Original Article

# Effect of perioperative immunonutrition on inflammatory and myocardial injury markers after myocardial revascularization surgery

*Efeito da imunonutrição perioperatória nos marcadores inflamatórios e de lesão miocárdica após cirurgia de revascularização do miocárdio*

DOI: 10.37111/braspenj.2026.41.1.20-en

Julia Souza Siqueira de Andrade[1]
Giovana Alves Carvalho[1]
Bruno Mahler Mioto[2]
Luiz Aparecido Bortolotto[2]

**ABSTRACT**
**Background:** Coronary artery bypass grafting is a complex surgical procedure often associated with a systemic inflammatory response, which may lead to postoperative complications. Perioperative immunonutrition has been investigated as a strategy to modulate inflammation. This study evaluated the effect of perioperative immunomodulatory supplementation on systemic inflammatory response, myocardial injury, and clinical outcomes in patients undergoing coronary artery bypass grafting. **Methods:** This was a non-randomized pilot clinical trial including patients undergoing coronary artery bypass grafting, in which a group receiving perioperative immunomodulatory supplementation (with omega-3 fatty acids, arginine, and nucleotides) was compared with a historical control group that did not receive supplementation. C-reactive protein levels, white blood cell count, and troponin were assessed, in addition to hospital and intensive care unit length of stay. **Results:** A total of 29 participants were included in the intervention group and 80 in the control group. Patients who received supplementation exhibited lower C-reactive protein levels (134.0: 83.2–178.5 vs. 94.0: 56.5–129.5) (p=0.03) on the fourth postoperative day compared with the historical control group, suggesting modulation of the inflammatory response. However, there was no significant impact on the other variables. **Conclusion:** The study suggests that perioperative immunomodulatory supplementation may be effective in reducing C-reactive protein levels. Nonetheless, the lack of impact on other biomarkers and clinical outcomes limits the generalizability of these findings. The results indicate that immunonutrition may represent a promising strategy to optimize recovery in cardiac patients, although further studies are needed to better evaluate its clinical impact.

**RESUMO**
**Introdução:** A cirurgia de revascularização do miocárdio é um procedimento complexo frequentemente associado a resposta inflamatória sistêmica, que pode levar a complicações pós-operatórias. A imunonutrição perioperatória tem sido investigada como uma estratégia para controlar a inflamação. Este estudo avaliou o efeito da suplementação imunomoduladora perioperatória sobre a resposta inflamatória sistêmica, injúria miocárdica e desfechos clínicos em pacientes submetidos à cirurgia de revascularização do miocárdio. **Método:** O estudo foi um ensaio clínico piloto não aleatorizado, incluindo pacientes submetidos à cirurgia de revascularização do miocárdio. Comparou-se um grupo que recebeu suplementação imunomoduladora perioperatória (com ácidos graxos ômega-3, arginina e nucleotídeos) com grupo controle histórico que não recebeu a suplementação. Foram avaliados níveis de proteína C-reativa, contagem de leucócitos e troponina, além de tempo de internação hospitalar e em unidade de terapia intensiva. **Resultados:** Foram incluídos 29 participantes no grupo intervenção e 80 no grupo controle. Os pacientes que receberam a suplementação apresentaram valores menores de proteína C-reativa (134,0: 83,2-178,5 vs. 94,0: 56,5-129,5) (p=0,03) no quarto dia pós-operatório em comparação com o grupo controle histórico, sugerindo modulação da resposta inflamatória. No entanto, não houve impacto significativo sobre as demais variáveis. **Conclusão:** O estudo sugere que a suplementação imunomoduladora perioperatória pode ser eficaz na redução da proteína C-reativa. No entanto, a falta de efeitos sobre outros biomarcadores e desfechos clínicos limita a generalização dos resultados. Os achados indicam que a imunonutrição pode ser uma estratégia com potencial para otimizar a recuperação de pacientes cardíacos, sendo necessário realizar mais estudos para melhor avaliar seu impacto.

**Keywords:**
Immunonutrition diet. Inflammation. Postoperative complications. Coronary artery bypass. C-reactive protein.

**Unitermos:**
Dieta de imunonutrição. Inflamação. Complicações pós-operatórias. Ponte de artéria coronária. Proteína C-reativa.

**Address for correspondence:**
Julia Souza Siqueira de Andrade
Rua José Alves Pereira, n° 387 – Vila Mury – Volta Redonda, Rio de Janeiro, Brasil – CEP: 27213-050
Email: julia.andrade1408@gmail.com

**Submission:**
December 1st, 2025

**Accepted for publication:**
January 5th, 2026

**Date of publication:**
January 26th, 2026

1. Nutricionista, especialista em Nutrição Clínica em Cardiologia pelo programa de Residência Multiprofissional do Instituto do Coração, São Paulo, SP, Brasil.
2. Médico, doutor em Cardiologia pela Faculdade de Medicina da Universidade de São Paulo, Instituto do Coração, São Paulo, SP, Brasil.

## INTRODUCTION

Coronary artery bypass grafting (CABG) is a widely performed procedure and represents the most common cardiac surgery in both Brazil and the United States in 2023[1,2]. However, despite advances in perioperative care, the morbidity rate associated with this procedure reaches up to 41%[3], which impacts patients' quality of life and the utilization of healthcare resources[4].

Surgical stress triggers an acute systemic inflammatory response through the activation of a cytokine cascade in the postoperative period. Cytokines play a crucial role in coordinating the inflammatory response at the site of injury. However, excessive cytokine production may lead to systemic complications and unfavorable postoperative outcomes[5].

These complications can be exacerbated by preexisting malnutrition, which increases the severity of organ dysfunction and worsens clinical and infectious outcomes, making nutritional support particularly important for this population[6]. Furthermore, pre-existing conditions such as obesity, diabetes mellitus, and smoking, common risk factors among patients undergoing CABG, are associated with increased rates of postoperative complications, including surgical site infections, atrial fibrillation, renal failure, reoperation, and others[3,4].

Among nutritional support strategies, the use of immunomodulatory supplementation is recommended in the perioperative period of major surgeries, particularly for high-risk patients[7]. The use of immunonutrition in such procedures has gained increasing attention due to its potential to modulate the inflammatory response and improve clinical outcomes, especially in oncologic surgeries, but also in abdominal, thoracic, and orthopedic procedures[8,9,10]. Nevertheless, its benefit in cardiac surgeries remains poorly investigated, and the guidelines for perioperative care in cardiac surgery recommended by the Enhanced Recovery After Surgery Society do not address this topic[11]. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines on clinical nutrition in surgery[12] recommend the administration of specific formulas enriched with arginine, omega-3 fatty acids, and ribonucleotides only for malnourished patients undergoing major cancer surgery. Conversely, an international consensus on cardiac surgery highlights the promising role of pharmaconutrition in mitigating the deleterious effects of the systemic inflammatory response[13].

Yu et al.[14] found that omega-3 supplementation improved immune function and reduced inflammatory marker levels in postoperative patients with gastrointestinal cancer. In a study involving patients undergoing cardiac surgery, supplementation with a combination of glutamine, β-hydroxy-β-methylbutyrate, and arginine was associated with a shorter hospital and intensive care unit (ICU) stay, as well as reduced myocardial injury, indicated by lower troponin levels, demonstrating the potential benefits of specific perioperative nutritional supplementation[15].

Supporting these findings, a recent meta-analysis[16] involving patients who underwent gastrointestinal cancer surgery demonstrated that preoperative oral nutritional supplementation reduced infectious complications and levels of inflammatory markers such as C-reactive protein (CRP) and leukocytes. These parameters are commonly used in clinical practice to assess the degree of inflammation, with elevated CRP levels indicating more severe systemic inflammation, which is associated with a higher risk of adverse outcomes and poorer disease progression[16]. Therefore, effective strategies to control these inflammatory markers warrant further investigation.

Given the high risk of postoperative complications and the potential protective effect of immunomodulatory supplementation, impacting patients' quality of life and healthcare resources, the present study aimed to evaluate the effect of perioperative immunomodulatory supplementation on systemic inflammatory response, myocardial injury, and clinical outcomes in patients with coronary artery disease undergoing CABG.

## METHODS

### Study design and participants

This study was designed as a non-randomized pilot clinical trial with historical controls. It was conducted at a single center, the Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (InCor-HCFMUSP), São Paulo, Brazil.

The intervention group included patients who underwent elective CABG between September and November 2024. Data from these patients were compared with those from a historical cohort of individuals who had undergone elective CABG during the corresponding months of 2023.

The sample size calculation was based on a broader research project, using the rate of surgical site infection as the primary variable. The elective CABG infection rate of 2023 at the institution (13.1%), obtained from the hospital's infection control center, was used as a reference. Since there were no prior studies involving immunomodulatory nutritional interventions in cardiac surgery, a multicenter clinical trial on colorectal resection was used as a reference[17]. Considering the same reduction in incidence (67%), a significance level (α) of 0.05, and a power of 80%

(1−β=0.80), a sample size of 90 individuals was estimated for the intervention group. The control group comprised 80 patients who underwent CABG between September and November 2023. However, due to logistical constraints, the intervention group included only 29 participants.

Inclusion criteria for the intervention group were: patients aged ≥18 years, eligible for elective CABG, and having signed the informed consent form. The control group included patients who underwent elective CABG by the same surgical team during the defined period, without immunomodulatory supplementation. Exclusion criteria, applied to both groups, were combined or emergency surgeries. In the intervention group, additional exclusions were allergy to any supplement component, inability to resume oral feeding in the postoperative period, or recent acute myocardial infarction.

Patients in the intervention group were invited to participate during the preoperative outpatient consultation or during hospitalization before surgery and were included by convenience sampling, following the surgical waiting list order. Each patient consumed two daily servings (400 ml total) of the liquid supplement IMPACT® (Nestlé Health Science, Switzerland), containing omega-3 fatty acids, arginine, and nucleotides. They took it for two days before surgery and three days postoperatively, resuming intake on the second postoperative day while hospitalized, according to the hospital's supplement distribution routine.

All participants were informed about the study procedures and signed the Informed Consent Form, in compliance with Resolution 466/12 of the National Health Council[18]. The study protocol was submitted to and approved by the institution's ethics committee (SDC: 5854/24/065; approval number: 7.025.215).

### Variables studied

Collected variables included sociodemographic, clinical, nutritional, biochemical, and surgical data. Nutritional assessment comprised body mass index (BMI) classification according to the World Health Organization[19] and the Pan American Health Organization[20], adjusted for age, as well as the Nutritional Risk Screening 2002 (NRS-2002) score[21]. To assess the inflammatory response, white blood cell count (WBC) and C-reactive protein (CRP) were measured, while myocardial injury was evaluated using high-sensitivity troponin I. Blood samples were collected at the following time points: preoperative baseline, immediately upon arrival in the postoperative ICU, and on postoperative days 1 through 4. Secondary outcomes included hospital length of stay, surgery duration, and ICU length of stay. All data for both groups were obtained from the electronic medical records, using only routine hospital biochemical test results.

### Statistical analysis

Quantitative variables were tested for normality and homogeneity of variance using the Shapiro-Wilk and Levene tests. For comparisons of quantitative variables between groups, Student's t-test or the Mann–Whitney U test was applied, as appropriate. Associations between categorical variables were analyzed using the Pearson's chi-square ($\chi^2$) test, Yates-corrected chi-square, or Fisher's exact test when applicable.

For significant results, Cramer's V and rank biserial correlation (rβ) were calculated to estimate effect size magnitude. A 95% confidence interval (CI) was adopted, and a p-value <0.05 was considered statistically significant for all analyses. Statistical analyses were performed using JAMOVI 2.2.5®[22] and RStudio 2024.04.2+764.

## RESULTS

The study sample consisted of a control group (n=80) and an intervention group (n=29). In both groups, there was a higher prevalence of male participants. The mean age in the control group was 62.9 years and in the intervention group, 64.0 years. When comparing sociodemographic variables, no significant differences were observed between groups regarding sex, age, race or ethnicity, and educational level (Table 1).

**Table 1 –** Sociodemographic variables in the control and intervention groups of patients undergoing coronary artery bypass grafting.

| Sociodemographic variables | Control (n=80) | Intervention (n=29) | Total (n=109) | Test statistic |
|---|---|---|---|---|
| **Sex, n (%)** | | | | $\chi^2_{(1)}$=0.92; p=0.34[1] |
| Female | 27 (33.8%) | 7 (24.1%) | 34 (31.2%) | |
| Male | 53 (66.2%) | 22 (75.9%) | 75 (68.8%) | |
| **Age, mean (±SD)** | 62.9±8.4% | 64.0±7.6% | 63.2±8.2% | $t^{(107)}$=-0.64; p=0.52[2] |

**Continuation Table 1 –** Variáveis sociodemográficas discriminadas entre grupos controle e intervenção de pacientes submetidos à cirurgia de revascularização do miocárdio.

| Sociodemographic variables | Control (n=80) | Intervention (n=29) | Total (n=109) | Test statistic |
|---|---|---|---|---|
| **Race or ethnicity, n (%)** | | | | $\chi^2_{(3)}$=1.15; p=0.82[3] |
| White | 61 (76.2%) | 21 (72.4%) | 82 (75.2%) | |
| Mixed race | 13 (16.2%) | 6 (20.7%) | 19 (17.4%) | |
| Black | 4 (5.0%) | 2 (6.9%) | 6 (5.5%) | |
| Asian | 2 (2.5%) | 0 (-) | 2 (1.8%) | |
| **Educational level, n (%)** | | | | $\chi^2_{(4)}$=5.09; p=0.28[4] |
| Not reported | 8 (10.0%) | 1 (3.4%) | 9 (8.3%) | |
| No formal education | 1 (1.2%) | 1 (3.4%) | 2 (1.8%) | |
| Primary education | 46 (57.5%) | 14 (48.3%) | 60 (55.0%) | |
| Secondary education | 17 (21.2%) | 6 (20.7%) | 23 (21.1%) | |
| Higher education | 8 (10.0%) | 7 (24.1%) | 15 (13.8%) | |

n = sample size; [1] = Pearson's chi-square test; [2] = Student's t-test; [3] = Fisher's exact test; [4] = Pearson's chi-square test with continuity correction.

Analysis of anthropometric data showed that the preoperative BMI was similar between groups. Regarding nutritional risk, most participants were classified as not at nutritional risk in both groups, with no significant difference observed (Table 2).

Regarding surgical data and clinical outcomes, the preoperative hospital stay was significantly longer in the intervention group compared to the control group. No significant differences were found in the other variables (Table 3).

Analysis of CRP levels over time revealed no statistically significant differences between groups at the preoperative moment or during the initial postoperative days. However, a significant difference was observed on postoperative day 4, with higher median values in the control group compared with the intervention group (Table 4).

White blood cell count and troponin levels showed no statistically significant differences between groups at any follow-up point. The values for each group and the respective between-group comparisons are shown in Tables 5 and 6.

The trends of CRP, WBC count, and troponin levels over time for each group are presented in Figures 1, 2, and 3, respectively.

**Table 2 –** Anthropometric and nutritional status variables of patients undergoing coronary artery bypass grafting, by control and intervention groups.

| Anthropometric and nutritional data | Control (n=80) | Intervention (n=29) | Total (n=109) | Test statistic |
|---|---|---|---|---|
| **Preoperative BMI (kg/m²) - Md (IQR)** | 28.5 (25.2-31.4) | 27.5 (25.2-30.4) | 27.9 (25.2-31.0) | U=1017; p=0.33[2] |
| **BMI classification - n (%)** | | | | $\chi^2_{(1)}$=2.40; p=0.49[1] |
| Underweight | 7 (8.8%) | 4 (13.8%) | 11 (10.1%) | |
| Normal weight | 24 (30.0%) | 12 (41.4%) | 36 (33.0%) | |
| Overweight | 20 (25.0%) | 5 (17.2%) | 25 (22.9%) | |
| Obesity | 29 (36.2%) | 8 (27.6%) | 37 (33.9%) | |
| **NRS classification - n (%)** | | | | $\chi^2_{(1)}$=0.01; p=0.90[1] |
| No risk | 75 (93.8%) | 27 (93.1%) | 102 (93.6%) | |
| At risk | 5 (6.2%) | 2 (6.9%) | 7 (6.4%) | |

n = sample size; BMI = body mass index; NRS = Nutritional Risk Screening; [1] = Pearson's chi-square test; [2] = Mann–Whitney U test.

**Table 3 –** Surgical and clinical outcomes of patients undergoing coronary artery bypass grafting, by control and intervention groups.

| Variable | Control (n=80) | Intervention (n=29) | Total (n=109) | Test statistic |
|---|---|---|---|---|
| Surgery duration (hours) - Md (IQR) | 4.6 (4.0-5.5) | 4.4 (4.2-4.8) | 4.5 (4.0-5.3) | U=1038; p=0.40[1] |
| ICU stay (days) - Md (IQR) | 3.0 (2.1-4.0) | 3.1 (2.7-4.0) | 3.0 (2.1-4.0) | U=1033; p=0.38[1] |
| Total hospital stay (days) - Md (IQR) | 9.1 (7.9-13.0) | 10.0 (8.0-17.0) | 9.2 (7.9-14.1) | U=1006; p=0.29[1] |
| Preoperative stay (days) - Md (IQR) | 1.0 (0.8-1.2) | 1.0 (0.9-4.7) | 1.0 (0.8-1.7) | **U=886; p=0.03[1]** |
| Postoperative stay (days) - Md (IQR) | 8.1 (7.0-10.6) | 8.0 (7.0-15.1) | 8.0 (7.0-11.4) | U=1093; p=0.65[1] |

n = sample size; ICU = intensive care unit; [1] = Mann–Whitney U test.

**Table 4 –** C-reactive protein levels over time in patients undergoing coronary artery bypass grafting, by control and intervention groups.

| CRP over time | Control (n=80) | Intervention (n=29) | Test statistic |
|---|---|---|---|
| **Preoperative CRP - Md (IQR)** | 2.4 (1.0-6.9) | 1.7 (1.1-5.6) | U=318; p=0.861 |
| Missing data | 39 | 13 | |
| **Postoperative day 0 CRP - Md (IQR)** | 1.9 (1.0-4.2) | 1.9 (1.0-3.2) | U=1038; p=0.721 |
| Missing data | 5 | 0 | |
| **Postoperative day 1 CRP - Md (IQR)** | 48.5 (25.2-75.8) | 54.0 (36.0-79.0) | U=953; p=0.211 |
| Missing data | 2 | 0 | |
| **Postoperative day 2 CRP - mean (±SD)** | 162.3 (65.0) | 178.3 (65.2) | $t_{(104)}$=-1.18; p=0.26[2] |
| Missing data | 2 | 1 | |
| **Postoperative day 3 CRP - mean (±SD)** | 171.6 (74.1) | 160.9 (78.6) | $t_{(79)}$=0.59; p=0.552 |
| Missing data | 25 | 3 | |
| **Postoperative day 4 CRP, Md (IQR)** | 134.0 (83.2-178.5) | 94.0 (56.5-129.5) | **U=462; p=0.03[1]** |
| Missing data | 20 | 8 | |

n = sample size; CRP = C-reactive protein; [1] = Mann–Whitney U test; [2] = Student's t-test.

**Table 5 –** White blood cell counts over time in patients undergoing coronary artery bypass grafting, by control and intervention groups.

| White blood cell count over time | Control (n=80) | Intervention (n=29) | Test statistic |
|---|---|---|---|
| **Preoperative WBC - Md (IQR)** | 7.165 (6.015-8.418) | 7.210 (6.400-7.910) | U=1032; p=0.77[1] |
| Missing data | 6 | 0 | |
| **Postoperative day 0 WBC - Md (IQR)** | 12.900 (9.310-17.100) | 15.600 (11.000-18.800) | U=889; p=0.10[1] |
| Missing data | 3 | 0 | |
| **Postoperative day 1 WBC - Md (IQR)** | 13.050 (10.245-16.825) | 13.000 (10.800-19.100) | U=1074; p=0.56[1] |
| Missing data | 0 | 0 | |
| **Postoperative day 2 WBC - Md (IQR)** | 13.300 (10.450-15.950) | 13.900 (11.100-16.400) | U=1035, p=0.45[1] |
| Missing data | 1 | 0 | |
| **Postoperative day 3 WBC - Md (IQR)** | 11.100 (8.810-13.900) | 10.500 (8.740-14.500) | U=843, p=0.92[1] |
| Missing data | 21 | 0 | |
| **Postoperative day 4 WBC - Md (IQR)** | 8.655 (6.870-11.100) | 9.960 (7.500-12.700) | U=692, p=0.44[1] |
| Missing data | 18 | 4 | |

WBC - White blood cell count; [1] = Mann–Whitney U test.

**Table 6 –** Troponin levels over time in patients undergoing coronary artery bypass grafting, by control and intervention groups.

| Troponin levels over time | Control (n=80) | Intervention (n=29) | Test statistic |
|---|---|---|---|
| **Preoperative troponin - Md (IQR)** | 8 (2-27) | 13 (4-23) | U=65; p=0.74[1] |
| Missing data | 56 | 23 | |
| **Postoperative day 0 troponin - Md (IQR)** | 1478 (674-3261) | 1424 (471-2886) | U=989; p=0.58[1] |
| Missing data | 4 | 1 | |
| **Postoperative day 1 troponin - Md (IQR)** | 1686 (932-3578) | 1976 (1272-3947) | U=934; p=0.34[1] |
| Missing data | 4 | 1 | |
| **Postoperative day 2 troponin - Md (IQR)** | 678 (367-1388) | 1120 (529-1573) | U=880; p=0.11[1] |
| Missing data | 4 | 0 | |
| **Postoperative day 3 troponin - Md (IQR)** | 388 (182-1238) | 708 (345-1063) | U=322; p=0.23[1] |
| Missing data | 42 | 8 | |
| **Postoperative day 4 troponin - Md (IQR)** | 233 (130-810) | 501 (173-956) | U=144; p=0.30[1] |
| Missing data | 56 | 14 | |

n = sample size; [1] = Mann–Whitney U test.

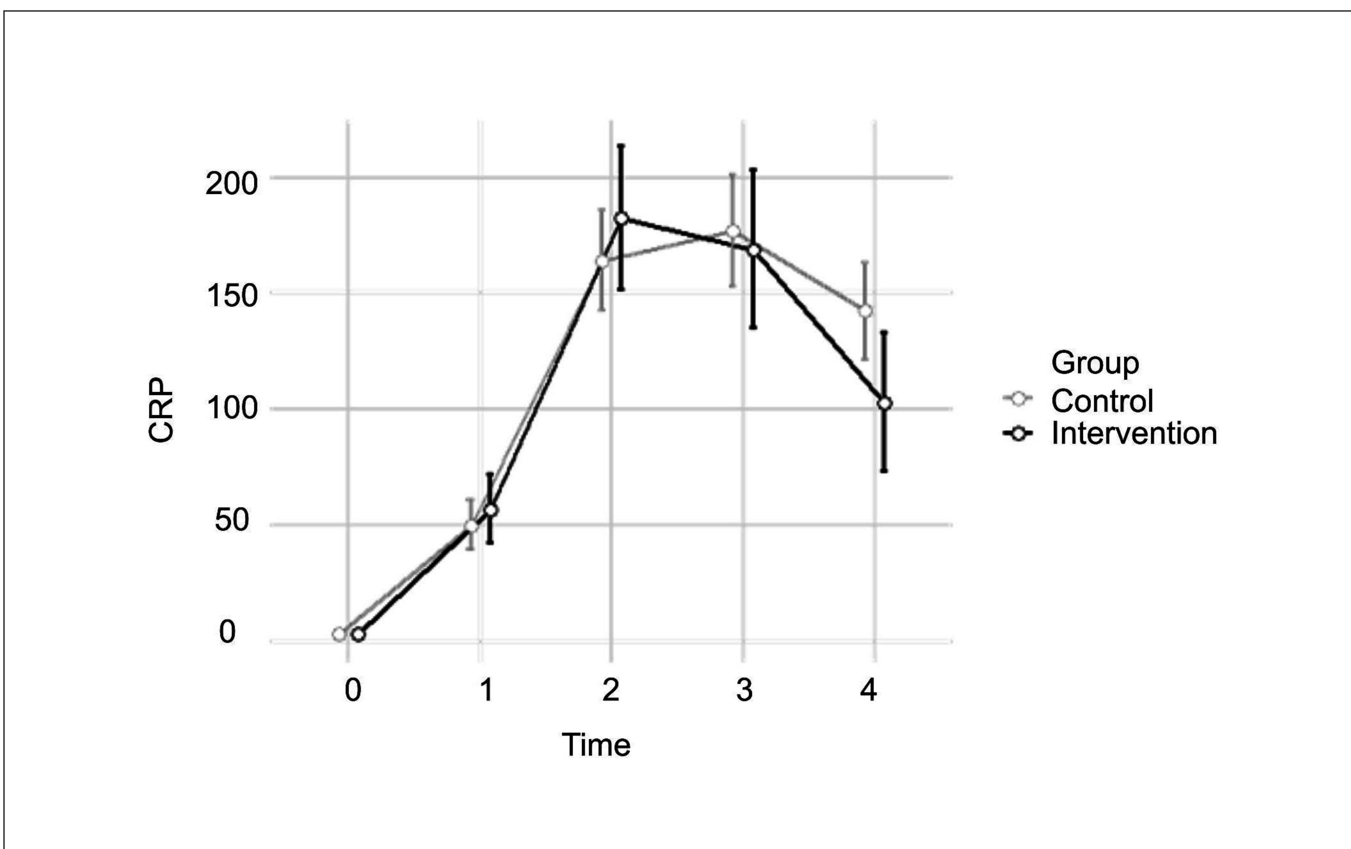


*Figure 1 -C-reactive protein levels over time in patients undergoing coronary artery bypass grafting, by control and intervention groups.*

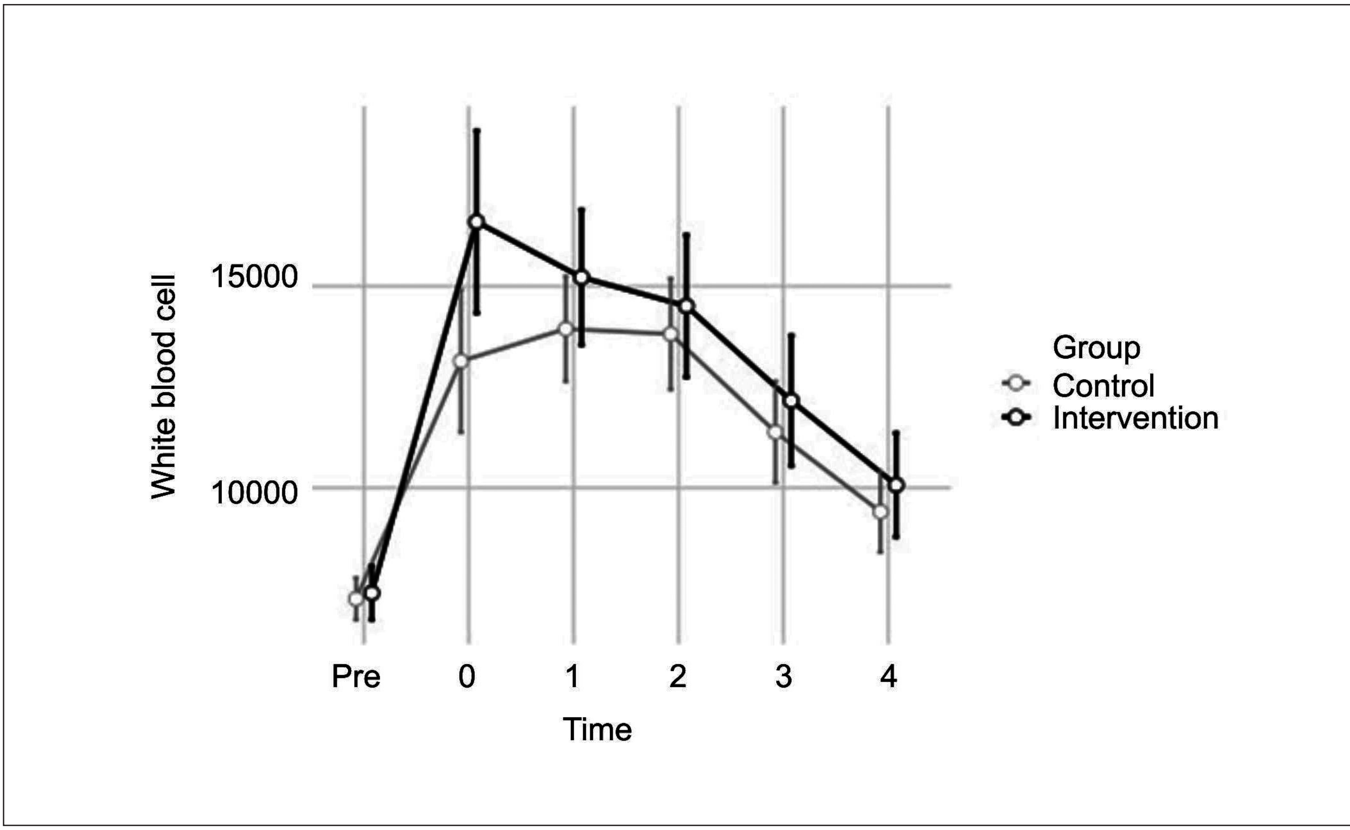


***Figure 2 -*** *White blood cell count over time in patients undergoing coronary artery bypass grafting, by control and intervention groups.*

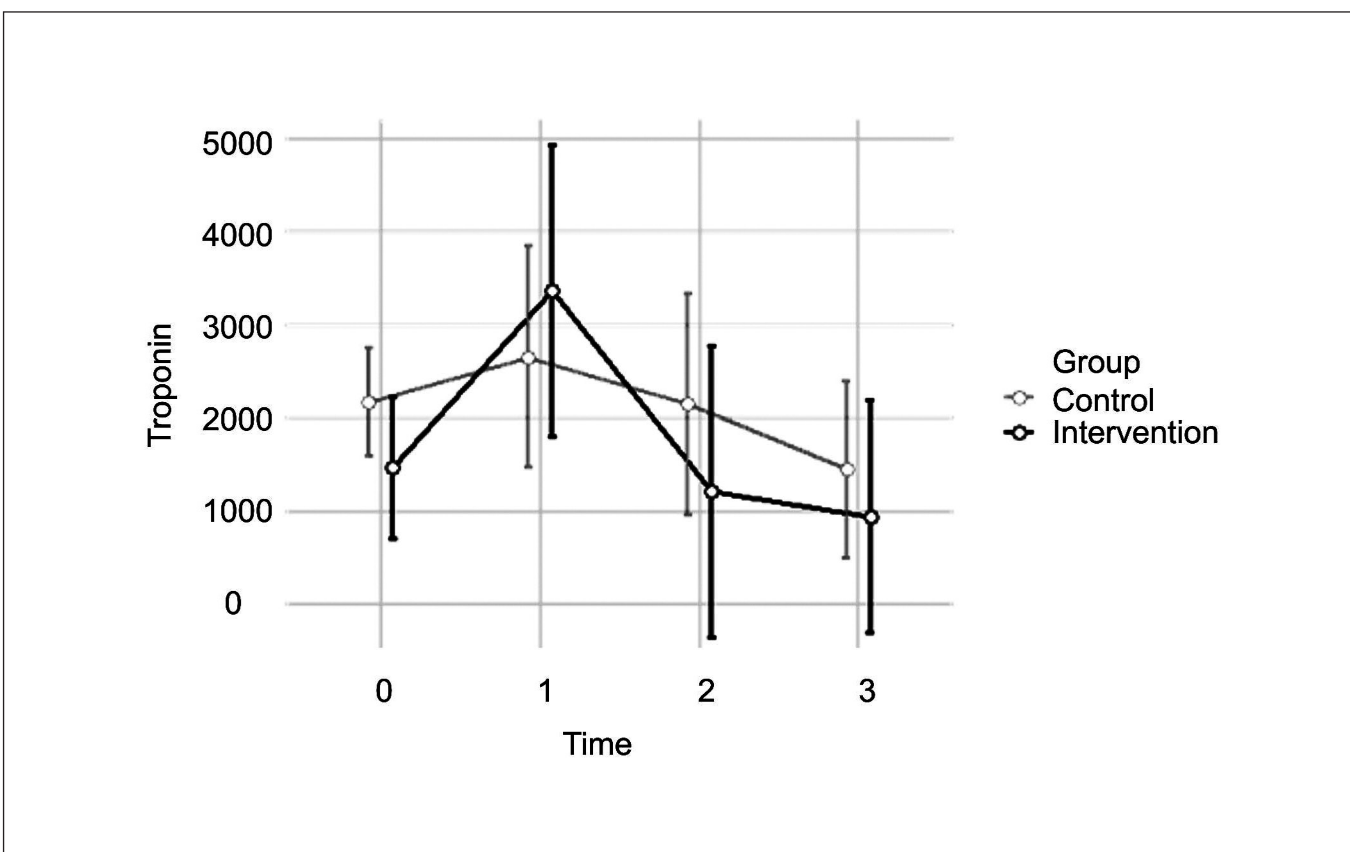


***Figure 3 -*** *Troponin levels over time in patients undergoing coronary artery bypass grafting, by control and intervention groups.*

## DISCUSSION

In this pilot study, we evaluated the effect of perioperative immunomodulatory supplementation on systemic inflammatory response, myocardial injury, and clinical outcomes in patients undergoing CABG. We found that patients who received supplementation had significantly lower CRP levels on postoperative day 4 compared to those who did not receive supplementation. However, no effect of supplementation was observed on white blood cell count, troponin levels, or clinical outcomes between groups, including hospital and ICU length of stay.

Reductions in inflammatory markers with immunomodulatory nutritional supplementation have been more frequently described in oncologic surgeries. In one such study, Yu et al.[14] demonstrated that omega-3 supplementation improved immune function and reduced certain biomarkers, such as CRP and interleukin-6, in patients with gastrointestinal cancer undergoing surgery. Another study[23] described the development and implementation of an oral immunonutrition protocol in the perioperative period of oncologic surgical patients, with preliminary results suggesting that immunonutrition may reduce the incidence of infectious complications and hospital stay. A meta-analysis[16] of patients undergoing gastrointestinal cancer surgery revealed that preoperative oral nutritional supplementation reduced infectious complications and inflammatory indicators such as CRP and WBC count. Another meta-analysis including 8375 patients concluded that postoperative oral or enteral immunonutrition may reduce morbidity rates in patients undergoing major abdominal surgery[9].

A randomized, double-blind clinical trial conducted in patients undergoing cardiac surgery reported that supplementation with a combination of glutamine, β-hydroxy-β-methylbutyrate, and arginine for 30 days prior to surgery reduced hospital stay, ICU time, and postoperative troponin levels[15]. Our findings of lower CRP levels on postoperative day 4 after CABG are consistent with these studies, but the limited impact on other markers and clinical outcomes raises questions regarding the duration and dosage of supplementation. Studies such as that of de-Aguilar-Nascimento et al.[7] suggest that longer protocols may be necessary to achieve consistent benefits.

The use of biomarkers as prognostic tools in the postoperative setting has become increasingly relevant, reducing morbidity, mortality, infections, hospital stay, and costs. In patients with colorectal cancer, elevated CRP levels on postoperative day 3 were associated with a higher need for reoperations[24]. In cardiology, these markers have also been linked to adverse cardiovascular and cerebrovascular events[25,26], highlighting the importance of strategies aimed at reducing their levels and improving clinical outcomes.

CRP is widely used in clinical practice and has strong evidence supporting its association with surgical outcomes[24,26,27]. A randomized trial evaluating immunonutrition in patients with gastric cancer cachexia showed that the preoperatively supplemented group had lower rates of infectious and overall complications, as well as reductions in white blood cell count, interleukin-6, and CRP on postoperative days 1 and 3, compared with standard nutrition[28]. Boćkowska et al.[29] found a significant increase in CRP levels on postoperative day 8 in pancreatic cancer patients who did not receive immunonutrition compared with those who did. However, some studies have shown different results[30,31], underscoring the need for more robust investigations, particularly in the field of cardiology.

In addition to C-reactive protein, WBC count is also widely studied as a marker of the inflammatory response in the perioperative period, as they play a crucial role in immune defense and inflammation regulation[32]. In the present study, immunomodulatory supplementation had no significant effect on postoperative white blood cell count. This finding contrasts with that of Yu et al.[28], a randomized trial in which preoperative immunonutrition strategies in patients with gastric cancer cachexia modulated leukocyte activation and reduced the release of pro-inflammatory cytokines. The benefits observed in that study may differ from ours due to differences in patient profiles, particularly the lower prevalence of malnutrition in our sample.

Troponin is a biomarker that provides diagnostic and prognostic information for coronary syndromes after cardiac surgery[25]. Pérez-Navero et al.[33] suggested that troponin levels measured two hours after cardiopulmonary bypass serve as an early independent predictor of low cardiac output syndrome. In the present study, immunomodulatory supplementation did not affect this marker. However, evidence from other studies suggests that perioperative nutritional interventions may influence troponin levels. Norouzi et al.[15] found that preoperative supplementation with glutamine, β-hydroxy-β-methylbutyrate, and arginine for one month improved recovery and reduced troponin levels after cardiac surgery, whereas Veljović et al.[34] demonstrated a reduction in troponin levels in patients who received preoperative intravenous omega-3 infusion. Nonetheless, the effects of immunonutrition on troponin remain not fully understood.

No statistically significant differences were observed in variables such as hospital or ICU length of stay between groups that received or did not receive perioperative immunonutrition. These findings contrast with many reports in the literature[10,15,35]. Conversely, studies such as those by Mohsen et al.[30] and Mudge et al.[36] also found no relevant differences in these outcomes. This suggests that although immunomodulatory supplementation may reduce some inflammatory markers, such as CRP, its direct impact on broader clinical outcomes remains controversial.

Our study presents some limitations. The small sample size of the intervention group may have affected the robustness of the results. As a historical control study, surgeries were performed at different times, which may have introduced variability in outcomes due to potential differences in clinical practices. The high rate of missing data also limited analytical accuracy. Another limitation was the lack of monitoring of supplement intake, which may have influenced intervention effectiveness. Furthermore, the literature lacks a standardized perioperative immunonutrition protocol, making comparisons across studies difficult. Adapting the supplement to hospital routines also proved challenging, as elective surgery dates vary, preventing a longer pre-operative consumption period, as observed in other studies[7,15,28].

Despite these limitations, this study provides relevant contributions. It adds knowledge about perioperative immunonutrition in cardiac surgeries, which is an area still scarcely explored. Although studies remain limited, preliminary findings suggest potential benefits in inflammatory response and reduction of postoperative complications[15,34,37]. Considering the magnitude of cardiovascular diseases[1], immunonutrition may enhance recovery, shorten hospital stay, reduce healthcare costs, and decrease the need for additional interventions. It may also improve patients' quality of life by accelerating recovery, reducing physical and psychological distress, and facilitating faster reintegration into daily life. These aspects underscore the importance of this study, which paves the way for future investigations into the use of immunonutrition in cardiac surgery and its potential to improve clinical outcomes.

## CONCLUSION

This pilot study provides encouraging insights into the potential effects of perioperative immunomodulatory supplementation in patients undergoing elective CABG, showing benefits in controlling the inflammatory response, with lower CRP levels on postoperative day 4. Although no significant effects were observed on myocardial injury, white blood cell count, or clinical outcomes, our findings suggest that perioperative immunonutrition may be a promising strategy to optimize recovery in cardiac patients. Immunonutrition has the potential to enhance not only patient recovery but also to reduce hospital costs. Future studies with standardized protocols and larger samples are warranted to clarify the impact of this intervention and optimize its clinical application.

## REFERENCES

1. Oliveira GMM, Brant LCC, Polanczyk CA, Malta DC, Biolo A, Nascimento BR, et al. Estatística cardiovascular – Brasil 2023. Arq Bras Cardiol. 2024;121(2):e20240079. Portuguese.
2. Ballmoos MCW, Kaneko T, Iribarne A, Kim KM, Arghami A, Fiedler A, et al. The Society of Thoracic Surgeons Adult Cardiac Surgery database: 2023 update on procedure data and research. Ann Thorac Surg. 2024;117(2):260-70.
3. Jawitz OK, Gulack BC, Brennan JM, Thibault DP, Wang A, O'Brien SM, et al. Association of postoperative complications and outcomes following coronary artery bypass grafting. Am Heart J. 2020;222:220-8.
4. Hadaya J, Downey P, Tran Z, Sanaiha Y, Verma A, Shemin RJ, et al. Impact of postoperative infections on readmission and resource use in elective cardiac surgery. Ann Thorac Surg. 2022;113(3):774-82.
5. Choileain NN, Redmond HP. Cell response to surgery. Arch Surg. 2006;141(11):1132-40.
6. Lopez-Delgado JC, Muñoz-Del Rio G, Flordelís-Lasierra JL, Putzu A. Nutrition in adult cardiac surgery: preoperative evaluation, management in the postoperative period, and clinical implications for outcomes. J Cardiothorac Vasc Anesth. 2019;33(11):3143-62.
7. de-Aguilar-Nascimento JE, Salomão AB, Waitzberg DL, Dock-Nascimento DB, Correa MITD, Campos ACL, et al. ACERTO guidelines of perioperative nutritional interventions in elective general surgery. Rev Col Bras Cir. 2017;44(6):633–48.
8. Tejera Pérez C, Guillín Amarelle C, Rodríguez Novo N, Lugo Rodríguez G, Mantiñán Gil B, Palmeiro Carballeira R, et al. Inmunonutrición, evidencias y experiencias. Nutr Hosp. 2023;40(1):186-199. Spanish.
9. Ricci C, Serbassi F, Alberici L, Ingaldi C, Gaetani L, Raffele E, et al. Immunonutrition in patients who underwent major abdominal surgery: A comprehensive systematic review and component network metanalysis using GRADE and CINeMA approaches. Surgery. 2023;174(6):1401-09.
10. Gregori P, Franceschetti E, Basciani S, Impieri L, Zampogna B, Matano A, et al. Immunonutrition in orthopedic and traumatic patients. Nutrients. 2023;15(3):537.
11. Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, et al. Guidelines for perioperative care in cardiac surgery: Enhanced Recovery After Surgery Society recommendations. JAMA Surg. 2019;154(8):755-66.
12. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, et al. ESPEN practical guideline: clinical nutrition in surgery. Clin Nutr. 2021;40(7):4745-61.
13. Stoppe C, Goetzenich A, Whitman G, Ohkuma R, Brown T, Hatzakorzian R, et al. Role of nutrition support in adult cardiac surgery: a consensus statement from an international multidisciplinary expert group on nutrition in cardiac surgery. Crit Care. 2017;21(1):131.
14. Yu J, Liu L, Zhang Y, Wei J, Yang F. Effects of omega-3 fatty acids on patients undergoing surgery for gastrointestinal malignancy: a systematic review and meta-analysis. BMC Cancer. 2017;17(1):271.
15. Norouzi M, Nadjarzadeh A, Maleki M, Khayyatzadeh SS, Hosseini S, Yaseri M, et al. Evaluation of the recovery after heart surgery following preoperative supplementation with a combination of beta-hydroxy-beta-methylbutyrate, L-arginine, and L-glutamine: a double-blind randomized placebo-controlled clinical trial. Trials. 2022;23(1):649.
16. Zou Q, Yin Z, Ding L, Ruan J, Zhao G, Wang X, et al. Effect of preoperative oral nutritional supplements on clinical outcomes in patients undergoing surgery for gastrointestinal cancer: a systematic review and meta-analysis. Medicine (Baltimore). 2024;103(39):e39844.
17. Moya P, Soriano-Irigaray L, Ramirez JM, Garcea A, Blasco O, Blanco FJ, et al. Perioperative standard oral nutrition supplements versus immunonutrition in patients undergoing colorectal resection in an enhanced recovery (ERAS) protocol: a multicenter randomized clinical trial (SONVI Study). Medicine (Baltimore). 2016;95(21):e3704.
18. Brasil. Ministério da Saúde. Resolução nº 466, de 12 de dezembro de 2012. Brasília: Ministério da Saúde; 2012. Portuguese.

19. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation on obesity. Geneva: World Health Organization; 1997.
20. Organización Panamericana de la Salud. División de Promoción y Protección de la Salud (HPP). Encuesta multicéntrica: salud, bienestar y envejecimiento (SABE) en América Latina y el Caribe: informe preliminar. In: XXXVI Reunión del Comité Asesor de Investigaciones en Salud; 2001 Jun 9-11; Kingston, Jamaica. Washington (DC): Organización Panamericana de la Salud; 2002. Spanish.
21. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z; Ad Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr. 2003;22(3):321-36.
22. The jamovi project (2024). jamovi. (Version 2.5) [Computer Software]. Disponível em: https://www.jamovi.org.
23. Carsten KI, Hermes DS. Elaboração e implementação de um protocolo de terapia nutricional oral imunomoduladora no perioperatório de pacientes cirúrgicos oncológicos em um hospital público da grande Florianópolis, Santa Catarina. BRASPEN J. 2022;37(2):183-90. Portuguese.
24. Correa Neto IJF, Nishiyama VKG, Theis C, Schelle G, Robles AG, Robles L. Proteína C-reativa como preditor de complicações pós-operatórias de cirurgias colorretais. Arq Gastroenterol. 2023;60(1):4–10. Portuguese.
25. Stef A, Bodolea C, Bocsan IC, Cainap SS, Achim A, Serban A, et al. The value of biomarkers in major cardiovascular surgery necessitating cardiopulmonary bypass. Rev Cardiovasc Med. 2024;25(10):355.
26. Min JJ, Nam K, Kim TK, Kim HJ, Seo JH, Hwang HY, et al. Relationship between early postoperative C-reactive protein elevation and long-term postoperative major adverse cardiovascular and cerebral events in patients undergoing off-pump coronary artery bypass graft surgery: a retrospective study. Br J Anaesth. 2014;113(3):391-401.
27. Kim DH, Shim JK, Hong SW, Cho KR, Kang SY, Kwak YL. Predictive value of C-reactive protein for major postoperative complications following off-pump coronary artery bypass surgery: prospective and observational trial. Circ J. 2009;73(5):872-7.
28. Yu J, Yuan A, Liu Q, Wang W, Sun Y, Li Z, et al. Effect of preoperative immunonutrition on postoperative short-term clinical outcomes in patients with gastric cancer cachexia: a prospective randomized controlled trial. World J Surg Oncol. 2024;22(1):101.
29. Boćkowska M, Kostro P, Kamocki ZK. Phase angle and postoperative complications in a model of immunonutrition in patients with pancreatic cancer. Nutrients. 2023;15(20):4328.
30. Mohsen G, Stroemer A, Mayr A, Kunsorg A, Stoppe C, Wittmann M, et al. Effects of omega-3 fatty acids on postoperative inflammatory response: a systematic review and meta-analysis. Nutrients. 2023;15(15):3414.
31. Svetikienė M, Trybė D, Strioga M, Vėželienė J, Isajevas V, Malickaitė R, et al. Impact of immunonutrition on T cell activation: a randomized control study in cardiac surgery patients. Acta Med Litu. 2021;28(2):240-52.
32. Graube SL, Okaseski KR, Ludvig BF, Bewanger SA, Bittencourt VLL, Colet CF, et al. Associação de exames hematológicos e bioquímicos e complicações pós-cirurgia cardiovascular. Mundo Saúde. 2022;46:e11642021. Portuguese.
33. Pérez-Navero JL, Torre-Aguilar MJ, Ibarra de la Rosa I, Gil-Campos M, Gómez-Guzmán E, Merino-Cejas C, et al. Cardiac biomarkers of low cardiac output syndrome after congenital heart disease surgery in children. Rev Esp Cardiol (Engl Ed). 2017;70(4):267-74.
34. Veljović M, Popadić A, Vukić Z, Ilić R, Trifunović Z, Antunović M, et al. Myocardial protection during elective coronary artery bypasses grafting by pretreatment with omega-3 polyunsaturated fatty acids. Vojnosanit Pregl. 2013; 70(5):484-92.
35. Zhang G, Zhao B, Deng T, He X, Chen Y, Zhong C, et al. Impact of perioperative immunonutrition on postoperative outcomes in pancreaticoduodenectomy: a systematic review and meta-analysis of randomized controlled trials. BMC Gastroenterol. 2024;24(1):412.
36. Mudge LA, Watson DI, Smithers BM, Isenring EA, Smith L, Jamieson GG. Multicentre factorial randomized clinical trial of perioperative immunonutrition versus standard nutrition for patients undergoing surgical resection of oesophageal cancer. Br J Surg. 2018;105(10):1262-72.
37. Damasceno NRT, Gowdak M, Oliveira L de, Passos A, Borba L. Emergências cardiológicas: suplementos nutricionais e imunomoduladores – parte 2. Rev Soc Cardiol Estado São Paulo. 2018;28(4):479-85. Portuguese.

---

**Study location:** Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP, Brazil.

**Conflict of interest:** The authors declare there are none.