

Preoperative C-reactive protein can predict early clinical outcomes following elective off-pump CABG surgery in patients with severe left ventricle dysfunction

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ABSTRACT

Purpose: Atrial fibrillation (AF) is the most common type of arrhythmia following elective off-pump coronary bypass graft (CABG) surgery, occurring on the 2nd or 3rd postoperative day. Postoperative atrial fibrillation and early complications may be the cause of long term morbidity and mortality after hospital discharge. High sensitive C-reactive protein (hsCRP) seems to be most significantly associated with cardiovascular disorders. This study was designed to evaluate whether preoperative hsCRP (≥ 3 mg/dl) can predict post-elective off-pump CABG, AF, and early complications in patients with severe left ventricle dysfunction (Ejection Fraction (EF) $< 30\%$). **Methods:** This study was conducted on 104 patients with severe left ventricular dysfunction (EF $< 30\%$), undergoing elective off-pump CABG surgery during April to September 2011 at the Afshar Cardiovascular Center in Yazd, Iran. Patients undergoing emergency surgery and those with unstable angina, creatinine higher than 2.0 mg/dl, malignancy, or immunosuppressive disease were excluded from the study. The subjects were divided into two groups: Group I with preoperative increased hsCRP (> 3 mg/dl) ($n=51$) and group N with preoperative normal hsCRP (< 3 mg/dl) ($n=53$). We evaluated post-CABG variables including incidence, duration, and frequency of AF, early morbidity (bleeding, infection, vomiting, renal and respiratory dysfunctions), ICU or hospital stay and early mortality. Data were then analyzed by Analysis of Variance (ANOVA), Chi-square and Fisher exact test for quantitative and qualitative variables. **Results:** The average age of the patients was 62.5 years, 75 cases (72.1%) were male, and 39 (37.5%) were female. Postoperative AF occurred in 19 cases (18.2%); 17 cases (33.3%) had hsCRP ≥ 3 mg/dl and 2 cases (3.8%) had hsCRP ≤ 3 mg/dl ($P=0.03$). Postoperative midsternotomy infection, respiratory dysfunction, and hospital stay were significantly higher in group I compared with group N ($P<0.05$). No statistical significant differences were identified between the two groups concerning other postoperative complications (bleeding, vomiting, renal dysfunction and ICU stay) ($P>0.05$). **Conclusion:** Preoperative hsCRP ≥ 3 mg/dl can predict incidence of postoperative atrial fibrillation and early complications such as midsternotomy infection, respiratory dysfunction, and hospital stay following elective off-pump CABG.

Key words: Atrial fibrillation, C-reactive protein, early complications, elective off-pump CABG

INTRODUCTION

Coronary Artery Disease (CAD) is one of the most

important causes of morbidity and mortality in man. Coronary artery bypass graft (CABG) is the most common cardiac surgery which has early and late postoperative complications, compared to other surgical procedures.^[1] Atrial fibrillation (AF) is the most common type of arrhythmia following CABG surgery. Incidence of AF is observed in 20-50% of the patients following CABG and is even higher after combined CABG and valve surgery. It occurs on the 2nd or 3rd postoperation day.^[2] Factors contributing to early postoperative complications and atrial arrhythmia are old age, preoperative leukocytosis, low ejection fraction, increase in plasma level of inflammatory

Access this article online	
Quick Response Code:	Website: www.saudija.org
	DOI: 10.4103/1658-354X.105852

marker and postoperative pericarditis.^[3] Postoperative AF and early complications may be the causes of long-term morbidity and mortality after hospital discharge. Early complications include stroke, hypertension, pulmonary edema, heart failure, and hemodynamic instability.^[4] Such complications can increase the cost of therapy. Inflammatory reaction may contribute to the development of postoperative complications such as myocardial injury and organ failure. These reactions have been shown to play a role in acute coronary syndrome, from pathogenesis of atherosclerosis to death of myocardial cells. Inflammatory markers are therefore present in different stages of coronary artery disease and can be used to predict subsequent cardiovascular events.^[5,6] High sensitive C-reactive protein (hsCRP) seems to be most significantly associated with cardiovascular disorders. Elevation of hsCRP is associated with a prognosis of worsening condition in patients with acute myocardial infarction (AMI) or those undergoing angioplasty or mitral valvuloplasty.^[5-7] Early complications following elective off-pump CABG which are associated with elevated preoperative levels of hsCRP have not been markedly investigated. This study was designed to evaluate the relation between preoperative hsCRP and the occurrence, duration, and frequency of AF, as well as other early complications, after off-pump CABG in patients with severe LV dysfunction (EF < 30%).

METHODS

Our prospective cross-sectional study was approved by the regional committee of our university. Written consent was received from all patients ($n=104$) who voluntarily underwent off-pump CABG surgery at the Afshar Cardiovascular Center of Yazd from April to September 2011. All the operations were performed by a skilled surgical team. One hundred and four patients with severe left ventricular dysfunction (EF < 30%), undergoing elective off-pump CABG enrolled in this study and were assigned into two groups according to their level of hsCRP: Group I with preoperative increased hsCRP (>3 mg/dl) ($n=51$) and group N with preoperative normal hsCRP (<3 mg/dl) ($n=53$). Patients undergoing emergency surgery and those with unstable angina, creatinine >2.0 mg/dl, malignancy or immunosuppressive disease were excluded from the study. As premedication, all the patients received morphine (10-15 mg) and oral diazepam (10 mg), 30-60 minutes before introduction into the theatre. Induction of anesthesia was performed with diazepam (20 mg), fentanyl (10-15 μ g/kg), and pentobarbital (0.1 mg/kg). In order to continue the anesthetic state, fentanyl (4-5 μ g/kg/h) and pentobarbital (0.3-0.4 mg/kg/h) were used. After adequate exposure

and stabilization, the target vessel was exposed and snared above the anastomosed site with 4-0 prolene suture and a soft plastic snigger to prevent coronary injury. The coronary artery was then opened and anastomosis was performed. Visualization was enhanced by utilizing a surgical blower and humidifier.

The demographic variables and early postoperative complications such as occurrence, duration and frequency of recurrence of atrial fibrillation and infection, bleeding, vomiting, renal and respiratory dysfunction, ICU and hospital stay were all recorded. The patients underwent Holter monitoring after ICU discharge and during their hospital stay. Our data were then analyzed by SPSS software version 15. We used ANOVA, Chi-square and Fisher exact test for quantitative and qualitative variables.

RESULTS

One hundred and four patients with severe left ventricle dysfunction were enrolled as possible candidates for off-pump CABG surgery in this study. The demographic characteristics of the patients are presented in [Table 1]. The prevalence of risk factors was hypertension (38%), HLP (22%), and cigarette smoking (15%). Of all the patients, 51 cases (49%) had increased preoperative hsCRP levels (≥ 3 mg/dl). AF was observed in 19 cases (18.2%); 12 were male (11.5%) and 7 female (6%). There was no significant relationship between sex and AF. The incidence of significant stenosis of vessels was identified as the following: 4 cases (3.8%) with one stenosis, 29 (27.8%) with 2, 61 (58.6%) with 3, and 10 cases (9.6%) with left main vessel stenosis. Regarding AF, 1 case (25%) was found with one vessel, 3 cases (10%) with two vessels, 12 cases (19.6%) with three vessels, and 3 cases (30%) with patients suffering from left main artery disease. There was no significant variation between the number of vessels involved and postoperative AF.

On the other hand, postoperative AF occurred in 19 cases totally (18.2%) [Table 2]. Of these, 17 cases (33.3%) were affected with hsCRP ≥ 3 mg/dl (group I) but 2 cases (3.8%) had hsCRP ≤ 3 mg/dl (group N) ($P=0.03$). The mean duration of AF was 1101+1140 min., which in group I was elevated to 1185+1180, compared to 1018+1100 min. in group N ($P=0.44$). Moreover, the frequency of AF recurrence was 2.8+1.8 and 2.3+1.2 in groups I and N respectively ($P=0.77$). These findings revealed that duration and frequency of recurrence of AF was not significantly different between the groups. Preoperative hsCRP ≥ 3 mg/dl could however predict a greater incidence of AF compared to hsCRP ≤ 3 mg/dl. Early postoperative complications were compared between the groups as well

Table 1: Demographic characteristics of both groups

Variables	hsCRP \geq 3 mg/dl (N=51)	hsCRP \leq 3 mg/dl (N=53)	P value
Age (year)	62 \pm 21	63 \pm 11	0.61
Sex (M/F) (n)	33/18	36/27	0.35
HTN [n (%)]	17 (33)	23 (43)	0.22
Diabetic mellitus [n (%)]	15 (29.4)	17 (32)	0.38
HLP [n (%)]	13 (25)	10 (18)	0.63
Cigarette smoking [n (%)]	11 (21)	5 (9)	0.25
Addiction [n (%)]	3 (5)	4 (7.5)	0.57
Cigarette smoking [n (%)]	18 (35)	10 (18.8)	0.09

Table 2: POAF and early complications after surgery in both groups

Variables	hsCRP \geq 3 (N=51)	hsCRP \leq 3 (N=53)	P value
Incidence of POAF [n (%)]	17 (33.3)	2 (3.8)	0.03
Duration (min)	1185 \pm 1180	1018 \pm 1100	0.44
Recurrence	2.8 \pm 1.8	2.3 \pm 1.1	0.77
Bleeding [n (%)]	7 (13)	6 (11)	0.81
Midsternotomy infection [n (%)]	8 (15)	1 (1.8)	0.03
Vomiting [n (%)]	7 (13)	9 (16)	0.67
Resp. dysfunction [n (%)]	10 (19)	2 (3.7)	0.04
Renal dysfunction [n (%)]	6 (11)	5 (9.4)	0.73
Mortality [n (%)]	1 (1.9)	1 (1.8)	1.0
ICU stay (days)	3.34 \pm 1.41	3.2 \pm 0.6	0.58
Hospital stay (days)	7.12 \pm 2.69	5.4 \pm 1.8	0.001

[Table 2]. Midsternotomy infection was detected in 9 cases (8.6%); of these, 8 cases (15%) were in group I and one (1.8%) in group N ($P=0.03$). Respiratory dysfunction was also observed in 11 cases (11.5%); 10 (19%) and 2 (3.7%) cases in groups I and N respectively ($P=0.04$). In addition, the mean value of hospital stay reached 6.25 \pm 2.24 days; it being 7.12 \pm 2.69 days and 5.4 \pm 1.8 days for groups I and N respectively. Postoperative midsternotomy infection, respiratory dysfunction, and hospital stay turned out to be more in group I than in group N. It therefore follows that preoperative hsCRP can predict occurrence of AF, midsternotomy infection, respiratory dysfunction, and hospital stay following elective off-pump CABG. No significant differences were identified between the two groups in terms of other postoperative complications such as bleeding, vomiting, renal dysfunction, and ICU stay ($P>0.05$). Early postoperative mortality occurred in 2 cases (1.9%) in hospital, one in each group. With regard to mortality, no significant relationship was detected between preoperative hsCRP and post-CABG.

DISCUSSION

Atrial fibrillation (AF) is one of the most prevalent arrhythmia after cardiac surgery. AF and other early complications following CABG are important causes of morbidity among patients.^[2,8] Occurrence of

postoperative AF and early complications are related to patients' particulars and type of surgical operation as well as the procedure and duration of postoperative management and monitoring. High sensitive C-reactive protein (hsCRP) seems to be most significantly associated with cardiovascular disorders. Elevation of hsCRP is associated with a worse prognosis in patients with acute myocardial infarction (AMI) or those undergoing angioplasty.^[6,7,9,10] This study was designed to evaluate the association of preoperative hsCRP with early complications and hospital stay in patients undergoing elective off-pump CABG.

Totally, 19 cases (18.2%) of prevalence of AF were identified in this study, whereas other studies have reported an incidence of 20-50%.^[2,8,11] Of the patients who had developed AF, there were 17 cases (33.3%) with preoperative hsCRP \geq 3 mg/dl and 2 cases (3.8%) with hsCRP \leq 3 mg/dl. Preoperative hsCRP values could predict the occurrence of postoperative atrial fibrillation but not the duration or frequency of recurrence of AF. Our study detected midsternotomy infection in 9 cases (8.6%); 8 (15%) were found in group I and one (1.8%) in group N ($P=0.03$). Respiratory dysfunction was also observed in 11 cases (11.5%); 10 (19%) and 2 cases (3.7%) in groups I and N respectively ($P=0.04$). The mean hospital stay turned out to be 6.25 \pm 2.24 days; it was 7.12 \pm 2.69 and

5.4+1.8 days in groups I and N respectively. Postoperative midsternotomy infection, respiratory dysfunction and hospital stay were observed to be greater in group I than N. It thus follows that preoperative hsCRP can predict occurrence of midsternotomy infection, respiratory dysfunction, and hospital stay after elective off-pump CABG. In a study conducted by Agda Mezzomo, it was indicated that hsCRP levels higher than 3 mg/dl can be used to predict respiratory infections associated with old age and increased mechanical ventilation (>24 h) and that preoperative hsCRP cannot predict cardiovascular events such as atrial arrhythmias (atrial fibrillation) or death.^[12] In a study carried out by Biancari *et al.*, it was detected that patient candidates for coronary bypass surgery with CPB and preoperative serum concentration of CRP ≥ 1.0 mg/dl would carry a higher risk of overall, low cardiac output syndrome, and postoperative cardiac death.^[13] Preoperative serum concentration of CRP ≥ 1.0 mg/dL was significantly more frequent among patients with a history of myocardial infarction and low left ventricular ejection fraction in patients undergoing surgery.^[13] Preoperative CRP in patients, undergoing on-pump coronary artery bypass surgery is an important determinant of postoperative outcome.^[13] These findings are therefore in line with those of our study, irrespective of the different surgical procedures applied. In a study conducted by Ahlsson *et al.*, it was shown that preoperative CRP cannot predict incidence of atrial fibrillation following open heart surgery,^[14] the results of which are not consistent with our findings. Cappabianca *et al.* reported that patients undergoing cardiac surgery with a CRP level of 0.5 mg/dL or more are predisposed to a higher risk of hospitalization mortality and postoperative infections.^[15] Despite correction of the surgical procedure, a high preoperative CRP value is regarded a risk factor for mid-term survival and hospitalization.^[15] A study conducted by Kangasniemi *et al.* in patients undergoing on-pump CABG reported that increased preoperative levels of CRP are associated with significantly decreased overall survival after surgery.^[16] These results are in line with those of our study in some respects. Palmerini *et al.* also identified that elevated preoperative levels of C-reactive protein can indicate an increased risk of post-coronary bypass surgery mortality in the treatment of unprotected left main coronary artery stenosis.^[17] Inflammatory risk assessment in patients with unprotected left main coronary artery stenosis provides incremental prognostic value for adequate preoperative patient stratification.^[17] These findings are not consonant with our results. Our study, however, focused on elective off-pump CABG whereas other studies chose on-pump CABG for their operations.

We conclude that preoperative hsCRP ≥ 3 mg/dl can predict

incidence of postoperative AF and early complications such as midsternotomy infection, respiratory dysfunction and hospital stay, following elective off-pump CABG.

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How to cite this article: Mirhosseini SJ, Forouzannia SK, Ali-Hassan-Sayegh S, Ravan HV, Abdollahi MH, Mozayan MR. Preoperative C-reactive protein can predict early clinical outcomes following elective off-pump CABG surgery in patients with severe left ventricle dysfunction. *Saudi J Anaesth* 2012;6:327-31.

Source of Support: Nil, **Conflict of Interest:** None declared.

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