Incidence and Predisposing Factors of Atrial Fibrillation After Coronary Artery Bypass Surgery

Koroner Arter Bypass Cerrahisi Sonrasında Atriyal Fibrilasyon Görülme Sıklığı ve Etki Eden Faktörler

Atrial Fibrillation and CABG

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Özet

Amaç: Koroner arter bypass cerrahisi yapılan hastalarda yeni gelişen ortaya çıkan atriyal fibrilasyon daha fazla postoperatif komplikasyonlar ile ilişkilidir. Bu çalışmada izole koroner arter bypass cerrahisi uyguladığımız hastalarda gelişen postoperatif atriyal fibrilasyonu ve en sık görülen sebeplerini saptamayı ve kontrol altına almayı amaçladık. Gereç ve Yöntem: Kliniğimize 2008 ve 2012 yılları arasında koroner arter bypass cerrahisi uyguladığımız tüm hastaların (n=149) verilerini retrospektif olarak inceledik. Olası predispozan risk faktörlerin arasından, yaş, vücut kitle indeksi, diabetes mellitus varlığı, postoperatif kreatinin değeri, ameliyat sonrası verilen eritrosit süspansiyonlarının sayısı, postoperatif ejeksiyon fraksiyonu ve distal baypas sayısını özellikle inceledikaraştırdık. Bulgular: Postoperatif atriyal fibrilasyon 149 hastanın 55' inde (%36.9) meydana geldi. İleri yaş ve postoperatif atriyal fibrilasyon arasında anlamlı bir korolesyon vardı (p<0.001). Toplam hastanede kalış süresi postoperatif atriyal fibrilasyon görülmeyen hastalarda 8.31±1.88 gün, postoperatif atriyal fibrilasyon görülenlerde 11.45±4.35 gün idi (p<0.001). Postoperatif atriyal fibrilasyon görülmeyen hastalarda ortalama yoğun bakımda kalış süresi 2.57±0.95 gün iken, postoperatif atriyal fibrilasyon görülenlerde 5.13±3.20 gün idi (p<0.001). Tartışma: Postoperatif atriyal fibrilasyona bağlı mortalite ve morbiditeyi azaltmak için risk altındaki hastaları tam olarak belirlemek ve gerekli önlemleri almak önemlidir. Bu çabalar gereksiz ilaç kullanımını ve buna bağlı yan etkileri engellerken, aynı zamanda yoğun bakımda kalış süresini kısaltarak sağlık harcamalarının miktarını da azaltmaya yardımcı olur.

Anahtar Kelimeler

Koroner Arter Bypass Cerrahisi; Atriyal Fibrilasyon; İleri Yaş

Abstract

Aim: In patients undergoing coronary artery bypass grafting (CABG), development of new-onset postoperative atrial fibrillation (POAF) is related with more postoperative complications. In this study we aim to detect and try to control the most common predictors of POAF among our patients who underwent solely CABG operation. Material and Method: We retrospectively examined retrospectively the data of all the patients (n=149) who had undergone CABG operation at our institution between 2008 and 2012. While evaluating the possible predisposing factors, we specifically investigated age, body mass index, diabetes mellitus, preoperative creatinine value, the number of postoperative erythrocyte suspension replacement, preoperative ejection fraction levels and the number of distal bypasses. Results: POAF occurred in 55 of 149 patients (36.9%). There was a significant correlation between advanced age and occurrence of POAF (p<0.001). Among the patients with no-POAF the total hospital stay was 8.31±1.88 days, compared to 11.45±4.35 days in the POAF group (p<0.001). In no-POAF group the mean postoperative intensive care unit (PICU) stay was 2.57±0.95 days, whereas in the POAF group the mean PICU stay was 5.13±3.20 days (p<0.001). Discusion: It is important to accurately identify patients who are at greater risk for POAF and to take the required precautions pre-, intra- and postoperatively in order to decrease the mortality and morbidity related to POAF. These efforts can also help to prevent unnecessary drug use and their adverse effects, shortens the length of PICU and hospital stay and decrease amount of health expenses.

Keywords

Coronary Artery Byapss Grafting; Atrial Fibrillation; Advanced Age

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Introduction

Atrial fibrillation is a common postoperative complication of cardiac operations and can be as frequent as 20-40 % after coronary artery by-pass grafting (CABG) or 38-64 % after valve operations [1]. Atrial fibrillation generally occurs in the first week of postoperative period, especially on the 2nd and 3rd days [2]. Risk factors that are associated with postoperative atrial fibrillation (POAF) include, Aatrial trauma due to cannulation, long aortic cross clamping time, acute atrial enlargement, atrial ischemia, postoperative electrolyte imbalance, pericarditis, epicardial inflammatory reaction, sick euthyroid syndrome, grafting of right coronary artery, increased postoperative sympathetic tone, increased levels of circulating catecholamines, advanced age, lack of postoperative beta blockade, hypertension and male sex are considered among the common culprits [1,3].

The underlying pathology in occurrence of POAF is multifactorial and is not yet well understoodthe specific causes remain unknown. Multiple re-entry waves arising due to dispersion ofduring the atrial refractory period is considered the electrophysiological mechanism of POAF but it is still remains unclear why some patients have an increased tendency to develop POAF [4]. Some authors have tried to explain this with an increased preoperative constitutional tendency to arrhythmias or the intraoperative atrial damage that is created by atrial incisions or perioperative ischemia [1,5].

It is possible to categorize the factors that play an important role in the development of AF as preoperative, intraoperative and postoperative. The most important preoperative factor is the patient's age. Male sex is also an important preoperative risk factor. Akazawa et al. reported a higher incidence of AF among males compared to females in all age groups [6]. The effects of ion channel expression and hormones on autonomic tone can be used to explain this difference. It is also reported a close relation between the aortic cross clamping time and POAF. It is thought to be due to prolonged atrial ischemia. The location of venous cannulation is also found to be related to POAF and it is suggested that bicaval cannulation avoiding an atrial incision can lower the rates of POAF [7]. Moreover, Postoperative postoperative pneumonia, chronic obstructive pulmonary disease and prolonged ventilation periods are also thought to beas important factors in the occurrence of POAF. Although, some studies failed to show the efficacy of preoperative beta blocker use on prevention of POAF, meta-analyses show that beta blockers lower the incidence of POAF and routine use of these agents are suggested by the American Heart Association [8-11]. Also it is reported in a meta-analysis of twelve clinical trials that preoperative use of statins can decrease incidence of POAF in post-CABG patients [12]. In this study we aim to detect and try to control the most common predictors of POAF based on our experience among our patients who underwent solely CABG operation.

Material and Method

Permission of this study was granted by the local ethics committee. The participants of the study were chosen among our patients who had undergone CABG operation at our institution between January, 2008 and May, 2012. The we excludexclusion chiriteriased the patients from the study were,ho had a prior AF or arrhythmia, hypo or hyperthyroidism history, redo cases, had undergone left ventricular aneurysm repair, emergent CABG operations and patients who have a severe valve disease. We examined retrospectively the data of all the patients (n=149) who matched our selection criteria in order to detect risk factors in the development of POAF.

Risk Factors

The variables assessed were: age ≥65 years; left ventricular ejection fraction (EF) ≤40; number of postoperative erythrocyte suspension replacement; preopeative creatinine level ≥ 1.4 mg/dL; DM; obesity: (defined by body mass index ≥ 30 kg/m2); and number of distal anastomosis >3.

Anesthesia and Operational Technique:

All of our patients operated under general anesthesia that was provided by intravenous narcotic anesthetic technique. Left internal mammary artery and saphenous venous grafts were prepared and used for revascularization. All the patients were operated under cardiopulmonary bypass. Aortic arterial, unicaval venous cannulation were applied and antegrad aortic cardioplegia cannula was placed. After aortic cross clamping, antegrad, hyperpotasemic blood cardiplegia and systemic hypothermia were applied for myocardial protection. Distal anastomoses were done under aortic cross clamping, after removal of aortic cross clamp proximal anastomoses were done under lateral clamp. After decannulation and completion of the operation the patients were transferred to postoperative intensive care unit (PICU).

All of the patients were extubated in the PICU on the day of the operation and were followed there for two days. ECG monitorization was done with standard D-II derivations in a 5 lead monitor. Electrolyte levels were also monitored closely and replaced if needed. After two days the patients were transferred to ward, pulse and blood pressure were obtained every four hours and when necessary. Daily ECG was performed in all patients. After detection of an arrhythmia, continuous, 12 derivation ECG monitoring was obtained.

Statistical Methods

To compare mean values of variables with normal distribution for two different groups t test, for more than two groups 'One way variant analysis' (One-way ANOVA), if a significant difference found between groups then post-hoc 'Tukey HSD' tests were used. If necessary (according to the number of subjects and controlling homogenicity) non-parametrical "Mann-Whitney U" and "Kruskal-Wallis One-way variant analysis" were applied. To detect the associations between variables and to expose these associations in mathematical relations correlation (Pearson, Spearman etc.), regression analysis were done. Multivariate statistical analysis methods (ANOVA, Logistic regression analysis etc.) were used to explain the research data. Results were interpreted as significant by p values of <0.05.

Results

We examined retrospectively the data of 149 patients whothat had undergone CABG at our institution between 2008 and

2012. 51.7 % (n=77) of the patients were under age of 65 and 48.3 % (n=72) were older than 65. Body mass index (BMI) was lower than 30 in 76.5 % (n=114) of the patients, higher than 30 in 23.5 % (n=35). POAF developed in 36.9 % (n=55) of the patients. Preoperative creatinine levels were below 1.4 mg/dl in 83.2 % (n=124) of the patients and were higher than 1.4 mg/dl in 16.8 % (n=25). 43 % (n=64) of the patients had Diabetes Mellitus (DM). In 84.6 % (n=126) of the patient population ejection fraction (EF %) was higher than 40 % and was below 40 % in 14.8 % (n=23; Table 1).

Table 1. Patient Demographics and Preoperative Data Related to the Predetermined Risk Factors

		(n)
Age (years)	<65	77 (51.7%)
	≥65	72 (48.3%)
BMI (kg/m2)	<30	114 (76.5%)
	≥30	35 (23.5%)
Preoperative Creatinine (mg/dl)	<1.4	124 (83.2%)
	≥1.4	25 (16.8%)
Type II DM	Yes	85 (57.0%)
	No	64 (43.0%)
EF	>%40	126 (84.6%)
	≤%40	23 (14.8%)
Distal Anastomosis (n)	1	1 (0.7%)
	2	10 (6.7%)
	3	35 (23.5%)
	4	38 (25.5%)
	5	47 (31.5%)
	6	14 (9.4%)
	7	4 (2.7%)
Postoperative ES Replacement (n)	0	28 (18.8%)
	1	69 (46.3%)
	2	45 (30.2%)
	3	7 (4.7%)

The earliest time POAF developed was day 1, while the latest was day 6 (Table 2). Among these patients with POAF (n=55)

Table 2. Timing of Development of POAF

Potoperative Day	(n)
1	7 (12.7%)
2	25 (45.5%)
3	19 (34.5%)
4	2 (3.6%)
5	1 (1.8%)
6	1 (1.8%)

POAF = Postoperative atrial fibrillation

the mean time in the development of AF was found day 2.42 ± 0.96. The minimum hospital stay length was 5 days and the maximum was 28 days. The mean value of total hospital stay length was 9.47 ± 3.38. Among the patients with no-POAF the total hospital stay was 8.31 ± 1.88 days, whereas it was found 11.45 ± 4.35 days in the POAF group. The difference betweenin hospital stay inbetween patients with POAF and no-POAF was found to be statistically significant (p<0.001) Minimum PICU stay was 1 day and maximum was 23 days. The mean PICU stay was 3.52 ± 2.42 days. In no-POAF group the mean PICU stay was 2.57 ± 0.95 days, whereas in POAF group the mean PICU stay was 5.13 ± 3.20 days. The difference in PICU stay between patients with POAF and no-POAF was found to be statistically significant (p<0.001). Minimum number of distal anastomoses was 1 and maximum was 67. The mean number of distal anastomoses was 4.19 ± 1.21. Iin the no-POAF group the number of distal anastomoses was 4.22 ± 1.25 and, in POAF group it was 4.15 ± 1.16. This difference was not found to be statistically significant (p=0.542). Among our patients minimum postoperative erythrocyte suspension replacement was 0, maximum was 3. . For the entire group of patents, Tthe mean value of the number of postoperative erythrocyte suspension replacement was 1.21 ± 0.80. In no-POAF group the number of postoperative erythrocyte suspension replacement was 1.18 ± 0.75, in POAF group it was 1.25 ± 0.87. The difference between patients with POAF and no-POAF was not found to be statistically significant (p=0.624).

Distribution and comparison of categorical variables in patients with POAF and no-POAF is shown in Table 3. 67.3 % (n=37) of

Table 3. Distribution and comparison of Predetermined Risk Factors in patients with POAF and no-POAF

Risk Factors	POAF (n)	No-POAF (n)	p
Age (years) ≥65	35 (37.2%)	37 (67.3%)	<0,001
BMI ≥30	20 (21.3%)	15 (27.3%)	0.405
Preoperative Creatinine (mg/dl)	17 (18.1%)	8 (14.5%)	0.577
DM	45 (47.9%)	19 (34.5%)	0.113
EF ≤40%	11 (11.7%)	11 (20.4%)	0.154
Distal anastomosis	4.15 ± 1.15	4.22 ± 1.25	0.542
Postoperative ES Replacement	1.25 ± 0.87	1.18 ± 0.75	0.624

BMI = Body mass index; DM = Diabetes mellitus; EF = Ejection fraction; ES = Erythrocyte Suspension; POAF = Postoperative atrial fibrillation

patients with AF were 65 and older, 32.7 % (n=37) of patients with AF were younger than 65. The difference between POAF and no-POAF groups was found to be statistically significant (p<0.001). Among the patients with POAF body mass index (BMI) was below 30 in 72.7 % (n=40) and above 30 in 27.3 % (n=15). The difference between patients in both groups was not found to be statistically significant (p=0.405). In 14.5 % (n=8) of patients with POAF, pPreoperative creatinine levels were below 1.4 mg/dl in the 85.5 % (n=47) of patients with POAF and above 1.4 mg/dl in 14.5 % (n=8). The difference between patients with POAF and no-POAF was not found to be statistically significant (p=0.577). In POAF group, 34.5 % (n=19) of patients had DM, 65.5 % (n=36) did not have DM. The difference between both groups was not found to be statistically significant (p=0.113). EF was over 40 % in 79.6 % (n=43) of all patients with POAF, whereas below 40 % in 20.4 % (n=12). The difference between patients with POAF and no-POAF was not found to be statistically significant (p=0.154). The number of distal bypasses wereas >3 and below in 30.9 % (n=17) of patients with AF, more than 3 in 69.1 % (n=38) of patiebts in POAF greoupall patients with AF. and Tthe difference between patients with POAF and no-POAF was not found to be statistically significant (p=0.994).

Number of postoperative erythrocyte suspension replacement was 3 in 7.3 % (n=4) of patients with AF, 2 in 32.7 % (n=18) and, , 1 in 38.2 % (n=21). . 21.8 % (n=12) of patients with POAF did not receive any erythrocyte suspension and the difference between patients with POAF and no-POAF was not found to be statistically significant (p=0,379).

Discussion

Although it is generally considered as a temporary and relatively less dangerous condition, atrial fibrillation is associated with increased early and long term morbidity and mortality [13]. In patients who have undergone CABG, development of postoperative AF is related with more postoperative complications. Even though AF is the most common clinically detected arrhythmia, the true incidence of POAF following cardiac surgery is unclear. However the with reported incidence ranges from 10 to- 65%. The reason of this wide range can be derived from patient characteristics or type of surgery. In recent years the incidence of POAF is found to be increasing and advanced age of patients who have undergone CABG can be considered as the main reason of this problem. In our patients POAF developed in 36.9 % (n=55), these results were similar to other reports in the literature. Advanced age was reported several times as the most important predictor of AF after CABG [14]. Leitch et al [15] reported a 70 % increased AF risk with every decade. Advanced age is closely related with myocardial fibrosis and atrial dilation and it is also suggested changes that come with aging such as loss of nodal fibers, muscle atrophy, increased fat and fibrous tissue in sinus node, local interstitial amyloidal deposits are important factors in the pathology of AF. These structural changes may explain why AF is more common in the elderly population. 67.3 % of our patients with AF were 65 and older ($p < 0.001$).

Obesity can be considered as a risk factor for occurrence of AF [16]. People who are categorized as overweight (BMI >= 25 and < 30) or obese (BMI > 30) have a larger left atrium in size. Atrial dilation is a common condition in patients with chronic AF and mostly accompanied by ruptures in muscle fibers. Ducceschi et al [17] reported more AF cases among people with BMI ≥ 30. Hakala et al [18] reported that BMI ≥ 30 is an independent risk factor for development of POAF. In both studies increased left atrial sizes were detected by preoperative echocardiography and this relation between enlarged left atrium and POAF was found to be statistically significant. Also in a recent meta-analysis obese patients have been found to have a modestly higher risk of POAF compared with non-obese patients (p=0.002) [19]. In our patient population 15 patients with AF BMI were ≥ 30 and in contrast to before mentioned studies, the results were not statistically meaningful (p=0.405). Nardi et al [20] demonstrated that large left atrium volumes were independently correlated to the occurrence of POAF in patients undergoing isolated CABG. We could not find any relationship between the left atrium size with the occurrence of POAF.

Rubin et al [21] stated the importance of number of coronary artery lesions in development of POAF. In a recent retrospective study the authors confirmed that POAF results in worse in-hospital and 30-day outcomes but no correlation was found between POAF and number or type of grafts [22]. In our study the difference between patients with AF and no-AF concerning the number of anastomoses was not found to be statistically significant (p=0.994).

Koch et al [23] evaluated the risk of POAF in patients who receive erythrocyte transfusions after CABG and reported an increased risk for POAF with every unit of erythrocyte transfusion. Alameddine et al [24] also pointed out an increased risk of POAF with higher number of erythrocyte transfusions, they reported AF risk increases 61 % with each increasing level of erythrocyte transfusion. Although the mechanism is not yet well understood, it is suggested increased inflammatory responses related with transfusions can trigger AF by damaging atrial tissue due to activated leukocytes. In our study postoperative erythrocyte suspension replacement ranged between 0 and 3, 1.21 being the mean value. We did not find any statistically significant results for occurrence of POAF but Koch et al [23] stated their mean value of transfusion was 2.13 so the statistical difference between studies can be explained by the different numbers of transfusion.

Renal dysfunction is related to long-term mortality and myocardial infarction after CABG. In a recent study Chua et al [25] reported renal dysfunction (Glomerular Filtration Rate < 60 mL min−1 1.73 m−2) associated with left ventricular diastolic dysfunction is an important risk factor for POAF after cardiac surgery and can be used to improve the diagnostic accuracy of the CHA2DS2-VASc score. In our study only 8 of 25 patients with AF had higher than 1.4 mg/dl preoperative creatinine levels and it was not found to be statistically significant. Preoperative low EF % (EF ≤ 40 %) is also suggested as one of the predictors of POAF. It has been offered that preoperative low EF % can create an expansion in atria plus the effects of intraoperative ischemia may cause an abundant environment for POAF. In our study, we did not find a significant relation between low EF % and POAF.

We also found that POAF can increase the time that was spent in PICU and the ward ($p < 0,01$). In a recent trial, based on the patient database of The Veterans Affairs Randomized On/Off Bypass Trial, it's been reported that POAF patients had longer postoperative hospital stay (+3.9 days) and higher discharge costs compared to no-POAF patients. At 1 year, POAF patients found to have more than twice the adjusted odds of dying ($p < 0.01$), with higher 1-year total cumulative costs [13]. In our study, among the patients with no-POAF the total hospital stay was 8.31±1.88 days, whereas it was found 11.45 ± 4.35 days in the POAF group. The difference in hospital stay between patients with POAF and no-POAF was found to be statistically significant ($p<0.001$). In no-POAF group the mean PICU stay was 2.57 ± 0.95 days, whereas in POAF group the mean PICU stay was 5.13 ± 3.20 days. The difference in PICU stay between patients with POAF and no-POAF was found to be statistically significant ($p<0.001$).

The biggest restriction of our study was lack of telemetry monitorization of patients for detection of POAF. ECG monitorization was done with standard D-II derivations in a 5 lead monitor at PICU. At ward pulse and blood pressure were obtained every four hour and when is necessary. After detection of arrhythmia, 12 derivation ECG was obtained so in the mean time short term, asymptomatic, paroxysmal AF attacks might have been

stayed undetected.

In conclusion, AF is the most common clinically detected arrhythmia after CABG. Despite the advancements in surgical techniques, myocardial protection and anesthesiology incidence of POAF is still not in the desired range. AF increases postoperative short and long term mortality and morbidity. There is also an increase in total hospital stay length and total health care expenses. In our study we detected a higher incidence of POAF with advanced age. We also observed that AF most commonly occurs at postoperative 2nd and 3rd days and patients with AF requiring longer stays at PICU and hospital. We believe that a thorough preoperative evaluation of risk factors in patients who undergo CABG may help health care providers to take the necessary precautions in order to prevent and detect POAF and decrease the mortality and morbidity related to it. These efforts can also help to prevent unnecessary drug use and their adverse effects, shortens the length of PICU and hospital stay and decrease amount of health expenses.

Competing interests

The authors declare that they have no competing interests.

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