Cardiovascular Surgery

Can Off-Pump Coronary Artery Bypass Graft Surgery Decrease the Incidence of Postoperative Atrial Fibrillation?

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Background: Atrial fibrillation (AF) remains the most common cardiac arrhythmia encountered after coronary artery bypass grafting (CABG) and leads to a significant source of morbidity and mortality after the surgery. Due to its involving less manipulation of the atria, off-pump CABG was thought to have a lower incidence of postoperative AF compared with on-pump CABG.

Methods: Two hundred and twenty-five patients (154 male) underwent CABG. Preoperative permanent AF patients were excluded (n = 12). Group 1 consisted of 78 patients (53 male, 68.6 ± 11.9 years old; 25 female, 70.7 ± 7.9 years old) who received off-pump CABG, and group 2 included 135 patients (93 male, 72.1 ± 10.1 years old; 42 female, 72.3 ± 7.9 years old) who underwent on-pump CABG with cardiopulmonary bypass (CPB) during the same study period. The incidence and predictors of postoperative AF were analyzed.

Results: AF developed in 60 cases (28.2%) after CABG. There were higher incidence of myocardial infarction, history of paroxysmal atrial fibrillation, NYHA Fc $\geqq$ 2, β-blocker use, and longer intubation in the on-pump group compared with the off-pump group. However, there was no significant difference relating to the incidence of AF between off-pump (23.1%) and on-pump (31.1%) groups. The predictors of AF were old age (> 65 years, OR: 5.008, 95% CI: 1.4-17.9, $p = 0.013$), history of paroxysmal AF (OR: 7.851, 95% CI: 2.4-25.6, $p = 0.001$) and prolonged postoperative intubation days (> 3 days, OR: 5.303, 95% CI: 2.2-13.1, $p < 0.001$).

Conclusion: In this retrospective study, off-pump CABG surgery did not decrease the incidence of postoperative AF.

Key Words: Atrial fibrillation • Coronary artery bypass grafting • Electrophysiology

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia encountered after conventional coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB). The reported incidence of postoperative AF was high, up to 40%,[1] and was thought to be associated with poor early clinical outcome, complicated with increased incidence of postoperative hypotension, risk of stroke, prolonged hospitalization, needed anti-arrhythmic treatment and increased resource utilization.[2,3] However, the pathophysiological mechanism responsible for the high incidence of AF after CABG remains unclear. Due to its involving less frequent manipulation of the atria and stretch of the thoracic veins, off-pump CABG has been thought to have a lower incidence of AF than the on-pump technique.[4]

In this retrospective study, we compared the inci-

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dence of postoperative AF between on-pump and off-pump groups and searched for the predictors of AF after CABG.

MATERIAL AND METHODS

Patient population

Two hundred and twenty-five patients underwent CABG at our hospital between Jan. 1997 to Jan. 2001. Patients with preoperative permanent AF (n = 12) were excluded. Thus, our study population included 213 patients (146 male, mean age 71.4 ± 9.9 years). None of these patients had a history of hyperthyroidism. Preoperative data collection included age, gender, left atrial diameter (LAD), left ventricular ejection fraction (LVEF), New York Heart Association Functional Class (NYHA Fc), history of myocardial infarction (MI), history of paroxysmal AF (PAF), hypertensive cardiovascular disease (HCVD), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), history of chronic renal failure (CRF) and use of anti-arrhythmic medications. Postoperative AF was defined as new-onset AF with the duration ≧ 20 minutes, detected by EKG monitoring, and requiring anti-arrhythmic treatment during the hospital stay after CABG. The anti-arrhythmic medications included β-blockers and calcium channel blockers for rate control and amiodarone for pharmacological conversion.

Group 1 (off-pump) consisted of 78 patients (53 male, mean age 69.3 ± 10.7 years) who underwent CABG without the use of CPB. Group 2 (on-pump) consisted of 135 patients (93 male, mean age 72.1 ± 9.4 years) who underwent CABG using CPB.

The surgical techniques were median sternotomy, with or without takedown of the left internal thoracic artery. In the on-pump group, cardiopulmonary bypass was achieved by cannulating the ascending aorta and right atrium. Myocardial protection was carried out through anterograde and retrograde administration of cardioplegia with either blood or crystallolid solution. The degree of hypothermia was 28 °C, and we used the side-bite proximal anastomosis technique.[5] The mean aorta clamping and bypass times were 82 ± 27 and 147 ± 58 minutes, respectively. Patients with high comorbidity risks such as low left ventricular ejection fraction and myocardial infarction with NYHA functional class ≧ 3 were arranged to receive on-pump CABG. All the surgical procedures were performed by the same cardiovascular surgery teams throughout the whole study period.

Statistical analysis

All continuous variables were expressed as mean ± SD. Categorical variables between the off-pump group and on-pump group were compared using chi-square test or Fisher's exact test. Continuous variables between the off-pump group and the on-pump group were compared using Student t-test. Multivariate logistical regression analysis was used to determine the independent correlates of AF. All clinical or procedural factors with a p value < 0.05 in the univariate analysis were entered into this analysis. A p value < 0.05 was considered statistically significant.

RESULTS

Patient characteristics and incidence of AF after operation

The baseline clinical and demographic characteristics of the patients are summarized in Table 1. Sixty patients (28.2%) developed postoperative AF during the study period. The incidences of AF in off-pump and on-pump group were 23.1% and 31.1% (p = 0.209), respectively. The diseased coronary arteries number, described as CAD 2 VD and CAD 3 VD between off-pump and on-pump groups, were 47.4% versus 14.1% and 42.3% versus 44.4% (p > 0.05), respectively. The graft vessel numbers in these two groups were similar (off-pump 2.6 ± 0.7, on-pump 2.7 ± 0.8, p = 0.258).

Most AF occurred within 3 days after CABG, and the duration was less than 3 days (n = 50, 83.3%). There was no difference in the incidence of male gender, history of HCVD, COPD, DM, CRF and use of ACEI/ARB (Angiotensin-converting enzyme inhibitor/Angiotensin receptor blocker) or statin between the two groups. More patients in group 2 received preoperative β-blocker (BB) (56.4% versus 67.4%, p = 0.001) than in group 1. However, more group 1 patients received BB (57.7% versus 17.0%, p < 0.001) and calcium channel blocker (CCB) (65.4% versus 45.9%, p = 0.006) than patients in group 2 for treatment of postoperative AF. Group 2 patients had higher incidence of MI, history of PAF, NYHA Fc ≧ 2, longer intubation (> 3 days) and higher complication

Table 1. Demographic and clinical characteristics of patients (n=213) who underwent CABG using off-pump and on-pump technique

Variables	Off-pump (n = 78)	On-pump (n=135)	*p* value
Pre-CABG			
Age ≥ 65	61 (78.2)	116 (85.9)	0.147
Male	53 (67.9)	93 (68.9)	0.887
LAD (mm)	38.7 ± 6.8	39.3 ± 6.4	0.623
LVEF (%)	54.3 ± 17.2	45.2 ± 14.6	0.0002
NYHAFc ≥ 2	21 (26.9)	62 (45.9)	0.006
MI	22 (28.2)	66 (48.9)	0.003
PAFHx	2 (2.6)	14 (10.4)	0.037
HCVD	49 (62.8)	77 (57.0)	0.408
COPD	6 (7.7)	9 (6.7)	0.778
DM	35 (44.9)	52 (38.5)	0.363
CRF	8 (10.3)	26 (19.3)	0.084
1 VD	6 (7.7)	8 (5.9)	0.135
2 VD	22 (28.2)	43 (31.9)	0.356
3 VD	50 (64.1)	84 (62.2)	0.889
BB	44 (56.4)	91 (67.4)	0.001
CCB	37 (47.4)	66 (48.9)	0.737
ACEI/ARB	22 (28.2)	38 (28.1)	0.733
Statin	15 (19.2)	17 (12.6)	0.290
Post-CABG			
Intubation day > 3	2 (2.6)	24 (17.8)	0.001
BB	45 (57.7)	23 (17.0)	< 0.001
CCB	51 (65.4)	62 (45.9)	0.006
Digoxin	27 (34.6)	61 (45.2)	0.15
Amiodarone	14 (17.9)	39 (28.9)	0.075
Diuretics	61 (78.2)	102 (75.6)	0.660
Mortality	2 (2.6)	8 (5.9)	0.332
Complication	1 (1.3)	20 (14.8)	0.001
AF	18 (23.1)	42 (31.1)	0.209

Values are expressed as mean ± SD or number (%) of patients.

Student t-test, Fisher exact test and Chi-square tests were used for statistical analysis.

1 VD: single-vessel disease; 2 VD: two-vessel disease; 3 VD: triple-vessel disease; ACEI/ARB: Angiotensin-converting enzyme inhibitor/Angiotensin receptor blocker; AF: atrial fibrillation; BB: β-blocker; CABG: coronary artery bypass grafting; CCB: calcium channel blocker; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; DM: diabetes mellitus; HCVD: hypertensive cardiovascular disease; LAD: left atrial diameter; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHAFc: New York Heart Association functional class; PAFHx: paroxysmal atrial fibrillation history.

rate. Twenty patients developed complications in the on-pump group, including 7 sepsis, 3 re-bleeding, 2 cerebral vascular accident, 2 ischemic bowel disease, 2 ventricular septal defect, 1 sick sinus syndrome, 1 wound infection, 1 acute renal failure and 1 cardiac rupture. However, only one patient developed sepsis in the off-pump group. The mortality rate in the off-pump group was lower than in the on-pump group, although the difference did not reach statistical significance (2.6% versus 5.9%, $p = 0.332$).

Predictors of AF

In Table 2, the demographic and clinical characteristics between patients with or without postoperative AF are compared. By univariate analysis, there was no difference in terms of NYHAFC, CHF, MI, PAFHX, INTUBA, BB and CCB use ($p < 0.05$). However patients who developed AF were older (74.8 ± 6.9 versus 69.7 ± 10.7, $p = 0.002$), had higher incidence of PAF history (18.3% versus 3.3%, $p < 0.001$), lower incidence of statin and CCB use before surgery, and longer intubation

Table 2. Univariate analysis of demographic and clinical characteristics of patients (n = 213)

Variables	AF (n = 60)	No AF (n = 153)	*p* value
Pre-CABG			
Age (years)	74.8 ± 6.9	69.7 ± 10.7	0.002
Male	42 (70.0)	104 (68.0)	0.775
LAD (mm)	40 ± 6.5	38.6 ± 6.5	0.866
LVEF (%)	46 ± 16.1	49.8 ± 16.1	0.845
NYHAFc ≥ 2	29 (48.3)	54 (35.3)	0.079
MI	22 (36.7)	66 (43.1)	0.388
PAFHx	11 (18.3)	5 (3.3)	< 0.001
HCVD	37 (61.7)	89 (58.2)	0.640
COPD	5 (8.3)	10 (6.5)	0.645
DM	25 (41.7)	62 (40.5)	0.879
CRF	5 (8.3)	29 (19.0)	0.057
BB	28 (46.7)	32 (20.9)	0.279
CCB	20 (33.3)	83 (54.2)	0.041
ACEI/ARB	16 (26.7)	44 (28.8)	0.195
Statin	1 (1.7)	31 (20.3)	0.006
Post-CABG			
Intubation days	3.9 ± 8.8	1.5 ± 2.3	< 0.001
BB	15 (25.0)	53 (34.6)	0.175
CCB	28 (46.7)	85 (55.6)	0.242
Amiodarone	47 (78.3)	6 (4.4)	< 0.001
Diuretics	57 (95.0)	106 (69.3)	< 0.001
Mortality	3 (5.0)	7 (4.6)	0.571
Off-pump CABG	18 (30.0)	60 (39.2)	0.209

Values are expressed as mean ± SD or number (%) of patients. Student t-test and chi-square tests were used for statistical analysis. Abbreviations are the same as in Table 1.

(3.9 ± 8.8 versus 1.5 ± 2.3, $p < 0.001$) after CABG.

In multivariate analysis, three variables emerged as the independent predictors of AF: Age ≧ 65 years (OR 5.008; 95% CI, 1.4-17.9, $p = 0.013$), history of PAF (OR 7.851; 95% CI, 2.4-25.6, $p = 0.001$) and intubation > 3 days (OR 5.303; 95% CI, 2.2-13.1, $p < 0.001$) (Table 3).

Mortality between AF and non-AF patients

Ten patients (3 AF, 7 non-AF) died after CABG (Table 4). Five patients were due to pneumonia with septic shock and five were related to preoperative complications of acute MI (1 cardiac rupture, 1 ventricular septal defect, 3 cardiogenic shock). However the mortality rate between AF and non-AF patients was not significantly different (5.0% to 4.6%, $p = 0.571$).

Therapeutic treatment of AF patients

In this study, several anti-arrhythmic medications were used, including BB, CCB, digitalis and amiodarone. Eighteen and 42 patients developed postoperative AF in groups 1 and 2, respectively. Once AF developed, digitalis (n = 12, 66.7%; n = 33, 78.6%) and amiodarone (n = 13,72.2%; n = 34, 80.9%) were more frequently used in acute treatment of AF as compared with BB (n = 10, 55.5%; n = 5, 11.9%) and CCB (n = 12, 66.7%; n = 16, 38.1%) in groups 1 and 2, respectively.

Table 3. Multivariate predictors of AF

	OR	95% CI	*p* value
Age ≥ 65	5.008	1.4-17.9	0.013
PAFHx	7.851	2.4-25.6	0.001
Intubation days > 3	5.303	2.2-13.1	< 0.001

OR: odds ratio
95% CI: 95% confidential interval
PAFHx: paroxysmal atrial fibrillation history

Table 4. Perioperative morbidity and mortality between AF and non-AF patients

	AF	Non-AF
Morbidity		
Acute renal failure	1	0
CVA	2	0
Cardiac rupture	1	0
Ischemic bowel disease	0	2
Pneumonia with sepsis	4	4
Rebleeding	0	3
SSS	0	1
VSD	0	2
Wound infection	0	2
Mortality		
Cardiac rupture	1	0
Cardiogenic shock	1	2
Pneumonia with septic shock	1	4
VSD	0	1

CVA: cerebrovascular accident; SSS: sick sinus syndrome; VSD: ventricular septal defect.

DISCUSSION

AF incidence after CABG

AF remains the most common cardiac arrhythmia after CABG and leads to an increased risk of thromboembolic events, as well as longer hospital stays. Reported

postoperative AF incidence varies from 3.1% to 40%, and the possible mechanisms of AF include withdrawal of anti-arrhythmic medications administered preoperatively such as β-blockers, the effects of cardiopulmonary bypass, cardioplegic solution, pericardial inflammation, autonomic imbalance in the early postoperative period and release of systemic mediators.[1-4,6-9] Whether the occurrence of postoperative AF is related to CPB is inconclusive. Allen et al. reported that 23 patients who underwent minimally invasive Redo CABG without using CPB had lower incidence of postoperative AF as compared with traditional on-pump CABG.[3] However, Saatvedt et al. found no reduction of AF incidence in off-pump CABG and recommended that postoperative AF was not caused solely by extracoporeal circulation.[7] In a recent study, Salamon et al. also reported similar incidence of postoperative AF in off-pump and on-pump CABG.[8] The possible explanations for that observation may be due to routine use of prophylactic β-blockers and limited pericardial inflammation. In this study, more patients in the on-pump group received preoperative β-blocker than in the off-pump group, and this may account for the similar incidence of postoperative AF between on-pump and off-pump groups in this study. In our current study, the use of statins seemed to have the ability to reduce the AF incidence (1.7% versus 20.3%, $p = 0.006$), however, further investigation is recommended due to the small numbers of patient receiving statins. In our study, the overall incidence of AF after cardiac surgery was 28.2%, which is compatible with previous studies. However, there was no statistically significant difference of AF incidence between off-pump (23.1%) and on-pump (31.1%) patients ($p = 0.209$).

Predictors of AF after CABG

Several parameters have been raised as the predictors of AF after CABG, including male gender, old age, history of AF, history of CHF, previous stroke, pulmonary vein venting and longer aorta cross-clamping time.[2,4] In our study, we found three variables to be independent predictors of AF after CABG, including age ≧ 65 years (OR 5.008; 95% CI, 1.4-17.9, $p = 0.013$), history of PAF (OR 7.851; 95% CI, 2.4-25.6, $p = 0.001$), and prolonged postoperative intubation > 3 days (OR 5.303; 95% CI, 2.2-13.1, $p < 0.001$). Age-related atrial structural dilatation, myocardial fibrosis and non-uniform anisotropic conduction may explain the strong association of AF with old age. In addition, prolonged ventilation due to pneumonia, poor left ventricular function and congestive heart failure have been associated with increased vulnerability to occurrence of AF due to hypoxia, sepsis and electrolyte imbalance.[11-13]

Acute treatment of postoperative AF

To treat postoperative AF, Ommen et al.[1] recommended prompt anticoagulation and the administration of an atrioventricular nodal blocking agent, including BB and CCB to control the heart rate. Digitalis may be useful for patients with left ventricular dysfunction, and membrane-active anti-arrhythmic drugs should be started if AF recurs. Lee et al. also reported the safety and efficacy of perioperative low-dose intravenous amiodarone in the prevention of AF after CABG.[10] In our study, intravenous digoxin and amiodarone were used more often than BB and CCB, due to the limited choice of intravenous anti-arrhythmic agents in our hospital.

Mortality rate between AF and non-AF patients

In a recent large retrospective cohort study reported by Villareal et al, patients who developed AF after CABG had significantly greater incidence of stroke, early death and long-term mortality.[9] In our current study, ten patients (3 AF, 7 non-AF) developed in-hospital death, however, the mortality rate of AF and non-AF patients did not differ (5.0% versus 4.6%, $p = 0.571$). This may be due to the small case number in our study and higher incidence of pneumonia with septic shock in the non-AF group (57.1% versus 33.3%, $p = 0.105$).

Limitations of study

This was a retrospective and non-randomized study. The second limitation of this study was that the true incidence and duration of postoperative AF might have been underestimated, as Holter monitoring was not routinely performed in this study.

CONCLUSION

In this retrospective study, off-pump CABG surgery did not decrease the incidence of postoperative AF.

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非體外循環式冠狀動脈繞道手術能否降低術後心房顫動之發生機率？

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背景 心房顫動是冠狀動脈繞道術後最常發生之心律不整，同時也增加了術後之合併症及死亡率。由於減少對心房的撥動，非體外循環式冠狀動脈繞道手術被認為可以減少術後心房顫動之發生。

方法 225 位病人接受冠狀動脈繞道手術，其中有 12 位病人術前即是慢性心房顫動，因此不予以分析。第一組有 78 位病人 (53 位男性，平均年齡 68.6 ± 11.9 歲；25 位女性，平均年齡 70.7 ± 7.9 歲) 接受非體外循環式冠狀動脈繞道手術，第二組有 135 位病人 (93 位男性，平均年齡 72.1 ± 10.1 歲；42 位女性，平均年齡 72.3 ± 7.9 歲) 接受體外循環式冠狀動脈繞道手術。本研究分析這兩組病人心房顫動之發生機率及其預測因子。

結果 60 位病人產生術後心房顫動 (28.2%)。雖然第二組病人有較高比率之心肌梗塞、陣發性心房顫動病史、鬱血性心臟衰竭、較長之插管時間及較高之併發症發生率。但是第一組 (23.1%) 跟第二組 (31.1%) 之術後心房顫動發生機率並無統計學上有意義之差別。至於術後心房顫動發生之預測因子則有：年齡大於 65 歲、有陣發性心房顫動病史者以及術後插管時間大於三天者。

結論 在這個回朔性的研究中，非體外循環式冠狀動脈繞道手術並不能減少術後心房顫動之發生機率。

關鍵詞：心房顫動、冠狀動脈繞道手術、心臟電生理學。