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Original Article

Preoperative CRP levels is not predictive early renal dysfunction after coronary artery bypass surgery

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Abstract: Background: The aim of this retrospective study is to determine the correlation between preoperative CRP levels and the early renal dysfunction after cardiac surgery. Methods: From January 2012 to December 2013, values for preoperative CRP were available for 546 unselected patients undergoing cardiac operations. CRP was used to divide this cohort in two groups: a normal CRP levels group (Group I) of 432 patients with CRP of less than 0.5 mg/dL, and a high CRP levels group (group II) of 114 patients with a CRP of 0.5 mg/dL or more. Results: Median CRP preoperative values were significantly different in the group II (2.49±1.03 mg/dL) than in the group I (0.32±0.14 mg/dL; $P < 0.0001$). Median CRP postoperative values were significantly different in the group I (17.62±2.99) than in the group II (23.13±3.01; $P < 0.0001$). Preoperative levels of serum blood urea nitrogen (BUN), creatinine and CrCl were not significantly different between group I and group II. Postoperative levels of BUN, Cr and CrCl between the two groups were not significantly different. Conclusions: The early Cr and CrCl levels after surgery are not significantly different in group I and group II. The early renal function after CABG is not correlated with the preoperative CRP levels.

Keywords: C-reactive protein, renal function, cardiopulmonary bypass

Introduction

C-reactive protein (CRP) is a sensitive, although nonspecific marker of inflammation that has been shown in multiple prospective epidemiological studies to predict incident myocardial infarction, stroke, peripheral arterial disease, and sudden cardiac death [1]. Increased levels of C-reactive protein (CRP) were presented with angina pectoris in some patients recently [2]. Because these patients are potential candidates for cardiac operation, some patients will be operated on with preoperatively increased CRP levels.

Most of the recent studies showed that the cardiac surgery with cardiopulmonary bypass (CPB) induces a systemic inflammatory response syndrome (SIRS) [3, 4]. This inflammatory reaction may contribute to the development of postoperative complications, including myocardial dysfunction, respiratory failure, renal and neurologic dysfunction, bleeding disorders, altered liver function, and ultimately, multiple organ failure (MOF) [3, 5]. Even though advances in methods and technologies, postoperative acute renal insufficiency continues to be a significant cause of morbidity and mortality after CABG performed with using cardiopulmonary bypass (CPB). The etiology of this condition is multifactorial, including the factors correlated to conduct and management of CABG for instance; bypass time, use of vasopressors before CABG, systemic inflammatory response, hypoperfusion, and loss of pulsatile perfusion [6, 7].

Preoperatively increased CRP levels in cardiac surgical patients have been shown to correlate with the postoperative complications such as infections, atrial fibrillations and stroke [8]. However, whether there is a relationship between preoperatively increased CRP levels and postoperative renal dysfunction has not established yet.

Patients and methods

Patients

From January 2012 to December 2013, 925 patients underwent cardiac surgery at our institution. We performed a retrospective analysis of prospectively collected data. Exclusion criteria for registration were emergent surgery, reoperations, respiratory failure including asthma, adult respiratory distress syndrome, and clinical signs of infection before the operation (temperature > 37.5°C, CRP level ≥ 5 mg/dL or white blood cells > 12000/μL), history of neoplastic diseases including benign and malignant tumors, acute or chronic renal failure, determined by serum creatinine (Cr) values greater than 1.5 mg/dl and creatinine clearance (CrCl) using Cockroft-Gault equation [7] < 50 ml/min, autoimmune diseases, recent history of steroid or non-steroidal anti-inflammatory drug therapy in the last 2 weeks before surgery treatment with corticosteroids or immunosuppressive drugs.

The study was planned, and approval of the hospital ethics committee was obtained. 546 patients were suitable for inclusion in this study of among 925 patients. Patients were divided this cohort in two groups: a normal CRP level (group I) of 432 patients with CRP levels of less than 0.5 mg/dL, and a high CRP level (group II) of 114 patients with CRP levels of 0.5 mg/dL or more.

Operative techniques

All patients received an opioid-based anesthetic supplemented with muscle relaxants and volatile anesthetic drugs to facilitate early extubation. Endotracheal tube, urinary catheter, as well as radial artery and pulmonary artery catheters were inserted. After heparin administration, extracorporeal circulation was performed with hypothermic, nonpulsatile flow and esophagus temperature was 28°C. Cold blood cardioplegia was used to induce and maintain cardioplegic arrest and warm blood cardioplegia was used to terminate of the cardiac arrest. Mean arterial blood pressure during cardiopulmonary bypass was maintained between 50 mm Hg and 80 mm Hg with phenylephrine, sodium nitroprusside, or by altering the concentration of volatile anesthetic delivered to the cardiopulmonary bypass circuit. Pericardial aspirate was returned to the cardiopulmonary bypass circuit. To reverse heparin, protamine was administered at the rate of 1 mg for each milligram of total heparin given before and during CPB.

Biochemical parameters

Venous blood samples were obtained immediately before operation and 48 h after operation. Samples were collected in sterile tubes, centrifuged at 4,000 r.p.m. for 10 min at 4°C, and Serum levels of creatinine (Cr) and blood urea nitrogen (BUN) were measured using an automated chemical analyzer (Cobas 6000-c501 module).

Levels of CRP and were measured by the turbidimetric method using commercial kits (Cobas İntegra CRPLX). CrCl was determined by using the standard formula - Cockroft-Gault equation.

Statistical analyses

The quantitative data are presented as means ± SD, and the qualitative data are expressed as numbers and percentages. Student's t test for independent samples, and Mann-Whitney U and Wilcoxon signed rank tests were used to assess the differences between stages when applied. Comparison of qualitative data was also performed by χ^2 test and correlation assessed using Pearson's correlation test. Also, multivariable analysis using a multiple regression test was performed to assess effects of the changes in levels of preoperative CRP on the postoperative Cr and CrCl changes. A p value < 0.05 was considered significant. Statistical analyses were performed using the SPSS statistical package version 17.0 (SPSS Inc., Chicago, Ill., USA).

Results

A total of 546 consecutive patients who had coronary bypass operations were evaluated. The preoperative demographic values of patients were not significantly different between the two groups. The mean age of the patients was 64.1±4.9 years (range, 42 to 78 years); 421 patients (77.1%) were men and 125 patients (22.9%) were women. Mean duration of cardiopulmonary bypass was 109±36 minutes in group I and 106±32 in group II (P=0.62),

Table 1. Risk factors in the study groups

	CRP < 0.5 mg/dL (432 Patients)	CRP ≥ 0.5 mg/dL (114 patients)	*p*-value
Patients	432	114	
Mean age	64.25±4.8	63.9±5.4	0.50
Male (%)	337 (78)	84 (73.6)	0.33
Pulmonary disease (%)	115 (26.6)	29 (25.4)	0.67
Extra cardiac arteriopathy (%)	70 (16.2)	20 (17.5)	0.13
Hypertension (%)	293 (67.8)	72 (63.1)	0.09
Hyperlipidemia (%)	221 (51.5)	55 (48.2)	0.17
Diabetes (%)	129 (29.8)	33 (28.9)	0.68
Transient ischemic attack/stroke (%)	13 (3)	2 (1.75)	0.21
Unstable angina pectoris (%)	62 (14.3)	14 (12.2)	0.37
Emergency operation	5 (1.15)	6 (5.2)	< 0.0001
Recent myocardial infarction < 3 months (%)	196 (45.3)	51 (44.7)	0.57
Atrial fibrillation (%)	20 (4.6)	5 (4.3)	0.76
Left Ventricular ejection fraction < 30 (%)	19 (4.3)	4 (3.5)	0.24
Intra-aortic balloon pump (%)	4 (0.9)	1 (0.8)	0.78
Number of distal anastomoses	3.49±0.66	3.37±0.72	0.08
CPB time (minutes)	109±36	106±32	0.62
	116±43	0.17	
Clamp time (minutes)	65±26	63±21	0.54
	67±31	0.65	
Postoperative hospitalization (day)	5.4±0.3	5.6±1.2	0.73
Hospital mortality (%)	4 (0.92)	1 (0.87)	0.82

Continuous variables are reported as the mean ± standard deviation, or as percentage of group total. CPB, Cardiopulmonary bypass.

Table 2. Summarizing of renal function parameters between CRP < 0.5 mg/dL and CRP ≥ 0.5 mg/dL, and preoperative and postoperative

		CRP < 0.5 mg/dL (432 patients)	CRP ≥ 0.5 mg/dL (114 patients)	*P*-value
Cr, mg/dl	Preop	0.91±0.15	0.93±0.15	0.34
	Postop	0.97±0.17	0.96±0.17	0.64
CrCl, ml/min	Preop	104.11±10.96	103.56±11.22	0.63
	Postop	102.76±12.55	103.03±12.29	0.84
BUN, mg/dl	Preop	20.60±3.52	20.35±3.57	0.89
	Postop	21.19±3.79	21.43±3.06	0.73
CRP, mg/dl	Preop	0.32±0.14	2.49±1.03	< 0.0001
	Postop	17.62±2.99	23.13±3.01	< 0.0001

Cr: creatinine; CrCl: Creatinine clearance; BUN: blood urea nitrogen; CRP: C-reactive protein.

mean duration of aortic cross-clamp time was 65±26 minutes in group I and 63±21 in group II (P=0.54). The length of postoperative hospital stay was not significantly longer in patients with group I than in those with group II (5.4±0.3 versus 5.6±1.2 days; P=0.73). The mortality rate in patients with group I (0.92%) was significantly different from that in patients with group II (4.38%) P < 0.0001. Demographic and clinical data stratified according to preoperative CRP group are listed in **Table 1**. As per protocol, preoperative median CRP values were significantly different in the group II (2.49±1.03 mg/dL) than in the group I (0.32±0.14 mg/dL; P < 0.0001). Postoperative median CRP values were significantly different in the group I (17.62±2.99) than in the group II (23.13±3.01) P < 0.0001.

As demonstrated in **Table 2** and **Figures 1**-**3**, preoperative levels of serum BUN, Cr and CrCl were not significantly different between group I and group II. Postoperative levels of BUN, Cr and CrCl between the two groups were not significantly different.

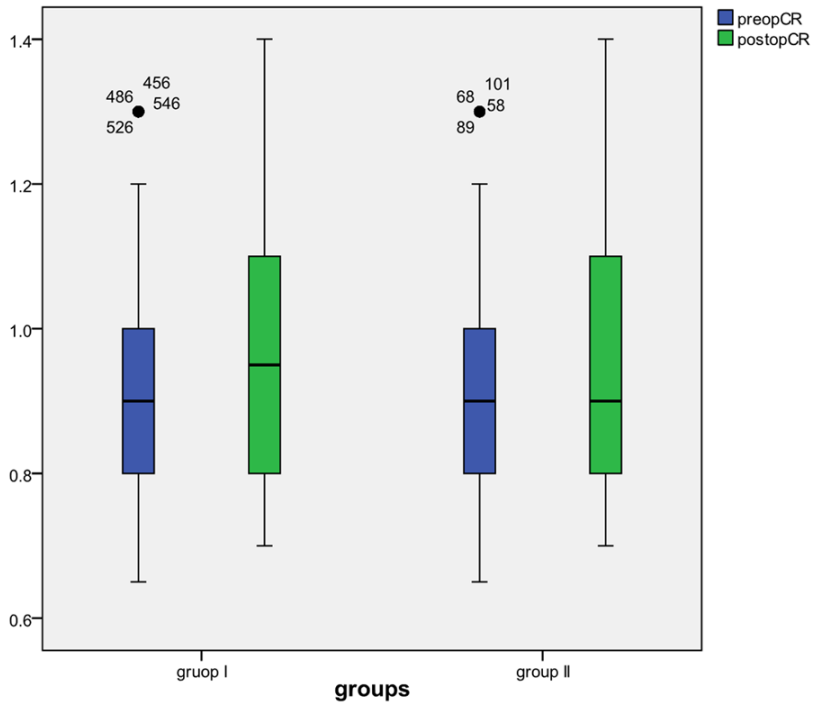

Figure 1. Preoperative and postoperative CR levels.

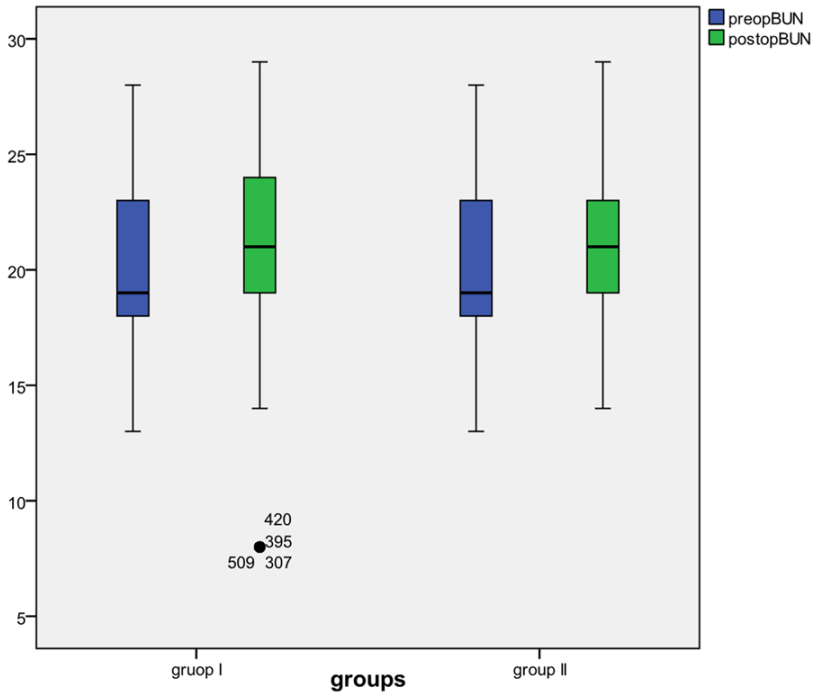

Figure 2. Preoperative and postoperative BUN levels.

Discussion

Classification of factors associated with an increased risk to develop complications after coronary artery bypass surgery is of main importance for a sufficient preoperative patients selection. Although the new scoring systems have been shown to be good predictors of outcome after cardiac surgery, they invariably suffer a certain inaccuracy in predicting the individual risk of postoperative mortality and morbidity.

CRP is an acute-phase protein, and elevated levels may be an indication of an underlying infectious disease or other inflammatory process. The last few studies showed that the CRP has emerged as an important predictor of cardiovascular events in healthy subjects and in those with known coronary artery disease [1, 2]. Numerous studies showed that the preoperatively increased CRP levels in cardiac surgical patients have been shown to correlate with the postoperative incidence of infections, atrial fibrillations and stroke [8, 9]. However Gaudino et al. [12] showed in small series that preoperative CRP levels did not have any impact on the postoperative adverse events of these patients.

It is well recognized that CABG may lead to major organ dysfunction. However, the role of an extracorporeal circulation in the development of renal injury is not completely clear. One study of CABG patients with normal preoperative renal function found no change in glomerular filtration rate (GFR) [13]. In addition, several factors are known to affect renal function during CPB

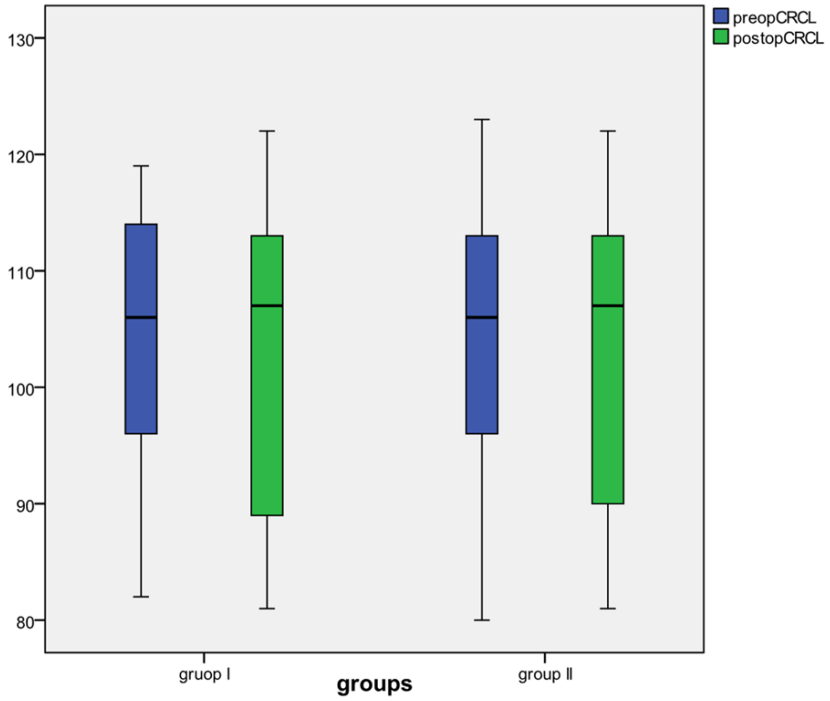

Figure 3. Preoperative and Postoperative CrCl levels.

including hypothermia, haemodilution, changes in haemodynamics, surgical stress, inflammatory response, and ischaemia reperfusion injury [14]. Cardiac surgery with CPB provokes a SIRS [3, 4, 16]. Contact of the blood components with the artificial surface of the bypass circuit, ischemia-reperfusion injury, endothelial damage, endotoxemi, and subsequent tissue edema and organ malfunction. This inflammatory reaction may cause to the development of postoperative complications, including cardiac dysfunction, respiratory failure, renal and neurologic dysfunction and eventually multiple organ failure (MOF) [3, 5, 17].

Preoperatively elevated CRP-concentrations for predicting complications after cardiac surgery has been controversially discussed. One study of Boeken et al. showed that retrospectively reviewed the files of a group of 50 patients undergoing coronary and valvular procedures with a preoperative CRP level > 5 mg/l and compared their results with those of a cohort of 50 matched cases with a normal preoperative CRP value, finding a superior incidence of postoperative complications among the high CRP level group [18]. However, some of the studies showed that there was no evidence of a relationship between a preoperative CRP-elevation in clinically unapparent patients and postoperative complications, especially renal dysfunction after extracorporeal circulation [17, 22]. We therefore made a retrospective study of one group of patients with elevated CRP-levels and another group of patients with preoperatively normal CRP-values. The results of the present study did not show a consistent association between the preoperative CRP levels and renal dysfunction, none of our patients in two group developed renal failure, and renal dysfunction, determined by early postoperative Cr and CrCl levels, was not different between the LCL and HCL groups.

In conclusion, none of our patients in either group developed early renal failure, and renal dysfunction, determined by early postoperative Cr and CrCl levels, was not different between the two groups. In our study preoperative CRP levels in patients who underwent cardiac operations were independent of inflammatory markers in early renal function.

Disclosure of conflict of interest

None.

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