

Original article

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**ANALYSIS OF THE IMMUNOLOGICAL RESPONSE DURING EXTRACORPOREAL
CIRCULATION IN PATIENTS UNDERGOING MYOCARDIAL REVASCULARIZATION**

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Extracorporeal circulation (ECC) used during coronary artery bypass grafting (CABG) may induce significant systemic inflammatory and immunological responses, contributing to postoperative complications. The aim of this study was to evaluate perioperative immunological changes in patients undergoing myocardial revascularization with and without ECC, with particular emphasis on inflammatory biomarkers, cytokine profiles, and the development of systemic inflammatory response syndrome (SIRS). This prospective study included 100 patients who underwent single-, double-, or triple-vessel myocardial revascularization at the Clinic for Cardiac Surgery, University Clinical Center Niš, between January 2020 and January 2021. Patients were divided into two groups: ECC group (n=51) and off-pump group (n=49). Preoperative and postoperative (8 hours after surgery) analyses included complete blood count parameters, C-reactive protein (CRP), presepsin, and serum cytokine concentrations (TNF- α , IL-1 β , IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17, and IFN- γ). Patients undergoing surgery with ECC demonstrated significantly higher postoperative CRP ($p < 0.001$) and presepsin concentrations ($p < 0.05$) compared with the off-pump group. Presepsin values above 600 pg/mL were significantly more frequent in ECC patients ($p < 0.01$), while four patients in the ECC group exhibited concentrations above 1000 pg/mL, indicating increased risk of sepsis. SIRS was more frequently observed in the ECC group (17.64%) compared with the off-pump group (4.08%). Furthermore, ECC patients exhibited significantly higher preoperative TNF- α and postoperative IL-10 concentrations ($p < 0.05$). Extracorporeal circulation during myocardial revascularization is associated with enhanced systemic inflammatory activation and more pronounced immunological alterations. Presepsin may represent a valuable early biomarker for identifying patients at increased risk of postoperative inflammatory complications and sepsis.

Keywords: extracorporeal circulation, myocardial revascularization, SIRS, presepsin, cytokines

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**ANALIZA IMUNOLOŠKOG ODGOVORA TOKOM EKSTRAKORPORALNE CIRKULACIJE KOD
BOLESNIKA PODVRGNUTIH HIRURŠKOJ REVASKULARIZACIJI MIOKARDA**

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Ekstrakorporalna cirkulacija (ECC), koja se koristi tokom aortokoronarnog bypassa (CABG), može izazvati značajan sistemski inflamatorni i imunološki odgovor, doprinoseći razvoju postoperativnih komplikacija. Cilj ovog istraživanja bio je da se procene perioperativne imunološke promene kod bolesnika podvrgnutih hirurškoj revaskularizaciji miokarda sa i bez primene ekstrakorporalne cirkulacije, sa posebnim osvrtom na inflamatorne biomarkere, citokinske profile i razvoj sistemskog inflamatornog odgovora (SIRS). Ova prospektivna studija obuhvatila je 100 bolesnika

koji su podvrgnuti jednostrukoj, dvostrukoj ili trostrukoj hirurškoj revaskularizaciji miokarda na Klinici za kardiohirurgiju Univerzitetskog kliničkog centra Niš, u periodu od januara 2020. do januara 2021. godine. Bolesnici su bili podeljeni u dve grupe: ECC grupu (n=51) i grupa bez ECC (n=49). Preoperativno i postoperativno (8 sati nakon operacije) analizirani su parametri kompletne krvne slike, C-reaktivni protein (CRP), presepsin i serumske koncentracije citokina (TNF- α , IL-1 β , IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17 i IFN- γ). Kod bolesnika operisanih uz primenu ekstrakorporalne cirkulacije zabeležene su značajno više postoperativne koncentracije CRP-a ($p < 0,001$) i presepsina ($p < 0,05$) u poređenju sa grupom bez ECC. Vrednosti presepsina iznad 600 pg/mL bile su značajno češće u ECC grupi ($p < 0,01$), dok su četiri bolesnika u ovoj grupi imala koncentracije veće od 1000 pg/mL, što je ukazivalo na povećan rizik od sepse. SIRS je bio češće prisutan u ECC grupi (17,64%) u odnosu na grupu bez ECC (4,08%). Pored toga, bolesnici u ECC grupi imali su značajno više preoperativne koncentracije TNF- α i postoperativne koncentracije IL-10 ($p < 0,05$). Ekstrakorporalna cirkulacija tokom hirurške revaskularizacije miokarda povezana je sa izraženijom sistemskom inflamatornom aktivacijom i značajnijim imunološkim promenama. Presepsin može predstavljati značajan rani biomarker za identifikaciju bolesnika sa povećanim rizikom od postoperativnih inflamatornih komplikacija i sepse.

Ključne reči: ekstrakorporalna cirkulacija, revaskularizacija miokarda, SIRS, presepsin, citokini

Introduction

Surgical myocardial revascularization, most commonly performed as coronary artery bypass grafting (CABG), remains one of the most important therapeutic strategies for patients with advanced coronary artery disease. Despite significant advances in surgical techniques, perioperative management, and myocardial protection, CABG performed with extracorporeal circulation (cardiopulmonary bypass, CPB) continues to represent a highly complex procedure associated with considerable immunological and inflammatory alterations. In elective procedures, perioperative mortality rates are generally low; however, postoperative complications related to systemic inflammation remain a major clinical concern (1).

The use of extracorporeal circulation enables temporary replacement of cardiac and pulmonary function, thereby ensuring adequate tissue oxygenation, systemic perfusion, and thermoregulation during surgery. Nevertheless, blood contact with nonphysiological artificial surfaces within the extracorporeal circuit, together with ischemia–reperfusion injury, mechanical shear stress, endotoxemia, and operative trauma, may induce profound activation of the innate and adaptive immune systems (2). These mechanisms contribute to endothelial dysfunction, complement activation, leukocyte and platelet activation, oxidative stress, and the release of numerous inflammatory and vasoactive mediators into the systemic circulation (3).

One of the most important complications associated with extracorporeal circulation is the development of systemic inflammatory response syndrome (SIRS), which may significantly contribute to postoperative organ dysfunction, prolonged intensive care unit stay, and increased morbidity and mortality (4). The severity of the inflammatory response depends on multiple factors, including patient-related characteristics (age, sex, comorbidities, and preexisting inflammatory status), duration of cardiopulmonary bypass and aortic cross-clamping, surgical technique, anesthetic management, and the type of biomaterials used in the extracorporeal circuit (5).

Cytokines are considered central mediators in the pathogenesis of postoperative inflammatory responses during cardiac surgery. Among proinflammatory cytokines, tumor necrosis factor- α (TNF- α), interleukin-1 beta (IL-1 β), and particularly interleukin-6 (IL-6) play a pivotal role in the initiation and amplification of systemic inflammation. IL-6 is of special importance because it stimulates hepatic synthesis of acute-phase reactants, including C-reactive protein (CRP), which is widely used as a marker of postoperative inflammatory activity (6). In

parallel, anti-inflammatory cytokines such as interleukin-10 (IL-10) are activated as compensatory mechanisms aimed at limiting excessive immune activation.

Recent studies have additionally emphasized the importance of immune response polarization during and after extracorporeal circulation. Changes in cytokine profiles associated with Th1-mediated immunity (IL-12p70 and interferon-gamma [IFN- γ]), Th2-mediated responses (IL-4), Th17-associated pathways (IL-17), and regulatory T-cell activity (IL-10) may substantially influence postoperative recovery and susceptibility to complications, including SIRS and sepsis (7). However, despite extensive investigation, the precise immunological mechanisms induced by extracorporeal circulation and their clinical implications remain insufficiently clarified.

In addition to conventional inflammatory biomarkers, soluble CD14 subtype (presepsin) has recently emerged as a promising early biomarker of systemic inflammation, bacterial infection, and sepsis. Elevated presepsin concentrations have been associated with increased inflammatory activation and adverse postoperative outcomes in critically ill and cardiac surgical patients (8).

The aim of this study was to evaluate the immunological response in patients undergoing myocardial revascularization with and without extracorporeal circulation by analyzing perioperative inflammatory biomarkers and cytokine profiles. In addition, the study aimed to determine the impact of extracorporeal circulation on systemic inflammatory response syndrome (SIRS) and postoperative complications.

Materials and Methods

Study Design and Patient Population

This prospective study included 100 patients who underwent single-, double-, or triple-vessel surgical myocardial revascularization at the Clinic for Cardiac Surgery, University Clinical Center Niš, between January 15, 2020, and January 15, 2021. The study population consisted of 22 female patients (22.0%) and 78 male patients (78.0%). The mean age of the participants was 64.63 ± 7.48 years, ranging from 43 to 80 years.

Study Groups and Surgical Procedure

Following preoperative preparation, all patients underwent surgery according to standard cardiac surgical protocols. The patients were divided into two groups:

- 1) the extracorporeal circulation group (ECC group), consisting of 51 patients who underwent surgery with the use of an extracorporeal circulation system during the procedure; and
- 2) the off-pump group (off-ECC group), consisting of 49 patients in whom extracorporeal circulation was not used intraoperatively.

Hematological and Inflammatory Biomarker Analysis

Preoperatively and 8 hours after surgery, the following parameters were determined in all study participants:

Complete blood count parameters, including erythrocyte count (RBC), hemoglobin concentration (Hgb), hematocrit (Hct), leukocyte count (WBC), platelet count (Plt), and C-reactive protein (CRP; ng/mL), were measured using the Microsemi CRP LC-667G hematology analyzer (Horiba Medical, France). Analyses were performed from 4 mL of whole blood collected in EDTA-anticoagulated tubes.

Determination of Presepsin Concentration

Soluble CD14 subtype (sCD14), known as presepsin (pg/mL), was determined using an immunofluorescence assay with dedicated reagent cartridges on the PATHFAST analyzer (Mitsubishi Chemical Medience Corporation, Japan). Measurements were performed from 4 mL of whole blood collected in EDTA-anticoagulated tubes. Presepsin concentrations above 600 pg/mL were considered indicative of a pre-septic state and were used as the cut-off value for differentiating systemic inflammatory response syndrome (SIRS) from sepsis.

Cytokine Analysis

Serum concentrations of cytokines, including TNF- α , IL-1 β , IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17, and IFN- γ (pg/mL), were determined using the enzyme-linked immunosorbent assay (ELISA) technique. Serum samples were obtained by centrifugation of 4 mL of peripheral venous blood collected in tubes without anticoagulants. Cytokine concentrations were determined using the Magnetic Luminex® Performance Assay. Standard cytokine detection panels manufactured by Bio-Techne R&D Systems were used, while sample acquisition and analysis were performed on the FlexMap 3D flow analyzer (Invitrogen, Thermo Fisher Scientific) in accordance with the manufacturer's instructions.

Monitoring of Postoperative Complications

Early postoperative complications, including systemic inflammatory response syndrome (SIRS), sepsis, and septic shock, were prospectively monitored throughout the study period. According to the criteria of the American Society of Anesthesiologists, the diagnosis of SIRS was established when two or more of the following criteria were present: body temperature ≥ 38 °C or ≤ 36 °C, heart rate ≥ 90 beats/min, respiratory rate ≥ 20 breaths/min or partial pressure of carbon dioxide ($p\text{CO}_2$) ≤ 32 mmHg, and leukocyte count $\geq 12,000/\text{mm}^3$ or $\leq 4,000/\text{mm}^3$.

Sepsis was defined as the presence of SIRS associated with a confirmed infection, whereas septic shock was defined as sepsis accompanied by persistent hypotension and clinically significant tissue hypoperfusion.

Statistical Analysis

Data were presented as mean \pm standard deviation (SD), minimum and maximum values, and as absolute and relative frequencies. The normality of continuous variable distribution was assessed using the Kolmogorov–Smirnov test. For variables with normal distribution, comparisons between preoperative and postoperative values were performed using analysis of variance (ANOVA), whereas the Friedman test was applied for variables that did not follow a normal distribution. Comparisons between the two study groups were performed using the independent-samples t-test for normally distributed variables and the Mann–Whitney U test for variables with non-normal distribution. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics software, version 26.0.0.

Results

Distribution of Surgical Myocardial Revascularization Procedures

This prospective study included 100 patients who underwent single-, double-, or triple-vessel surgical myocardial revascularization at the Clinic for Cardiac Surgery, University Clinical Center Niš, between January 15, 2020, and January 15, 2021.

Figure 1 presents the distribution of different types of surgical myocardial revascularization, including single-, double-, and triple-vessel coronary artery bypass grafting (CABG I, CABG II, and CABG III). The highest proportion of patients (43.0%) underwent single-vessel coronary artery bypass grafting (CABG I).

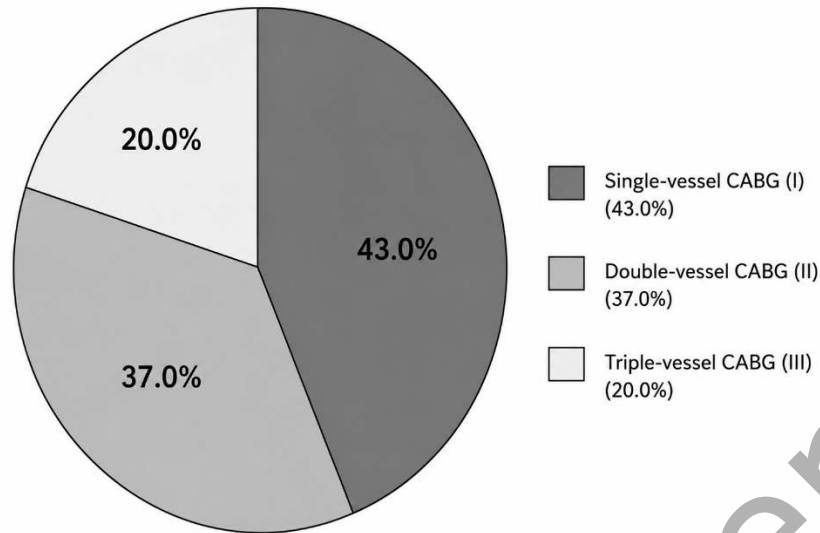


Figure 1. Distribution of patients according to the type of aorto-coronary bypass grafting (single-, double-, and triple-vessel CABG) in the studied population

Distribution of Patients According to the Use of Extracorporeal Circulation

The patients were further divided into two groups according to the use of extracorporeal circulation (ECC) during surgery. Extracorporeal circulation was applied in 51 patients (51.0%), whereas 49 patients underwent off-pump surgery without the use of extracorporeal circulation.

Comparison of Preoperative Laboratory Parameters Between the Study Groups

Table 1 shows the intergroup differences in preoperative laboratory parameters of the examined patients (RBC, Hgb, Hct, WBC, Plt, CRP, and PSEP). No statistically significant differences were observed in the levels of these parameters between the ECC and off-ECC groups. All patients in both groups had normal preoperative presepsin values (≤ 600 pg/mL).

Table 1. Preoperative hematological and immunological characteristics of patients undergoing surgical treatment with and without extracorporeal circulation (ECC)

| Parameter | ECC (N=51) | off-ECC (N=49) | P= |
|------------------------------|---------------------|---------------------|-------|
| RBC ($1 \times 10^{12}/L$) | 4,45 ± 0,46 | 4,49 ± 0,49 | 0,707 |
| HGB (g/L) | 136,80 ± 11,68 | 138,80 ± 10,25 | 0,368 |
| HCT (%) | 38,78 ± 4,48 | 39,58 ± 3,80 | 0,337 |
| WBC ($1 \times 10^9/L$) | 7,34 ± 1,51 | 6,95 ± 1,13 | 0,156 |
| PLT ($1 \times 10^9/L$) | 241,72 ± 70,05 | 232,51 ± 56,70 | 0,472 |
| CRP (ng/mL) | 9,0 (4,0-14,0) | 10,0 (5,0-13,0) | 0,801 |
| PSEP (pg/mL) | 246,0 (167,0-366,0) | 235,0 (166,0-337,0) | 0,591 |
| PSEP (≥ 600 pg/mL) | 0 (0,0%) | 0 (0,0%) | / |

RBC - erythrocyte count; HGB - hemoglobin; HCT - hematocrit; WBC - leukocyte count; PLT - platelet count; CRP - C-reactive protein; PSEP - presepsin

Postoperative Changes in Inflammatory Biomarkers

During surgical myocardial revascularization, patients in whom extracorporeal circulation was applied exhibited significantly higher postoperative CRP concentrations ($p < 0.001$), as well as higher presepsin concentrations ($p < 0.05$), compared with patients operated on without the use of extracorporeal circulation (Table 2). In addition, a significantly higher proportion of patients in the extracorporeal circulation group had presepsin values above the established cutoff level of 600 pg/mL ($p < 0.01$).

Table 2. Postoperative hematological and immunological characteristics of patients undergoing surgical treatment with and without extracorporeal circulation (ECC)

| Parameter | ECC (N=51) | off-ECC (N=49) | P= |
|------------------------------|---------------------|---------------------|--------------|
| RBC ($1 \times 10^{12}/L$) | 3.9 (3.6-4.3) | 3.7 (3.5-4.0) | 0.060 |
| HGB (g/L) | 115.0 (110.0-119.0) | 114.0 (108.5-116.0) | 0.090 |
| WBC ($1 \times 10^9/L$) | 10.76 \pm 3.69 | 9.34 \pm 3.56 | 0.053 |
| PLT ($1 \times 10^9/L$) | 154.67 \pm 59.75 | 141.33 \pm 53.00 | 0.241 |
| CRP (ng/mL) | 110.0 (90.0-132.0) | 92.0 (76.5-104.5) | 0.001 |
| PSEP (pg/mL) | 419.0 (315.0-625.0) | 343.0 (300.0-419.5) | 0.011 |
| PSEP (≥ 600 pg/mL) | 14 (27.5%) | 2 (4.1%) | 0.002 |

RBC – erythrocyte count; HGB – hemoglobin; HCT – hematocrit; WBC – leukocyte count; PLT – platelet count; CRP – C-reactive protein; PSEP – presepsin

Presepsin Levels and Incidence of Systemic Inflammatory Response Syndrome

Overall, 4 of 51 patients (7.84%) in the extracorporeal circulation (ECC) group had postoperative presepsin values exceeding 1000 pg/mL, which, according to established clinical criteria, indicated a high risk for the development of systemic bacterial infection and sepsis. No such cases were recorded in the off-ECC group.

Furthermore, in the extracorporeal circulation group, 17.64% of patients (9/51) fulfilled the clinical criteria for systemic inflammatory response syndrome (SIRS) while simultaneously exhibiting elevated presepsin concentrations above 600 pg/mL. In contrast, only 2 of 49 patients (4.08%) in the off-ECC group met the clinical and laboratory criteria for SIRS.

Comparison of Cytokine Profiles Between the Study Groups

Patients who were not subjected to extracorporeal circulation exhibited significantly lower preoperative TNF- α levels ($p < 0.05$), as well as lower postoperative IL-10 concentrations ($p < 0.05$), compared with patients in whom extracorporeal circulation was applied (Table 3).

Table 3. Serum cytokine levels before and after the intervention

| | Cytokine | ECC | off-ECC | P= |
|-------------------------|----------------------|---------------------|---------------------|--------------|
| Before operation | TNF α (pg/ml) | 261.39 \pm 53.12 | 239.03 \pm 44.23 | 0.025 |
| | IL-2 (pg/ml) | 47.5 (43.0-49.6) | 45.3 (40.6-47.5) | 0.068 |
| | IL-1 β (pg/ml) | 17.2 (15.6-20.1) | 18.7 (13.7-22.6) | 0.336 |
| | IL-6 (pg/ml) | 79.9 (70.0-92.3) | 84.8 (54.7-109.0) | 0.986 |
| | IL-10 (pg/ml) | 32.26 \pm 18.43 | 36.69 \pm 19.19 | 0.252 |
| After operation | TNF α (pg/ml) | 261.2 (232.8-315.5) | 246.7 (221.3-271.5) | 0.056 |
| | IL-2 (pg/ml) | 65.8 (41.7-81.7) | 62.6 (47.5-81.5) | 0.656 |
| | IL-1 β (pg/ml) | 34.2 (25.8-40.1) | 30.9 (22.6-39.1) | 0.598 |
| | IL-6 (pg/ml) | 905.20 \pm 361.19 | 857.30 \pm 399.69 | 0.531 |
| | IL-10 (pg/ml) | 114.9 (93.9-151.2) | 85.9 (58.6-146.3) | 0.012 |

Discussion

The present prospective study evaluated perioperative immunological responses in patients undergoing surgical myocardial revascularization with and without extracorporeal circulation (ECC). The obtained results demonstrated that the use of ECC was associated with significantly more pronounced postoperative inflammatory activation, reflected by elevated CRP and presepsin concentrations, a higher incidence of presepsin values above the clinically relevant threshold of 600 pg/mL, and a greater frequency of systemic inflammatory response syndrome (SIRS). In addition, differences in cytokine profiles between the ECC and off-ECC groups further confirmed the important role of extracorporeal circulation in modulating perioperative immune responses.

Cardiac surgery performed with cardiopulmonary bypass is well recognized as a potent trigger of systemic inflammation. Exposure of blood to artificial surfaces of the extracorporeal circuit, ischemia–reperfusion injury, operative trauma, endotoxemia, hypothermia, and mechanical shear stress collectively activate multiple inflammatory pathways involving leukocytes, platelets, endothelial cells, complement proteins, and cytokine cascades (9,10). The inflammatory response observed in our ECC group is therefore consistent with the currently accepted pathophysiological concept of extracorporeal circulation–induced immune activation.

One of the most important findings of this study was the significantly higher postoperative CRP concentration in patients undergoing ECC-assisted myocardial revascularization. CRP is an acute-phase reactant synthesized in hepatocytes predominantly under the influence of IL-6 stimulation and represents one of the most widely used biomarkers of systemic inflammatory activity following cardiac surgery (11). Previous investigations have demonstrated that cardiopulmonary bypass significantly enhances postoperative CRP production compared with off-pump procedures, which is in agreement with our results (12,13). Elevated postoperative CRP concentrations have additionally been associated with prolonged intensive care unit stay, postoperative atrial fibrillation, and increased risk of organ dysfunction (14).

The role of presepsin as an early biomarker of inflammatory activation and sepsis has attracted increasing attention in recent years. In the present study, postoperative presepsin concentrations were significantly higher in the ECC group, while presepsin values above 600 pg/mL were substantially more frequent in patients subjected to extracorporeal circulation. Importantly, four patients in the ECC group exhibited presepsin concentrations exceeding 1000 pg/mL, suggesting a markedly increased risk of systemic bacterial infection and sepsis. No such findings were observed in the off-ECC group. These results support the hypothesis that extracorporeal circulation induces a more profound activation of innate immune mechanisms and may contribute to postoperative immune dysregulation.

Presepsin is generated through cleavage of membrane-bound CD14 receptors on activated monocytes and macrophages following exposure to bacterial components and inflammatory stimuli (15). Several recent studies have suggested that presepsin may represent a sensitive early biomarker capable of differentiating postoperative SIRS from developing sepsis in critically ill and cardiac surgical patients (16,17). Memiş et al. (2016) demonstrated that postoperative presepsin concentrations significantly increase after cardiopulmonary bypass and correlate with the severity of systemic inflammatory activation (18). Similarly, Masson et al. (2014) reported that elevated presepsin values were associated with unfavorable postoperative outcomes and increased mortality risk in intensive care patients (19). Our findings are in accordance with these observations and further support the clinical utility of presepsin in perioperative monitoring after myocardial revascularization.

Another important observation of the present study was the significantly higher frequency of SIRS among patients undergoing surgery with extracorporeal circulation. Nearly one-fifth of ECC patients fulfilled clinical SIRS criteria while simultaneously exhibiting elevated presepsin

concentrations above 600 pg/mL, whereas this phenomenon was considerably less frequent in the off-ECC group. These findings emphasize the strong relationship between cardiopulmonary bypass and postoperative systemic inflammatory activation. Previous studies have shown that excessive inflammatory response during extracorporeal circulation contributes to endothelial dysfunction, capillary leakage, coagulation abnormalities, and postoperative organ injury (20,21). Furthermore, severe inflammatory activation may predispose susceptible patients to secondary infectious complications and sepsis due to subsequent immune exhaustion and immunoparalysis (22).

The cytokine profile observed in this study additionally supports the existence of significant perioperative immune modulation during extracorporeal circulation. Patients in the off-ECC group exhibited significantly lower preoperative TNF- α levels and lower postoperative IL-10 concentrations compared with the ECC group. TNF- α is among the earliest proinflammatory cytokines released during systemic immune activation and plays a crucial role in leukocyte recruitment, endothelial activation, and amplification of cytokine cascades (23). Elevated TNF- α concentrations during cardiopulmonary bypass have been repeatedly associated with increased postoperative inflammatory complications and myocardial dysfunction (24).

On the other hand, IL-10 is considered one of the most important anti-inflammatory cytokines involved in limiting excessive immune activation. Increased IL-10 concentrations in the ECC group may reflect a compensatory anti-inflammatory response syndrome (CARS), which develops in parallel with systemic inflammation in an attempt to restore immunological homeostasis (25). However, excessive anti-inflammatory activation may also contribute to postoperative immunosuppression and increased susceptibility to infections (26). Therefore, the simultaneous activation of proinflammatory and anti-inflammatory pathways observed in our study confirms the complex biphasic nature of immune responses induced by extracorporeal circulation.

Our findings additionally support the growing body of evidence favoring off-pump myocardial revascularization as a potentially less inflammatory surgical strategy. Several previous studies have demonstrated that off-pump CABG is associated with reduced cytokine release, diminished complement activation, lower oxidative stress, and decreased postoperative inflammatory response compared with conventional on-pump surgery (27,28). Nevertheless, the

clinical superiority of off-pump procedures remains controversial, as long-term cardiovascular outcomes depend on multiple technical and patient-related factors (29).

This study has several limitations that should be acknowledged. First, the sample size was relatively limited, which may reduce the generalizability of the findings. Second, postoperative cytokine and biomarker measurements were performed only at a single postoperative time point (8 hours after surgery), whereas serial measurements could provide more detailed information regarding the dynamics of immune activation. Third, microbiological confirmation of infection was not available in all patients with elevated presepsin concentrations, limiting definitive differentiation between sterile inflammatory activation and early sepsis. Finally, the study was conducted at a single tertiary center, and multicenter investigations are needed to validate the obtained results.

Despite these limitations, the present study provides important clinical evidence regarding the immunological impact of extracorporeal circulation during myocardial revascularization. The results suggest that ECC significantly enhances systemic inflammatory activation and increases the incidence of postoperative SIRS and elevated presepsin concentrations. Monitoring of inflammatory biomarkers and cytokine profiles, particularly presepsin, may therefore contribute to earlier identification of patients at increased risk for postoperative inflammatory complications and sepsis. Future studies should focus on the development of individualized perioperative anti-inflammatory and immunomodulatory strategies aimed at reducing immune-mediated postoperative complications in cardiac surgical patients.

Conclusion

Extracorporeal circulation during surgical myocardial revascularization was associated with significantly more pronounced postoperative systemic inflammatory activation, reflected by elevated CRP and presepsin concentrations, a higher incidence of SIRS, and increased TNF- α and IL-10 levels. In contrast, myocardial revascularization performed without extracorporeal circulation was associated with a less pronounced inflammatory response, while presepsin may represent a valuable early biomarker for identifying patients at increased risk of postoperative inflammatory complications and sepsis.

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