New-onset atrial fibrillation after coronary artery bypass grafting: A prospective study between off-pump and on-pump surgery

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Background
Atrial fibrillation (AF) is one of the most common complications after cardiac surgery. It occurs mostly between the second and the third postoperative day. The aim of this study was to compare the distribution of the incidence of AF between patients operated upon with the standard on-pump coronary artery bypass grafting (CABG) and off-pump CABG techniques.
Materials and methods
This was a prospective analysis of 173 patients with coronary artery disease operated upon at the Dar Al Fouad Hospital and the National Heart Institute. Eighty-five patients undergoing off-pump CABG were matched for age and number of distal anastomoses with another 88 patients undergoing on-pump CABG. The possible risk factors for postoperative new-onset AF were recorded.
Results
AF occurred in 42 (24.3%) of the 173 patients for whom data could be analyzed. AF occurred in 19 patients (22.4%) in the off-pump group versus 23 (26.14%) in the on-pump group, but this difference was not statistically significant. On univariate analysis, age and serum creatinine levels were found to be the significant risk factors for the occurrence of AF. In a multivariate analysis that included operative technique, age was found to be the only significant risk factor. Also, the length of hospital stay was significantly longer in the on-pump group ($P < 0.05$).
Conclusion
The occurrence of AF after CABG does not depend on the type of operation of CABG.

Keywords:
atrial fibrillation, coronary, coronary artery bypass grafting, grafting, off-pump

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia following coronary artery bypass grafting (CABG), with a reported incidence of 20–40% [1,2]. Although AF is a benign arrhythmia, it may result in hemodynamic compromise, anxiety, thromboembolism, and prolonged hospital stay. The pathophysiological mechanism of AF after cardiac surgery is uncertain, but it has been suggested to be related to the extracorporeal circulation (ECC), atrial cannulation, myocardial ischemia, and the preservation techniques required during these procedures. Off-pump CABG does not require atrial cannulation, ECC, or cardioplegic arrest. This study compared the incidence of postoperative new-onset AF in patients undergoing first-time elective off-pump CABG through median sternotomy with that in patients undergoing first-time elective on-pump CABG.

Materials and methods

Patients were divided into two groups: (a) patients undergoing first-time elective off-pump CABG and (b) patients undergoing first-time elective on-pump CABG with ECC and cardioplegic arrest. Patients were allocated alternately to these two groups, which were matched for age and number of distal anastomoses performed.

Exclusion criteria included concomitant operations, such as valve repair or replacement, aneurysmectomy, myocardial infarction (MI) less than 1 month before surgery, second or third degree atrioventricular block, sick sinus syndrome, a previous history of AF, a previous stroke or transient ischemic attack, a left ventricular ejection fraction of less than 30%, and redo CABG. Patients in the off-pump CABG group converted to on-pump CABG during surgery and also patients on corticosteroid therapy were excluded from the study.

Preoperative and postoperative medications

Medications such as β-blockers, calcium channel blockers, and antihypertensives were stopped on the possible day of surgery. On the first postoperative day, medications were restarted depending on the clinical situation.

Anesthetic technique

Premedication was performed on the night of the operation by administration of oral bromazepam (Lexotanil, 1.5 mg) and morphine sulfate (10 mg) intramuscularly 1 hour before surgery.

Induction of anesthesia

When the patient reached the preparation room, a peripheral cannula (18 G) was inserted and midazolam (2 mg) was administered as soon as the standard pulse oximeter and ECG monitor were applied. An intra-arterial catheter (20 G) was placed in the radial artery of the nondominant hand under local anesthesia before induction, and if the left radial artery was harvested as a graft, it was placed in the right radial artery. Also, the central venous catheter (triple lumen) was placed in the right internal jugular vein under local anesthesia before induction. All patients were preoxygenated with a 100% O_2 mask for 2 min.

A smooth induction was performed using fentanyl (5–10 mcg/kg) and a sleeping dose of thiopental (2–4 mg/kg); endotracheal intubation was performed after the administration of a nondepolarizing muscle relaxant (rocuronium, 0.6 mg/kg), followed by initiation of mechanical ventilation. Succinylcholine (1 mg/kg) was used if difficult intubation was anticipated.

Monitoring of all patients was carried out using continuous ECG (five-lead), invasive arterial blood pressure monitoring, O_2 saturation by a pulse oximeter, end-tidal CO_2 by capnogram, central venous pressure, blood gas analysis, serum electrolytes, temperature by nasopharyngeal temperature probe, and urine output.

Maintenance of anesthesia

Maintenance of anesthesia was performed using 2% sevoflurane in a mixture of 70% O_2 and 30% air; maintenance of muscle relaxation was performed by rocuronium infusion (0.02 mg/kg/min). Mechanical ventilation was adjusted to maintain end-tidal CO_2 tension between 32 and 36 mmHg for the off-pump group. After surgery, the patients were transferred to the ICU and were extubated when they are awake, oriented, and cooperative with stable hemodynamics with a temperature higher than 36.5°C, minimal chest drain loss, and acceptable blood gases (PCO_2 < 45 mmHg and SaO_2 > 93%).

Operative technique

In all patients, surgical access was gained through a median sternotomy. For the on-pump group, after harvesting the conduits, 300 U/kg heparin was administered before aortic cannulation. Cardiopulmonary bypass was instituted with ascending aortic and two-stage venous cannulation of the right atrium. A roller pump, a nonheparinized circuit, and a hollow fiber membrane oxygenator were used. The pump flow rate was maintained between 2.0 and 2.4 l/min/m^2 body surface area to maintain a mean arterial pressure of 60–70 mmHg. A systemic normothermia of 37°C was induced. Anticoagulation was maintained during cardiopulmonary bypass and monitored using activated clotting time (ACT) measurements.

Myocardial protection was achieved by an initial antegrade infusion of the warm blood cardioplegia (miniplegia) as the use of all blood miniplegia provided superior protection when compared with global ischemia or crystalloid cardioplegia in acutely ischemic hearts [3]; then, it was continued with intermittent antegrade warm blood cardioplegia. The advantages of blood cardioplegia include the oxygen-carrying capacity, superior oncotic and buffering properties, and endogenous antioxidants contained in the blood; although blood cardioplegia (miniplegia) have disadvantages, these do not have an impact on the pathogenesis of infarct size or recovery of regional contractile function [4]. Distal anastomoses were constructed during one period of aortic cross-clamping; 'warm induction' was applied just before the removal of the cross-clamp. Proximal anastomoses were constructed in the ascending aorta with the aid of a partially occluding ascending aortic side clamp. Heparin was antagonized with protamine sulfate guided by the ACT after the removal of the side clamp.

For the off-pump group, after harvesting the bypass grafts, 150 U/kg heparin was administered. An octopus tissue stabilizer was used for stabilization of the target coronary artery. In all cases, the left anterior descending artery was the first artery to be revascularized. The target coronary artery was stabilized and occluded proximally with the aid of a silastic suture and then the distal anastomosis was performed. No coronary shunts were used during the distal anastomosis. Finally, the proximal anastomosis of the vein graft was constructed in the ascending aorta with the aid of a partially occluding ascending aortic side clamp. Heparin was then antagonized with protamine sulfate guided by the ACT.

Postoperative monitoring

After the operation, the heart rate and rhythm were monitored continuously using bedside monitors for the first 72 h. All persistent arrhythmias were confirmed with 12-lead ECG. After 72 h, trained nurses performed clinical observation every 4 h. If there was any clinical suspicion of arrhythmia, an ECG was performed and continuous ECG monitoring was restarted in cases of documented arrhythmia. For the purpose of this study, postoperative AF was defined as an episode of AF lasting longer than 10 min. Potassium

levels were monitored and deficiencies were treated promptly to maintain the electrolyte balance within the normal range.

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS; SPSS Inc., Chicago, Illinois, USA). All continuous variables were expressed as mean ± SD. Categorical variables were compared in the two groups using the c^2-test and Fisher's exact test. An independent-samples *t*-test was used to assess differences in noncategorical or continuous variables between the two groups.

The relationship between the occurrence of AF and perioperative variables was investigated using univariate analysis. Age, sex, left ventricular ejection fraction, previous MI, transient stroke, preoperative use of β-blockers, hypertension, diabetes mellitus, hypercholesterolemia, preoperative serum creatinine level, chronic obstructive pulmonary disease, use of the left internal thoracic artery, grafting of the right or posterior descending coronary artery, chest infection, requirement for inotropic agents, perioperative MI, drainage, length of hospital stay, and deaths were included in the analysis.

Independent predictors of AF were then determined using a multivariate logistic regression analysis of those variables with a *P*-value of less than 0.10 on univariate analysis, together with the type of operation (on-pump or off-pump). A *P*-value of less than 0.05 was considered to be statistically significant.

Results

The study included 85 patients undergoing off-pump CABG who were matched with another 88 patients undergoing on-pump CABG. During surgery, three patients in the off-pump CABG group were converted to on-pump CABG because of hemodynamic instability and severe rhythm disturbance, and were also excluded from the study.

The preoperative and intraoperative variables for each group are shown in Tables 1 and 2.

The two groups were almost similar without statistically significant differences in terms of sex, previous MI, hypertension, diabetes mellitus, transient stroke, preoperative use of β-blockers, left ventricular ejection fraction, and surgical data, including left internal thoracic artery usage and right coronary artery or posterior descending artery grafting. Postoperative clinical data and adverse outcomes are presented in Table 3.

There were a total of four deaths: Two in the off-pump group because of low cardiac output and two in the on-pump group because of multiorgan failure and low cardiac output. The overall incidence of AF was 24%, being 22.2% in the off-pump group and 26.5% in the on-pump group; this difference was not statistically significant. The patients in the off-pump group required significantly less inotropic support ($P < 0.05$). The length of hospital stay was slightly, although not significantly, longer in the on-pump than in the off-pump group.

Table 1 Characteristics of patients undergoing off-pump or on-pump coronary artery bypass grafting

Variables	On-pump (*n* = 88)	Off-pump (*n* = 85)	*P*-value
Male : Female	67:21 (76.14%) (male)	58:27 (68.24%) (male)	0.322
Diabetes mellitus [*n* (%)]	17 (19.32)	21 (24.71)	0.501
Hypertension [*n* (%)]	47 (53.4)	52 (61.2)	0.377
Hypercholesterolemia [*n* (%)]	42 (47.7)	35 (41.2)	0.480
Previous MI [*n* (%)]	34 (38.6)	31 (36.5)	0.898
Left ventricular ejection fraction (%)	48.3 ± 6.2	48.9 ± 7.1	0.554
Creatinine (mg/dl)	1.01 ± 0.41	1.1 ± 0.38	0.137
COPD [*n* (%)]	7 (7.95)	12 (14.12)	0.291
β-blockers [*n* (%)]	32 (36.36)	34 (40)	0.741

Data are expressed as either number percent or mean ± SD. MI, myocardial infarction. $P > 0.05$, nonsignificant. COPD, chronic obstructive pulmonary disease.

Table 2 Intraoperative data

Variables	On-pump (*n* = 88)	Off-pump (*n* = 85)	*P*-value
Cross-clamp time (min)	73.6 ± 25.4	NA	–
Cardiopulmonary bypass time (min)	94.5 ± 32.7	NA	–
Left internal mammary artery usage [*n* (%)]	82 (93.2)	79 (92.9)	0.825
RCA or PDA [*n* (%)]	41 (46.6)	44 (51.8)	0.595

Data are expressed as either number percent or mean ± SD. NA, not applicable. $P > 0.05$, nonsignificant. RCA, right coronary artery; PDA, posterior descending artery.

Table 3 Postoperative data and adverse outcomes

Variables	On-pump (*n* = 88) [*N* (%)]	Off-pump (*n* = 85) [*N* (%)]	*P*-value
Atrial fibrillation	23 (26.14)	19 (22.4)	0.692
Death	3 (3.41)	2 (2.35)	0.970
Postoperative MI	3 (3.41)	1 (1.18)	0.642
Chest infection	8 (9.09)	4 (4.71)	0.404
Transient stroke	2 (2.27)	3 (3.53)	0.968
Inotropic support	40 (45.5)	21 (25.4)	0.009*
Cessation of β-blockers	3 (3.41)	2 (2.35)	0.970
Drainage (ml)	496.5 ± 150.3	474.3 ± 131.6	0.303
Length of hospital stay (days)	7.2 ± 1.6	6.5 ± 1.2	0.001*

Data are expressed as either number percent or mean ± SD. MI, myocardial infarction. *$P < 0.05$, significant. $P > 0.05$, nonsignificant.

The results of the univariate and multivariate analyses of the relationships between each variable and AF are presented in Tables 4 and 5.

On univariate analysis, advanced age was associated with an increase in the incidence of new-onset AF. On multivariate logistic regression analysis of AF predictors, including the type of operation (on-pump or off-pump), the only independent predictor of postoperative new-onset AF was advanced age (P = 0.005, odds ratio = 1.06, confidence interval = 1.01–1.11).

Discussion

Despite advances in ECC, cardioplegic arrest, and surgical techniques, postoperative new-onset AF remains a common arrhythmia after CABG, possibly because of the increasing age and illness of patients undergoing CABG and advances in continuous monitoring technology. Various preoperative and postoperative factors, including advanced age, hypertension, discontinuation of β-blockers, bleeding, and right coronary artery stenosis, have all been suspected to increase the incidence of postoperative AF. Strategies for the prevention of postoperative AF have focused mainly on antiarrhythmic medication such as digitalis, β-blockers, calcium channel blockers, and amiodarone [5,6].

Table 4 Univariate analysis

Variables	AF (n = 42)	No AF (n = 131)	P-value
Type of operation (on-pump/off-pump)	24/18 (57.14%) (on-pump)	64/67 (48.85%) (on-pump)	0.449
Age (years)	61.2 ± 7.6	57.8 ± 7.1	0.009*
Sex (male/female)	31/11 (73.81%) (male)	94/37 (71.76%) (male)	0.952
Diabetes mellitus [n (%)]	13 (30.95)	25 (19.08)	0.161
Hypertension [n (%)]	24 (57.14)	75 (57.25)	0.868
Hypercholesterolemia [n (%)]	21 (50)	56 (42.75)	0.519
Perioperative MI [n (%)]	17 (40.48)	52 (39.69)	0.928
Left ventricular ejection fraction (%)	46.9 ± 6.7	47.6 ± 7.8	0.602
Creatinine (mg/dl)	1.21 ± 0.14	1.01 ± 0.42	0.003*
COPD [n (%)]	5 (11.9)	14 (10.69)	0.948
Grafts (n)	3.04 ± 0.8	3.2 ± 0.6	0.169
Distal grafts [n (%)]			
1 graft	4 (9.5)	18 (13.7)	0.656
2 grafts	20 (47.62)	66 (50.38)	0.893
3 grafts	18 (42.86)	47 (46.53)	0.812
Left internal mammary usage [n (%)]	38 (90.48)	123 (93.89)	0.683
RCA or PDA [n (%)]	24 (57.1)	61 (46.6)	0.314
Cross-clamp time (min)	74.3 ± 27.1	75.1 ± 24.6	0.858
Cardiopulmonary bypass (min)	93.7 ± 29.8	94.8 ± 31.7	0.843
Inotropic support [n (%)]	18 (42.86)	43 (32.82)	0.318
Drainage (ml)	485.3 ± 129.4	490.2 ± 131.5	0.833

Data are expressed as either number percent or mean ± SD.
AF, atrial fibrillation; MI, myocardial infarction. *P < 0.05, significant P > 0.05, nonsignificant; COPD, chronic obstructive pulmonary disease; RCA, right coronary artery; PDA, posterior descending artery.

Table 5 Multivariate analysis

Variables	Odds ratio	95% confidence interval	P-value
Type of operation (on-pump/off-pump)	1.396	0.69–2.81	0.351
Age (years)	1.06	1.01–1.11	0.005*
Creatinine (mg/dl)	1.54	0.84–2.72	0.08

*P < 0.05, significant P > 0.05, nonsignificant.

Cohn *et al.* [7] compared the incidence of postoperative AF after a minimally invasive coronary surgery and standard CABG and did not find a reduction, but the extent of revascularization was different in the two groups, with a mean number of grafts of 1.1 and 3.6, respectively. Saatvedt *et al.* [8] compared the occurrence of AF in patients after conventional CABG with the occurrence in those operated on with a beating heart through a median sternotomy and found no difference, but the mean number of distal anastomoses was 3.6 and 1.9, respectively. In their prospective randomized study with a similar cohort of 200 patients, Ascione *et al.* [9] found that ECC including cardioplegic arrest was the major predictor of postoperative AF.

The aims of treatment for postoperative AF are the control of the ventricular rate, anticoagulation, and conversion to sinus rhythm. Recently renewed interest in performing CABG on the beating heart has enabled the influence of ECC and cardioplegic arrest on postoperative new-onset AF to be studied. Several studies have reported reduced postoperative AF after off-pump CABG, although others reported no significant reduction [2].

In the present matched study, we failed to find a statistical difference between the on-pump and the off-pump CABG group, with incidences of AF of 26.14 and 22.4%, respectively; ECC was not a risk factor for postoperative AF after univariate analysis and multivariate logistic regression.

According to the Framingham study [10], the overall average incidence of AF in all populations is 1.7%; it is age dependent and attains a level of 2–4% among those older than 70 years of age. The incidence of AF in those with ischemic heart disease may reach 4.8% in women and 6.2% in men depending on the severity of the disease.

In the present study, advanced age is well documented as a risk factor for postoperative AF; structural changes such as hypertrophy of the myofibrils, decreased

conduction tissue, and progressive fibrosis (which are more common in the elderly) probably play an important role [2]. To overcome these predictors, we chose a study design with a cohort of patients matched for age and number of grafts.

Mueller *et al*. [11] reported that age and history of supraventricular arrhythmia were the dominant predictors of postoperative AF in their study of patients undergoing isolated left internal thoracic artery–left anterior descending artery grafting with either minimally invasive CABG or on-pump CABG. In agreement with these results and the literature [1,2,6], in the present study, we found that age was the only significant factor for postoperative AF after ECC-inclusive multivariate logistic regression ($P = 0.0046$, odds ratio = 1.06, 95% confidence interval = 1.01–1.11). Other possible risk factors, such as hypertension, male sex, bleeding, and grafting of the right coronary artery [1,2,6] were not found to be risk factors for postoperative AF on univariate analysis.

Many of the intraoperative factors that might influence the occurrence of postoperative new-onset AF are related to ECC, myocardial preservation, and global myocardial ischemia. Ischemia of the myocardium occurs both in on-pump and in off-pump CABG. Although it is only transient in off-pump CABG, there is still a potential risk of myocardial injury because of inadequate perfusion and reperfusion of the normothermic metabolically active myocardium during the occlusion of the target coronary artery. The use of intracoronary shunts in off-pump CABG may provide continuity of the coronary blood flow, but further prospective studies are needed to show whether this influences the incidence of postoperative new-onset AF or not.

As the incidence of postoperative AF is similar after on-pump and off-pump CABG, mechanisms common to both types of coronary surgery should be looked for, such as the opening of the pericardium and the resulting local inflammatory response.

Saatvedt *et al*. [8] reported a reduced incidence of AF after transmyocardial revascularization in comparison with conventional and minimally invasive coronary surgery.

In lung resection operations, Krowka *et al*. [12] found a higher incidence of supraventricular tachyarrhythmia in patients with intrapericardial dissection.

In another study, a relationship between AF and significant pericardial effusion was shown after cardiac valve surgery [13,14]. All these findings suggest the need for further study of the importance of a local inflammatory response in postoperative AF.

Limitation of the study

The main limitation of the present study is the small population investigated. In order to set up a prospective study to demonstrate at least a 16% reduction (from 26.14 to 22.4% in our study) in the occurrence of AF between on-pump and off-pump CABG, over 2900 patients would be needed to detect a difference at a significance level of 0.05.

The lack of randomization with respect to which patients would undergo off-pump or on-pump CABG is another limitation. In addition, continuous ECG monitoring was not performed after the first 72 h; thus, it is possible that short episodes of asymptomatic AF might have been missed after this time.

Conclusion

Although there was a slight decrease in the occurrence of postoperative new-onset AF after off-pump CABG compared with on-pump CABG (26.14 vs. 22.4%), this difference was not statistically significant. Age was shown to be the most important predictor of postoperative new-onset AF, which suggests that further efforts should be focused on factors other than ECC and cardioplegic arrest in order to reduce the incidence of this common postoperative arrhythmia.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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