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Determining the Relative Frequency of the Factors Predicting Atrial Fibrillation after Coronary Artery Bypass Grafting

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ABSTRACT

Title: Relative frequency of predictive factors of Atrial Fibrillation after coronary artery bypass grafting in Patients that referred to Dr. Heshmat hospital of Rasht from January till May 2015.
Introduction and objective: Atrial fibrillation (AF) is the most common arrhythmia after coronary artery bypass grafting (CABG), that its etiology remains poorly understood. Several factors are linked to postoperative AF (POAF), including advanced age, sex and etc. that also controversial. This study focuses on factors that may affect the occurrence of AF. The aim is to identify those factors to develop AF after CABG.
Material & Methods: 184 patients underwent CABG in our hospital from Jan 2015 till May 2015 were enrolled to study. variables such as existence of Atrial fibrillation, age, sex, BMI, history of MI, Hyper lipidemia, Hypertension, Diabetic mellitus, COPD, Smoking, cross clamp time, number of graft, Kind of surgery (off-pump or on-pump) , consumption of beta-blocker were analyzed by SPSS version 16.
Results: Mean age of the patients was 59.7±8.86 years old that most of them (44%) were in range of 50-60yers old. The overall incidence of postoperative AF was 13%. Preoperative factors presenting significant correlation with the incidence of post-operative AF included: 1) age (P<0.015), 2) Sex (p<0.04), 3) chronic obstructive pulmonary disease (P<0.03), 4) Smoking (P<0.0001). After logistic regression multivariate analyze predictors of post operative AF was Age (odd ratio: 1.07) 95%CI (1.14-1.02) and smoking (odd ratio:4.48) 95%CI (12.26-1.64) .
Conclusions: Our results suggest that the incidence of post-CABG Atrial fibrillation can be predicted by specific preoperative. The preoperative age and Smoking can be predictable factor for post operative AF. For those patients at risk we would suggest to follow up them for recurrent AF and also survey of the effect of anti arrhythmic drugs on recurrent AF.
KEY WORD: Atrial Fibrillation, Coronary Artery Bypass, Risk Factor

INTRODUCTION

Atrial Fibrillation (AF) is the most common arrhythmia which occurs after the coronary artery bypass grafting (CABG) and leads to increased mortality and hospitalization period after surgery [20]. CABG surgery is an effective form of treatment for patients with cardiac ischemia. Although this treatment is well tolerated by most patients, it has its own side effects [21]. AF is a common complication after CABG surgery [22-28] which occurs in 20-40%of patients [3, 29, and 30]. Based on the definition of arrhythmia, patient's characteristics, type of surgery, and heart rhythm monitoring method, AF may appear in different forms [6]. AF usually occurs t2 to 4 days after the surgery [31] and most likely on the second day [31, 32] and causes malignant tachycardia, hypotension, heart failure, and increased risk of cerebrovascular events in some cases [33]. Several studies have shown that AF is associated with greater incidence of CHF, renal failure, and stroke [4]. The risk of perioperative stroke in patients with AF is higher by three times [34]. According to many researchers, postoperative AF is a benign and self-limiting arrhythmia that is rarely fatal, but it may lead to thrombotic complications, additional drug treatment [35], patient instability, prolongation of hospitalization period, and increased medical costs [21, 31, 36-38]. Therefore, despite the benignity of AF, its treatment requires greater medical and nursing care [3]. Etiology, prevention, and treatment of AF after the operation has still remained a controversial subject [24, 39]. Although the pathophysiological cause of AF after CABG surgery is not filly known [17, 26, and 35], a number of clinical and intraoperative factors have been identified to be related to this condition. However, there is no reliable method to predict postoperative AF [26]. The incidence of AF is also associated with age, chronic lung disease, low magnesium levels, previous history of AF, renal failure [43], heart disease such as hypertension, ventricular dysfunction, valvular heart disease, and ischemic heart disease [44]. Pre-existed comorbidities and surgical factors that lead to atrial inflammation and ischemia may

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increase the risk of postoperative AF [17]. The risk of postoperative AF increases as age and complexity of the surgical procedure increase [45]. Traditional CABG with CPB cardioplegia has been the gold standard treatment of ischemic heart disease for decades. CABG allows the surgeon to have an operation without additional blood which leads to effective myocardial revascularization and coronary reconstruction through providing adequate protection of the myocardium. The use of cardiopulmonary bypass (CPB), cardioplegia effect, and myocardial ischemia are the possible risk factors for the occurrence of AF [21]. Therefore, CPB avoidance may be effective in reducing the incidence of AF. However, postoperative AF has been reported to occur in surgeries with or without the use of CPB [22]. Arrhythmia after heart surgery seems to be a controversial issue [21]. The results of available studies are not adequate for corroborating the definite relationship between CPB and AF occurrence after CABG surgery [35]. There are contradictions about the clinical and electrocardiographic characteristics of patients with postoperative AF [48]. Hence, the present study aims to determine the relative frequency of atrial fibrillation after CABG surgery in patients with coronary artery disease.

METHODOLOGY

In this cross-sectional, descriptive-analytic study, patients with CAD who were under CABG treatment in Dr. Heshmat Hospital of Rasht**,** Guilan Province, Iran after the diagnosis of a cardiologist. At first, the patients were asked to fill out a questionnaire about cardiovascular risk factors such as age, gender, hypertension, hyperlipidemia, diabetes, affliction with COPD, smoking, history of MI, and beta-blocker use. Systolic and diastolic blood pressure of patients were measured at the same time using a calibrated mercury manometer after 5 minutes of rest in the sitting position. Then, the patients' height (without shoes) and weight (with thin clothes) were measured in order to calculate their Body Mass Index (BMI) through dividing the weight in kilogram by square of the height in centimeter. To assess atrial fibrillation in these patients, 12-lead electrocardiogram was recorded before and after the surgery and then daily until the discharge. Cardiovascular monitoring was done daily during the hospitalization in the ICU after surgery and also in the electrocardiography unit. Standard 12-lead electrocardiograms were recorded using an electrocardiogram device with a paper speed of 25 mm per second and a voltage of 10 mm per mV. The obtained electrocardiograms were observed and read by a cardiologist who was unaware other information of patients. Aortic clamp time, number of links, the type of surgery, cardiopulmonary bypass time, and the use of beta-blockers were recorded even after the surgery.

Exclusion criteria included being under other surgical procedures such as valve repair or replacement, aneurysmectomy, myocardial infarction less than a month before surgery, second-degree or third-degree of atrioventricular blockage, sick sinus syndrome, previous history of AF, the history of transient ischemic attack or stroke, and having an EF value less than 30%.

The obtained data and information were analyzed in SPSS-16 software. The normality distribution of data was examined using Kolmogorov-Smirnov test. If the distribution of data follows a normal pattern, parametric tests such as independent t-test are used, otherwise nonparametric tests are used for comparison. To estimate the intensity of relationship and relative probability of risk factors associated with atrial fibrillation, odd ratios indicators based on multivariate logistic regression model were used. Level of significance of was considered to be $p<0.05$.

After obtaining an informed consent, patients were entered into the study and their characteristics and information were kept confidential. In addition, all measures related to vascular reconstruction, electrocardiography, and tests were performed by having the indication.

Findings:

The mean age of subjects was 59.7±8.9. Table 1 shows the frequency distribution of age groups of the subjects. In this study, 103 subjects (55.9%) were male and 81 subjects (44.2%) were female. In addition, 86.96% of subjects were under CABG without AF and the frequency of atrial fibrillation was 13.04%, at a confidence level of 95% (8-18%). The mean age of patients with atrial fibrillation and without atrial fibrillation was 63.67±7.74 and 59.11±8.88, respectively. According to independent t-test, there is a significant difference between these two groups ($p<0.018$).

The mean BMI of patients with atrial fibrillation and without atrial fibrillation was 27.15±2.85 and 27.84±4.2, respectively. These figures suggest no significant different between two groups.

The percentage of atrial fibrillation in women (4.7%) was almost less than half of atrial fibrillation in men (15.7%), which is statistically significant ($p<0.04$). Atrial fibrillation in men was higher than that of women by 2.6 times with an odd ratio of 1.292 and confidence level of 95% (1-7.02).

In terms of atrial fibrillation with a history of hyperlipidemia, 12.4% of patients with HLP had arterial fibrillation, while 13.8% of patients without a history of HLP showed atrial fibrillation. Distribution of atrial fibrillation in two groups with and without a history of HLP indicates no significant difference ($p<0.752$).

Also, 3.13% of patients with diabetes had atrial fibrillation and no significant difference was observed about affliction with diabetes and atrial fibrillation (p<0.869).

1.13%of patients with HTN had arterial fibrillation and there was no significant difference between patients with and without hypertension in terms of affliction with atrial fibrillation (p<0.981).

The frequency of atrial fibrillation in patients with a history of COPD (40%) was almost 4 times more than that of people without a history of COPD (11.88%), which suggests significant different between these two groups of patients (p<0.03). Odd ratio for COPD at a confidence level of 95% (1.29-19.25) was equal to 5.

In terms of the frequency of atrial fibrillation in smokers and nonsmokers, Table 11 and Figure 6 show that the frequency of atrial fibrillation in smokers (25.9%) is about 4 times more than that of nonsmokers (6.7%), indicating a significant different between two groups (p<0.0001). Odd ratio for smoking at a confidence level of 95% (1.9-12.3) was obtained equal to 4.9.

According to Table 1, there is no significant difference between on-pump and off-pump types of surgeries in terms of atrial fibrillation frequency (p<0.446).

Table 1: Comparing the frequency of atrial fibrillation by the type of surgery

P-Value	Total		No		Yes		Arterial fibrillation / Type of surgery
Fisher's Exact Test P = NS (P < 0.46)	Percentage	Number	Percentage	Number	Percentage	Number	
	100	10	80	8	20	2	Off Pump
	100	174	68.3	153	13.7	21	On Pump
	100	184	87	160	13	24	Total

In terms of the frequency of atrial fibrillation among the subjects and taking beta-blockers, Table 2 shows that there is no significant difference between taking beta-blockers and atrial fibrillation (p<0.718).

Table 2: Comparing the frequency of atrial fibrillation by taking beta-blockers

P-Value	Total		No		Yes		Atrial fibrillation / Taking beta-blockers
Chi-square Test P = NS (P < 0.71)	Percentage	Number	Percentage	Number	Percentage	Number	
	100	63	85.7	54	14.3	9	Yes
	100	121	86.7	106	12.4	15	No
	100	184	87	160	13	24	Total

About the relationship of aortic clamp time with the number of graft and bypass time, Table 3 shows that the mean of these quantitative variables calculated by Mann Whitney U test was not significant. The significance level of aortic clamp, the number of graft, and bypass time was p< 0.429, p<0.888, and p<0.517, respectively.

Table 3: Comparing the frequency of atrial fibrillation by surgical factors

Bypass time		Number of graft		Aortic clamp		Surgical factors / Arterial fibrillation
Mean ± SD	Number	Mean ± SD	Number	Mean ± SD	Number	
56.18±13.2	22	3.12±0.85	24	63.77±9.34	22	Yes
57.65±20.66	162	3.16±0.77	160	37.03±14.52	162	No
57.47±19.85	184	3.16±0.78	184	63.99±13.95	184	Total
P = NS P < 0.52		P = NS P < 0.88		P = NS P < 0.43		P-Value (Mann Whitney U)

Table 4 shows that Age (p<0.013) and smoking (p<0.003) are the only cardiovascular predictors of atrial fibrillation in the final model of logistic regression analysis.

Table 4: Regression coefficients and odd's ratio of cardiovascular risk factors and predictive factors for atrial fibrillation surgery in the logistic regression model

Significance level of 95%		Sig	S. E	Odd ratio	Variables
High limit	Low limit				
1.182	1.032	0.004	0.034	1.104	Age
5.157	0.324	0.71	0.736	1.292	Gender
1.137	0.829	0.71	0.706	0.829	BMI
1.515	0.087	0.16	0.729	0.363	History of MI
4.122	0.302	0.85	0673	1.130	Hyperlipidemia
7.190	0.553	0.29	0.654	1.995	Diabetes
7.993	0.534	0.29	0.690	2.066	Hypertension
52.940	0.662	0.11	1.118	5.920	COPD
22.425	1.633	0.01	0.668	6.051	Smoking
1.138	0.909	0.88	0.052	1.008	Aortic clamp
7.182	0.828	0.10	0.551	2.439	Number of graft
1.054	0.903	0.53	0.040	0.976	Bypass time
2.913	0.298	0.90	0.581	0.932	Taking beta-blocker

In this study, the risk of atrial fibrillation in smokers was 4.48 times more than that of nonsmokers.

DISCUSSION

Atrial fibrillation is a common arrhythmia after heart surgeries that there is still no consensus on its prevention [56]. Atrial fibrillation not only increases the length of hospitalization and the risk of cardiovascular events but also can increase the long-term mortality rates caused by tachycardia-induced cardiomyopathy [57]. Several factors such as aging and systemic inflammation have been reported to be associated with atrial fibrillation. However, these predicting factors are still being debated [58-60]. In the present study which dealt with the predictive factors for atrial fibrillation after CABG surgery, 184 patients with indication for CABG underwent this type of cardiac surgery by a surgeon. Postoperative arterial fibrillation was observed in 24 patients (13%) in this study.

The frequency of atrial fibrillation after CABG surgery have been reported to be 27.4%, 25.6%, 32.1%, 18.5%, 9%, 35%, 26%, 26%, and 19% by Svagzdiene *et al.* [40], Mariscako *et al.* [24], Knyazer *et al.* [55], El-chami *et al.* [61], Siebert *et al.* [47], Amar *et al.* [48], Gabrielle *et al.* [10], Tayyarei *et al.* [62], and Choi *et al.* [30], respectively. The difference in the rate of atrial fibrillation after surgery in the present study compared to other studies may be attributed to the number of studied patients or the individual characteristics of them. In this study, most patients undergoing CABG were in a lower age range. This would be the reason for the reduction of atrial fibrillation in this study.

In this study, the mean age of patients with and without atrial fibrillation after CABG was 63.7±67.7 and 59.11±8.8, respectively. These figures represent a significant difference between these two groups. In the study conducted by Filardo *et al.* [8] on 6889 patients undergoing CABG, the mean age of patients with and without postoperative atrial fibrillation was 69.1 and 62.2, which also show a significant difference like the present study ($p<0.001$). In the study of Budeus *et al.* [32], there was also a significant difference between two groups in terms of age ($p<0.01$). By contrast, Koletsis *et al.* [57] did not found a significant difference between patients with and without atrial fibrillation in terms of age. Attaran *et al.* [6] also reported that patients with and without atrial fibrillation after CABG were in the age range 64-79 and there was no significant between them. Generally, the results of the present study and other similar studies show that the prevalence of atrial fibrillation may increase with age.

About the gender distribution in the study, among 24 patients with atrial fibrillation, 18 patients were male and 6 patients were female which account for 17.5% and 7.4% of total patients, respectively. According to these results, men were significantly more afflicted with postoperative atrial fibrillation than women were ($p<0.04$).

In the study carried out by Koletsis *et al.* [57], among 157 patients with postoperative arterial fibrillation, 137 patients were male and 160 patients out of 191 patients without postoperative arterial fibrillation were male. Unlike the present study, there is no significant difference in this regard. Attaran *et al.* [6] and Chamchad [6] obtained the same results as Koletsis *et al.* [57]. Zaman *et al.* [3] also found a significant difference between patients with and without postoperative arterial fibrillation in terms of age, with higher frequency in men. Zacharias *et al.* [16] also reported the same results.

In the present study, only 4 patients with arterial fibrillation had a history of myocardial infarction in the past and 20 patient lacked such a history, which suggests no significant difference. Topal *et al.* [64], Chamchad *et al.* [63], and Koletsis *et al.* [57] also reported the same result.

Among 24 patients with postoperative AF in this study, 12 patients had a history of hyperlipidemia and treatment with statins. No significant relationship was found between hyperlipidemia history and AF occurrence after CABG.

Like the present study, Koletsis *et al*. [57] did not observed a significant relationship between hyperlipidemia history and postoperative AF occurrence. In the study conducted by Sakamato *et al*. [65], frequency of postoperative AF was determined 26% and there was a significant relationship between statin use and postoperative atrial fibrillation, as AF occurred less frequently in patients who had taken statins. In the study conducted by Kinoshita *et al*. [66] on 584 patients undergoing CABG, 364 patients received statins five days before the surgery and the incidence of atrial fibrillation among them was 14.4%, while this figure was obtained 26.4% for those who had not taken statins ($p<0.001$).

In the present study, no significant relationship was found between the use of beta-blockers in the past and the decrease or increase in the incidence of postoperative atrial fibrillation. In the study carried out by Fuji *et al*. [67], frequency of postoperative AF was reported to be 21.7% and taking beta-blockers significantly reduced the incidence of AF after surgery ($p<0.042$). They also stated that treatment with intravenous landiolol during CABG surgery is more effective than carvedilol therapy alone. Tadic *et al*. [58], Topal *et al*. [64], and Koletsis *et al*. [57] did not found a significant relationship between taking beta-blockers and occurrence of AF after CABG, but Zacharias *et al*. [16] and Marasco *et al*. [49] reported such a significant relationship.

In the present study, the relationship of the history of diabetes and hypertension with the occurrence of atrial fibrillation was not statistically significant. In addition, the frequency of atrial fibrillation after CABG was higher in patients with a history of COPD than in patients without a history of COPD ($p<0.03$). This is consistent with the findings of Topal *et al*. [64], Tadic *et al*. [58], Koletsis *et al*. [57], and Straus *et al*. [68].

In this study, the incidence of atrial fibrillation was significantly higher in smokers. Filardo *et al*. [8] and Attaran *et al*. [6] found no significant relationship between smoking and postoperative AF incidence after CABG surgery. This difference between the results can be attribute to the amount and duration of smoking in various studies. However, no study has determined the cut-off number for smoking.

In studies conducted by Zangrillo *et al*. [50], Sezai *et al*. [52], and Pastuszelc *et al*. [53], patient's age was reported to be the only predictor of AF occurrence after CABG. On the other hand, Straus *et al*. [68] and Koletsis *et al*. [57] also stated that high BMI and history of COPD are other predictors of postoperative AF, in addition to age. Echahidi *et al*. [34] introduced age and high BMI as the predictors of postoperative AF. Additionally, Auer *et al*. [33], Marasco *et al*. [49], Kinoshita *et al*. [66], and Arribas-leal *et al*. [51], respectively, reported age and type of surgery; age and taking beta-blockers; the use of statins; and the use of statins to be the predictors of postoperative AF after CABG.

What is generally observed in most studies is the predictive role of high age in the occurrence of atrial fibrillation after CABG. The occurrence of heart problems and thereby the need for cardiac surgeries such as CABG increase with age which increases the risk of postoperative complications such as cardiac arrhythmias. Also, given the greater willingness to the use of percutaneous coronary interventions (angioplasty balloon) in recent decades instead of CABG, the number of CABG in higher ages has reduced.

One of the limitations of the present study was that intraoperative factors influencing the occurrence of atrial fibrillation after surgery were no investigated. In addition, it was not possible to determine whether postoperative atrial fibrillation is caused by an underlying myocardial disease or originated from inflammation and neurohormonal activity.

In the present study, it was shown that the occurrence of atrial fibrillation after CABG surgery can be predicted by some criteria. Hence, it is recommended that closer monitoring to be conducted and rapid and timely treatment to be provided for patients who are at greater risk based on these criteria. In addition, it is recommended that multicenter studies with larger samples and more influential factors to be carried out. Also, the study of prophylaxis treatment in patients at high risk can be an interesting area of research for future studies. This can be done through following up the patients with AF for at least 2 years and determining the frequency of attack repetition. In addition, the frequency of arterial fibrillation can be compared between two groups treated with placebo and anti-arrhythmic drugs during a period of 2 years. Exploring the benefits and harms of anti-arrhythmic drugs in the prevention of atrial fibrillation can be another recommendation for future studies.

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