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The effects of serum CRP level on postoperative atrial fibrillation in patients who had coronary bypass surgery

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ABSTRACT

Coronary artery bypass grafting (CABG) is the most common cardiac operation performed worldwide. We aimed to evaluate the relationship between post-operative serum C-reactive protein (CRP) level and atrial fibrillation (AF) in patients who received CABG.

A total of 198 patients who had undergone CABG between January 2016 and February 2018 in our cardiovascular surgery clinics were included in the study. According to CRP levels, patients were into 2 groups; Group 1 serum CRP level <8.0mg/L and Group 2 serum CRP level ≥8.0mg/L. There were 82 patients in Group 1 (31 Female, 51 Male) and 116 patients (48 Female, 68 Male) in Group 2. Patients who died within 30 days after CABG were excluded.

While the mean age of the cohort was 61.2 ± 8.1 years; it was 59.8 ± 9.4 years and 61.5 ± 7.4 years in Group 1 and 2, respectively. AF was observed in 65 patients (32.8%) including 13 patients in Group 1 (15.8%) and 52 patients (44.8%) in Group 2. The rate of AF was significantly higher in Group 2 ($p<0.05$).

Coronary artery disease itself is significant risk factor of mortality and morbidity. Our study showed that post-operative serum CRP level would be an indicator of AF. Although increased levels of CRP alone cannot be the primary cause of AF, the rate of post-operative AF was higher in CABG patients with high CRP level.

Key Words: C-Reactive Protein, Atrial Fibrillation, Coronary Artery Bypass Surgery

Introduction

Generally, atrial fibrillation (AF) occurs after valvular heart disease with a ratio of 30% following CABG (1). In AF, the atrial contraction rate increases to 300-600 beats/minute. Although a ventricular systole should follow each atrium systole in normal physiologic condition, ventricular contraction does not follow each atrial systole in AF which leads to ineffective ventricular contraction. The most undesirable complication of AF is systemic embolism including cerebral infarction (2). AF is diagnosed through lack of p waves in electrocardiogram with unequal spaces between R-R waves. Atrial contractions provide a 20-30% contribution to the cardiac output in normal sinus rhythm. Sudden disruption of this contribution constitutes a severe condition in patients with borderline cardiac reserve. AF is an unfavourable prognostic factor in patients with coronary artery disease thus, AF should be treated rapidly in patients with coronary artery disease.

AF is the most common arrhythmia after CABG with a ratio of 30%. It is important to maintain sinus rhythm especially at the time of weaning from cardiopulmonary bypass (CPB) in CABG operations. CPB duration is lengthened when this cannot be achieved or with the occurrence of AF. Because CPB is a non-physiological circulation, the patients who underwent cardiac surgery should be separated from CPB at once, and a normal physiological order should be provided. If AF develops in patients after removing the aortic cross clamp, the sinus rhythm should be provided through epicardial defibrillation.

Many factors have been defined as the cause of AF. Use of blood and blood products, advanced age, long CPB time, local cold application, over-manipulation of the heart during operation, electrolyte imbalance, incomplete revascularization

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Table 1. Demographic and clinical characteristics of the study population

Variable	Group 1 (n=82) (CRP<8mg/dl)	Group 2 (n=116) (CRP>8 mg/dl)	p value
Age (Years)	59.8 ± 9.4	61.5 ± 7.4	p >0.05
Gender (Female/Male)	31 F, 51 M	48 F, 68 M	p >0.05
BMI (kg/m2)	21 ± 2.4	24 ± 1.5	p >0.05
EF (%)	46 ± 5	48 ± 7	p >0.05
Hypertension n (%)	56 (68.2%)	85 (73.2%)	p >0.05
Chronic Obstructive Lung Disease n (%)	16 (19.5%)	22 (18.9%)	p >0.05
Smoking n (%)	65 (79.2%)	84 (72.4%)	p >0.05
Hyperlipidaemia n (%)	52 (63.4%)	86 (74.1%)	p >0.05
DM n (%)	45 (54.8%)	62 (53.4%)	p >0.05
WBC	9300 ± 2100	8200 ± 1900	p >0.05
Hb Level (gr/dl)	13 ± 2	12 ± 4	p >0.05
INR	1.2 ± 0.3	1.1 ± 0.15	p >0.05
Platelet Level	256 ± 65	294 ± 70	p >0.05
NYHA Functional Class (1-5)	2.7 ± 0.5	2.8 ± 0.9	p >0.05
EUROSCORE	3.2 ± 2.1	3.1 ± 2.4	p >0.05

The values are n (%) for categorical variables and mean ± standard deviation for constant variables
MI: Myocardial infarction
INR: International normalized ratio,
NYHA: New York Heart Association
BMI: Body mass index

and infection are some of these causes (3). In this article, we aimed to investigate the relationship between CRP level, as an acute phase reactant, and the development of postoperative AF.

Material and Method

A total of 198 patients who undergone CABG surgery in our clinics between January 2016 and March 2018 were included in the study. Patients enrolled in the study were evaluated after separating into Group 1 (CRP<8 mg/L) and Group 2 (CRP≥8 mg/L). Congenital hemodialysis-dependent chronic kidney patients and those who had preoperative valve pathology, preoperative rhythm disorder or additional surgical operation were excluded from the study. Additionally, patients who had fever and suspected infection in the postoperative early period within 3 days were excluded from the study. Demographical data of the patients were registered before the operation. Hypertension, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), smoking, hypercholesterolemia, medicine use were registered and compared in detail. EUROSCORE risk stratification was used for operation risk scoring. All patients were operated under general anaesthesia. Left internal mammary artery (LIMA) was used for left anterior descending (LAD) artery grafting in both groups. Saphenous vein graft (SVG) was used for other coronary artery revascularisations. A complete dose of heparin was given to the patients for CPB. CBP was initiated with aortic arterial and right atrial two stage venous cannulation after activated clotting time (ACT) was reached to 420 seconds. Cold blood cardioplegia solution was administered every 20 minutes through aortic root cannula for myocardial protection. ACT level was adjusted between 200 and 400 seconds for the CABG operations performed on beating heart. Octobus and Starfish (Medtronic, Inc., Minneapolis, MN, USA) coronary stabilizers were used for coronary stabilization. Revascularised coronary artery number, CPB time, cross clamp time, blood product use and inotropic agent usage ratios were registered. Post-operative biochemical and haematological values, duration of postoperative intensive care unit and hospitalization were registered and compared in detail.

Results

The total number of the participants was 198, and there were 82 patients in Group 1 (31 Female, 51 Male) and 116 patients (48 Female, 68 Male) in Group 2. The mean age of the patients was 59.8 ± 9.4 in Group 1 and 61.5 ± 7.4 in Group 2.Preoperative characteristics of the patients are revealed in (Table 1). The number of off-pump

Table 2. The comparison of Group 1 and 2

	Group 1 (n=82) (CRP<8mg/dl)		Group 2 (n=116) (CRP>8 mg/dl)		
Characteristics	Off-pump n (35)	On-pump n (47)	Off-pump n (52)	On-pump n (64)	p value
Total operation duration (Hours)	2.5 ± 1.3	3.8 ± 2.1	2.6 ± 1.8	4.1 ± 1.5	p >0.05
Anastomosis number	1.5 ± 0.6	2.4 ± 0.64	1.4 ± 0.63	2.9 ± 0.7	p >0.05
Inotrope use n (%)	13 (37.1%)	24 (51%)	22 (42%)	28 (43.7%)	p >0.05
Aortic cross clamp time	-	58.2 ± 21.1	-	60.7 ± 15.4	p >0.05
Cardiopulmonary bypass time	-	74.5 ± 18.6	-	78.5 ± 15.6	p >0.05
Average Hemoglobin level during operation (mg/dl)	11.4 ± 1.2	8.3 ± 1.4	10.8 ± 1.4	9.1 ± 1.3	p >0.05*
Intubation duration (hours)	3.4 ± 1.5	4.0 ± 1.2	3.5 ± 1.5	4.3 ± 2.0	p >0.05
WBC	11200 ± 1100	13400 ± 2100	10400 ± 1100	14200 ± 1300	p >0.05
Intensive care unit stay (days)	2.1 ± 1.6		2.5 ± 2.4		p<0.05*
Total drainage amount (ml)	550 ± 260	950 ± 150	450 ± 150	850 ± 200	p >0.05
Hospitalization duration (days)	6.5 ± 2.2		8.4 ± 2.5		p<0.05*
Postoperative hemoglobin level	11.2 ± 1.4		9.6 ± 2.2		p >0.05
Mortality	4 (4.8%)		6 (5.1%)		p<0.05*

The values are n (%) for categorical variables and mean ± SD for constant variables

Table 3. Atrial fibrillation occurrence ratios among the groups

	Group 1 (n=82) (CRP<8mg/dl)		Group 2 (n=116) (CRP>8mg/dl)		
Characteristics	Off-pump n (35)	On-pump n (47)	Off-pump n (52)	On-pump n (64)	p value
CRP level (mg/dL)	6.4 ± 1.1	7.1 ± 0.5	11.2 ± 2.3	15 ± 3.2	p<0.05
Atrial fibrillation occurrence time (day)	1.2 ± 0.5	2.1 ± 0.6	1.4 ± 0.7	2.3 ± 0.4	p>0.05
Atrial fibrillation	4 (4.8%)	9 (10.9%)	12 (10.3%)	40 (34.4%)	p<0.05

and on-pump CABG were 35 and 47 in Group 1, and 52 and 116 in Group 2. There was no statistical difference in regards to hypercholesterolemia, hypertension, DM, COPD, smoking among the two groups (p>0.05). In total, AF occurred in 65 (32.8%) patients. Preoperative CRP levels were 3.2 ± 1.8 mg/L in Group 1 and 2.8 ± 1.5 mg/L in Group 2. In postoperative second day, in comparison to Group 2 (13.2 ± 2.7 mg/L), the CRP level was significantly higher (p<0.05) in Group 1 (6.8 ± 1.7 mg/L). AF occurred in four patients (4.8%) who had off-pump and nine patients (10.9%) who had on-pump surgery in Group 1. In group 2, AF developed in twelve patients (10.3%) who had off-pump and 40 patients (34.4%) who had on-pump surgery (Table 2). This difference was statistically significant (p<0.05). The mean duration of AF was 1.8 ± 0.5 days in Group 1 and 1.6 ± 0.6 days in Group 2. Anastomosis counts were 2.1 ± 0.7 in Group 1 and 2.4 ± 0.4 in Group 2, which revealed no statistically significant difference (p>0.05). Aortic cross clamp time in patients who had on-

pump CABG was 58.2 ± 21.1 minutes in Group 1 and 60.7 ± 15.4 minutes in Group 2 ($p>0.05$).

Duration of intensive care unit stay was 2.1 ± 1.6 days in Group 1, 2.5 ± 2.4 days in Group 2. The hospital stay was 6.5 ± 2.2 days in Group 1 and 8.4 ± 2.5 days in Group 2, which revealed statistically significant difference ($p<0.05$). Same standard treatment protocol was applied for all patients who had AF (Table 3). After development of AF, sinus rhythm was provided by administration of amiodaron tablet 200 mg three times a day and metoprolol 50 mg tablet once a day following loading, and with continuation treatments containing 900 mg of Amiodaron in total. During the discharge of the patients and their first out-patient visit, it was observed that the sinus rhythm was preserved.

Discussion

Atrial fibrillation is the most common arrhythmia observed after cardiac surgery (4). While the rate of postoperative AF was 3% after major non-cardiac surgeries, it was stated that AF prevalence could rise up to 70% following cardiac surgery (5). Different prevalence rates are reported according to the cardiac surgery type. Although AF occurs most commonly after isolated cardiac valve operations, this prevalence was shown to be lower in those who received CABG under beating heart compared to those who had CABG under CPB (6).

Obesity, hypertension, COPD, advanced age and pre-operative AF were also reported to be related to post-operative AF prevalence (7). Cardiac output decreases in AF patients as synchronised atrial contraction in sinus rhythm does not occur and intra-atrial stasis increases. AF also increases post-operative mortality, stroke rates and duration of hospitalization. Ability to predict postoperative AF is important in order to prevent postoperative AF-related complications. Thus, biochemical blood analyses should also be used in addition to the clinical markers. Many biochemical markers, such as tumour necrosis factor alpha, hemoglobin A1c, CRP and interleukin 8 are investigated (8). The validity of CRP, which is an acute phase reactant, continues in the studies as a biochemical marker.

The importance of the follow-up of CRP levels in infection, acute damage and inflammation evaluations is shown (7). As histopathological inflammatory cell infiltration was noticed, especially in the biopsies of AF patients, correlation evaluation studies among CRP levels and AF gained speed (9,10).

In the study by Liu et al (11) which constitutes 420 patients, it was stated that high CRP level was related to AF prevalence in patients who had cardioversion following recurrent AF. Mathew et al (12) also reported that non-steroid anti-inflammatory medicine use decreased AF prevalence in the study they performed on 4657 patients.

It was reported that age, gender and race could cause different CRP levels (13). It was shown that infectious and inflammatory diseases, trauma and necrosis also cause increases in CRP level (14). It was also stated that medicines such as statin, angiotensin converting enzyme inhibitor and angiotensin receptor antagonist, exercise and weight loss can decrease CRP level (15). It is also considered that medicines such as statin, angiotensin receptor antagonist can be anti-arrhythmogenic due to their anti-inflammatory effects (16).

It is stated that CRP, which is a proinflammatory marker produced in liver, may have an arrhythmogenic characteristic by retaining the phosphocholine in damaged cell membrane (17). As the result of a meta-analysis including 17 researches, it was shown that pre-operative CRP level could be related to post-operative AF prevalence (18). But there are also studies stating that there is no relationship between serum CRP level and AF prevalence. Ahlsson et al (19) examined 524 patients who had cardiac surgery and reported no correlation between serum CRP levels and post-operative AF.

In studies evaluating post-operative AF prevalence, beta-blocker use was also investigated. Erdem et al (20) reported that post-operative AF was less commonly observed in patients who used beta-blocker before operation. But in studies evaluating the relationship between CRP and AF, no study presented how long the medicines like beta-blocker were continued after the operation or when they were discontinued.

In this study, we examined 198 patients through comparing the two groups according to their CRP levels. We detected that post-operative AF prevalence and duration of hospital stay were significantly higher in Group 2 with high CRP level compared to Group 1. It has not been clarified whether inflammation induced development of AF, or inflammatory phase was effective after AF occurrence. We think that fatal complications secondary to AF and the AF-related

high treatment expenses can be decreased by predicting the AF. From this point of view, this prediction can be achieved by the level of CRP which is an inflammatory biochemical marker.

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