Risk Factors for Atrial Fibrillation following a Cardiac Surgery

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Abstract

Background: Atrial fibrillation (AF) following cardiac surgery is common and has clinical impact on morbidity. The preoperative and intraoperative risk factors are still not well defined. The objective of the study was to examine preoperative and intraoperative risk factors for AF following cardiac surgery. Methods: A retrospective analysis of a database of cardiac surgeries was performed during 2017-2019 at Poriya Medical Center. Preoperative factors and intraoperative were recorded. Results: 208 patients were included in this analysis. Overall AF following cardiac surgery was detected in 50 (24%) patients. Of 175 patients who did not have history of AF prior to surgery, 27 (15.5%) had post-operative AF. In the 33 patients with previous AF, AF following surgery was detected in 23 (70%). Patients with AF following surgery who were older ($66.2\pm8.0 \text{ vs. } 60.7\pm11.4 \text{ years}, p=0.002$), were treated more with anti-arrhythmic drugs (18.9% vs 4.5, p<0.001), and had higher rates of pre-operative AF (46% vs 6.3%, p=0.0001), prior cerebral vascular accidents (14% vs 4.4%, p=0.019), and prior valve replacement (10% vs 1.9%, p=0.006) and history of preoperative AF (HR 6.01, CI 3.42-10.57, P<0.001) were predictors of AF following cardiac surgery. The probability of being free of postsurgical AF was 80% among patients without history of AF following cardiac surgery. The probability of being free of postsurgical AF was 80% among patients without history of AF following cardiac surgery.

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Abstract

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Methods: A retrospective analysis of a database of cardiac surgeries was performed during 2017-2019 at Poriya Medical Center. Preoperative and intraoperative factors were recorded.

Results: 208 patients were included in this analysis. Overall AF following cardiac surgery was detected in 50 (24%) patients. Of 175 patients who did not have history of AF prior to surgery, 27 (15.5%) had post-operative AF. In the 33 patients with previous AF, AF following surgery was detected in 23 (70%). Patients with AF following surgery who were older (66.2±8.0 vs. 60.7 ± 11.4 years, p=0.002), were treated more with anti-arrhythmic drugs (18.9% vs 4.5, p<0.001), and had higher rates of pre-operative AF (46% vs 6.3%, p=0.0001), prior cerebral vascular accidents (14% vs 4.4%, p=0.019), and prior valve replacement (10% vs 1.9%, p=0.009) compared to patients without AF following surgery. In multivariate Cox regression analysis, age (HR 1.04, CI 1.01-1.07, P=0.006) and history of preoperative AF (HR 6.01, CI 3.42-10.57, P<0.001) were predictors of AF following cardiac surgery. The probability of being free of postsurgical AF was 80% among patients without history of AF compared to 30% in patients with previous AF history (p<0.001).

Conclusion: Preoperative AF and age were predictors of AF following cardiac surgery.

Background

Atrial fibrillation (AF) is a common arrhythmia in the general population and is more common in specific conditions such as cardiac and non-cardiac surgery [1,2]. AF following surgery could occur in patients who were or were not previously diagnosed with AF. Post-operative atrial fibrillation (POAF) is defined as the development of AF in the postoperative period in a patient who was not previously diagnosed with AF [2,3].

Focusing on POAF following cardiac surgeries is important since it is considered a common complication affecting patients following abundant surgical procedures including coronary artery bypass grafting (CABG), valve surgery, combined CABG and valve surgery, congenital defects surgery, and even percutaneous coronary revascularization but with a much lower risk than major surgical intervention [3-6]. The occurrence of POAF increases in correlation with increasing invasiveness of cardiac surgery, and may reach up to 60%, usually appearing within the first 6 days after surgery with a peak in the 2nd-4th days [4-6].

POAF is associated with major morbidities such as prolonged mechanical ventilation support, postoperative stroke, myocardial infarction, cardiac arrest, permanent pacemaker, respiratory failure, pneumonia, gastrointestinal complications, acute kidney injury, and a new onset of dialysis. Furthermore, POAF leads to a longer hospital and intensive care unit stay, higher treatment costs, hospital readmission, and most importantly, 2 folds of increased mortality [6-8].

Risk factors that were reported to correlate with increased incidence of POAF, were derived from epidemiological studies, and can be divided into 3 main groups: preoperative, intraoperative and postoperative factors [9,10]. In the last 20 years, research has expanded in the field of POAF and several modifications have been implemented to perioperative management and surgical techniques, in an attempt to decrease POAF incidence or its subsequent complications. However, more progress needs to be made [11]. The aim of this study is to evaluate preoperative, intra-operative risk factors and predictors of occurrence of overall AF following cardiac surgery including patients previously diagnosed and who were not previously diagnosed with AF (POAF).

Materials and Methods

A retrospective (case control) observational study was conducted in the cardiovascular department of Baruch Padeh Medical Center – Poriya to determine predictive risk factors that lead to developing AF in patients who had cardiac surgeries. The study was approved by the institutional ethics review board and the research was conducted in accordance with the Helsinki Declaration. Preoperative, intraoperative, and postoperative clinical data and laboratory tests were collected and summarized. Moreover, 30 days after surgery morbidities and mortality were recorded.

The population study included 208 patients who underwent cardiac surgeries at Baruch Padeh Medical Center in the years 2017-2019. Inclusion criteria consisted of: patients undergoing cardiac surgeries in a sinus rhythm with and without a history of AF. Exclusion criteria consisted of: patients with permanent atrial fibrillation, patients who were not in sinus rhythm prior to surgery, and patients with missing data. Patients were divided into 2 groups: patients with and without AF post cardiac surgery irrespective of their AF history prior to cardiac surgery. Pre, intra, and post-operative factors were compared between the 2 groups.

Statistical Methods

Values were presented as mean and standard deviation, and Categorical variables were represented by percentage and prevalence. Comparison between patients who developed AF post cardiac surgery and those who did not was conducted using t- test or Mann Whitney U for the continues data, and Chi Squared Test for categorical data. Logistic regression analysis was used for identifying pre and intraoperative risk factors for developing AF post cardiac surgery.

Kaplan Meir survival curve was utilized for evaluating the prevalence of AF post-surgery based on the history of pre-surgery AF. P value of less than 0.05 was considered statistically significant.

Results

208 patients who underwent cardiac surgeries at Baruch Padeh Medical Center in the years 2017-2019 who met the inclusion criteria participated in our study. Overall, AF post cardiac surgery was detected in 50 out of 208 (24%) patients. POAF was detected in 27 (15.5%) out of 175 patients without history of documented AF before cardiac surgery (Table 1). Among the 33 patients with history of AF before cardiac surgery, AF following surgery was detected in 23 (70%) patients.

The participants' demographic and preoperative clinical data are summarized in Table 2. Patients with AF post cardiac surgery were older ($66.2\pm8.0 \text{ vs } 60.7\pm 11.4 \text{ years}$, p<0.001), utilized more preoperative anti arrhythmic drugs (AADs) (18.9% vs 4.5%, p<0.001), and had more AF history (46% vs 6.3%, p>0.001), previous cerebrovascular accident (CVA) (14% vs 4.4%, p=0.019) and prior valve replacement (10% vs 1.9%, p=0.009) compared to patients without AF post cardiac surgery. Hypertension tended to be more prevalent among patients with AF post cardiac surgery (74% vs 59.5%, p=0.06). In contrast, gender, height, weight, BMI, BSA, prior beta blockers , diabetes mellitus , dyslipidemia, chronic obstructive pulmonary disease (COPD) and interstitial lung disease, peripheral vascular disease (PVD), renal failure, undergoing dialysis, previous (TIA), coronary vascular disease, congestive heart failure (CHF), ejection fraction (EF), previous CABG, and prior percutaneous coronary intervention (PCI) were not statistically different between the two groups.

Table 3 presents intraoperative factors and laboratory results. Pump time, minimum PH, Pre and postoperative hemoglobin, pre and post-operative creatinine were not statistically different between patients with and without AF following cardiac surgery. Aortic clamp time tended to be longer among patients with AF post cardiac surgery, compared to patients without AF post cardiac surgery (116.7 \pm 52.0 vs 101.7 \pm 50.2 minutes, respectively, p=0.07).

Post surgical major bleeding, and infection were not statistically different between the two groups as presented in Table 4. In hospital mortality, including cardiovascular and non-cardiovascular within 30 days and mortality in the first year following the surgery were not statistically different between the two groups. Readmission within 30 days tended to be more prevalent among patients with AF post cardiac surgery compared to patients without AF post cardiac surgery (26% vs 14.6%, respectively , p=0.06).

Predictors of AF Post-Cardiac Surgery

As shown in table 5, univariate Cox regression analysis revealed that age (HR 1.05, CI 1.01-1.08, P=0.002) and history of AF (HR 6.48, CI 3.69-11.37, P<0.001)) were predictors of AF post-surgery. Type of surgery (HR 1.34, CI 0.95-1.91, p=0.09) and hypertension (HR 1.72, CI 0.91-3.24, p=0.09) tended to predict AF following cardiac surgery. In multivariate Cox regression analysis, age (HR 1.04, CI 1.01-1.07, P=0.006) and history of preoperative AF (HR 6.01, CI 3.42-10.57, P<0.001) were independent predictors of AF following cardiac surgery (table 6).

Kaplan Meir survival curve was utilized for evaluating the probability of AF post-surgery based on the history of AF before surgery (figure 1). The probability of being free of AF post cardiac surgery was 80% among patients without history of preoperative AF compared to 30% among patients with history of preoperative AF (p<0.001). Most of AF episodes occurred between postoperative 2 and 5 as showed in figure 1.

Discussion

Overall AF following cardiac surgery was detected in 24% of patients. POAF (AF following cardiac surgery without history of AF) was detected in 15.5% of patients without history of AF prior to surgery. Among patients with history of AF, AF following surgery was detected in 70%. History of AF and age were independent predictors of AF following cardiac surgery.

The true incidence of POAF following cardiac surgery remains unclear due to variability in methods of detection and definitions of POAF [12]. The majority of studies reported POAF rates between 20-40% following CABG, 40-50% after valve surgery, up to 60% following combined valve and CABG surgery, and as high as 80% following multiple valve surgery [11]. Mariscalco et al. reported that among 17,262 cardiac surgery patients, 4,561 (26.4%) developed POAF, primarily within 2 days of surgery [13]. Bessissow et al. reported that the incidence of POAF among adults aged 45+ ranges from 20% to 40% among those undergoing thoracic or cardiac surgery [14]. In our study, the overall AF following cardiac surgery was 24%, and POAF was 15.5%. This rate (15.5%) of POAF seems to be lower than the rate reported in the literature if we take into account only patients with no history of AF. The discrepancy could be attributed to differences in definition and detection of POAF. Part of patients undergoing cardiac surgeries who are considered to have no history of AF actually have undetected and or asymptomatic paroxysmal AF before surgery as many of them have risk factors for AF. Thus, to overcome this limitation, we decided to investigate the overall AF following cardiac surgery irrespective of history of AF before surgery.

Many risk factors for POAF were reported in different studies. In general, older patients and those with more preoperative comorbidities are more likely to develop POAF. These risk factors were used to create predictive scoring systems and risk models [2]. Risk models are based on known risk factors such as age, race, CHF, a high EuroSCORE rating, COPD, emergency operation, decreased preoperative left ventricular EF, and decreased estimated glomerular filtration rate (eGFR) [13, 15-17]. However, Current risk prediction models for POAF are derived from epidemiological studies and are not based on pathophysiologic mechanisms. Due to that they are moderately accurate at best, these models are infrequently used in clinical settings [9]. Currently, no validated, evidence-based threshold exists to stratify patients according to risk of developing POAF, and there are no published studies that delineate risk factors for POAF based on significantly differentiating factors.

In general, the major risk factors for POAF among both non-cardiac surgery and cardiac surgery patients are male sex, advancing age, CHF history, and hypertension [14,18]. Among cardiac surgery patients, specifically, history of arrhythmias and AF, history of vascular and coronary artery diseases, valvular heart disease, decreased preoperative kidney function, and type of surgery are also implicated [11,13,14,16,19-23]. Our results are consistent with the previous reports in some aspects. In univariate Cox regression analysis, age and history of AF were found to be predictors of AF post-surgery. Type of surgery and hypertension tended to predict AF following cardiac surgery. In multivariate Cox regression analysis, age and history of preoperative AF were independent predictors of AF following cardiac surgery. Indeed, history of AF was previously reported to be strongly associated with POAF complicating cardiac surgery [24]. However, this report emphasizes the importance of cautious interpretation of the data from different studies as some studies included patients with history of arrhythmias and AF. The risk of POAF increases non-linearly with age, and a large retrospective study of nearly 15000 patients who have undergone cardiac surgery showed that POAF incidence increases at higher rates over the age of 55 years [25]. Recently, Eikelboom *et al.* reported in systemic review and meta-analysis that POAF occurred in 36,988 (23.7%) out of 155,575 patients [9]. Patients with POAF were older than those without it (mean, 68.7 vs 63.7 years). There were no sex differences between the groups. Hypertension, dyslipidemia, diabetes, and smoking occurred equivalently in patients who did and did not develop POAF [9]. With respect to intraoperative factors, there was no difference between patients with and without AF post cardiac surgery, except for aortic clamp time which tended to be longer among patients with AF post cardiac surgery (p=0.07). In some studies, procedural factors such as the duration of the aortic cross-clamp time, location of the venous cannulation, and duration of cardiopulmonary bypass have been shown to affect the rates of POAF [4].

Finally, POAF after cardiac surgery was reported to be associated with increased short-term and long-term morbidity and mortality, including an eightfold increase in the risk of subsequent AF, as well as a higher rate of stroke and cardiovascular death [3,7,9,26,27]. In our study, there was no difference in complications between the two groups, except for readmission within 30 days, which tended to be more frequent among patients with AF following cardiac surgery.

Limitations

This is a retrospective analysis of a relatively small number of patients. We decided to include all patients with AF following cardiac surgery irrespective of history of AF to overcome the variation in definition of POAF in different studies. Thus, our results applied to all patients with AF following cardiac surgery and not specifically to patients with POAF (patients with no history of AF).

In summary, preoperative AF and age were independent predictors of AF following cardiac surgery.

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Table 1: Atrial fibrillation post-cardiac surgery

	No atrial fibrillation post surgery $(n=158)$	Atrial fibrillation post surgery (n=50) $*$	P value
History of atrial fibrillation $(n=33)$	10~(6.3%)	23 (46%)	< 0.001
No history of atrial fibrillation (n=175)	148 (93.7%)	27 (54%) **	

*Atrial fibrillation post cardiac surgery= 50 out of 208 (24%). ** POAF= 27 out of 175 (15.5%)

Table 2: Demographic and preoperative clinical data

	No atrial fibrillation post surgery (n= 158)	Atrial fibrillation post surge
Male n(%)	125 (79.1%)	33 (70%)
Female $n(\%)$	33 (20.9%)	15 (30%)
Age (years)	60 ± 11	66±8
Height (cm)	169 ± 8	169 ± 10
Weight (Kg)	$80.4{\pm}14.6$	81.1 ± 12.7
$BMI (kg/m^2)$	$27.8 {\pm} 4.3$	28.3 ± 3.5
$BSA(m^2)$	$1.9{\pm}0.1$	1.9 ± 0.1
Beta blockers $n(\%)$	90~(7.3%)	33~(67.3%)
Pre-operative antiarrhythmic drugs $n(\%)$	7(4.5%)	9(18.4%)
Hypertension $n(\%)$	94~(59.5%)	37(74%)
Diabetes Mellitus treated with insulin $n(\%)$	31 (19.6%)	6(12%)
Diabetes Mellitus not treated with insulin $n(\%)$	39~(24.7%)	11 (22%)
Dyslipidemia n(%)	105~(66.5%)	32(64%)
COPD and Interstitial lung disease $n(\%)$	7(4.4%)	1 (2%)
Peripheral Vascular Disease $n(\%)$	5(3.2%)	1 (2%)
Renal failure $n(\%)$	5~(3.2%)	3(6.1%)
Patients undergoing dialysis $n(\%)$	2(1.3%)	0 (0%)
Permanent pacemaker $n(\%)$	3(1.9%)	1 (2%)
Previous CVA $n(\%)$	7(4.4%)	7 (14%)
Previous TIA $n(\%)$	1 (0.6%)	1 (2%)
Coronary Vascular disease $n(\%)$	97~(61.4%)	32(64%)
Chronic heart failure $n(\%)$	8 (5.1%)	4 (8%)
Ejection Fraction (%)	53.6 ± 16.3	52.5 ± 23.6
Previous CABG $n(\%)$	3~(1.9%)	2 (4%)
Prior Valve Replacement n(%)	3~(1.9%)	5(10%)
Prior PCI $n(\%)$	43 (27.2%)	16 (32%)

Table 3: Intra-operative factors and laboratory results:

	No atrial fibrillation post surgery (n= 158)	Atrial fibrillation post surgery (n=
Pump Time (min)	130.6 ± 59.2	144.9 ± 17.6
Aortic clamp time (min)	101.7 ± 50.2	116.7 ± 52.0
Minimum PH	7.2 ± 0	7.2 ± 0
Pre-operative Hemoglobin (g/L)	13.3 ± 1.9	13.3 ± 1.8
Pre-operative Creatinine (mg/dL)	$0.9{\pm}0.6$	$0.9 \pm .25$

	No atrial fibrillation post surgery (n= 158)	Atrial fibrillation post surgery (n
Post-operative Hemoglobin (g/L)	10.8 ± 1.9	10.9 ± 1.3
Post-operative Creatinine (mg/dL)	$0.9{\pm}0.8$	$0.9{\pm}0.2$
Post-operative Hemoglobin, Day1 (g/L)	$9.9{\pm}1.2$	$9.5{\pm}1.7$
Post-operative Creatinine, Day1 (mg/dL)	$0.9{\pm}0.4$	$0.9 {\pm} 0.3$

 Table 4: Post-operative complications

	No atrial fibrillation post surgery (n= 158)	Atrial fibrillation post surger
Major Bleeding [*] n(%)	7 (4.4%)	3 (6%)
Infection $n(\%)$	2(1.3%)	2(4%)
Cardio-vascular disease (CVD) mortality $n(\%)$	6(3.8%)	1(2%)
Non -CVD mortality $n(\%)$	1(0.6%)	0(0%)
Mortality within 30 days $n(\%)$	7 (4.4%)	1(2%)
Mortality in 1 year $n(\%)$	9(5.7%)	3(6%)
Readmission within 30 days $n(\%)$	23~(14.6%)	13~(26%)
Multiple readmissions $n(\%)$	31~(19.6%)	9~(18%)

*blood transfusion is needed

Tab	le	5:	Univa	aria	ble	\mathbf{C}	ox	regression	of	predictor	s of	A	١F	post-s	urge	ry.
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	B Coefficients	Hazard Ratio (CI)	P Value
Age	0.05	1.05(1.01-1.08)	0.002
Gender	0.41	1.51(0.82 - 2.76)	0.18
Beta blockers	0.38	1.47(0.81-2.67)	0.20
Surgery Type	0.29	1.34(0.95-1.91)	0.09
History of atrial fibrillation	1.86	6.48(3.69-11.37)	$<\!0.001$
Pump time	0.00	1.00(0.99-1.00)	0.18
Aortic clamp time	0.00	1.00 (0.99-1.00)	0.11
Minimum PH	2.64	14.05 (0.10-1870.71)	0.29
BMI	0.014	1.01 (0.95-1.08)	0.66
Hypertension	0.54	1.72(0.91-3.24)	0.09
Chronic heart failure	0.39	1.48 (0.53-4.13)	0.44

Table 6: Multivariable Cox regression predictors of AF post-surgery.

	B Coefficients	Hazard Ratio (CI)	P Value	
Age	0.04	$\begin{array}{c} 1.04 \ (1.01 - 1.07) \\ 6.01 \ (3.42 - 10.57) \end{array}$	0.006	
History of atrial fibrillation	1.79		<0.001	



Figure 1: Kaplan Meir survival curve evaluating the probability of AF post-surgery based on the history of AF before surgery.

