

Effect of Off-Pump Coronary Artery Bypass Surgery on C-Reactive Protein Level

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Abstract

Context: Off-Pump Coronary Artery Bypass Surgery (OPCAB) induces ischaemic injury of varying degree. The inflammation associated with such ischaemia causes rise in CRP level. Heart failure is an important consequence of OPCAB in immediate postoperative (postop) period and may affect overall recovery. *Aims:* Our study investigated a relationship between CRP level and parameters of heart failure in postoperative period, so that, CRP level can guide us to predict the prognosis of such patients. *Settings and Design:* This is a retrospective study done on the population of eastern India with ischaemic heart disease, underwent OPCAB from January 2018 to June 2019. 83 male patients were selected depending on various exclusion criteria including abnormal lung function. All patients were investigated for preoperative cardiac, renal, liver and haematological parameters along with assessment of preoperative (preop) CRP level. *Materials and Methods:* 44 patients (pts) were seen to have normal CRP level preoperatively. These pts in postoperative day one (POD 1) were checked for CRP level and were divided into two groups, ≥ 10 milligram/litre (mg/L) and < 10 mg/L. Other postoperative investigations on various organ system were done. *Statistical analysis used:* Two sample t-tests for a difference in mean involved independent samples or unpaired samples. p value less than or equal to 0.05 was considered statistically significant. *Results:* Heart failure parameters like brain natriuretic peptide (BNP), left ventricular ejection fraction (LVEF) and Left Ventricular End Systolic Volume (LVESV), postoperative ventilation time and hospital stay were significantly increased in the group having ≥ 10 mg/L CRP. *Conclusion:* High CRP level in postoperative OPCAB patients has a predictive power as good as LVEF and LVESV. It can guide us regarding overall recovery.

Keywords: CRP; Heart failure; Ischaemic injury; OPCAB, Prognosis.

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Introduction

Inflammation characterizes all phases of atherothrombosis.¹ It provides a critical link

between plaque formation and all its consequences.² In clinical practice, the best studied and most easily applied biomarker of such inflammatory process is the acute phase reactant C-reactive protein (CRP). It is produced and released from liver within 6 hours of injury and peaks at 48 hours.³

It is known that OPCAB operation induces inflammatory changes in our body and may inflict an ischaemic injury during the procedure. The influence of such operation on blood CRP level and on our body physiology is variable.⁴ It depends upon internal factors like inflammatory response of

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the individual and on external factors like degree of perioperative injury and many others.

Elevated postoperative inflammatory response may influence the recovery. Heart failure is the important consequence in postoperative ischaemic heart disease patients and affects the overall recovery.^{4,5} Simple indices like Left Ventricular Ejection Fraction (LVEF) and End Systolic Volume (LVESV) determined by Trans Thoracic Echocardiography are the good indicators of heart failure.^{5,6} The present study, investigated on the relationship between elevated CRP and parameters of heart failure (clinical and investigational) in postoperative patients of OPCAB, so that, CRP level can guide us to predict the prognosis of these patients in immediate postop period. Moreover, as per available literature, no study has been done on such relationship of CRP and heart failure on the ethnic population of eastern India.

Materials and Methods

From January 2018 to June 2019, among patients who underwent OPCAB in IPGME & R and SSKM Hospital, 83 patients with following criteria, were consecutively selected and enrolled retrospectively in this study. As this is a retrospective record based study, our Institutional Ethics Committee has granted our request for waiver of the written informed consent for the study.

Criteria of inclusion were strictly followed –

1. Only male patients with diagnosed triple vessel disease were included, as causal factors and disease prognosis are different in male and female genders in ischaemic heart disease;
2. Age limit 45–65 years, the most common age group affected by ischaemic heart disease;
3. All patients were afebrile preoperatively as fever induces CRP level;⁷
4. All patients were on Atorvastatin tablets (40 mg) – as it checks CRP level;⁸
5. Left ventricular ejection fraction more than 45% (with such ejection fraction hemodynamic stability during operation would be better maintained);⁹
6. All patients selected were nondiabetic, as diabetes increases CRP level;¹⁰
7. Patients were screened for serum Thyroid Stimulating Hormone (TSH) and free T4 level. Only those patients were selected for the study who showed normal parameters as abnormality

of thyroid profile, induce lipid profile thus may cause CRP rise;¹¹

8. Our patients had no history, symptoms and signs of peripheral arterial disease (PVD) – as PVD is mostly associated with increased CRP level¹²
9. No other associated co morbidities like chronic kidney and lung diseases as chronic inflammation increases CRP.
10. All patients had 4 grafts – as number of grafting is the function of time and may influence ischaemic time;¹³
11. The preop NYHA (New York Heart Association classification for heart failure) class was either III or IV in all patients.

All patients had preoperative (preop) CRP level measured, the day before surgery and postoperative (postop) measurement done on POD 1 morning i.e., 14–16 hours after surgery. Measurement was done by nephelometry method. The normal value was considered as < 3 mg/dl. CRP level ≥ 10 mg/dl were considered as significant rise. All patients were divided into two groups, postop CRP ≥ 10 mg/dl and postop CRP < 10 mg/dl. All patients were evaluated with preop and postop 2D Echocardiography and colour doppler study. Postop Echo evaluation was done in POD 5.

Patients Characteristics All patients underwent the operation, under same surgical team, with general anesthesia and intubation and midline sternotomy. All patients received LIMA to LAD grafting, RSVG to one diagonal artery (sequential), one obtuse marginal (sequential) and one PDA/distal RCA grafting(end anastomosis). 2 pts (4.54%) had GSV harvesting done from right lower limb and the rest had (95.46%) it from left lower limb. Suction stabiliser, Deep Pericardial Stays and Gauge packing were used in all patients.

All patients received infusion nitroglycerin and/or dobutamine, low-dose of noradrenaline and diuretic therapy perioperatively and postoperatively. Reopening was done in one patient in ICU due to bleeding issues. Postoperatively 8 patients had signs and symptoms of heart failure, mild to moderate in presentation, with variable incidence of increased heart rate, pedal edema, rales at the base of the lungs, night cough, distress on lying down, anorexia but all of them were treated successfully.

Respiratory complications included post-operative prolonged mechanical ventilation (more than 36 hours) and no tracheostomy needed, no death happened. One pt underwent hemodialysis.

Wound infection occurred in single patient (pt), who needed sternal wire removal later on.

Among 83 selected patients, 44 (53.01%) pts had normal preoperative CRP level and considered for further evaluation, the rest 39 pts had elevated preoperative CRP level and were excluded from the study. There were 26 patients (59.09%) with significant rise in CRP level postoperatively (≥ 10 mg%) and 18 patients (40.90%) had CRP rise not reaching the significant level (< 10 mg/dl).

Statistical analysis

For statistical analysis data were entered in a Microsoft Excel spread sheet and then analysed by SPSS (version 25.0; SPSS Inc, Chicago, IL, USA). Data had been summarised as mean and standard deviation for numerical variables and count and percentages for categorical variables, Two sample t-tests for a difference in mean involved independent samples or unpaired samples. p - values of ≤ 0.05 was considered for statistical significance.

Results

Table 1 compares the preoperative characteristics of patients who belong to two groups with postoperative CRP ≥ 10 mg/dl and CRP < 10 mg/dl. Age, height, renal function, nutritional status along with left ventricular function were not different between the two groups. Body weight (wt), BMI, Blood pressure status were also not different in these two groups.

In table 2 early postop hospital outcomes are depicted. Packed RBC transfusions were different in two groups but FFP transfusion were not. The need for prolonged ventilation (> 36 hrs), the heart failure marker BNP level, postoperative hospital stay were significantly different in two said groups. The difference between LVEF and ESV were significantly different in groups with $p = 0.003$ and $p = 0.0001$ respectively.

No significant difference were found in, renal dysfunction, postop wound infection between two groups. No in-hospital death occurred.

Table 1: Comparative preop data for two groups with postop CRP > 10 mg/dl vs postop CRP < 10 mg/dl

Characteristics	CRP > 10 mg/dl ($n = 26$)	CRP < 10 mg/dl ($n = 18$)	p - value
Age	53.75 \pm 10.90	56.40 \pm 7.32	0.37
Height	1.63 \pm 0.05	1.60 \pm 0.05	0.06
Body weight	58.44 \pm 7.38	55.20 \pm 7.19	0.15
BMI	22.37 \pm 2.30	21.63 \pm 2.15	0.29
Systolic Blood pressure	123.75 \pm 17.19	116.15 \pm 13.34	0.12
Diastolic Blood pressure	76.25 \pm 7.79	79.50 \pm 7.32	0.17
Creatinine	1.25 \pm 0.70	1.21 \pm 0.30	0.796
Albumin	2.5 \pm 1.1	2.9 \pm 1.20	0.259
Hemoglobin	8.42 \pm 1.60	8.97 \pm 1.69	0.279
ALT	51.33 \pm 19.22	49.60 \pm 17.0	0.760
AST	44.00 \pm 22.80	33.13 \pm 17.70	0.097
LVEF	55.00 \pm 3.50	52.50 \pm 5.78	0.08
ESV	40.12 \pm 3.0	40.62 \pm 5.33	0.69

BMI - Body Mass Index, ALT- Alanine Transaminase, AST - Aspartate Transaminase.

Table 2: Comparative data of postoperative outcomes between two groups with postop CRP > 10 mg/dl vs postop CRP < 10 mg/dl.

Characteristics	CRP > 10 mg/dl ($n = 26$)	CRP < 10 mg/dl ($n = 18$)	p - value
BNP	1054.79 \pm 684.69	672.34 \pm 229.98	0.027
LVEF	45.67 \pm 9.62	54.05 \pm 7.26	0.003
ESV	43.57 \pm 4.47	32.0 \pm 5.50	0.0001
Transfusions			
PRBC (units)	4.20 \pm 1.76	3.0 \pm 1.23	0.016
FFP (ml)	786.9 \pm 646.90	540.00 \pm 560.15	0.196
Postop Hospital stay (days)	7 \pm 1.25	4.6 \pm 2.3	0.0001
Ventilator support(hours)	32.37 \pm 4.75	17.15 \pm 5.50	0.0001
Dialysis	1	0	1.0
Wound Infection	1	0	1.0

BNP - Brain Natriuretic Peptide; PRBC - Packed Red Blood Cells; FFP - Fresh Frozen Plasma.

Discussion

Shifting of burden of Cardio Vascular Disease (CVD) is happening globally. Between 1990 and 2013, deaths from CVD increased from 26% to 32% of all world deaths, a reflection of rapid epidemiological transition, particularly in low and middle income countries (LMICs). In absolute numbers, CVD causes four-five times as many deaths in LMICs than in High Income Countries (HICs).¹⁴ India, the country with unique diversity, belongs to this LMIC group.

The nature and environment, looks and body stature, lifestyle and food habits are significantly different amongst the habitants of northern, southern, western and eastern parts of India. Our center has the wide drainage area of eastern Indian population. People in this demographic area use to have high carbohydrate and fat-rich diet, sedentary life style with low propensity to sports and other outdoor activities and high rate of tobacco abuse. There is a steep rise of incidences of diabetes and ischemic heart disease and bursting number of CABGs in past few decades especially OPCABs in eastern India.¹⁵ Our study was based on this demographic group which has not been done by any other study earlier.

Inflammation plays a critical role in cardiovascular diseases. Inflammatory cytokines like Interleukin (IL)-1 or Tumor Necrosis Factor (TNF), implicated in atherogenesis, elicit the expression of messenger cytokine IL-6 which induces the liver to release acute phase reactant protien CRP. It is a member of pentraxin family with homopentameric 23 kDa subunits, responsible for human-innate immunity.³ CRP is the best studied and easily assessable down-stream acute phase reactant. It was discovered in 1930 by Tillet and Francis while investigating the sera of patients suffering from the acute stage of *Pneumococcus* infection and was named for its reaction with the capsular (C)-polysaccharide of *Pneumococcus*.²¹ It is released from the liver within 6 hours of infliction of injury/inflammation and peaks up in next 2-3 days. It continues to be so, the next 7-8 days.¹⁶ In chronic inflammatory condition it remains elevated for longer duration. The average levels of CRP in serum in a healthy individual is around 0.8mg/L, but this baseline can vary due to other factors including age, gender, smoking status, weight, lipid levels and blood pressure.¹⁵ More than 50 large scale prospective cohorts conducted worldwide, CRP when measured with high sensitivity assays (hs CRP), independently predicts risk of various

illnesses like acute ischaemia, Infarction, heart failure, peripheral vascular disease etc.¹⁷

Literature has categorized CRP levels of less than 1, 1-3, >3, and ≥ 10 mg/L and is to be interpreted as with lower, moderate, high and very high cardiovascular risk.¹⁷ Assesment of the CRP is done by nephelometry method in our center. It is an automated blood test that uses particle-enhanced immunonephelometry to quantify CRP in serum samples. Polystyrene particles coated with monoclonal antibodies against CRP become agglutinated when mixed with samples containing CRP. The intensity of light scattering due to agglutination reaction was measured using nephelometer and directly related to the concentration of CRP. The lower detection limit is 0.5 mg/l.²² On this basis, we considered < 3 mg/lit as preoperative cut off value for inclusion of patients in our study. We divided postop OPCAB patients into two groups based on ≥ 10 mg/L and < 10 mg/L as significant cut off level because studies have depicted C reactive protein levels ≥ 10 mg/L correlate in a statistically significant manner ($p < 0.001$) with a risk higher than 4% to develop a fatal cardiovascular event in next 10 years.¹⁸

OPCAB is one of the most commonly performed operation in our centre and it highly outnumbers onpump coronary artery bypass surgery (ONCAB). Many studies have shown, CRP level rises up after OPCAB, the real issue is still under research. In our center we routinely perform CRP estimation by nephelometry test before and after operation in all cardiac cases. To eleminate the variables producing ischaemia during the procedure like time of application of stabilizer, grafting time, no of grafts, types and quantities of drugs used, incidence of intraop hypotension,¹⁹ we selected only those cases done by the same surgical and anaesthetic team.

CRP level is increased in heart failure and all postop OPCAB patients suffer from variable degrees of heart failure, subtle to overt in range. Thus, measurement of CRP and heart failure parameters have the potential to play an important role as for risk assessment in postoperative OPCAB patients. After ischaemia postoperatively, there is cardiac dilation from day 3 to day 21. Studies support that addition of ESV to LVEF clearly added prognostic power to stratification of morbidity risk.²⁰ In our study, we included both these parameters therefore.

In our study, we hypothesize that high-postop CRP, after OPCAB, like a simple index similar to LVEF and LVESV could be an indicator for guiding treatment and prognosis. Between two study groups, there were no significant difference

between different preoperative parameters like renal function (urea, creatinine), liver function (albumin, AST, ALT), cardiac function (LVEF, ESV) and inflammation and general well-being (CRP and hemoglobin level). In our center lung function test is not routinely done before OPCAB unless history and clinical features suggest. In our study, clinically abnormal lung function was an exclusion criteria. Therefore, theoretically CRP level could be related to postoperative result. However, between two groups with postoperative high (≥ 10 mg/lit) and low (< 10 mg/lit) CRP values, there were no differences in regard to dialysis, wound infection rate. There is significant difference regarding heart failure parameters like BNP level ($p = 0.027$), LVEF ($p = 0.003$) and LVESV ($p = 0.0001$) values. There was significant difference between hours of mechanical ventilation ($p = 0.0001$), no tracheostomy was needed in either group. Though there is significant difference in postop cardiac function status in between two groups including PRBC transfusion ($p = 0.016$) but FFP transfusion was not significant ($p = 0.196$). The cause may be the size of study sample was small and this is the limitation of our study. The duration of hospital stay between two groups was significantly different ($p = 0.0001$).

Conclusion

High CRP level in postoperative OPCAB patients has a predictive power as good as LVEF and LVESV. It can guide us regarding overall morbidity like cardiac function, length of ventilator- support and prolonged hospital stay.

Prior publication Nil

Support Nil

Conflicts of interest Nil

Permissions: Ethical committee permission obtained.

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