Postoperative Atrial Fibrillation After Conventional and Beating Heart Myocardial Revascularization: Is there a culprit?

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This prospective randomized study was designed to determine the incidence and predictors of atrial fibrillation (AF) after conventional and off-pump coronary artery bypass (OPCAB) surgery and its impact on length of postoperative hospital stay. This is a prospective randomized study of two hundred patients who underwent first time coronary artery bypass operation in cardiac surgery department of Mayo hospital Lahore. There was equal number of patients in each group. (1) On-pump conventional surgery (100 patients, 82 men, mean age 62.5 years) using intermittent cross clamp fibrillation technique or (2) off-pump surgery (100 patients, 74 men, mean age 60.6 years) on the beating heart. Heart rate and rhythm were continuously monitored with an automated arrhythmia detector during the first 72 hours after surgery. Thereafter, routine clinical observation was performed and continuous monitoring restarted in the case of arrhythmia. There were no significant baseline differences among the two groups except that on-pump group received slightly higher mean number of distal anastomoses (3.3 v 3.0; p=0.028). 23 patients in the on-pump group and16 in the off-pump group had sustained AF (p=0.228). The median length of hospital stay was increased in-patients developing Atrial fibrillation. Atrial fibrillation is a common complication after procedures of myocardial revascularization, performed with or without cardiopulmonary bypass. Avoiding cardiopulmonary bypass does not seem to reduce the incidence of atrial fibrillation.
Key words: atrial fibrillation, on-pump, off-pump, and myocardial revascularization

Atrial fibrillation (AF) is the most common complication after heart surgery[1]. Its pathophysiology is unclear, and its prevention and management remain suboptimal.[2] Although it is not a life threatening event, it may lead to haemodynamic compromise, thromboembolic events, anxiety and increased costs[2,3,4].

Some factors reportedly associated with an increased incidence of postoperative AF relate to aspects of cardiopulmonary bypass (CPB) technique, such as bicaval venous cannulation and pulmonary venting.[5]. Myocardial ischemia and inadequate cardioplegic protection of the atria have also been reported to increase the incidence of postoperative AF[2,6]. Beating heart or "off-pump" coronary artery bypass (OPCAB) has become an accepted method of myocardial revascularization by reducing the perioperative morbidity related to cardiopulmonary bypass.[7] Myocardial revascularization on the beating heart does not require atrial cannulation, cardiopulmonary bypass and fibrillation or cardioplegic arrest[8,9,10,11,12]. Several studies have investigated the incidence of atrial fibrillation after CABG surgery without cardiopulmonary bypass. Rates of AF ranged from 7% to 40%[1,7,11,12,13,14,15,16,17].

The present prospective, randomized study investigated the incidence of AF in similar cohorts of patients undergoing CABG with or without CPB and its impact on length of postoperative hospital stay.

Patients Selection

Over a 41-month period, 258 patients underwent first time coronary artery surgery under the supervision of a single senior consultant. Based on their eligibility for off-pump surgery initially 214 patients were prospectively randomized for myocardial revascularization in two equal groups. The randomization sequence was obtained by card allocation and was strictly respected. Exclusion from the randomization was based on certain clinical and angiographic criteria. Preoperative clinical criteria included history of supraventricular arrhythmia, recent myocardial infarction (MI) (<1month), renal and respiratory impairment, preoperative amiodarone and digoxin intake, previous stroke or transient ischemic attack and nonelective operation. Angiographic criteria for exclusion were heavily diseased coronaries that were thought to be technically difficult for beating heart surgery, especially the obtuse marginal vessels. Out of 258 patients, 44 patients were excluded pre-operatively on these criteria. Thirty-four patients outs of these forty-four were rejected due to clinical criteria and remaining ten were excluded due to angiographic criteria.

On-Pump surgery (207 patents) patients were named as group 1 while group 2 consisted of Off-Pump surgery (207 patients) patients. In case of three patients in group 2, coronaries were found to be calcified during per-operative examination .In these three patients beating heart surgery plan was abandoned and CBP was established. They were operated on with conventional intermittent cross clamp fibrillation technique. Also in group 2 five

Patients had to be converted to conventional PCB during beating heart procedure due to haemodynamic instability. All these seven Patients were excluded from the study. In order to keep the number of patient's equal in each group seven patients out of 207 in group 1 were also excluded from the study. In order to eliminate any element of bias, exclusion of these seven patients of group 1 was totally blind from the mixture of patients in this group.

After exclusion of these fourteen patients, two groups had equal number of patients.

Finally Group 1 consisted of 100 patients who had on-pump conventional surgery [82 men, mean age 62.5 years] with hypothermic (32°C) CPB and intermittent cross clamp fibrillation technique and Group 2 consisted of 100 patients who had off-pump surgery [74 men, mean age 60.6 years]. All patients gave informed consent.

Perioperative medications

Preoperative medications including β-blockers, diuretics, antihypertensives, and calcium channel blockers were routinely omitted on the day of surgery. In order to avoid excessive vasodilatation during operation and in immediate post-operative period, ACE inhibitors were withdrawn on the evening before the operation. On the first postoperative day, in accordance with the intensive care unit (ICU) protocol (if heart rate >60bpm, systolic Blood pressure>110mmHg) β-blockers and anti-hypertensive drugs were restarted.

Anaesthetic technique

In both groups, anesthetic technique consisted of propofol infusion at 3 mg/kg/hr combined with fentanyl infusion at 0.5 to 1μg/kg/min. Neuromuscular blockade was achieved by 0.1 to 0.5 mg/kg pancuronium bromide or vecuronium and the lungs

Ventilated to normocapnia with air and oxygen (45% to 50%). Heparin was given at a dose of 300 IU/kg to achieve a target activated clotting time (ACT) of 480 seconds before commencement of CPB in the on-pump group. An additional 3000IU of heparin were administered if required. In the off-pump group, heparin (100 IU/kg) was administered before the start of the first anastomosis to achieve an ACT of 250- to 350 seconds. On completion of all anastomoses, protamine was given to reverse the effect of heparin and return the ACT to preoperative levels. Our routine prophylaxis against ulcers was done with ranitidine (3x50 mg/day) in intensive care unit. A proton pump inhibitor (omeprazole 20 mg/day) was only used in patients with a history of ulcers. Cefuroxime (750mgx3) was given perioperatively to all patients.

Operative technique

On-Pump

Cardiopulmonary bypass was instituted with the use of ascending aortic cannulation and 2-stage venous cannulation of the right atrium. A standard circuit was used: a Bard tubing set, which included a 40μm filter (Sorin Biomedica), and a hollow-fiber membrane oxygenator. A non-pulsatile blood flow rate of not less than 2.4L/min/m^2 was used

Whenever possible. Systemic temperature was kept at 32°C. In all patients intermittent cross clamp fibrillation technique was used.

Off-Pump

The anaesthetist plays an active role during the performance of OPCAB, as the maintenance of systolic pressure is important because heart does not tolerate haemodynamically unfavorable positioning. Alpha agents and inotropic agents are important to maintain cardiac output during manipulations. Median sternotomy was performed in all cases. All conduits were harvested as for traditional coronary artery bypass operation. The left internal mammary was made as long as possible. This helped to avoid excessive tension when the heart was elevated after the graft to the left anterior descending was performed. The coronary arteries were grafted in the following sequence; anterior wall vessels followed by inferior wall vessels and finally lateral wall vessels. The left internal mammary to left anterior descending graft was usually the first, the inferior wall grafts (posterior descending, right coronary) were usually next and the lateral wall grafts (obtuse marginal) were usually the last. The distal anastomoses were constructed first followed by proximal anastomoses. Stabilization of target site was accomplished with Medtronic Octopus-2 Stabilizer. Proximal occlusion of target vessel was accomplished with an encircling suture to the vessel proximal to the site chosen for anastomosis. No distal occlusion was necessary. Distal anastomoses were performed with a single suture continuous technique. A carbon dioxide gas/normal saline blower was used to keep

Operative field clear of blood, while keeping its flow less than 4 liters per minute to avoid damaging coronary endothelium.

For left anterior descending and diagonal grafting, a deep pericardial retraction suture with No 2 Silk was placed 1-2 centimeters above the left superior pulmonary vein pulled taut and secured to the drape on the left side of the patient. The retraction required for exposure not very uncommonly caused haemodynamic instability. The blood pressure recovered by keeping the patient head down and with preparatory volume loading. For grafting to Obtuse Marginal branches, heart "verticalizing technique" was used. Operation table was placed in steep Trendelenberg position and rotated toward the right. This allowed gravity to displace heart to the right and apex anteriorly. Suspensory sutures on the right side of the pericardium were removed and right pleural space was opened. These maneuvers allowed the heart to move toward the right pleural space. Additional deep pericardial retraction sutures were placed on the posterior pericardial surface on a line drawn from the left inferior pulmonary vein to the inferior vena cava, halfway between the cava and pulmonary vein. For grafting distal Right Coronary Artery and Posterior Descending Artery, with the table in steep trendelenberg position, the tension applied to the deep pericardial retraction sutures was modulated to expose the target vessel in the center of the operative field. The necessary temporary occlusion of the artery, proximal to the bifurcation, caused ischemia of the atrioventricular

node with resultant bradycardia. Anesthetist combated this with pharmacological means.

Postoperative management

At the end of surgery, patients were transferred to the intensive care unit (ICU). The lungs were ventilated with 60% oxygen with volume-controlled ventilation and a tidal volume of 10-15ml/kg with 5 cmH_2O of positive end-expiratory pressure. Adjustments in FIO_2 and respiratory rate were made according to the blood gas analysis to maintain PaO_2 between 90 and 100 mm Hg and $PaCO_2$ between 35 and 40 mm Hg. Patients were extubated as soon as they met the following criteria: hemodynamic stability, no excessive

Bleeding (<30 ml/hr), normothermia, consciousness with pain control and good muscle power. Fluid management after surgery consisted of 5% dextrose infused at 1ml/kg/hr, with additional colloid or blood to maintain normovolemia and hematocrit>28%. Potassium deficiency was promptly treated as necessary to maintain it within 4.0 to 5.5 millimoles/liter.

Monitoring and definitions

Heart rate and rhythm were continuously monitored and displayed on a screen with an automated arrhythmia detector (TCH 581, Hewlett-Packard, Andover, MA.) during the first 72 hours after surgery. Automatic printing of ECG was related to the inserted alarm levels and included heart rate>90 bpm and the presence of 6 consecutive normal R-R intervals varying by ≥ 100 ms. Twelve- lead ECG recordings were performed before surgery, 2 hours after surgery, and then daily thereafter until hospital discharge. After the first 72 hours, trained nurses performed clinical observations every 4 hours. Any ECG was recorded on the basis of any clinical suspicion of arrhythmia. In the case of documented arrhythmia, continuous ECG monitoring was restarted. Temporary pacing was instituted incase of symptomatic bradycardia unresponsive to treatment by drugs, acute conduction disturbances including second- or third degree atrioventricular (AV) block, and bifascicular or trifascicular block. Permanent pacemaker was inserted for long-lasting symptomatic bradycardia and second-degree (Mobitz type II) and third degree AV block.

Intraoperative and postoperative data, including complications and adverse events, were recorded. Clinical diagnostic criteria for perioperative MI were new Q waves of >0.04 milli-seconds and/or a reduction in R waves >25% in ≥2 leads. Chest infection was defined as the presence of purulent sputum associated with fever and requiring antibiotic therapy according to positive sputum culture. The need for anticoagulation, postoperative day of onset of AF and postoperative hospital length of stay were also compared between the two groups.

Statistical Analysis

Arrhythmias such as atrial flutter, atrial tachycardia, or others were not considered in the same group of AF because their mechanism differs. Only sustained episodes of AF persisting for more than 10 minutes, causing hemodynamic instability and / or requiring oral or intravenous drug treatment were included in the statistical analysis. Statistical analysis was performed using SPSS version 9.0 statistical software package (SPSS Inc. Chicago. IL). Univariate analysis was performed using the unpaired t-test or Mann-Whitney U tests for continuous data and Chi-square test for categorical data. Results were considered significant if $p< 0.05$.

Results

Preoperative patient characteristics and intraoperative data are shown in Tables 1 and 2, respectively. General demographics between the two groups were similar. The mean age of the on-pump patients was marginally greater (62.5 years v 60.6 years). There was a similar incidence of diabetes, hypertension, congestive heart failure and preoperative treatment with β-blockers. The mean preoperative left ventricle functional grade was slightly although not significantly worse in the on-pump surgery group (on-pump,1.82 v off-pump, 1.65; p=0.165). The mean number of distal anastomosis performed was less in the off-pump group (3.0 v 3.3; p=0.028). The incidence of perioperative arrhythmias is presented in Table 3. The incidence of sustained AF was slightly, although non-significantly higher in the on-pump group. (23% v 16%; p= 0.228). With a peak incidence on day 1 in both groups. Postoperative clinical data are presented in Table 4. There were 2 deaths, one in each group, due to multiorgan failure as a consequence of low cardiac output. 2 patients in the off-pump and 4 in the on-pump group had perioperative MI. The incidence of chest infection was almost similar in the two groups.

Table 1. Preoperative patient characteristics

Characteristic	Off-pump (n=100)	On-pump (n=100)	Univariate p
Mean age (years)*	60.6(10.6)	62.5(9.6)	0.165
Sex (male,n)	74	82	0.207
Hypertension (n)	18	25	0.228
Diabetes (n)	24	29	0.389
LV function grade*+	1.65(0.74)	1.82(0.78)	0.162
Preoperative β-blockers (n)	75	76	0.968
CHF (n)	10	13	0.522

LV, left ventricular, CHF, congestive heart failure
* Mean ± (SD), + left ventricular function grade, Grade1, ejection fraction ≥ 60%; grade2, ejection fraction 40% to 59%; grade3, ejection fraction 21% to 39%; grade4, ejection fraction≤ 20%.

Table 2. Intraoperative data

Variable	Off-pump (n=100)	On-pump (n=100)	Univariate p
CPB time, min+	-	63(25-202)	
Cross clamp time, min+	-	39(18-86)	
No. of distal anastomosis*	3.0±0.84	3.3±0.86	0.028
IMA to LAD or diag graft,(n) 98	98	1.0	
SV to diag graft,(n)	23	23	1.0
RCA/PDA graft,(n)	52	52	1.0
Proximal Cx graft, (n)	45	48	0.7

IMA indicates internal mammary artery; LAD, left anterior descending artery; diag, diagonal branch of LAD; SV, saphenous vein; and Cx, circumflex artery. +Median with range, *Mean ± SD

Table 3. Postoperative arrhythmias

Variable	Off-pump (n=100)	On-pump (n=100)	Univariate p
Arrhythmia incidence, (n)	22	33	0.380
Total AF,(n)19	29	0.338	
Sustained AF,(n)	16	26	0.228
Unsustained AF,(n)	3	3	1.0
Duration of sustained AF, h	11(5-38)	12(6-45) 0.317	
Atrial flutter, (n)	1	1	1.0
Second-degree AV block, (n)	1	1	1.0
Third-degree AV block, (n)	1	1	1.0

Data are presented as median with range or number of patients in parantheses.

Table 4. Postoperative data

Variable	Off-pump (n=100)	On-pump (n=100)	Univariate p
Sustained AF,(n)	16	26	0.228
Deaths,(n)	1	1	1.0
MI,(n)	2	4	0.456
Chest infection,(n)	10	13	0.522
Inotropic requirement, (n)	50	72	0.012
Fluid balance,(ml)*	1450(770)	2370(670)	<0.001
Temporary pacing over first 24h	1	17	<0.001
Permanent pacemaker,(n)	1	1	1.0
Hospital LOS (days)+	5(3-18)	6(5-32)	0.058

AF, atrial fibrillation; MI, myocardial infarction and LOS, length of stay.
* Mean ± SD, +Median (range)

Difference that reached statistical significance included a reduced mean positive fluid balance on admission to ICU in the off-pump group (1,450ml v 2,370ml; p<0.001), and more on-pump patients required pacing at some time in the postoperative period, including the time immediately post-cardiopulmonary bypass (18% v 2%; p< 0.001). Some form of inotropic support was used more commonly in the on-pump group (72% v 50%; p=0.012). The difference in median hospital length of stay in the off-pump group (5 days v 6 days; p= 0.058) did not reach statistical significance. Patients developing AF had a prolonged hospital length of stay as shown in Tables 5 &6.

Table 5. Characteristics of OPCAB patients who developed sustained AF

Characteristic	AF (n=16)	No AF (n=84)	Univariate p
Mean age (years)*	60.9 (10.6)	60.7 (10.3)	0.910
Sex (male,n)	12	62	0.521
Hypertension (n)	4	14	0.769
Diabetes (n)	6	18	0.628
CHF (n)	2	8	0.716
LV function grade*	2.20 (0.87)	1.73 (0.79)	0.013
Preoperative β-blockers (n)	12	63	0.996
No. of distal anastomosis	2.80 (0.81)	3.0 (0.91)	0.716
MI, (n)	1	1	1.0
Chest infection,(n)	3	7	0.520
Fluid balance(ml)*	1430 (705)	1525 (998)	0.650
Hospital LOS(days)+	7(4-15)	5(3-18)	0.004

LV, left ventricular, CHF, congestive heart failure
MI, myocardial infarction, LOS, length of stay*
Mean ± (SD) +Median(range)
Left ventricular function grade, Grade1, ejection fraction ≥60%; grade2, ejection fraction 40% to 59%; grade 3, ejection fraction 21% to 39%; grade 4, ejection fraction≤ 20%.

Table 6.Characteristics of on-pump patients who developed Sustained AF

Characteristic	AF (n=23)	No AF (n=77)	Univariate p
Mean age (years)*	62.9(9.6)	62.7(9.5)	0908
Sex (male)	19	62	0.521
Hypertension (n)	3	22	0.996
Diabetes (n)	8	21	0.921
CHF (n)	3	10	0.998
LV function grade	2.0(0.76)	1.57(0.67)	0.039
Preoperative β-blockers (n)	18	58	0.421
No. of distal anastomosis	3.36(0.95)	3.27(0.82)	0.655
MI, (n)	1	3	0.428
Chest infection,(n)	3	10	0.921
Fluid balance(ml)*	2580(650)	2370(680)	0.251
Hospital LOS(days)+	7(4-15)	6(5-32)	0.054

LV, left ventricular CHF, congestive heart failure MI, myocardial infarction
LOS, length of stay * Mean ± (SD) +Median(range)
Left ventricular function grade, Grade1, ejection fraction ≥ 60%; Grade 2, ejection fraction 40% to 59%; Grade3, ejection fraction 21% to 39%; Grade 4, ejection fraction≤ 20%.

In the off-pump group, the median hospital length of stay was increased from 5 to 7 days (p=0.004) in the patients developing AF. The patients in the on-pump group

had a greater positive fluid balance at admission to and discharge from the cardiovascular ICU, but there was no significant difference in fluid balance status between patients who developed AF and patients who did not in the two groups. All patients in the on-pump group who developed AF had reverted to sinus rhythm by the time of hospital discharge. Two (12.5%) patients in the off-pump group who developed AF remained in AF at the time of hospital discharge, and were anticoagulated (12.5%). For patients taking β-blockers preoperatively, there was no significant difference in the incidence of AF between patients who had restarted β-blockers by the time of ICU discharge and patients who had not in either the off-pump or on-pump groups.

Discussion

The results of this study agree with the findings of Koutlas et al[7] and Siebert et al[1]. Koutlas et al and Siebert et al found that in similar cohorts of patients there was no significant difference in the incidence of AF in patients undergoing coronary artery surgery with and without cardiopulmonary bypass. The incidence of AF in this study is similar to that seen in several other studies[1,7,11,12,13,14,15,16,17,18].

The pathophysiological mechanisms of postoperative atrial fibrillation have been the subject of speculation for decades despite extensive investigations focusing on identification of risk factors for initiation of arrhythmia. Patient age is an important predisposing factor for the development of postoperative AF[2,19,20,22]. Other reported predictors of postoperative AF after CABG include male gender, hypertension, right coronary artery disease, prolonged P wave duration, early postoperative withdrawal of β-blockers, need for an IABP, need for inotropes, postoperative chest infection, and prolonged aortic cross-clamp and cardiopulmonary bypass time[2,21,22,23]. However, this study did not show any of these factors as predictors of AF. In the off-pump and on-pump patients, who developed AF, there was a significantly poorer mean left ventricle functional grade (off-pump; 2.20[AF] v 1.73[noAF]; p=0.013; on-pump, 2.0[AF] v 1.57[noAF]; p=0.039). Poor left ventricular function has already been reported as risk factor for AF in patients undergoing surgery with CPB.[24,25]

The postoperative time of onset of AF was similar in the off-pump and on-pump surgery groups in this study, however the pattern of onset with a peak incidence on day 1 was contrary to that reported by Place et al[24]. The study was also in agreement with earlier finding of Tamis et al [26] that atrial fibrillation independently prolongs hospital stay after coronary artery bypass surgery.

In conclusion, despite the large number of studies on the subject, the cause of postoperative AF remains unclear, and the avoidance of cardiopulmonary bypass alone would not seem to reduce the risk of this postoperative complication, which is responsible for patient instability and a prolonged length of hospital stay.

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