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Case Report

Prognostic Value of Postoperative Changes in C-reactive Protein and Complete Blood Count after Cardiac Surgery with Cardiopulmonary Bypass

Kaoutar Zirhirhi*, Abdelhak Tissir, Lina Berrada, Sara Chabbar, Fatima Ezzahra Faouji, Anas Mounir and Mohamed Aziz Bouhouri

Surgical Intensive Care Unit, Ibn Rochd University Hospital, Casablanca, Morocco

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***Corresponding author:** Kaoutar Zirhirhi, Surgical Intensive Care Unit, Ibn Rochd University Hospital, Casablanca, Morocco

A B S T R A C T

Introduction: Cardiopulmonary bypass (CPB) induces a complex systemic inflammatory response combining leukocyte activation, platelet consumption and a rise in inflammatory markers. Identifying biological factors predictive of morbidity could improve risk stratification after cardiac surgery.

Objective: To study the postoperative changes in C-reactive protein (CRP) and the complete blood count (CBC) after cardiac surgery with CPB and to assess their predictive value for postoperative morbidity and mortality.

Methods: An analytical observational study of 75 patients operated on with CPB. Pre- and postoperative biological parameters were collected. Correlations between biological changes, patient characteristics and postoperative events were analysed in univariate and multivariate analyses.

Results: The median intensive care unit (ICU) stay was 6 days and the median hospital stay was 24 days. All biological parameters were significantly modified postoperatively ($p < 0.001$), confirming a marked inflammatory response. Haematological complications were the most frequent (76%), followed by cardiac (68%) and inflammatory complications (28%). In-hospital mortality was 8%. Postoperative CRP was correlated with age ($r = 0.348$; $p < 0.01$) and with renal failure ($r = 0.297$; $p = 0.01$). Postoperative lymphocytes were correlated with age ($r = 0.292$; $p < 0.05$) and with preoperative values ($r = 0.586$; $p < 0.01$). A rise in CRP was associated with a longer hospital stay ($p = 0.015$) and lymphopenia with a prolonged ICU stay ($p = 0.011$). Neither CPB duration nor aortic cross-clamp time was associated with the biological changes.

Conclusion: Postoperative changes in CRP and lymphocytes appear to be potential markers of outcome after cardiac surgery with CPB. Patient-related characteristics seem to play a more important role than operative parameters in the intensity of the inflammatory response.

Keywords: Cardiopulmonary bypass; Cardiac surgery; C-reactive protein; Lymphopenia; Systemic inflammatory response; Prognosis

Introduction

Cardiac surgery with cardiopulmonary bypass (CPB) remains associated with a systemic inflammatory response of variable intensity, whose pathophysiology is now well documented. Prolonged contact of blood with the non-endothelialised surfaces of the extracorporeal circuit, myocardial ischaemia–reperfusion related to aortic cross-clamping, haemodilution, hypothermia, surgical trauma and neuro-hormonal activation all contribute to triggering a complex inflammatory cascade involving complement activation, the release of pro-inflammatory cytokines (IL-6, IL-8, TNF-α) and the activation of neutrophil granulocytes[1-3].

Biologically, this reaction manifests as a rise in acute-phase proteins, foremost among them C-reactive protein (CRP), a predominantly neutrophilic leukocytosis, a transient lymphopenia and disturbances of haemostasis combining thrombocytopenia and platelet dysfunction[4]. Although these changes are most often transient and reversible, their intensity has been correlated in several studies with the occurrence of postoperative complications - infections organ failure, low cardiac output syndrome - and with prolonged lengths of stay[5,6].

CRP, a simple, inexpensive and widely available marker, together with the parameters of the complete blood count (CBC), could thus constitute prognostic tools accessible in routine practice. The objective of this study was to assess the postoperative changes in CRP and CBC after cardiac surgery with CPB and to analyse their predictive value for postoperative morbidity and mortality, as well as the clinical and operative determinants of these changes.

Materials and Methods

Study type and population

This was an analytical observational study carried out in 75 consecutive patients who underwent cardiac surgery with cardiopulmonary bypass. Demographic, clinical, operative and biological parameters were collected systematically for each patient.

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Data collected

The demographic and clinical variables analysed included age, sex and medical history. The operative parameters collected were cardiopulmonary bypass duration, aortic cross-clamp time and CPB temperature. The biological parameters, measured pre- and postoperatively, included haemoglobin, white blood cells, neutrophil granulocytes, lymphocytes, platelets and CRP.

Outcome measures

The primary outcome measures were the length of ICU stay, the total postoperative hospital length of stay, the occurrence of postoperative complications and in-hospital mortality.

Statistical analysis

Quantitative variables are expressed as mean ± standard deviation and qualitative variables as frequency and percentage. Comparison of pre- and postoperative values was performed using paired tests. Correlations between biological variables and postoperative events were assessed by univariate and multivariate analyses, with correlations expressed by the coefficient r. A p value below 0.05 was considered statistically significant.

Results

Population characteristics

The demographic and clinical characteristics of the 75 patients are presented in **(Table 1)**. The mean age was 58 ± 12 years, with a male predominance (62%). The main cardiovascular risk factors were arterial hypertension (48%), diabetes (32%) and dyslipidaemia (29%). The surgery performed was mostly coronary artery bypass grafting (55%), followed by valve replacement (35%) and combined surgery (10%).

Table 1: Demographic and clinical characteristics of the population (n = 75).

Variable	Result
Mean age	58 ± 12 years
Male sex	62%
Arterial hypertension	48%
Diabetes	32%
Dyslipidaemia	29%
Chronic renal failure	12%
Coronary artery bypass grafting	55%
Valve replacement	35%
Combined surgery	10%

Pre- and postoperative biological changes

All biological parameters were significantly modified postoperatively **(Table 2)**. A fall in haemoglobin, a markedly neutrophil-predominant leukocytosis, a lymphopenia, a thrombocytopenia and a major rise in CRP were observed, the mean value of which increased from 6 ± 4 mg/L to 148 ± 75 mg/L ($p < 0.001$) **(Figure 1)**. This profile reflects the intensity of the systemic inflammatory response induced by CPB.

Table 2: Pre- and postoperative changes in biological parameters (mean ± standard deviation). Neutrophils: neutrophil granulocytes; CRP: C-reactive protein.

Parameter	Preoperative	Postoperative	p
Haemoglobin (g/dL)	13.1 ± 1.4	10.4 ± 1.6	< 0.001
White blood cells (G/L)	7.2 ± 2.1	12.8 ± 4.3	< 0.001
Neutrophils (G/L)	4.8 ± 1.8	10.3 ± 3.7	< 0.001
Lymphocytes (G/L)	2.0 ± 0.7	0.9 ± 0.4	< 0.001
Platelets (G/L)	240 ± 65	145 ± 48	< 0.001
CRP (mg/L)	6 ± 4	148 ± 75	< 0.001

Lengths of stay

The median ICU stay was 6 days, with a range from 12 hours to 27 days. The median postoperative hospital stay was 24 days, with a range from 4 to 63 days.

Postoperative morbidity

Postoperative complications were dominated by

haematological complications, present in 76% of patients, followed by cardiac and inflammatory complications. The distribution of complications is presented in **(Table 3)**.

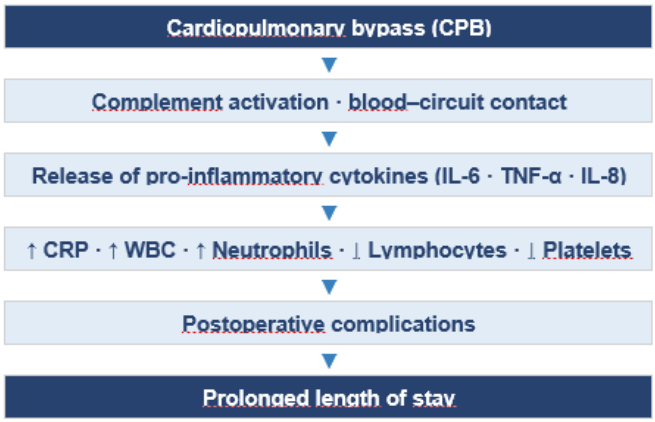

Figure 1: Pathophysiological scheme of the inflammatory response induced by cardiopulmonary bypass and its clinical consequences.

Table 3: Distribution of postoperative complications (n = 75)

Type of complication	Frequency
Haematological	76%
Cardiac	68%
Inflammatory	28%
Infectious	13.3%
Renal	13.3%
Respiratory	8%
Neurological	4%

Mortality

Overall, in-hospital mortality was 8%. The main causes of death were multiple organ failure, haemodynamic instability and severe respiratory distress.

Determinants of biological changes

Postoperative CRP levels were significantly correlated with age ($r = 0.348$; $p < 0.01$) and with the presence of preoperative renal failure ($r = 0.297$; $p = 0.01$). Postoperative lymphocyte counts were correlated with age ($r = 0.292$; $p < 0.05$) and with preoperative lymphocyte counts ($r = 0.586$; $p < 0.01$). Conversely, no significant correlation was found between the biological changes and cardiopulmonary bypass duration, aortic cross-clamp time or CPB temperature.

Predictors of morbidity and mortality

An increase in postoperative CRP was associated with a significant prolongation of the postoperative hospital stay ($p = 0.015$). A decrease in lymphocytes was associated with a significant prolongation of the ICU stay ($p = 0.011$). After multivariate adjustment, no biological marker was independently associated with in-hospital mortality.

Discussion

This study confirms the existence of a marked inflammatory and haematological response after cardiac surgery with cardiopulmonary bypass. All the biological parameters studied were significantly modified postoperatively: a rise in CRP, neutrophilic leukocytosis, lymphopenia and thrombocytopenia. This profile, found in almost all patients, illustrates the engagement of a stereotyped systemic inflammatory reaction, consistent with the pathophysiological mechanisms described in the literature and summarised in Figure 1, involving complement activation, the production of pro-inflammatory cytokines (IL-6, IL-8, TNF-α) and the recruitment of neutrophil granulocytes in contact with the extracorporeal circuit[1-3].

Comparison with the literature

Our results confirm four classic observations reported in many international series: the postoperative rise in CRP, neutrophilia, lymphopenia and thrombocytopenia. Wan et al. described in detail the cytokine cascade triggered by CPB and its central role in the genesis of postoperative organ dysfunction[1]. Paparella, et al. clarified the multiple activation pathways - contact, ischaemia-reperfusion, endotoxaemia - converging towards a generalised pro-inflammatory state[2]. More recently, Squiccimarro, et al. emphasised, in a narrative review, the considerable inter-individual variability of this response and its association with major adverse events[4]. Our data fit fully within this framework, while shedding light on the respective weight of patient background and operative parameters.

A notable finding of our work is indeed the absence of a significant association between cardiopulmonary bypass duration or aortic cross-clamp time and the intensity of the biological changes. This observation contrasts with some data in the literature reporting a relationship between CPB duration and the magnitude of the inflammatory response[6]. Our results suggest that individual patient characteristics may exert a more decisive influence than operative parameters alone. Several hypotheses can be put forward: the limited sample size, the heterogeneity of procedures and the inter-individual variability of inflammatory reactivity.

Role of patient background: Age and renal failure

In our series, age appears to be a major determinant of postoperative inflammatory changes, correlated with both the rise in CRP and lymphopenia. This finding is consistent with the concept of immunosenescence and chronic low-grade inflammation ("inflammaging") characterising the elderly, which may modulate the amplitude and duration of the postoperative inflammatory response. Likewise, the presence of preoperative renal failure seems to favour a more intense inflammatory response, which may be explained by a pre-existing pro-inflammatory state and a reduced clearance of inflammatory mediators.

The strong correlation between pre- and postoperative lymphocyte counts ($r = 0.586$) underlines the importance of baseline immune status in determining postoperative lymphopenia. Lymphopenia, a marker of immune dysregulation and transient immunosuppression, is increasingly recognised as a poor prognostic factor after surgical injury or in intensive care[5].

Prognostic value of biomarkers

From a prognostic standpoint, the association between the rise in CRP and prolonged hospitalisation on the one hand and between lymphopenia and prolonged ICU stay on the other, highlights the potential value of these biomarkers as risk-stratification tools. Their simplicity, low cost and immediate availability make them attractive candidates for integration

into routine practice. It should be noted, however, that CRP, because of its prolonged and non-specific elevation after CPB, must be interpreted with caution and ideally combined with other markers and with the kinetics of their evolution[4,7]. The joint monitoring of CRP and lymphocytes, rather than an isolated marker, could improve prognostic performance. In this regard, the neutrophil-to-lymphocyte ratio (NLR), which simultaneously integrates neutrophilia and lymphopenia, has been independently associated with mortality and prolonged ICU stay after cardiac surgery and constitutes a promising avenue of research[8,9]. Similarly, postoperative IL-6 levels have been correlated with age and the occurrence of organ failure, supporting the central role of pro-inflammatory cytokines in the genesis of complications[10-12].

Study limitations

This study has several limitations. Its observational and single-centre nature, the small sample size (75 patients) and the absence of specific cytokine assays limit the scope of the conclusions. The absence of an independent association with mortality in multivariate analysis may result from a lack of statistical power. Larger prospective studies, ideally multicentre, are needed to confirm the prognostic value of these biomarkers and to define their decision thresholds.

Clinical implications

Beyond their pathophysiological interest, our results have several direct practical implications for postoperative monitoring:

- An elevated postoperative CRP identifies patients at risk of a prolonged hospital stay and could justify enhanced monitoring.
- Postoperative lymphopenia could constitute an early marker of immunosuppression and vulnerability to infectious complications.
- Joint CRP–lymphocyte monitoring could improve postoperative surveillance compared with the use of an isolated marker.
- These biomarkers are inexpensive, reproducible and available in all centres, which facilitates their integration into follow-up protocols.

Conclusion

Cardiac surgery with cardiopulmonary bypass is accompanied by major postoperative inflammatory and haematological changes. Age and preoperative renal failure appear to be significant determinants of the intensity of this response, more so than operative parameters. Postoperative rise in CRP and lymphopenia are associated with prolonged lengths of stay and could constitute simple and useful prognostic markers in clinical practice. Larger prospective studies are needed to confirm these results and to clarify their therapeutic implications.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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