



Effect of combined epidural and general anesthesia on the systemic immune-inflammation index in colorectal surgery: a retrospective study

Does combining anesthesia change SII?

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Abstract

Aim: The surgical stress response is influenced by the type of anesthesia and may affect the inflammatory response. The systemic immune inflammation index (SII) is a parameter that helps to better characterize the inflammatory microenvironment. In this study, we aimed to compare the short-term postoperative effects of adding epidural analgesia to general anesthesia on the SII value in patients undergoing elective colorectal surgery.

Methods: Patients diagnosed with colon and rectal cancer who underwent elective operation were divided into two groups. Patients who received only general anesthesia were referred to as Group 1, and patients in whom epidural anesthesia was added to general anesthesia were referred to as Group 2. Demographic data and preoperative, postoperative 4th-hour, and 24th-hour SII values, as well as the statistical relationship between them, were analyzed.

Results: Neither group showed a statistically significant difference. ($P = .210$ and $P = .577$, respectively). In intragroup evaluations, SII values for the general anesthesia group increased statistically significantly [675.8 (217.0-6645.3)] after treatment [2329.7 (592.1-7730.6)] compared to the pre-treatment period ($P < .001$. 001), and similarly in the epidural + general anesthesia group, SII values increased statistically significantly [610.8 (161.6-3951.5)] after treatment [1990.6 (643.5-8651.0)] compared to the pre-treatment period ($P < .001$).

Conclusion: We believe that both methods of anesthesia have a negative effect on the systemic inflammatory microenvironment, and that the combined method and epidural anesthesia do not reduce the negative effects of general anesthesia.

Keywords

general anesthesia, epidural anesthesia, systemic immun-inflammation index, colorectal surgery

DOI: 10.4328/ACAM.22921

Ann Clin Anal Med 2025;17(10):1027-1030

Received: 28.09.2025

Accepted: 03.11.2025

Published Online: 11.11.2025

Printed: 01.10.2026

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Introduction

Surgical procedures trigger an inflammatory host response involving metabolic, hemodynamic, and hormonal pathways. Stress hormones and cytokines mainly mediate these reactions. The greater the resulting reaction and catabolic effects, the greater the surgical stress. Drugs used for anesthesia have been shown to disrupt the balance in the inflammation mechanism and negatively affect immunity. It is known that drugs used in anesthesia applications have a negative impact on cytokine balance, thereby reducing the immune response.¹ Local anesthetic agents have also been reported to inhibit the development and spread of tumor cells. This is said to be achieved by inducing the cell's self-destruction by acting directly on the cell, preventing the spread, and acting on its genetic structure.²

Neutrophil-to-lymphocyte ratio (NLR), platelet (PLT)- lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) are markers of active inflammation that can be used as prognostic factors for various cancers.³⁻⁶ The systemic immune inflammation index (SII) was first reported in 2014 and is a parameter that integrates inflammatory cells such as neutrophils, platelets, and lymphocytes, helping to characterize the inflammatory microenvironment.⁷ SII is calculated by the formula PLT count x neutrophil count/lymphocyte count. There are many studies on the prognostic significance of SII, and similar studies have been conducted for colon cancer, one of the most common malignancies of abdominal origin.⁸

Cancers of the colon and rectum are the 3rd most common malignancy in the world. Among these, it stands out as the 2nd leading malignancy causing death, and its incidence is increasing day by day, and it is also seen at younger ages and in Turkey, in the national cancer statistics published by the General Directorate of Public Health, Cancer Control Department in 2018; with 18750 new diagnoses, it ranks 3rd in women and men.^{9,10}

We designed this study to compare the early postoperative effects of epidural anesthesia in combination with general anesthesia in patients undergoing elective colorectal surgery.

The objective of this study was to evaluate whether adding epidural anesthesia to general anesthesia alters postoperative SII values in patients undergoing elective colorectal surgery.

Materials and Methods

This single-center retrospective study was conducted at Bilkent City Hospital. After obtaining ethics committee approval (study number TABED 1-24-596 dated 25.9.2024), 100 patients who underwent colorectal surgery in the department of General Surgery between February 2022 and February 2024 were included. Patient data were retrospectively obtained from medical records. Patients diagnosed with colon and rectal cancer and electively prepared for surgery were divided into two groups. Patients who received only general anesthesia were referred to as Group 1, and patients in whom epidural anesthesia was added to general anesthesia were referred to as Group 2. In Group 1, patients who received only general anesthesia were induced with propofol 3mg/kg, rocuronium 0.6 mg/kg, fentanyl 1mg/kg, and maintained with sevoflurane and remifentanyl (0.01/kg), and low flow anesthesia was performed with 1 L/min flow. Postoperative analgesia was provided with nonsteroidal anti-inflammatory analgesics and narcotic drugs (Tramadol). In Group 2, the epidural catheter was inserted at the T-10 level, and the same induction was performed as in Groups 1 and 1 liter of low-flow sevoflurane and bupivacaine (4cc/h at 0.025

cc) was administered through the epidural catheter, and epidural analgesia was continued until the postoperative 24th hour.

Demographic data and preoperative, postoperative 4th hour, and 24th hour SII values and the statistical relationship between them were analyzed.

Exclusion criteria were patients in whom epidural anesthesia was contraindicated, patients undergoing emergency surgery, patients with hematologic disease, patients receiving neoadjuvant CT, patients with chronic inflammatory disease, and patients with rheumatologic disease.

Ethical Approval

This study was approved by the Ethics Committee of Bilkent City Hospital (Date: 25.09.2024, Decision No: TABED 1-24-596).

Statistical Analysis

Continuous variables were expressed as median (min-max). In the intergroup analysis of continuous variables, normality analysis was performed with the Kolmogorov-Smirnov Goodness of Fit Test. Since the data did not fit the normal distribution, comparisons between independent groups were performed with the Mann-Whitney U Test. The Wilcoxon Signed Rank Test was used for within-group analyses before and after treatment. Categorical/ discrete variables were analyzed by the Chi-square Test. Analyses were performed with IBM SPSS version 27.0 (IBM Corporation, Armonk, NY, USA). Statistical significance level was considered as $P < .05$.

Reporting Guidelines

This study was reported in accordance with the STROBE guideline.

Results

Age, gender, and ASA were not significantly different in both groups ($P > .05$) (Table 1). No statistical difference was found between preoperative and 24th hour values ($P = .210$ and $P = .577$, respectively). In intragroup evaluations; SII values for the general anesthesia group increased statistically significantly [675.8 (217.0-6645.3)] after treatment [2329.7 (592.1-7730.6)] compared to the preoperative period ($P < .001$. 001), and similarly in the epidural + general anesthesia group, SII values increased statistically significantly [610.8 (161.6-3951.5)] postoperative [1990.6 (643.5-8651.0)] compared to the preoperative period ($P < .001$) (Table 2).

Discussion

Intraoperative anesthesia methods may facilitate the spread or disappearance of tumor cells left behind after surgery if oncologic

Table 1. Comparison of groups in terms of age, gender and ASA

	General anesthesia	Epidural + general anesthesia	P value
	Median (min-maks) (n = 50)		
Age	59.5 (28.0-82.0)	60.5 (30.0-79.0)	.669*
Sex			
Female	8 (16.0)	13 (26.0)	.220**
Male	42 (84.0)	37 (74.0)	
ASA			
II	27 (54.0)	24 (48.0)	.548**
III	23 (46.0)	26 (52.0)	

ASA, The American Society of Anesthesiologists;
*, Mann Whitney U Test; **, Ki-square Test

Table 2. Comparison of SII values between and within groups

	General anesthesia	Epidural + general anesthesia	P
	Median (min-maks) (n = 50)		
Preop SII	67.58 (217.0-6645.3)	610.8 (161.6-3951.5)	.210*
Postop 24. hour SII	2329.7 (592.1-7730.6)	1990.6 (643.5-8651.0)	.577*
P	< .001**		< .001***

SII, Systemic Inflammatory Index; *, Mann Whitney U Test; **, Wilcoxon Signed-Rank Test

surgery is performed.¹¹ This may suggest that the anesthesia method applied may affect the long-term outcomes of the patient. There are many studies investigating the effect of the anesthesia technique chosen in oncologic surgery on survival, disease-free survival, and recurrence.¹²⁻¹⁴

SII reflects the inflammation-immunity balance and has recently been used more frequently to express this condition, calculated by the number of neutrophils (N) * platelets (P) / lymphocytes (L) in peripheral blood.¹⁵ High SII values indicate an inflammatory state that is generally associated with poor prognosis in cancer patients, and there are studies indicating that it is associated with the number of circulating tumor cells.^{16,17} There are studies on the prognostic significance of SII in various cancers, and similar studies have been conducted for colon cancer, which is one of the most common malignancies of abdominal origin.^{7,8,17,18-24} The SII cut-off values obtained in studies using SII values as prognostic markers have a wide range. Therefore, a standard cut-off value has not yet been determined. This is also true for colorectal cancer. However, the common conclusion of almost all studies is that higher preoperative SII values have a negative effect on parameters such as prognosis, survival, infection, and recurrence.¹⁸⁻²⁰ Changes in the preoperative and postoperative periods have been emphasized rather than the cut-off value for SII.

We found that preoperative SII values were lower in the general anesthesia arm. This may be considered a favorable prognostic factor for this patient group. However, considering the studies in which high SII values were associated with poor prognosis, it is important to standardize the cut-off point for preoperative and postoperative values.^{1,13,24} Therefore, since one of the aims of our study was not to determine a cut-off value for SII, we think that it would not be correct to comment on the contribution of preoperative low SII values to prognosis without a cut-off value. There are studies related to whether anesthesia methods have an effect on survival after cancer surgery.^{12,13}

Although epidural analgesia during colorectal surgery has been included in guidelines for postoperative pain palliation, its effect on postoperative morbidity and mortality has not yet been proven.^{21,22} Compared with general anesthesia alone, a study examining immune function and metastatic formation in the postoperative period showed that epidural analgesia attenuated tumor growth and the likelihood of metastasis.²³ Therefore, intraoperative epidural analgesia may contribute positively to cancer prognosis by reducing stress factors.

In our study, although epidural blockade caused a decrease in SII values and seemed to slightly correct the negative effects of general anesthesia on inflammation parameters, we found that this was not statistically significant. Therefore, we think similarly to these studies that epidural anesthesia does not contribute to prognosis.

Limitations

The current study was retrospective and did not include long-term outcomes of SII.

Conclusion

Intraoperative epidural analgesia may contribute positively to cancer prognosis by reducing stress factors. This can be expressed by a decrease in SII values. In both groups of our study, there was an increase in postoperative SII values, but this was not statistically significant. We think that both methods of anesthesia have a negative effect on the systemic inflammatory microenvironment, and the combined method and epidural anesthesia do not reduce the negative effects of general anesthesia.

We think that epidural anesthesia may be meaningful when used for postoperative analgesia, but should not be applied with the idea of a positive contribution to patient prognosis. Our study differed from the studies we cited in that it focused only on the change in SII values in the short term. Nevertheless, we think that it would be more meaningful to combine our results with long-term prognostic studies.

Declarations

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Written informed consent was obtained from all participants.

Data Availability

The data supporting the findings of this study are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare no conflict of interest.

Funding

None.

Author Contributions (CRediT Taxonomy)

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AI Usage Disclosure

The authors declare that no AI-assisted technologies were used.

Abbreviations

ASA: American society of anesthesiologists

CT: Chemotherapy

NLR: Neutrophil-to-lymphocyte ratio

PLR: Platelet-to-lymphocyte ratio

PLT: Platelet count

SII: Systemic immune-inflammation index

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How to Cite

Eda Uysal Aydın, Oğuz Uğur Aydın, Suna Kızılet, Handan Güleş. Effect of combined epidural and general anesthesia on the systemic immune-inflammation index in colorectal surgery: a retrospective study. *Ann Clin Anal Med* 2025;17(10):1027-1030. doi:10.4328/ACAM.22921