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Postoperative Atrial Fibrillation is Associated with Higher Euroscore, but not with Hospital Mortality after Coronary Artery Bypass Graft Surgery

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Abstract

Background: Postoperative atrial fibrillation (POAF) is the most common arrhythmia after coronary artery bypass surgery (CABG) and is associated with an increased morbidity. Recently, it has been suggested that POAF is also associated with increased postoperative mortality.

Aim: To investigate whether POAF after isolated CABG was associated with a higher EuroSCORE, indicating greater in-hospital mortality risk.

Methods: We reviewed data from our prospective cardiac surgery database of all patients (n=2791) undergoing isolated CABG from January 2003 through December 2006 at a large university medical center. The Mann-Whitney test was used to test for differences in continuous variables between the POAF and non-POAF groups, while the Chi-square test was used for categorical variables. Cox proportional-hazards regression analysis was used to identify independent predictors of in-hospital mortality.

Results: The mean age was 68 ± 9.1yrs, and mean EuroSCORE was 6.91 ± 3.18. The overall incidence of POAF was 32.3%. The POAF group was older (70.5 ± 7.8 vs. 66.8 ± 9.5yrs non-POAF: p<0.0001), but there was no significant difference in ejection fraction (EF) between the two groups (p=0.13). There was a significant difference in the mean EuroSCORE (POAF, 7.6 ± 3.2 vs non-POAF, 6.6 ± 3.1, p<0.0001), indicating that the POAF group was at greater risk for postoperative mortality. Although, there was a significant association between EuroSCORE and POAF (p<0.0001), there was no significant difference in hospital mortality between the POAF and non-POAF groups. The overall hospital mortality was 1.9%, with no difference between the two groups (p=0.91). Furthermore, POAF was not predictive of hospital mortality after CABG.

Conclusion: POAF is associated with a higher EuroSCORE, but it is neither associated with, nor predictive of increased hospital mortality after CABG.

Keywords: Mortality; Bypass; Surgery; Prognosis; Atrial fibrillation

Introduction

Atrial fibrillation (AF), is the most common arrhythmia after cardiac surgery [1-3], occurring in as much as, forty to sixty-five percent of the patients [2,4-7]. Such occurrence of this arrhythmia in the post-operative setting has resulted in an escalation in hospitalization costs when compared to those without postoperative atrial fibrillation (POAF) [4,6]. Furthermore, POAF has been increasingly associated with greater hospital and 6-month mortality rates [4], as well as late mortality [2,8-10]. However, many of those studies documenting such an association between POAF and mortality utilized earlier cardiac surgery databases from the 1990s. Yet, since that time, there have been significant advances in cardiac surgery including implementation of clinical protocols with pharmacological agents (such as amiodarone and beta-blocker therapy) [11-13] in both the preoperative and postoperative periods [14-17] in an effort to try to prevent POAF.

Subsequent studies utilizing more recent databases from 2003-2007 found that new-onset POAF was not associated with increased hospital mortality [18] and was not an independent predictor of early mortality after coronary artery bypass graft [CABG] surgery [19]. In contrast, preoperative atrial fibrillation was associated with early [20] and late [20,21] mortality after CABG. Given the conflicting results between older studies and more recent research on the effect of POAF on mortality, we hypothesized that new-onset POAF is not associated with greater in-hospital mortality, using a more recent cardiac surgery database.

Aim

We investigated the relationship between new-onset POAF, EuroSCORE, and in-hospital mortality after isolated CABG surgery in the modern day era of cardiac surgery.

Methods

Study design

This was a retrospective study which examined whether new-onset

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POAF after CABG was associated with higher EuroSCORE and in-hospital mortality.

Study population: We reviewed data from our single-center, prospective cardiac surgery database of all patients (n=2791) undergoing isolated CABG from January 2003 through December 2006 at a large university medical center in northern Italy. Data extraction comprised demographic data, pre-existing co-morbidities, European System for Cardiac Operative Risk Evaluation (EuroSCORE), and postoperative clinical outcomes including POAF and mortality. The study protocol was in compliance with the Institutional Review Board.

The need for informed consent was waived since the data used in this study had already been collected for clinical purposes and for the surgical database registry maintained by the Department of Cardiothoracic Surgery. All personal identifying data had been removed from the study database so that individuals could not be identified.

The primary endpoint of hospital mortality was obtained from the cardiothoracic surgery database which was maintained by designated departmental staff.

POAF, the primary independent variable in this study, was detected by continuous cardiac monitoring in the intensive care unit and stepdown units, and was defined as the occurrence of any episode of AF (after CABG) which required treatment (including medication or cardioversion).

Statistical methods

Numerical variables were presented as mean ± SD and categorical variables were summarized by percentages. The Student *t* test [for Gaussian or normally distributed data] or Mann-Whitney test [for non-Gaussian data] was used to test for differences in continuous variables between the AF and non-AF groups, while the Chi-square test [$\chi 2$] was used for categorical variables. The Pearson correlation test was used to analyze for associations between hospital mortality and continuous variables [Spearman rank correlation was used for non-Gaussian data] while chi-square test was used for categorical variables.

Covariates of postoperative mortality risk were identified using the well-validated EuroSCORE risk model [22,23]. The 17 covariates of EuroSCORE consist of patient related factors, cardiac-related factors, and operation-related factors (Table 1) [22].

In order to evaluate the independent risk of POAF on in-hospital mortality, a stepwise multivariate Cox proportional-hazards regression analysis was used, adjusting for EuroSCORE (which reflects the 17 covariates of postoperative mortality risk) and those variables with significant differences between the two groups (POAF and non-POAF). Adjusted hazards ratios (HRs) and the 95% confidence intervals (CIs) were calculated for those variables which were found to be independent mortality predictors. The level of significance was p<0.05, and all tests were two-sided.

Patient-related factors	Definition	score
Age	(per 5 years or part thereof over 60 years)	1
Sex	female	1
Chronic pulmonary disease	Long-term use of bronchodilators or steroids for lung disease	1
Extracardiac arteriopathy	any one or more of the following: claudication, carotid occlusion or >50% stenosis, previous or planned intervention on the abdominal aorta, limb arteries or carotids	2
Neurological dysfunction disease	severely affecting ambulation or day-to-day functioning	2
Previous cardiac surgery	requiring opening of the pericardium	3
Serum creatinine	>200m micromol/L preoperatively	2
Active endocarditis	patient still under antibiotic treatment for endocarditis at the time of surgery	3
Critical preoperative state	any one or more of the following: ventricular tachycardia or fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before arrival in the anaesthetic room, preoperative inotropic support, intra-aortic balloon counterpulsation or preoperative acute renal failure (anuria or oliguria<10 ml/hour)	3
Cardiac-related factors	***Definition***	***Score***
Unstable angina	rest angina requiring iv nitrates until arrival in the anaesthetic room	2
LV dysfunction	moderate or LVEF30-50%	1
	poor or LVEF<30	3
Recent myocardial infarct	(<90 days)	2
Pulmonary hypertension	Systolic PA pressure>60 mmHg	2
Operation-related factors	***Definition***	***Score***
Emergency	carried out on referral before the beginning of the next working day	*2*
Other than isolated CABG	major cardiac procedure other than or in addition to CABG	*2*
Surgery on thoracic aorta	for disorder of ascending, arch or descending aorta	*3*
Postinfarct septal rupture		*4*

Table 1: European System for Cardiac Operative Risk Evaluation (EuroSCORE).

Results

Preoperative data

The mean age was 68 ± 9.1yrs, and mean EuroSCORE was 6.91 ± 3.18 among the entire study population. The overall incidence of POAF was 32.3% (Table 2). In comparison to the non-POAF group, the POAF group was older (70.5 ± 7.8 years vs 66.8 ± 9.5, p<0.0001), with a greater incidence of congestive heart failure (CHF, 5.7% vs 3.9%, p=0.04] and hypertension (HTN, 81.8% vs 78.5%, p=0.05). In addition, the incidence of POAF in our study was greater among women compared to men (37.3% vs 30.9%, p=0.003). Interestingly, smoking was significantly more prevalent among non-POAF patients (8.6% vs 5.5%, p=0.005). With regards to the incidence of diabetes mellitus (DM), emphysema, hypercholesterolemia, and cerebrovascular accident (CVA), there was no significant difference between the POAF and non-POAF groups. However, POAF patients were noted to have a higher preoperative creatinine (111.2 ± 71.6 mmol/dl vs 107.6 ± 70.4 mmol/dl, p=0.03). Although there was no significant difference in myocardial infarction (MI), left main disease, or surgical priority, the POAF group exhibited an increased pre-operative risk as evidenced by a greater need for preoperative intra-aortic balloon pump (IABP) support (8.1% vs 5.7%, p=0.02), as well as risk for increased postoperative mortality, as demonstrated by a higher EuroSCORE (AF: 7.6 ± 3.2 vs 6.6 ± 3.1, p<0.0001). Overall, 3.2% of the population underwent re-do CABG, with no significant difference between the AF and non-AF groups (Table 3) for preoperative risk factors based on the presence or absence of POAF).

Intraoperative data

While the use of internal mammary arteries (IMA) was significantly higher in non-POAF patients (Left IMA: 89.2 vs. 86.3%, p=0.03; Right IMA: 5.4% vs. 3.1%, p=0.01), patients in the POAF group had a significantly longer aortic cross clamp time (66.2 ± 34.3 vs. 62.8 ± 33.04 minutes, p=0.01) and cardiopulmonary bypass time (104.4 ± 45.5 vs 100.9 ± 51.2 minutes, p=0.02) (Table 4).

Variable	Overall study population (n=2,791)
Age (yrs), mean ±SD	68 ± 9.1
Euroscore	6.9 ± 3.2
Gender – Male (%)	2169 (77.7%)
Gender – Female (%)	622 (22.3%)
Ejection Fraction (%)	54.1 ± 12.5
Diabetes Mellitus (%)	800 (28.7%)
Hypertension (%)	2,223 (79.6%)
Preoperative creatinine (μmol/L)	108.7 ± 70.8 (1.2 ± 0.8 mg/dl)
CHF (%)	124 (4.4%)
Cerebrovascular Accident (CVA) (%)	186 (6.7%)
Chronic bronchodilator therapy (%)	69 (2.5%)
Smoker (%)	213 (7.6%)
Dialysis (%)	35 (1.3%)
Emphysema (%)	174 (6.2%)
Dyslipidemia (%)	1788 (64.1%)
Preoperative IABP (%)	204 (7.3%)
Left main disease>50% (%)	801 (28.7%)
Previous MI (%)	1228 (44%)
Re-do CABG (%)	90 (3.2%)
Extracardiac arteriopathy (%)	674 (24.1)
Body surface area (BSA)	1.71 ± 0.7

Table 2: Baseline characteristics of the study population.

Variable	Overall study population (n=2,791)	(+) POAF (n = 901)	(-) POAF (n = 1,890)	P value
Age (yrs) Mean ±SD	68 ± 9.1	70.5 ± 7.8	66.8 ± 9.5	<0.0001
Euroscore	6.9 ± 3.2	7.6 ± 3.2	6.6 ± 3.1	<0.0001
Gender - male	2169 (77.7%)	669 (74.2%)	1500 (79.4%)	0.002
Gender - Female	622 (22.3%)	232 (25.7%)	390 (20.6%)	0.003
Ejection Fraction (%)	54.1 ± 12.5	53.5 ± 12.7	54.3 ± 12.5	0.13
Diabetes Mellitus (%)	800 (28.7%)	259 (28.7%)	541 (28.6%)	0.99
Hypertension (%)	2,223 (79.6%)	737 (81.8%)	1486 (78.6%)	0.055
Preoperative creatinine (μmol/L)	108.7 ±70.8 (1.2 ± 0.8 mg/dl)	111.2 ± 71.6 (1.3 ± 0.8 mg/dl)	107.6 ± 70.4 (1.2 ± 0.8 mg/dl)	0.0324
CHF (%)	124 (4.44%)	51 (5.7%)	73 (3.9%)	0.04
Cerebrovascular Accident (CVA) (%)	186 (6.7%)	68 (7.5%)	118 (6.2%)	0.23
Pre-operative IABP (%)	204 (7.3%)	82 (9.1%)	122 (6.5%)	0.017
Previous MI (%)	1228 (44%)	402 (44.6%)	826 (43.7%)	0.68
Re-do CABG (%)	90 (32%)	27 (3%)	63 (3.3%)	0.76

Table 3: Preoperative risk factors based on the presence or absence of POAF.

Variable	Overall study population (n=2,791)	(+) POAF (n = 901)	(-) POAF (n = 1,890)	P value
Aortic cross clamp time (minutes)	63.8 ± 33.5	66.2 ± 34.3	62.8 ± 33	0.0124
Cardiopulmonary bypass (CPB) time (minutes)	102 ± 49.4	104.4 ± 45.5	101 ± 51.2	0.015
Venous grafts	2372 (85%)	772 (85.7%)	1600 (84.7%)	0.53
Number of vein grafts (mean ± SD)	1.76 ± 0.78	1.79 ± 0.77	1.74 ± 0.79	0.13
Right Internal Mammary artery graft	130 (4.7%)	28 (3.1%)	102 (5.4%)	0.009
Left Internal Mammary Artery graft	2461 (88.2%)	778 (86.3%)	1683 (89%)	0.045
Number of arterial grafts (mean ± SD)	1.12 ± 0.4	1.07 ± 0.34	1.14 ± 0.43	<0.0001
Intraoperative IABP	54 (1.9%)	18 (2%)	36 (1.9%)	0.97

Table 4: Intraoperative Variables based on the presence or absence of POAF.

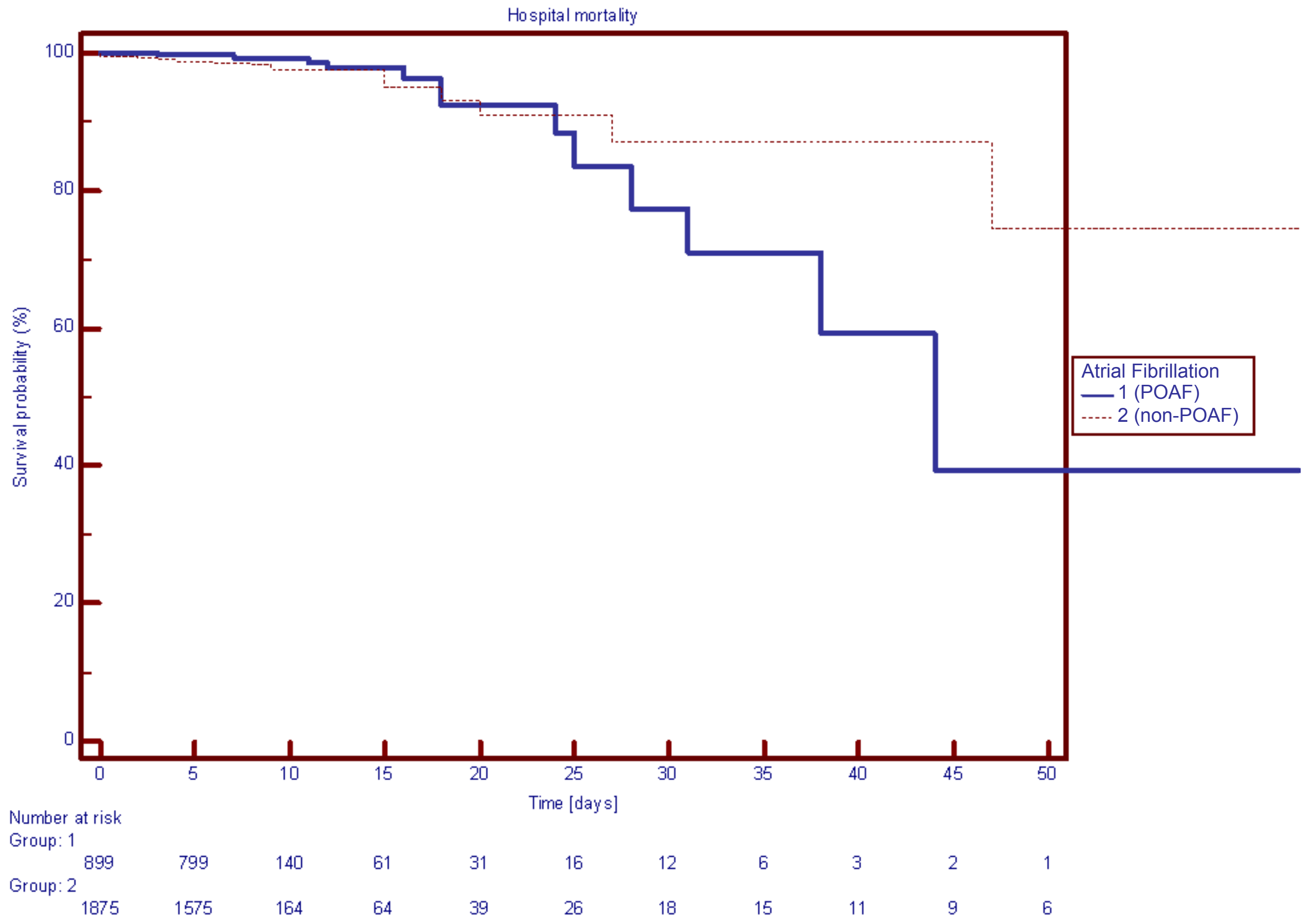
Postoperative data

The peak creatinine in the postoperative period was significantly higher among POAF patients (120.4 ± 70.1 mmol/dl vs. 117.4 ± 80.5 mmol/dl, p=0.04).

Furthermore, the POAF group had a longer period of mechanical ventilation (27.0 ± 72 hours vs 17.6 ± 42.1 hours, p<0.0001), greater incidence of blood transfusion (74.6% vs 61.4%, p<0.0001), and lengthier intensive care unit stays (3.0 ± 4.3 days vs. 2.4 ± 5.2 days, p<0.0001). The overall hospital length of stay was also prolonged in the POAF group (8.8 ± 11.3 days vs 7.8 ± 9.7 days, p<0.0001) (Table 5).

Outcomes

Despite a significant association between EuroSCORE and POAF (p<0.0001), there was no significant difference in in-hospital mortality between the POAF and non-POAF groups (Figure 1): the overall in-hospital mortality was 1.9% (1.88% in POAF group vs. 1.9% in non-



There was no difference in hospital mortality between the POAF (Group-1) and non-POAF (Group-2) groups [p=0.4, Hazard ratio 1.27, 95% CI 0.73 to 2.22]

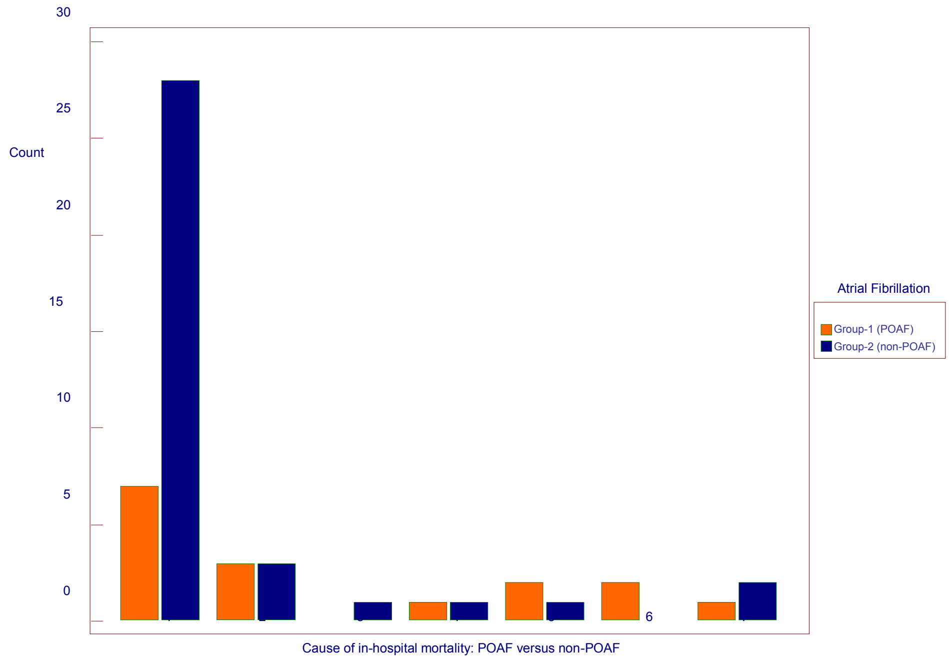
Figure 1: Kaplan-Meier survival curve of POAF versus non-POAF patients: hospital mortality.

Variable	Overall study population (n=2,791)	(+) POAF (n = 901)	(-) POAF (n = 1,890)	P value
Intensive care unit length of stay (days)	2.6 ± 4.9	3 ± 4.3	2.4 ± 5.2	<0.0001
Peak postop creatinine (μmol/L)	118.3 ± 77.2	120.4 ± 70.1	117.4 ± 80.5	0.041
Hospital length of stay (days)	8.1 ± 10.3	8.8 ± 11.3	7.8 ± 9.7	<0.0001
Pulmonary artery systolic pressure (PASP)	31.3 ± 6.3	31.7 ± 7.2	31 ± 5.8	0.07
Left ventricular end- diastolic pressure (LVEDP)	9.9 ± 10.5	10 ± 10.9	10 ± 10.3	0.84
Length of mechanical ventilation (hours)	20.6 ± 53.8	27 ± 72	17.6 ± 42.1	<0.0001
Postoperative IABP (%)	41 (1.5%)	19 (2.1%)	22 (1.2%)	0.0954
Blood transfusion (%)	1830 (65.6%)	672 (74.6%)	1158 (61.3%)	<0.0001

Table 5: Postoperative Variables based on the presence or absence of POAF.

POAF group, p=0.91) (Table 6). The cause of death was predominantly due to cardiac causes in both groups, with no significant difference between the two groups (Figure 2). Multivariate logistic regression analysis of univariate predictors of hospital mortality was performed (Table 7). Receiver Operating Characteristic (ROC) curve analysis showed the area under the curve was 0.951, 95% CI 0.942 to 0.96, indicating good discriminatory ability of the statistical model.

Using a stepwise Cox proportional-hazards regression model to identify independent predictors of hospital mortality, we entered the EuroSCORE (which incorporates those variables identified as mortality risk predictors) [22]. In order to adjust for baseline differences, we also entered those variables (not already included in EuroSCORE) for which there were significant differences between the two groups (i.e. postoperative AF, preoperative creatinine, peak postoperative creatinine, total cardiopulmonary bypass time, total aortic cross clamp time, use of right internal mammary artery graft, use of left internal mammary artery graft, number of arterial grafts, blood transfusion,



Cardiac=1; Pulmonary=2; Renal=3; Neurologic=4; Infective= 5; Valvular=6; Vascular=7

Cause of death	POAF (n=901)	Non-POAF (n=1890)	P value	total
Cardiac (1)	7 (0.8%)	28 (1.5%)	0.17	35
Pulmonary (2)	3 (0.3%)	3 (0.2%)	0.93	6
Renal (3)	0 (0%)	1 (0.1%)	0.86	1
Neurological (4)	1 (0.1%)	1 (0.1%)	0.52	2
Infective (5)	2 (0.2%)	1 (0.1%)	0.9	3
Valvular (6)	2 (0.2%)	0 (0%)	0.25	2
Vascular (7)	1 (0.1%)	2 (0.1%)	0.52	3

Figure 2: Cause of mortality in POAF versus non-POAF group.

Variable	Overall study population (n=2,791)	(+) POAF (n = 901)	(-) POAF (n = 1,890)	P value
Hospital mortality	53 (1.9%)	17 (1.9%)	36 (1.9%)	0.88
30-day mortality	25/remaining 2738(0.9%)	9/remaining 884 (1%)	16/remaining 1854 (0.86%)	0.88

Table 6: Mortality Outcomes.

and total number of hours of mechanical ventilation). POAF was not predictive of in-hospital mortality after CABG. Only EuroSCORE, peak postoperative creatinine, and total number of hours of mechanical ventilation were independent predictors of hospital mortality after CABG (Table 7).

Discussion

POAF is a frequent complication occurring in one-third to one-half of patients undergoing cardiac surgery. Both cardiopulmonary bypass and cardioplegic arrest have been identified as independent predictors of postoperative atrial fibrillation, suggesting that the inflammatory response to cardiopulmonary bypass, myocardial ischemia, and atrial cannulation may all contribute to the development of POAF after cardiac surgery [24].

However, the controversy remains whether cardiopulmonary bypass and cardioplegic arrest directly increase the risk of POAF, with conflicting results from several studies [25,26]. Similar to previous studies [27], a higher incidence of POAF was observed in patients with postoperative renal dysfunction in our study. Along with increased costs and use of resources [28], POAF is associated with increased risk of morbidity, including increased risk of stroke which significantly contributed to the long-term mortality rate with POAF patients after isolated CABG [29]. Late mortality in POAF patients was reported after CABG, but not after valvular surgery or combined CABG/valvular surgery [30]. In addition, independently of age, POAF was found to be strong risk factor for development of late AF [31]. Such late AF may occur as asymptomatic AF with uncontrolled ventricular response, thereby increasing the risk for not only stroke, but also for heart failure [due to loss of atrial kick and reduced ventricular diastolic filling time in AF with uncontrolled ventricular rates, with subsequent reduction in cardiac output], and arrhythmias which can lead to myocardial ischemia, myocardial infarction, and sudden death, all of which have been observed in POAF patients [10]. Whether closer surveillance for POAF recurrence after CABG, with subsequent rhythm control or rate control along with anticoagulation, would result in a reduction in mortality is unknown and remains to be elucidated, possibly by means of a prospective, randomized trial in which patients with POAF

Multiple stepwise logistic regression analysis of univariate predictors of hospital mortality:

Variable	Odds ratio	95% confidence interval	P value
EuroSCORE	1.1999	1.0854 to 1.3264	0.0004
Total hours of mechanical ventilation	1.0073	1.0040 to 1.0106	<0.0001
Cardiopulmonary bypass time	1.0038	1.0003 to 1.0074	0.036
Peak creatinine post-op (micromol/L)	1.0033	1.0007 to 1.0060	0.014
Intra-aortic balloon pump	7.2730	3.2704 to 16.1745	<0.0001

Cox-Proportional Hazards Regression analysis of independent predictors of hospital mortality:

Variable	Hazards Ratio	95% confidence interval	P value
EuroSCORE	1.1450	1.0089 to 1.2995	0.037
Peak creatinine post-op (micromol/L)	1.0049	1.0018 to 1.0080	0.002
Total hours of mechanical ventilation	1.0061	1.0028 to 1.0094	0.0003

Table 7

are randomized to rhythm or rate control strategy, and followed to determine if there is a difference in mortality. Such an investigation has previously been undertaken in non-surgical AF patients in several clinical trials [Atrial Fibrillation Followup Investigation of Rhythm Management (AFFIRM) [32], Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE) [33], and Rhythm control versus rate control for Atrial Fibrillation and Congestive Heart Failure (AF-CHF) [34], all of which found no significant difference in late mortality between the rhythm control versus rate control groups, after a mean follow-up period ranging from 2.3 yrs in one study up to 5 years in another study.

Study limitations

Given the low mortality rates [with no significant difference between the POAF and non-POAF groups for in-hospital and thirty-day mortality], the number of predictive variables used in the multivariate analysis for predictors of mortality was limited to variables collected for the registry, but included EuroSCORE [which incorporated those variables identified as mortality risk predictors], as well as variables for which there were significant differences between the POAF and non-POAF groups in an attempt to identify whether such differences contributed to mortality risk in the POAF group.

The current study is limited by lack of long-term follow-up, and data on long-term rhythm control, rate control, medication use such as beta-blockers and anti-arrhythmic drug therapy such as amiodarone, and anticoagulation status. Nonetheless, despite an increased baseline risk in the POAF group, there was no difference in hospital mortality between the POAF and non-POAF groups.

Conclusions

Our findings were in accordance with recently published studies which reported that new-onset POAF was neither associated with nor predictive of hospital mortality after CABG [18,19]. We report an association between POAF and a higher EuroSCORE, without any associated increase in postoperative mortality.

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