International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Inflammatory Biomarkers in the Intensive Care Unit: Postoperative Kinetics of C-Reactive Protein After Cardiac Surgery with Cardiopulmonary Bypass

Essalama Abderrahim[1], Derkaoui Ali[2], Benmlih Houda[3], Pr. Khatouf Mohamed[4], Pr. Shimi Abdelkarim[5], Pr. Bichri Ibrahim[6], Pr. Majdoub Amine[7]

[1,2,3,4,5,6]MD – Department of Intensive Care A1, Hassan II University Hospital, Fez, Morocco
[7]Department of cardiovascular Surgery, Hassan II University Hospital, Fez, Morocco

Abstract:
Cardiac surgery under extracorporeal circulation induced a significant inflammatory response, with CRP kinetics reflecting postoperative progression.
The aim of this study was to evaluate postoperative CRP kinetics and its association with complications.
We conducted a retrospective study including adult patients who underwent cardiac surgery under CPB and were admitted to the A1 intensive care unit at Hassan II University Hospital in 2023. Preoperative CRP levels, as well as those at 24 hours, 48 hours and 7 days, were analysed, and complications were classified as inflammatory, infectious, haemodynamic, haemorrhagic, neurological or thromboembolic.
Among the 88 patients included, CRP rose from 9.6 mg/L preoperatively to a peak of 216.9 mg/L at 48 hours before decreasing to 71.4 mg/L on day 7. Complications affected 55.7% of patients, predominantly inflammatory and haemodynamic. Univariate analysis identified male gender ($p = 0.031$) and length of stay in intensive care ($p = 0.021$) as significant risk factors, while the duration of CPB was not associated with complications. CRP values did not differ preoperatively or in the early stages, but remained significantly higher on day 7 in patients with complications (80.2 vs. 62.8 mg/L; $p \approx 0.03$).
These data suggested that persistent late elevation of CRP is a marker of poor outcome.

Introduction:
CRP is a robust marker of systemic inflammatory activation induced by extracorporeal circulation, incorporating the impact of surgical trauma, ischaemia–reperfusion and immune activation.
Its post-operative kinetics, characterised by a peak at 48–72 hours, reflect the intensity of the inflammatory response induced by CPB.
While early values are not very discriminating, the persistence of elevated CRP beyond D5–D7 is strongly correlated with inflammatory, infectious and haemodynamic complications.
Thus, CRP remains a relevant biomarker for post-operative monitoring, allowing early identification of patients at risk of unfavourable outcomes.

Materials and methods:

We conducted a retrospective descriptive and analytical study including all adult patients admitted to the A1 intensive care unit at Hassan II University Hospital in Fez after cardiac surgery under cardiopulmonary bypass (CPB) between January and December 2023. Patients with an intensive care unit stay of less than 48 hours, early death, or incomplete data were excluded. The variables collected included demographic data, comorbidities, type of procedure (valvular, coronary, or other), duration of CPB, and time to extubation.

Postoperative monitoring included assessment of haemodynamic parameters, vasopressor requirements, and screening for inflammatory, infectious, haemodynamic, haemorrhagic, neurological, or thromboembolic complications.

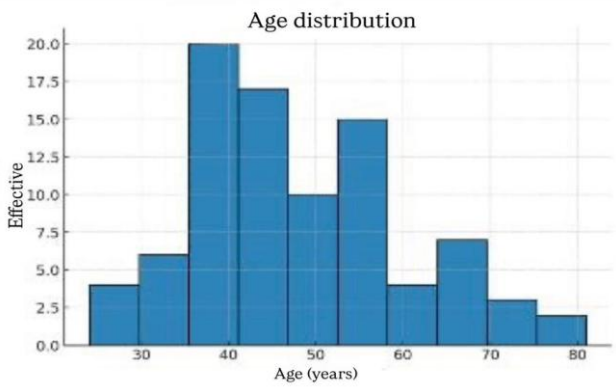
CRP was measured systematically at four time points: preoperatively, at 24 hours, at 48 hours, and on day 7. Length of stay in intensive care and in-hospital mortality were also documented.

Statistical analysis was performed using SPSS® version 26: quantitative variables were expressed as means ± standard deviation and compared using Student's t-test or Mann–Whitney test depending on their distribution, while qualitative variables were compared using the χ^2 test or Fisher's exact test. The significance threshold was set at $p \leq 0.05$.

Results:

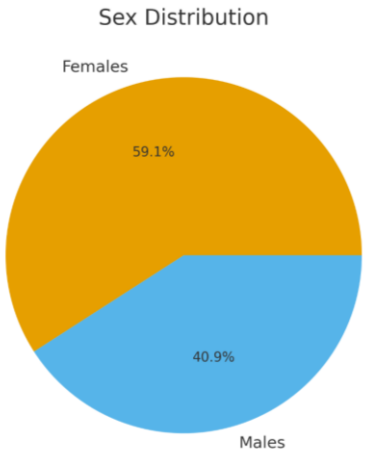
Of the 94 patients admitted to intensive care after cardiac surgery, 88 were included. The mean age was 48 years (range 24–81 years);

Figure 1. Age distribution of the study population.



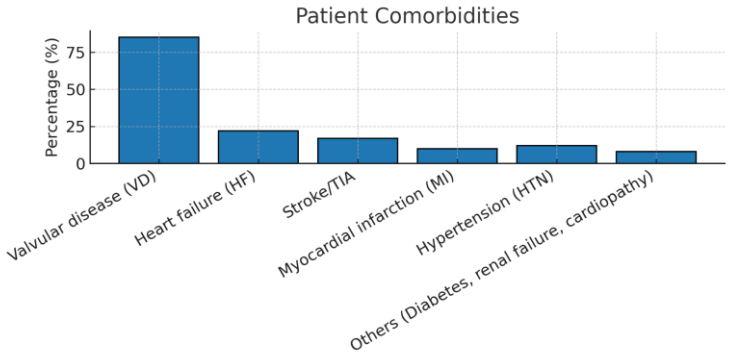
with a predominance of females (59.1%);

Figure 2. Sex distribution of the study population.



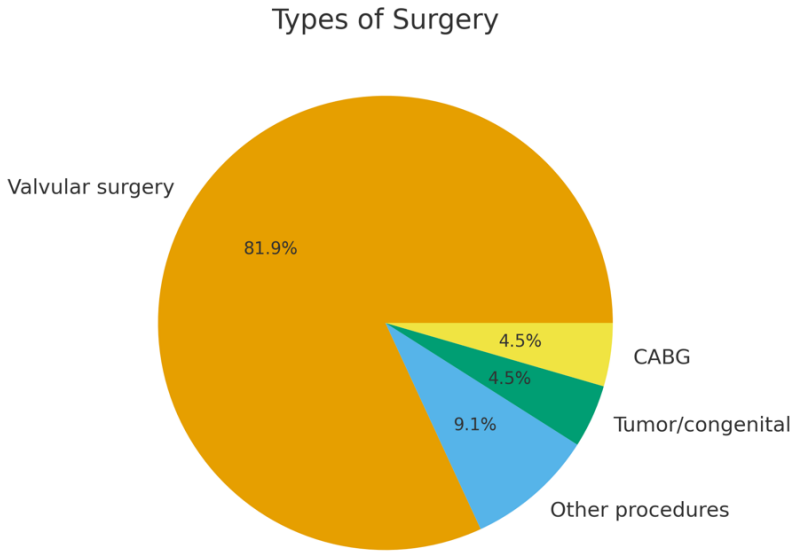
Valvular heart disease was the most common comorbidity (87.5%)

Figure 3. Patient comorbidities.



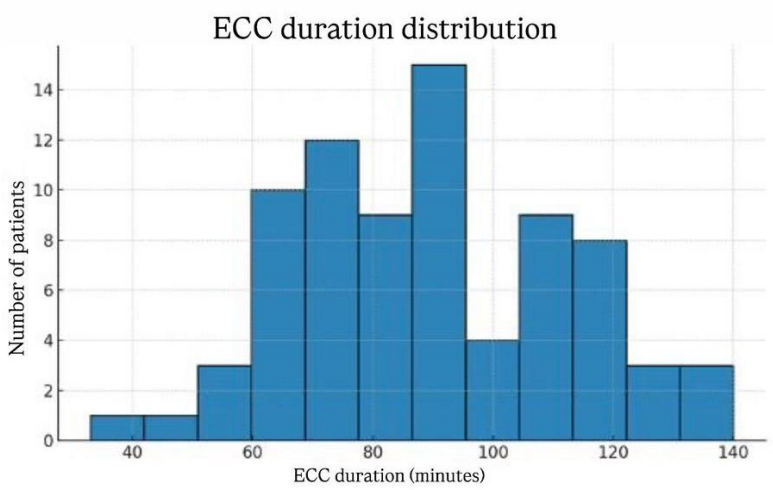
and valve surgery accounted for 81.8% of procedures

Figure 4. Types of cardiac surgery performed.



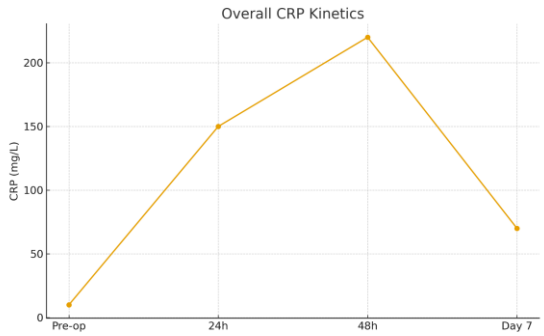
The duration of CPB varied between 33 and 140 minutes. 84.6% of patients had a CPB duration of between 60 and 120 minutes;

Figure 5. Cardiopulmonary bypass (CPB) duration distribution.



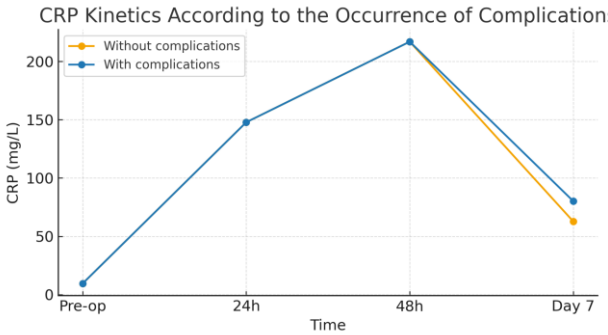
CRP increased from 9.6 mg/L preoperatively to 147.8 mg/L at 24 hours, peaked at 216.9 mg/L at 48 hours, and then decreased to 71.4 mg/L at 7 days;

Figure 6. Overall postoperative CRP kinetics



Postoperative complications were observed in 55.7% of patients, dominated by inflammatory complications (42%) and haemodynamic complications (27.3%), followed by haemorrhagic complications (14.8%), infectious complications (9.1%), neurological complications (9.1%) and thromboembolic complications (1.1%) .

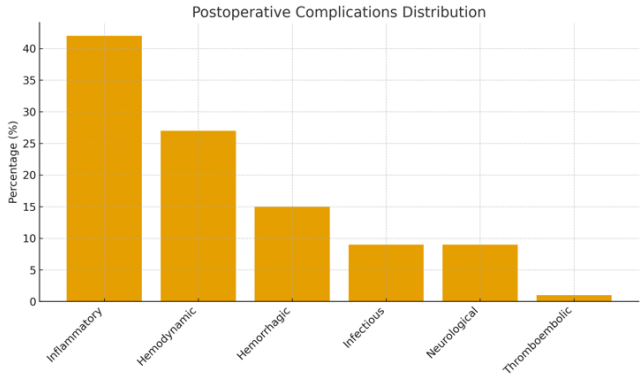
Figure 7. CRP kinetics according to the occurrence of complications.



Univariate analysis identified male gender ($p = 0.031$) and length of stay in intensive care ($p = 0.021$) as factors associated with complications, while the duration of CPB was not significantly related to their occurrence ($p = 0.302$). CRP values did not differ preoperatively or in the early stages, but remained

significantly higher on day 7 in patients with complications (80.2 vs 62.8 mg/L; p ≈ 0.03); Figure 8. Two deaths (2.3%) were recorded.

Figure 8. Postoperative complications distribution.



Discussion:

The inflammatory response induced by extracorporeal circulation (ECC) is a major factor in the post-operative pathophysiology of cardiac surgery. CRP, synthesised by the liver under the influence of IL-6, is one of the most widely studied biomarkers in this context. Several studies have shown that CRP accurately reflects the extent of postoperative immune activation, including complement activation, cytokine release and ischaemia-reperfusion mechanisms [1–3]. This kinetics is consistently characterised by an increase in the first 24 hours, a peak between 48 and 72 hours, and then a gradual decrease when the clinical course is favourable [4,5].

Regarding the reliability of CRP, studies converge on the idea that it is a sensitive but non-specific marker. WH Thomas et al. showed that CRP increases systematically after CPB, regardless of the presence of infection, highlighting its lack of specificity in the early phase [6]. In a recent meta-analysis, Larmann et al. confirmed that CRP values measured in the first 48 hours do not allow sterile inflammation to be differentiated from actual infection [7]. However, several studies show that late CRP, particularly after day 5, has real prognostic value: work by Kertai et al. [8], Brakenridge et al. [9] and Yamashita et al. [10] show that persistent high CRP is associated with the occurrence of major complications, a longer stay in intensive care and increased morbidity.

In cardiac surgery, CRP is of particular interest because it incorporates several inflammatory components characteristic of CPB: complement activation, tissue trauma, immune response to the extracorporeal circuit, endotoxemia, and myocardial and pulmonary ischaemia-reperfusion phenomena. Paparella et al. [11] showed that CRP kinetics closely reflect the intensity of postoperative SIRS. Furthermore, CRP remains widely available, inexpensive and reproducible, unlike other more specific biomarkers such as procalcitonin (PCT) or interleukin-6, whose use may be limited by availability or cost [3,12].

Comparison of our results with the literature confirms several points. First, the kinetics observed—early elevation, peak at H48, incomplete decline at D7—are fully consistent with the descriptions by Santonocito [4], Tomic [5] and Larmann [7]. Secondly, as in the series by Brakenridge [9] and Yamashita [10], only late CRP values (D7) were significantly associated with complications in our cohort, reinforcing the idea that late CRP is a superior prognostic marker to early values. Our study also identifies male gender as a risk factor, an association reported in some series but still insufficiently explored [13]. Finally, the

high frequency of inflammatory and haemodynamic complications is consistent with historical observations of the post-CPB inflammatory response described by Paparella [11] and Groom et al. [14].
Thus, the entire body of literature supports the use of CRP as a dynamic prognostic marker in cardiac surgery: while early values simply reflect the stress of surgery, late values — particularly on days 5–7 — make it possible to identify patients at risk of unfavourable outcomes, prolonged inflammatory complications or post-operative infection. A strategy incorporating serial CRP monitoring could therefore help to improve the early detection of complications and refine postoperative risk stratification.
Our study has certain limitations, notably a small sample size and a single-centre design, reducing statistical power, as highlighted by Larmann et al. [15]. The absence of complementary biomarkers, particularly procalcitonin, limits comparison with modern multimodal approaches; however, procalcitonin has been shown to have better specificity for postoperative bacterial infections, as described by Luyt et al. [16] and Schuetz et al. [17]. Despite this, our rigorous sequential monitoring of CRP at four time points is an original feature, allowing a dynamic description of its kinetics. The homogeneity of our cohort, dominated by valve surgery, reinforces the consistency of the data.
The persistence of elevated CRP on day 7, already identified as a prognostic marker in studies by Yamashita et al. [18] and Brakenridge et al. [19], is also evident in our series. These results encourage the joint integration of CRP and procalcitonin into multimodal monitoring to improve the early detection of postoperative complications.

Références :

1. Levy JH, Tanaka KA. Inflammatory response to cardiopulmonary bypass. Anesthesiology. 2020;133:1238–1245.
2. Laffey JG, Boylan JF, Cheng DC. The systemic inflammatory response to cardiac surgery. Anesthesiology. 2002;97:215–252.
3. Luyt CE, et al. Biomarkers after cardiac surgery: CRP vs PCT. Intensive Care Med. 2023;49:112–120.
4. Santonocito C, et al. Postoperative CRP kinetics after cardiac surgery. J Cardiothorac Surg. 2021;16:45.
5. Tomic V, et al. CRP dynamics after CPB. Eur J Cardiothorac Surg. 2020;58:540–546.
6. Thomas WH, et al. Early CRP response after cardiac surgery. Ann Thorac Surg. 2019;108:1631–1639.
7. Larmann J, et al. CRP as prognostic marker after cardiac surgery: meta-analysis. Crit Care. 2021;25:124.
8. Kertai MD, et al. Predictive biomarkers after cardiac surgery. Anesth Analg. 2020;130:1234–1244.
9. Brakenridge SC, et al. Persistent inflammation and poor outcomes. Crit Care Med. 2021;49:e447–e455.
10. Yamashita K, et al. CRP as predictor of complications after cardiac surgery. J Thorac Cardiovasc Surg. 2024;167:450–458.
11. Paparella D, et al. Inflammatory response and CPB. Ann Thorac Surg. 2022;114:123–131.
12. Schuetz P, et al. Procalcitonin vs CRP in postoperative infection. Clin Chem Lab Med. 2020;58:1025–1035.
13. Kieser TM, et al. Gender differences in outcomes after cardiac surgery. Circulation. 2019;139:2588–2596.
14. Groom RC, et al. SIRS after CPB: mechanisms and clinical implications. J Extra Corpor Technol. 2020;52:34–46.

15. Larmann J, et al. CRP AS PROGNOSTIC MARKER AFTER CARDIAC SURGERY. Crit Care. 2021;25:124.
16. Luyt CE, et al. BIOMARKERS AFTER CARDIAC SURGERY: CRP VS PCT. Intensive Care Med. 2023;49:112–120.
17. Schuetz P, et al. PROCALCITONIN VS CRP IN POSTOPERATIVE INFECTION. Clin Chem Lab Med. 2020;58:1025–1035.
18. Yamashita K, et al. CRP AS PREDICTOR OF POSTOPERATIVE COMPLICATIONS. J Thorac Cardiovasc Surg. 2024;167:450–458.
19. Brakenridge SC, et al. PERSISTENT INFLAMMATION AFTER CARDIAC SURGERY. Crit Care Med. 2021;49:e447–e455.