Original Article

Effect of the systemic immune-inflammation index on postoperative complications and the long-term prognosis of patients with colorectal cancer: a retrospective cohort study

Liping Feng[1#], Ruimin Xu[2#], Lin Lin[1], Xianghui Liao[1]

[1]Department of Oncology, Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; [2]Department of Anorectal, Shanghai Pudong New Area Hospital of Traditional Chinese Medicine, Shanghai, China

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[#]These authors contributed equally to this work.

Correspondence to: Xianghui Liao. Department of Oncology, Affiliated Hospital of Guangdong Medical University, No. 57 South Renmin Avenue, Zhanjiang 524000, China. Email: liaoxianghui5525@163.com.

Background: Colorectal cancer (CRC) is one of the most common malignant tumors of the digestive tract. Surgery is the main way to cure CRC, but the postoperative complication rate and recurrence rate remain high. The systemic immune-inflammation (SII) index reflects a patient's systemic inflammatory state and immune state. Postoperative recurrence and the occurrence of complications are closely related to the inflammatory state and immune state. Thus, the SII index may have some value in predicting postoperative complications and the long-term prognosis of CRC patients, but relevant studies are currently lacking. The present study sought to examine the effect of the SII index on the postoperative complications and long-term prognosis of patients with CRC.

Methods: From January 2014 to January 2017, the data of 440 patients with CRC who had been admitted to the Affiliated Hospital of Guangdong Medical University were retrospectively collected, and the patients were equally divided into the high and the low SII groups according to their preoperative SII index levels. The postoperative complication rate and postoperative progression-free survival (PFS) and mortality between the 2 groups were compared.

Results: Compared to the low SII group, the incidence of postoperative infection in the high SII group was significantly increased (15.45% *vs.* 9.09%, P=0.042), mortality was significantly increased at 5 years postoperatively (20.91% *vs.* 7.27%, P<0.001), and PFS was significantly shortened (P<0.001). The SII index had certain predictive value for postoperative infection in CRC patients, and the area under the curve (AUC) was 0.645 [95% confidence interval (CI): 0.559–0.731, P=0.001]. The SII index also had certain predictive value for the progression of CRC patients within 5 years of surgery, and the AUC was 0.670 (95% CI: 0.610–0.729, P<0.001). Additionally, the SII index had certain predictive value for death within 5 years of surgery in patients with CRC, and the AUC was 0.660 (95% CI: 0.593–0.726, P<0.001). CRC patients with postoperative infection had a significantly shorter PFS period than those who did not develop postoperative infection (P=0.029).

Conclusions: The SII index has certain predictive value for the diagnosis of postoperative infectious complications and the long-term prognosis of CRC patients.

Keywords: Systemic immune-inflammation index (SII index); colorectal cancer (CRC); postoperative complications; long-term prognosis

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Introduction

Colorectal cancer (CRC) is the 3rd most common cancer in the world, and it was estimated that there were 1.8 million new cases and >800,000 deaths worldwide in 2018 (1). The vast majority of CRC cases are sporadic, with no family history or significant genetic predisposition, and people aged >50 years are at high risk of CRC (2). Surgery is one of the main methods of treating CRC, but postoperative complications are common. A study in China showed that the incidence of postoperative infectious complications in patients with CRC was as high as 16% (3). Similarly, a foreign study showed that the incidence of postoperative infectious complications in patients with CRC was as high as 16.59% (4). Postoperative complications can lead to increased recurrence and mortality; moreover, Chen *et al.* showed that in patients with CRC liver metastases, postoperative infectious complications were associated with worse progression-free survival (PFS) and overall survival (5).

The systemic immune-inflammation (SII) index is a comprehensive indicator of the neutrophil, platelet, and lymphocyte counts in the peripheral blood, which can reflect the balance of inflammatory factors and immunity in the body. Inflammatory status and immune function are closely related to postoperative complications, recurrence, and mortality; thus, we speculated that the SII index may be able to predict postoperative complications and the long-term prognosis of CRC patients. Previous studies have confirmed that the SII index is associated with the PFS and mortality of CRC patients preoperatively, a higher level of SII index was associated with poor prognosis (6,7), but no studies have examined the relationship between the SII index and postoperative complications in CRC patients. We present the following article in accordance with the STARD reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-716/rc).

Methods

General information

From January 2014 to January 2017, the data of 440 patients with CRC who had been admitted to the Affiliated Hospital of Guangdong Medical University were retrospectively and continuously collected, and the patients were equally divided into the high SII group (n=220) and the low SII group (n=220) according to their preoperative SII index levels. Patients were included in the study if they met the following inclusion criteria: (I) had CRC (as confirmed by postoperative routine pathological results); (II) were aged ≥18 years; (III) had not received systematic treatment before surgery and underwent surgical treatment at the Affiliated Hospital of Guangdong Medical University; and (IV) had complete clinical pathology data. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had a pre-existing immune disease; (II) had a preoperative infectious disease; (III) had perforation of the digestive tract; (IV) had a disease of the blood system; (V) had received special treatments, such as radiotherapy, chemotherapy, and molecular targeting before surgery; (VI) had other concomitant malignant tumors; (VII) had stage IV CRC; (VIII) had not received standardized adjuvant therapy after surgery; (IX) had hepatic and renal insufficiency; (X) had missed visits during the 5 years of follow-up; and/or (XI) had died from a non-tumor-related death. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Hospital of Guangdong Medical University (No. 20210165). Individual consent for this retrospective analysis was waived.

Observation data

The primary outcomes were as follows: (I) blood neutrophil, lymphocyte, and platelet levels, and the SII index score; (II) the postoperative complication rate (i.e., the incidence of infectious complications, deep vein thrombosis, anastomotic fistula, postoperative bleeding, and perioperative death); and (III) long-term prognosis (i.e., mortality and PFS). The clinical factors of subjects were as follows: age, sex, surgical methods, body mass index, tumor location (colon or rectum), maximum tumor diameter, pathological type, lymph node metastasis, peripheral invasion, and length of hospital stay.

Definitions

We defined the SII index score as follows: platelet count × neutrophil count/lymphocytes. We defined PFS as follows: the time from operation to recurrence, metastasis or death for the first time.

Statistical analysis

The data analysis of this study was completed using SPSS26.0 (IBM, USA), and a difference was considered

statistically significant when the P value was <0.05 (two-sided). The measured data of the 2 patient groups are expressed as the mean ± standard deviation, and the differences were analyzed by independent sample *t*-tests. The differences in the count data between the 2 groups were analyzed using chi-square tests, and the results are expressed as the number (%). The predictive value of the SII index for postoperative complications and postoperative death in CRC patients was analyzed using the receiver operator characteristic curve. A Kaplan-Meier survival function analysis was conducted to study the effect of the SII index and postoperative infection on the prognosis of CRC patients.

Results

Comparison of the clinical and pathological factors, and the prognosis of patients between the 2 groups

Compared to the low SII group, the incidence of postoperative infection in the high SII group was significantly increased (15.45% *vs.* 9.09%, P=0.042), mortality was significantly increased at 5 years postoperatively (20.91% *vs.* 7.27%, P<0.001), and PFS was significantly shortened (P<0.001). There were no statistically significant differences between the 2 groups in terms of patients' age, body mass index, maximum tumor diameter, number of lymph node dissections, lengths of hospital stay, surgical method, sex, degree of differentiation, pathological type, lymph node metastasis rate, peripheral invasion rate, postoperative deep vein thrombosis, anastomosis fistula, postoperative bleeding, or perioperative mortality (P>0.05; see *Table 1* and *Figure 1*).

Diagnostic value of SII index for postoperative infection in CRC patients

The SII index had certain diagnostic value for postoperative infection in CRC patients. The area under the curve (AUC) was 0.645 [95% confidence interval (CI): 0.559–0.731, P=0.001; see *Figure 2*].

Diagnostic value of the SII index for disease progression within 5 years of CRC surgery

The SII index had certain diagnostic value for the progression of CRC patients within 5 years of surgery, and the AUC was 0.670 (95% CI: 0.610–0.729, P<0.001; see *Figure 3*).

Diagnostic value of the SII index for death within 5 years of CRC surgery

The SII index had certain diagnostic value for death within 5 years of surgery in CRC patients, and the AUC was 0.660 (95% CI: 0.593–0.726, P<0.001; see *Figure 4*).

Effect of postoperative infection of CRC on long-term prognosis

CRC patients with postoperative infection had a significantly shorter PFS period than those who did not develop postoperative infection (P=0.029; see *Figure 5*).

Discussion

Scholars have studied many indicators in order to analyze the clinical characteristics and prognosis of various cancers (8-10). Patients with malignant tumors often have low immune function, and the immune system's ability to monitor and remove abnormal cells in the body is weakened, making it difficult for patients to effectively remove tumor cells from the body. Decreased immune function can also lead to an increased incidence of postoperative infectious complications, which can further worsen a patient's long-term prognosis. Patients with malignant tumors also have increased levels of inflammation throughout the body, which can promote the proliferation and metastasis of tumor cells. The SII index reflects the level of inflammation and immune function in patients with malignant tumors; thus, it has been used in the diagnosis and treatment of a variety of malignant tumors, and has been found to have high value in predicting the prognosis of cancer patients (10-12). In this study, the diagnostic value of the SII index for postoperative complications in and the long-term prognosis of CRC patients was explored, and it was found that an increased SII index score was associated with increased postoperative infectious complications and mortality.

The SII index measures 3 metrics, that is, neutrophils, lymphocytes, and platelets. In patients with malignant tumors, neutrophils are inflammatory cells that indicate that the patient's systemic level of inflammation is increased, which is conducive to the local tissue angiogenesis of tumors, which in turn promotes the proliferation and metastasis of CRC cells (13). Additionally, this systemic inflammation also promotes an increase in intestinal permeability, which in turn leads to the

Table 1 Comparison of the clinical and pathological factors, and the prognosis of patients between the 2 groups

Groups	High SII group	Low SII group	t/χ^2 value	P value
Age (years) (mean ± SD)	63.58±12.43	64.52±11.73	0.821	0.412
Body mass index (kg/m^2) (mean ± SD)	23.40±3.60	24.01±3.46	1.825	0.069
Maximum tumor diameter (cm) (mean ± SD)	5.26±2.63	4.90±2.26	1.526	0.128
Number of lymph node dissections (mean ± SD)	16.40±6.44	16.56±6.28	0.262	0.793
SII (mean ± SD)	1,061.42±997.69	308.67±90.04	11.146	<0.001
Length of hospital stays (d) (mean ± SD)	12.95±7.31	13.84±8.83	1.147	0.252
Surgical methods, n (%)	–	–	3.404	0.065
Laparoscopic assistance	195 (88.64)	206 (93.64)	–	–
Open surgery	25 (11.36)	14 (6.36)	–	–
Gender, n (%)	–	–	0.943	0.331
Male	136 (61.82)	126 (57.27)	–	–
Female	84 (38.18)	94 (42.73)	–	–
Degree of differentiation, n (%)	–	–	0.176	0.675
Medium-low differentiation	207 (94.09)	209 (95.00)	–	–
High differentiation	13 (5.91)	11 (5.00)	–	–
Pathological type, n (%)	–	–	0.000	1.000
Adenocarcinoma	219 (99.55)	219 (99.55)	–	–
Non-adenocarcinoma	1 (0.45)	1 (0.45)	–	–
Lymph node metastases, n (%)	92 (41.82)	77 (35.00)	2.162	0.141
Peripheral invasion, n (%)	11 (5.00)	13 (5.91)	0.176	0.675
Postoperative infection, n (%)	34 (15.45)	20 (9.09)	4.137	0.042
Deep vein thrombosis, n (%)	17 (7.73)	23 (10.45)	0.990	0.320
Anastomotic fistula, n (%)	4 (1.82)	3 (1.36)	0.145	0.703
Postoperative bleeding, n (%)	2 (0.91)	4 (1.82)	0.676	0.411
Perioperative death, n (%)	2 (0.91)	2 (0.91)	0.000	1.000
5-year mortality rate, n (%)	46 (20.91)	16 (7.27)	16.897	<0.001

SD, standard deviation; SII, systemic immune-inflammation.

displacement of intestinal flora, causing postoperative infectious complications, such as intraoperative infection. Lymphocytes are the main immune cells of the body that kill tumor cells, which can be divided into T cells, B cells, and natural killer (NK) cells in terms of type. T cells, B cells, and NK cells can kill tumor cells after activation, and when lymphocyte levels decrease, tumor cells can proliferate and metastasize rapidly (13), and immune function declines at this time, and the incidence of postoperative infectious complications increases. Platelets are small pieces of cytoplasm that fall off from the cytoplasm of mature megakaryocytes in the bone marrow, and are involved in the development of tumors, including tumor growth, tumor cell extravasation, and tumor metastasis (13-15), which can inhibit the apoptosis of tumor cells and maintain the integrity of tumor blood vessels.

Elevated SII index scores indicate elevated platelets and neutrophils, and decreased lymphocytes. CRC patients are prone to infection, recurrence, or metastasis after surgery, which ultimately leads to a poor prognosis, and previous

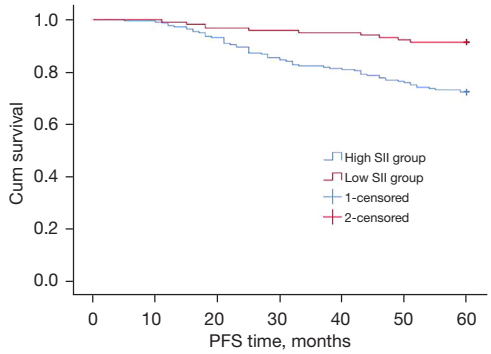

Figure 1 Comparison of PFS between the 2 groups. SII, systemic immune-inflammation; PFS, progression-free-survival.

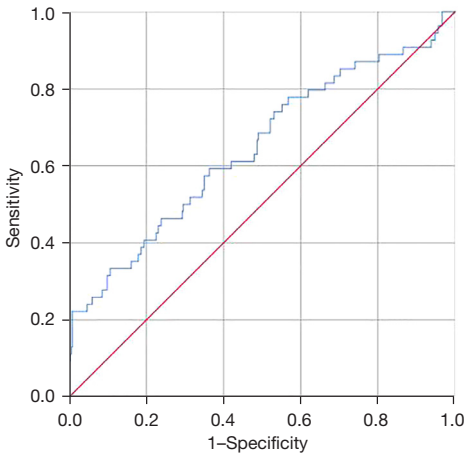

Figure 2 Diagnostic value of the SII index for postoperative infection in CRC patients. SII, systemic immune-inflammation; CRC, colorectal cancer.

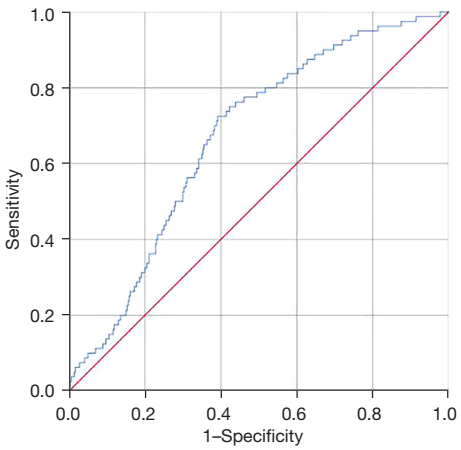

Figure 3 Diagnostic value of the SII index for disease progression within 5 years of CRC surgery. SII, systemic immune-inflammation; CRC, colorectal cancer.

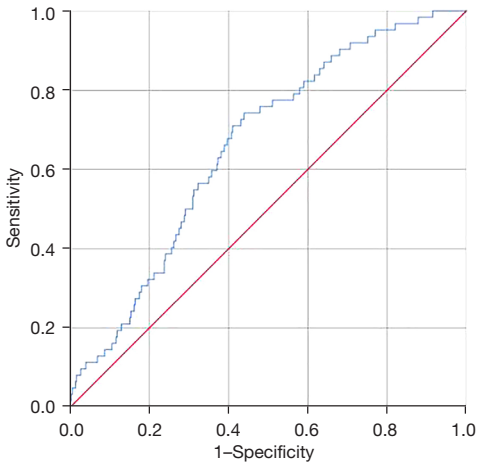

Figure 4 Diagnostic value of the SII index for death within 5 years of CRC surgery. SII, systemic immune-inflammation; CRC, colorectal cancer.

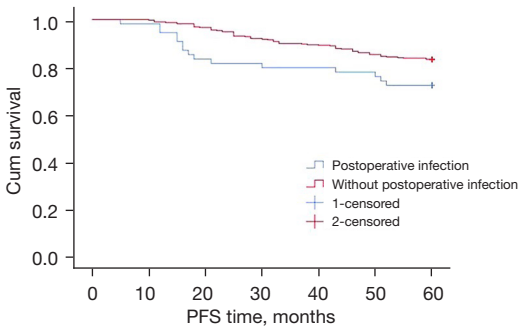

Figure 5 Effect of postoperative infection of CRC patients on long-term prognosis. PFS, progression-free-survival; CRC, colorectal cancer.

studies have confirmed that an increased SII index score is the main risk factor for the poor postoperative prognosis of CRC patients, which supports the findings of this study (16-20). However, compared to previous studies, this study is somewhat innovative; we did not find any other study that explored the relationship between the SII index and postoperative infectious complications in CRC patients, and this study confirmed that an increased SII index score indicates an increased incidence of postoperative infectious complications. Finally, this study found that postoperative infectious complications were associated with the poor postoperative prognosis of CRC patients, and that the PFS of patients with postoperative infection was significantly reduced, which is consistent with previous findings (4,21).

Our findings provide more targets for the prevention and treatment of postoperative infectious complications in CRC patients.

Limitations: this study was a retrospective clinical study, and the relationship between the SII index and T cells, B cells, NK cell function, and intestinal flora could not be explored, a previous study has showed that CRC patients may have intestinal flora and immune dysfunction (22).

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-716/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-716/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-716/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Hospital of Guangdong Medical University (No. 20210165). Individual consent for this retrospective analysis was waived.

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