹⁾ also found that amiodarone medication during the perioperative phase reduced the incidence of POAF by 16 percent in the amiodarone group compared to 25 percent in the placebo group.

Also, in **Fuster et al.** ⁽²⁰⁾ preventing atrial fibrillation in high-risk individuals can also be done with amiodarone, which has been shown to be superior to placebo in CABG patients.

A non-significant statistical difference in POAF treatment responses in our study was found between the analyzed groups. Many studies have shown that amiodarone reduces the risk of postoperative atrial fibrillation, as documented in **Buckley et al.** ⁽²¹⁾, prophylactic amiodarone has been shown to minimize the risk of atrial fibrillation following CABG, with a significant response in the prophylaxis group of patients.

Onk and Erkut ⁽²²⁾ found that amiodarone was well tolerated and did not produce substantial problems postoperatively, in keeping with our findings. Amiodarone has a number of negative effects that have been discovered as a result of its increased use. These are generally well tolerated and can easily be reduced in dosage, so cessation of therapy is rarely necessary. It was shown that the incidence of postoperative sustained ventricular tachyarrhythmia was lower in amiodarone patients (1/299; 0.3 percent) than in placebo patients (8/302; 2.6%, $P=0.25$). It was found that three of these occurrences resulted in death in patients who received placebos. Both treatment groups had similar rates of serious nonfatal postoperative complications and operative mortality due to these and other factors.

CONCLUSION

Our study shows that, amiodarone prophylaxis strategy dramatically decreased incidence of POAF risk. All previous estimates of POAF risk reduction using prophylactic amiodarone were consistent with this effect. Amiodarone was more effective in preventing postoperative atrial fibrillation with no serious side effects and decrease postoperative ICU stay.

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