2026, Volume 2 (Issue 1) Nutrition and Metabolism Journal: Clinical and Experimental

Original Article

Impact of immunonutrition on inflammatory and nutritional biomarkers in perioperative HIPEC patients

Leticia Cappelletto Luvisa[1], Graziele Fardin[1], Maristenia Machado Araujo[1], Joane Severo Ribeiro[1], Rafaela Alvarez Martins[1], Ana Carolina Bathelt Fleig[2], Rafael Seitenfus[2], Alessandra Peres[1]

[1]1Federal University of Health Sciences of Porto Alegre (UFCSPA), Porto Alegre, Rio Grande do Sul, Brazil

2 Surgical Oncology Department, Santa Rita Hospital, Irmandade Santa Casa de Misericórdia Hospital Complex of Porto Alegre (ISCMPA), Porto Alegre, Rio Grande do Sul, Brazil

Corresponding author:
Alessandra Peres (peres@ufcspa.edu.br)
Federal University of Health Sciences of Porto Alegre (UFCSPA)

Open Access

Published: June 16, 2026

Copyright, 2026 by the authors. Published by Ascend Solutions and the work is licensed under the Creative Commons Attribution 4.0 International License. To view a copy of this *license, visit http://creativecommons.org/licenses/by/4.0/*

Nutrition and Metabolism Journal: Clinical and Experimental: *2026, Volume 2 (Issue 1)*

DOI: 10.66154/nmetj.v2i1.19

Highlights

- HIPEC induces an intense systemic inflammatory response.
- CRP and albumin reflect postoperative metabolic stress.
- CRP variation may predict clinical complications.
- Immunonutrition acts as perioperative metabolic support.

Abstract

Introduction: To evaluate C-reactive protein (CRP) and albumin behavior in patients undergoing cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) receiving immunonutrition.
Methods: Retrospective observational cohort of nine patients with peritoneal carcinomatosis (2021–2024). Biomarkers were assessed at five perioperative time points. Normality was tested using the Shapiro-Wilk. Spearman correlation and nonparametric tests were applied.
Results: CRP peaked 48h after HIPEC, while albumin decreased during the same period. Preoperative CRP variation showed positive correlation with complications (R^2=0.542; p=0.156). Discharge BMI correlated negatively with complications (r=-0.66).
Conclusion: HIPEC induces severe metabolic stress reflected by inflammatory and nutritional biomarkers. Dynamic monitoring of these markers may support early identification of patients at higher risk of postoperative complications.

Keywords: Immunonutrition; HIPEC; Inflammation; Albumin; C-reactive protein

Introduction

Peritoneal cancer, characterized by the spread of neoplastic cells in the abdominal cavity, represents one of the greatest challenges in contemporary oncology. Whether as a primary neoplasm (mesothelioma or primary serous carcinoma) or secondary (carcinomatosis originating from colorectal, gastric, or ovarian tumors) [1,2], the disease requires aggressive interventions. The combination of cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) has become the gold standard for selected cases, significantly increasing overall survival [3,4].

However, the magnitude of this procedure is proportional to its metabolic impact. Exposure of the abdominal cavity to heat (hyperthermia) and chemotherapeutic agents

triggers a massive systemic inflammatory response [5]. This "surgical stress" is marked by the exacerbated release of pro-inflammatory cytokines, which alter protein and energy metabolism.

In this scenario, C-Reactive Protein (CRP) emerges as a crucial biomarker of inflammation, while albumin acts as an indicator of nutritional reserves and the severity of the inflammatory state (being a negative acute phase protein). Both increased C-Reactive Protein and albumin depletion are direct predictors of morbidity and mortality [6,7].
Given this scenario, specific nutritional strategies have been investigated as adjuvant tools to cancer treatment. Immunonutrition, characterized by the supply of nutrients with immunomodulatory properties, such as omega-3 fatty acids, arginine, and nucleotides, has shown potential to attenuate the exacerbated inflammatory response, preserve immune function, and promote postoperative recovery [8-10]. Previous studies suggest the benefits of this intervention in patients undergoing cancer surgery, although there are still gaps regarding its specific impact in the context of HIPEC [11].

Thus, the present study is justified by the need to better understand the behavior of inflammatory and nutritional biomarkers in patients undergoing cytoreductive surgery with HIPEC under an immunonutrition protocol. The hypothesis is that immunonutrition contributes to the modulation of systemic inflammation and the preservation of nutritional status, reflecting in smaller variations in CRP and albumin and, potentially, in better clinical outcomes. The general objective was to evaluate the evolution of CRP and albumin in the perioperative period of HIPEC, while the specific objectives included analyzing the association of these biomarkers with postoperative complications, body mass index (BMI), and length of hospital stay.

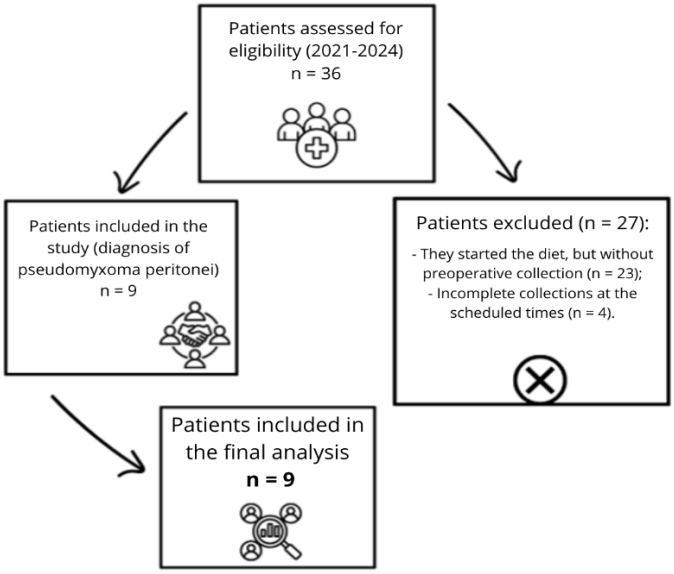
Methods

This is a retrospective observational cohort study. The study used secondary data from medical records. The project was approved by the Research Ethics Committee of the Irmandade da Santa Casa de Misericórdia de Porto Alegre (number 5.222.351, CAAE 52927421.0.0000.5335), respecting the guidelines of the Declaration of Helsinki.

The study population consisted of adult patients treated at the Oncology Surgery Service of Hospital Santa Rita, of the Irmandade da Santa Casa de Misericórdia de Porto Alegre, who underwent cytoreductive surgery associated with HIPEC between September 2021 and June 2024. Patients over 18 years of age, of both sexes, with a biopsy-confirmed diagnosis of peritoneal carcinomatosis of different origins (colorectal, ovarian, gastric, pancreatic, or primary peritoneal), eligible for the procedure, and who followed an immunonutrition protocol approved by the attending team were included. All participants signed the Informed Consent Form.

Patients with contraindications to HIPEC, such as extraperitoneal disease progression, bowel obstruction, functional performance below 2 according to ECOG, high risk of chemotherapy toxicity, renal failure (GFR < 40 mL/min), heart failure NYHA functional class > II, or liver failure with total bilirubin greater than 1.5 mg/dL, were excluded.
The selection of participants followed the STROBE initiative guidelines for observational studies (Malta et al., 2010). Of the 36 patients initially assessed for eligibility, 27 were excluded due to lack of preoperative collection (n = 23) or incomplete collections at the defined times (n = 4). Thus, 9 patients diagnosed with pseudomyxoma peritonei were included in the study and comprised the final analysis. The flowchart of the selection process is shown in **Figure 1**.

Figure 1: STROBE flowchart for patient inclusion.



Clinical, laboratory, and nutritional data were collected using an electronic medical record (Tasy System). Biological samples were collected at five perioperative time points: preoperative nutritional consultation, day of surgery (pre-HIPEC), 48 hours after surgery, 7 days, and 15 days after the procedure. Serum CRP was measured by immunoturbidimetry, based on the formation of immune complexes between latex particles sensitized with anti-CRP antibodies and the CRP of the sample, with automated absorbance reading proportional to the analyte concentration, using a calibrator traceable to the international standard NIBSC 85/506. Serum albumin was measured by a colorimetric method with Bromocresol Green, with spectrophotometric reading at 630 nm, with the color intensity proportional to the albumin concentration, according to Lambert-Beer's Law.

Statistical analysis was conducted using Python software (version 3.11). Initially, a descriptive analysis of the variables was performed. Normality was assessed using the Shapiro-Wilk test, and, in the absence of a normal distribution, non-parametric tests were used. Spearman correlations, Mann-Whitney U tests, and simple exploratory linear regressions were applied. The significance level adopted was $p < 0.05$..

Results

The Clinical Profile and Severity of the Cohort

The final sample consisted of nine patients diagnosed with pseudomyxoma peritonei, all of whom underwent cytoreductive surgery with HIPEC and an immunonutrition protocol. **Table 1** presents the clinical characteristics of the sample.

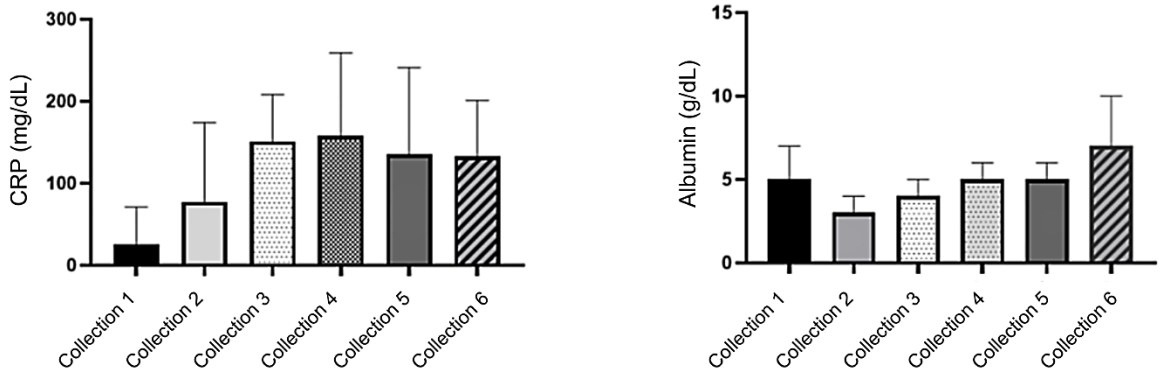
Table 1: Clinical characteristics of the sample.

Variable	Value
Number of patients	9
Gender (%) Man Woman	 33.3 66.7
Diagnosis	Pseudomyxoma peritonei
Average Peritoneal Carcinomatosis Index (PCI)	19.67
Average length of stay (days)	37.67
Postoperative complications (%)	88.9 (Serious: ~44)

Evolution of Inflammation Markers

Perioperative variations in CRP and albumin are shown in **Figure 2**. The variation in CRP between the preoperative time point (T2) and 48h postoperative time (T3) showed a positive correlation with the number of complications ($R^2 = 0.542$; $p = 0.156$).

Figure 2: Perioperative behavior of inflammatory and nutritional biomarkers in patients undergoing HIPEC.



Caption: To the left, C-reactive protein (CRP, mg/dL) is presented as mean ± standard deviation at the five perioperative collection times. A marked elevation is observed 48 hours after the procedure, reflecting the systemic inflammatory response to surgical stress. To the right, serum albumin (g/dL) is presented as mean ± standard deviation at the same periods. A reduction is noted in the first postoperative days, consistent with a negative acute phase response and metabolic changes associated with surgical trauma.

Nutritional Status and Outcomes

During hospitalization, the patients' average BMI decreased from 26.98 kg/m² to 24.56 kg/m². A negative correlation was found between BMI at hospital discharge and the number of complications (r = -0.66). The average length of stay was 37.67 days.

Discussion

The high complexity of the sample, reflected by the high mean PCI, is associated with a greater need for extensive surgical procedures and a higher risk of complications, as reported in other studies on peritoneal carcinomatosis [13,14]. The acute inflammatory response induced by HIPEC is evidenced by the CRP peak in the first 48h, a pattern consistent with the intense metabolic stress described in the literature.

The progressive reduction of albumin up to T3 reinforces its nature as a negative acute phase protein, compromised by hepatic synthesis redirected to inflammatory proteins [15]. The positive correlation between ΔCRP (T2–T1) and the number of complications, although without statistical significance (p = 0.156), suggests relevant clinical value, corroborating findings that point to the usefulness of dynamic inflammatory biomarkers as predictors of adverse outcomes [16].
The observed weight loss and the negative correlation of BMI at discharge with complications indicate that patients with lower nutritional reserves or greater depletion face more difficult recovery, which is consistent with previous evidence on the importance of nutritional status in oncological prognosis.

Immunonutrition, included as part of the care protocol, may have played a modulating role in the inflammatory response exacerbated by HIPEC. Although albumin levels decreased, the supply of immunomodulatory nutrients may have prevented more pronounced drops and their clinical consequences, such as delayed healing and immune dysfunction. It is important to emphasize that the purpose of immunonutrition is not to completely suppress the inflammatory response, but to promote adequate modulation that favors the resolution of the inflammatory process and tissue recovery [17]. The literature supports the analysis of deltas (variations) as more sensitive in predicting complications than isolated values, which reinforces the clinical relevance of serial CRP [18].

Finally, hypoalbuminemia in the context of HIPEC is multifactorial and should be interpreted as a marker of severity, not just as a sign of malnutrition, which justifies the need for aggressive and individualized nutritional support [19]. This study has important limitations that should be considered when interpreting the findings. The small sample size limits the generalizability of the results and reduces the statistical power to detect significant associations. In addition, the retrospective design is subject to information and selection biases. Also noteworthy is the lack of detailed quantification of caloric and protein intake during the perioperative period, which prevents a more precise assessment of the isolated impact of immunonutrition on the biochemical markers evaluated.

Conclusions

The study confirmed that cytoreductive surgery with HIPEC imposes extreme metabolic stress, evidenced by elevated CRP and decreased albumin. The correlation between these markers and clinical complications, although limited by the sample size, points to the importance of rigorous biochemical monitoring.

Immunonutrition remains an essential pillar in perioperative management. Its benefits in modulating the inflammatory response and supporting the immune system are fundamental to addressing the high morbidity associated with peritoneal cancer treatment. It is concluded that early and specialized nutritional intervention is indispensable to optimize clinical outcomes and promote functional recovery in these patients..

References

1. McQuade C, Renton M, Chouhan A, et al. Review of imaging peritoneal disease and treatment. Can Assoc Radiol J. 2024;0(0):08465371241296778. doi: https://doi.org/10.1177/08465371241296778

2. Torres EM. Peritoneal tumors of Mullerian origin: a case report and review of the literature. Int J Med Sci Clin Res Stud. 2022;2(11):1598-1601. doi: https://doi.org/10.47191/ijmscrs/v2-i11-16

3. Cortés-Guiral D, Cascales-Campos PA, Sugarbaker PH, et al. Primary and metastatic peritoneal surface malignancies. Nat Rev Dis Primers. 2021;7(1):50. doi: https://doi.org/10.1038/s41572-021-00326-6

4. Sarvestani AL. Malignant peritoneal mesothelioma literature review: past, present, and future. Diagnostic and Interventional Research. 2022;2(4):30. doi: https://doi.org/10.21037/dmr-22-19

5. Rubio-López J, Durán-Martínez M, Moreno-Blázquez A, et al. Intraoperative metabolic changes associated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Langenbecks Arch Surg. 2023;408(1):31. doi: https://doi.org/10.1007/s00423-023-02770-2

6. Valencia-Sola L, Becerra-Bolaños Á, Mateo-Ferragut M, et al. Cytoreductive Surgery (CS) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC): Postoperative Evolution, Adverse Outcomes and Perioperative Risk Factors. Healthcare (Basel). 2025;13(7):808. doi: https://doi.org/10.3390/healthcare13070808

7. Guven D, Şahin T, Erul E, et al. The association between albumin levels and survival in patients treated with immune checkpoint inhibitors: A systematic review and meta-analysis. Front Mol Biosci. 2022;9:1039121. doi: https://doi.org/10.3389/fmolb.2022.1039121

8. Adiamah A, Skořepa P, Weimann A, et al. The Impact of Preoperative Immune Modulating Nutrition on Outcomes in Patients Undergoing Surgery for Gastrointestinal Cancer: A Systematic Review and Meta-analysis. Ann Surg. 2019;270(2):247-56. doi: https://doi.org/10.1097/SLA.0000000000003256

9. García-Malpartida K, Aragón-Valera C, Botella-Romero F, et al. Effects of Immunonutrition on Cancer Patients Undergoing Surgery: A Scoping Review. Nutrients. 2023;15(7):1776. doi: https://doi.org/10.3390/nu15071776

10. Raczyńska A, Leszczyńska T, Skotnicki P, et al. The Impact of Immunomodulatory Components Used in Clinical Nutrition—A Narrative Review. Nutrients. 2025;17(5):752. doi: https://doi.org/10.3390/nu17050752

11. Tan G, Chia C, Wong J, Ong W, Zhu H, Ong C, Teo M. Randomized controlled trial investigating perioperative immunonutrition for patients undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Ann Surg Oncol. 2023;30:777-789. doi: https://doi.org/10.1245/s10434-022-12509-w

12. Thorgersen E, Asvall J, Frøysnes I, Schjalm C, Larsen S, Dueland S, Andersson Y, Fodstad Ø, Mollnes T, Flatmark K. Increased local inflammatory response to MOC31PE immunotoxin after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol. 2021;28:5252-5262. doi: https://doi.org/10.1245/s10434-021-10022-0

13. Elias D, Glehen O, Gilly F, et al. Carcinose peritoneal de origem digestiva e primitiva. In: Relatório do 110º Congresso da AFC. Paris: Arnette: Wolters Kluwer França; 2008. p. 23-30.

14. Sugarbaker PH. Procedimentos de peritonectomia. Surg Oncol Clin N Am. 2003;12(4):703-27. doi: https://doi.org/10.1016/S1055-3207(03)00048-6

15. Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. Int J Gen Med. 2016 Jul 15;9:229-55. doi: https://doi.org/10.2147/IJGM.S102819

16. Kim EY, Yim HW, Park CH, Song KY. C-reactive protein can be an early predictor of postoperative complications after gastrectomy for gastric cancer. Surg Endosc. 2017 Jan;31(1):445-454. doi: https://doi.org/10.1007/s00464-016-5272-4

17. Adiamah A, Skořepa P, Weimann A, Lobo DN. The Impact of Preoperative Immune Modulating Nutrition on Outcomes in Patients Undergoing Surgery for Gastrointestinal Cancer: A Systematic Review and Meta-analysis. Ann Surg. 2019 Aug;270(2):247-256. doi: https://doi.org/10.1097/SLA.0000000000003256

18. Platt JJ, Ramanathan ML, Crosbie RA, Anderson JH, McKee RF, Horgan PG, McMillan DC. C-reactive protein as a predictor of postoperative infective complications after curative resection in patients with colorectal cancer. Ann Surg Oncol. 2012 Dec;19(13):4168-77. doi: https://doi.org/10.1245/s10434-012-2498-9

19. Guven DC, Sahin TK, Erul E, Rizzo A, Ricci AD, Aksoy S, Yalcin S. The association between albumin levels and survival in patients treated with immune checkpoint inhibitors: A systematic review and meta-analysis. Front Mol Biosci. 2022 Dec 2;9:1039121. doi: https://doi.org/10.3389/fmolb.2022.1039121