A novel nomogram based on nutritional and immune status predicting postoperative intra-abdominal infection in colorectal cancer

doi: 10.6133/apjcn.202209/PP.0007
Published online: September 2022

Running title: Nomogram in colorectal cancer

Guibing Pei MD[1], Shuguang Zhen MD[2], Bo Zhang MD[1]

[1]Department of Anorectal Surgery, Zhongda Hospital, Southeast University, Jiangsu, PR China
[2]Department of Anorectal Surgery, Suzhou TCM Hospital Affiliated to Nanjing University of Chinese Medicine, Jiangsu, PR China

Authors' email addresses and contributions:
Conceptualization, Guibing Pei, Shuguang Zhen, and Bo Zhang; methodology and formal analysis, Guibing Pei and Shuguang Zhen; writing—original draft preparation, Guibing Pei; writing—review and editing, Bo Zhang.

Corresponding Author: Dr Bo Zhang, Department of Anorectal Surgery, Zhongda Hospital, Southeast University, Nanjing 210009, Jiangsu, PR China. Tel: . Email: 13400057505@163.com

ABSTRACT

Background and Objectives: This study aimed to investigate independent risk factors for intra-abdominal infection and to construct a nomogram to identify colorectal patients at a high risk of intra-abdominal infection. **Methods and Study Design:** Clinical data of patients undergoing radical resection of colorectal cancer from January 2019 to December 2021 were retrospectively included in this study. Patients were divided into two groups according to postoperative intra-abdominal infection. Clinicopathological indicators, intraoperative conditions, and postoperative complications were compared between the two groups, logistic regression was used to look for independent risk factors for intra-abdominal infection, and a nomogram was constructed based on independent risk factors. **Results:** 402 colorectal cancer patients were enrolled in this study, and 46 patients (11.4%) developed intra-abdominal infections after surgery. The independent risk factors for intra-abdominal infection were preoperative albumin, lymphocyte-white cell ratio (LWR) <0.17, low subcutaneous fat mass, and low skeletal muscle mass. The nomogram model for intra-abdominal infection was able to reliably quantify the risk of intra-abdominal infection with strong optimism-adjusted discrimination (concordance index=0.931). Furthermore, decision curve analysis showed that the nomogram was clinically useful and had a better discriminative ability to recognize patients at high risk than the risk factors alone. **Conclusions:** In conclusion, we found that preoperative albumin, LWR <0.17, low subcutaneous fat mass, and low skeletal muscle mass were significantly correlated with intra-abdominal infection. Our nomogram was a simple and practical instrument to quantify the individual risk of intra-abdominal infection.

Key Words: colorectal cancer, intra-abdominal infection, LWR, L3MI, L3FI

INTRODUCTION

In recent years, the incidence of colorectal cancer has remained high, and surgery is often the first treatment. Surgical site infections (SSIs) are the most common nosocomial infection among surgical patients. The definition of surgical site infection provided by the Centers for Disease Control in 1992 and updated in 2003 proposed that SSIs can be roughly divided into incision infections and organ/space infections.[1,2] After radical resection of colorectal cancer, organ/space infections often manifest as intra-abdominal infections, which is a serious complication. According to previous literature reports, although the incidence of intra-abdominal infection varies from center to center (1%-30%), it can cause systemic inflammatory response syndrome, sepsis, and even death, which seriously affects the

prognosis of patients.[3-6] Intra-abdominal infection should be highly suspected when clinical signs such as fever, tachycardia, oliguria, elevated white blood cell count and even shock occur after an operation. There are many reasons for postoperative abdominal infection, such as anastomotic leakage, pelvic inflammatory disease, and abdominal abscess. The main cause of postoperative intra-abdominal infection is anastomotic leakage. Postoperative intra-abdominal infection usually occurs between the 6th and 9th days after the operation, although anastomotic leakage may occur long ago.[7]

Finding the risk factors of postoperative intra-abdominal infection is conducive to early identification of high-risk groups and immediate preventive measures, which plays an important role in reducing the incidence of postoperative intra-abdominal infection of colorectal cancer and improving the clinical outcomes of patients. Previous studies have found that the risk factors for postoperative SSIs include advanced age, increased BMI, higher American Society of Anesthesiologists (ASA) score, longer operation time, and diabetes mellitus.[8] However, there are few similar studies on postoperative intra-abdominal infection in patients with colorectal cancer, so the purpose of this study is to retrospectively collect data from our center to determine the risk factors of intra-abdominal infection after radical resection of colorectal cancer and to construct a nomogram based on nutritional and immune status.

MATERIALS AND METHODS

Patients

A total of 402 adult patients aged 18-80 who underwent radical resection for colorectal cancer from January 2019 to December 2021 were included in this retrospective analysis. With the permission of the Research Ethical Committee, we can collect patient files. The exclusion criteria for this study were: (1) previous colorectal resection (2) palliative surgery only (3) age older than 80 years (4) colorectal cancer with TNM stage IV. All patients were operated on by a group of experienced surgeons. Before the operation, the intestinal tract was cleaned with sodium phosphate oral liquid, and intravenous antimicrobial prophylaxis (cefuroxime) was given to all patients. Besides, a combination of ceftazidime and ornidazole was administered twice daily for one or three consecutive days after surgery. Finally, the treatment process and postoperative intra-abdominal infections were recorded in detail. The clinical management of all patients in this study followed the guidelines for the treatment of colorectal cancer published by the National Comprehensive Cancer Network (NCCN) in 2018.[9]

Data collection

The data collected in this study included the following: (1) preoperative patient characteristics, including age, gender, body mass index (BMI), NRS 2002 score (NRS 2002 score ≥3 indicated at risk of malnutrition), American Society of Anesthesiologists (ASA) score, neoadjuvant chemotherapy and radiotherapy, diabetes mellitus, hematological indicators [hemoglobin, albumin (< 35 g/L was defined as hypoproteinemia), C-reactive protein (CRP), white cell count (WBC), absolute lymphocyte count and lymphocyte-white cell ratio (LWR)]; (2) surgical condition: surgical resection mode, combined organ resection, obstruction, and intraoperative blood loss; (3) postoperative: TNM stage, the time of removing abdominal drainage tube, hospitalization days and total expenses; (4) clinical outcome: whether there is an intra-abdominal infection and the results of pathogenic bacteria of infection. The eighth edition of the American Joint Committee on Cancer (AJCC) cancer staging system was used in this study to define pathological classification.[10]

Measurement of subcutaneous fat mass and skeletal muscle mass

The OsiriX open-source software (version 8.5.2: Pixmeo Sarl, Geneva, Switzerland) was used to analyze preoperative abdominal computerized tomography (CT) images. The tissue cross-sectional area (cm^2) of tissue in the para-lumbar section of the third lumbar spine (L3) was calculated, –190 Hounsfield unit (HU) to –30 HU corresponded to the subcutaneous fat tissue and –29 HU to +210 HU corresponded to the skeletal muscle tissue.[11] The ratio of subcutaneous fat mass and skeletal muscle mass to height squared (m^2) was used to acquire the L3 subcutaneous fat mass index (L3FI, cm^2/m^2) and L3 skeletal muscle mass index (L3MI, cm2/m2).

Definition of low subcutaneous fat mass and low skeletal muscle mass

Due to a lack of consensus in defining L3FI and L3MI using a CT image, we defined sex-specific cut-off values for our population using the first quartile. The L3FI <46.1 cm^2/m^2 for men and L3FI <61.8 cm^2/m^2 for women were defined low subcutaneous fat mass, the L3MI <43.6 cm^2/m^2 for men and L3MI <38.1 cm^2/m^2 for women were defined low skeletal muscle mass.

Diagnosis of clinical intra-abdominal infection

The diagnosis of postoperative intra-abdominal infection is based on the patient's symptoms and signs, imaging diagnosis, laboratory examination, or intraoperative direct vision within 30

days after surgery. The criteria were as follows: (1) the contents of the intestine drained out of the abdominal drainage tube and accompanied by a bad smell of feces; (2) high fever was difficult to be relieved after the operation until localized peritonitis or diffuse peritonitis appeared, which could be accompanied with a significant increase of white blood cells; (3) low rectal fistula was found in the digital rectal examination; (4) imaging examination such as gastrointestinal radiography, abdominal CT found fistula or abdominal abscess: (5) reoperation found under direct vision. If two or more of the above criteria are met, it can be diagnosed as a postoperative intra-abdominal infection.

Management of clinical intra-abdominal infection

Under the guidance of the attending physician, the treatment measures for patients with intra-abdominal infection included reoperation drainage, image-guided percutaneous drainage, continuous irrigation of double cannula, antibiotics, and nutritional support (Supplementary Table 1).

Statistical analysis

All data analysis in this study was completed by software SPSS version 25.0 (IBM, New York, USA) and R version 4.0.5 (R Project for Statistical Computing, Vienna, Austria). Quantitative variables were described as mean ± standard deviation or median ± quartile interval, while classified or ranked variables were described as the number with proportion. The data of continuous distribution between the two groups were evaluated by t-test or Mann–Whitney U test, and Pearson's Chi-square test analyzed categorical variables. Univariate and multivariate logistic regression models determined the independent risk factors of intra-abdominal infection, and the interaction of these factors was analyzed. In univariate analysis, the variables with p values < 0.1 were included in multivariate analysis. Using the predictive factors, the nomogram was formulated. The predictive factors were then incorporated into the receiver-operating characteristic (ROC) analysis. The performance of the nomogram was assessed using the area under the curve (AUC) and calibration curve. Decision curve analysis (DCA) was used to evaluate the clinical benefits and utility of the nomogram compared with risk factors alone. A ROC modeling LWR against any intra-abdominal infection was analyzed (Supplementary Figure 1). Youden index was derived to determine the optimal threshold value. The optimal cut-off point of 0.17 was used for subsequent analysis. Two-sided $p \leq 0.05$ was considered to be statistically significant.

RESULTS

Clinicopathological characteristics of the patients in this study

A total of 402 patients were eventually included in the analysis after 68 patients were excluded from the initial 470 patients. The basic clinicopathological characteristics of all patients are presented in Table 1. The mean age of all patients was 59.6 years, and males accounted for the majority (61.7%). Although the mean BMI of the patients in the study was normal, a small minority (7%) had a lower BMI (<18.5 kg/m^2). Preoperative with nutritional risk and high ASA score (≥3) was 116 patients and 32 patients. The prevalence of colon cancer (54.7%) was similar to that of rectal cancer (45.3%) in the included group, while 42 patients had diabetes. Preoperative concentrations or counts of hemoglobin, albumin, CRP, WBC, and lymphocytes were normal. 144 and 82 patients underwent neoadjuvant chemotherapy and radiation, respectively. The majority of patients underwent laparoscopic surgery (n=324, 80.6%), with TNM stage I (n=66), II (n=200) and III (n=136). Finally, intra-abdominal infection occurred in 46 patients, accounting for about 11.4%.

As shown in Table 2, patients with intra-abdominal infection were older (p<0.001), had higher nutritional risk (p<0.001), had lower preoperative hemoglobin concentration (p<0.001) and lymphocyte (p=0.045). Patients who experienced intra-abdominal infection had lower L3FI and L3MI (p<0.001), lower LWR (p=0.045), higher rates of intestinal obstruction (p<0.001) and combined multiple organ resection (p<0.001). After intra-abdominal infection, the removal of the abdominal drainage tube was more difficult (p<0.001). Furthermore, intra-abdominal infections prolonged hospital stays (p<0.001) and total hospitalization costs (p<0.001). Other factors showed no significant difference between the two groups.

Results of microbial culture in abdominal drainage fluid

Only 36 of forty-six patients with intra-abdominal infection had positive results from the microbial culture of abdominal drainage (Supplementary Table 2). A total of 48 strains of bacteria were identified from the drainage fluid, among which 12 patients isolated more than 1 strain. Among the identified bacteria, 75% were gram-negative (*escherichia coli* was the most common) and 25% were gram-positive (cocci were the most common). But there were no anaerobes or fungal infections.

Independent risk factors for intra-abdominal infection

We used the logistic regression model to find independent risk factors for intra-abdominal infection. First, a univariate analysis was established. Through this analysis, it was found that

NRS2002 score ≥3 (p=0.01), preoperative albumin (p <0.001), preoperative intestinal obstruction (p<0.001), intraoperative multiple organ resection (p=0.001), LWR <0.17 (p=0.013), low L3FI and low L3MI (p<0.001) were significantly related to the occurrence of intra-abdominal infection (Table 3). The variables with p<0.1 were again included in the multivariate analysis, and Table 4 shows the results. Through multivariate analysis, we finally found that the independent risk factors affecting intra-abdominal infection were preoperative albumin (OR: 1.32, p<0.001), LWR<0.17 (OR: 5.84, p=0.041), low L3FI (OR: 28.48, p<0.001) and low L3MI (OR: 15.10, p=0.001). Meanwhile, there was an interaction between preoperative albumin, low L3MI and low L3FI.

Establishment and validation of a nomogram for intra-abdominal infection

Based on the four independent risk factors, a simple and practical nomogram was established to quantify the risk of intra-abdominal infection (Figure 1). To examine the discriminative ability of the nomogram, the ROC curve of the nomogram was plotted (Figure 2A), and the area under the ROC (AUROC, Table 5) was calculated. The AUROC value for the nomogram was 0.931 (95% CI, 0.815–0.971). The calibration of nomograms was checked by the calibration curve. The calibration curves of the nomogram showed high consistencies between the predicted and observed intra-abdominal infection probability in the cohort (Figure 2B). The clinical benefits of the nomogram were compared with those of the risk factors alone. DCA curves showed that the nomogram could better predict the probability of intra-abdominal infection, as it added more net benefits compared with the risk factors alone for almost all threshold probabilities in the cohort, and with both the treat-all-patients scheme and the treat-none scheme (Figure 3B). The above results indicate that the prediction model of preoperative albumin, LRM<0.17, low L3FI, and low L3MI have high reliability.

DISCUSSION

Based on the above study results, we found that the incidence of intra-abdominal infection after colorectal cancer surgery in this study was 11.4%, which was similar to previous reports.[12] Patients with intra-abdominal infection are older, have a higher incidence of preoperative anemia, have a higher nutritional risk, have lower L3FI and lower L3MI. At the same time, they will significantly extend the postoperative hospital stay and increase the economic burden on patients. The bacterial culture of the abdominal drainage fluid was mainly gram-negative bacteria. After comprehensive treatment, all the patients were discharged successfully. Finally, the independent risk factors of intra-abdominal infection

were preoperative albumin, the LMR <0.17, low L3FI, and low L3MI preoperatively found by logistic regression. Simultaneously, this is the first study creating a nomogram that can be directly used in clinical settings to visually quantify the risk of intra-abdominal infection. Therefore, taking measures to reduce the incidence of postoperative intra-abdominal infection has important clinical significance.

The NRS200 score is used to assess the nutritional risk of patients. Nutritional risks exist when NRS2002 score ≥3. Such patients may have malnutrition, which will damage their immune and circulatory functions and make them prone to complications. Previous studies have found that in patients with colorectal cancer, a high preoperative NRS200 score can predict the incidence of major postoperative complications,[13] and increase the risk of postoperative anastomotic leakage and incision infection.[14] At the same time, a study included 1063 patients undergoing radical resection of rectal cancer and found that 11.2% of patients had nutritional risk, and NRS2002 >4 points were an independent risk factor for anastomotic leakage after surgery.[15] This study also obtained similar results. Although there was no significant statistical difference in the multivariate analysis, it was found in the univariate analysis that the NRS2002 score ≥3 was a risk factor for intra-abdominal infection.

Lymphocyte count, a well-known indicator of immune status in cancer patients,16 is associated with prognosis in colorectal patients. Colorectal patients with a preoperative lymphocyte count lower than 1700/mm^3 had significantly lower 5-year overall survival after surgery (71.4% vs 81.1%, p=0.002).[17] Not only that, decreased postoperative lymphocyte (<680) also significantly reduced 5-year disease-free survival in colorectal patients (71.1% vs 88.5%, p<0.001).[18] At the same time, LWR<0.18 was an independent risk factor for overall morbidity, multiple morbidities, and severe morbidity after colorectal surgery.19 These results suggest that lymphocyte count or LWR, as a simple preoperative indicator, can better predict the short-term and long-term prognosis of patients with colorectal cancer after surgery. This study also found that preoperative LWR<0.17 is an independent predictor of postoperative intra-abdominal infection and deserves further study.

To date and to our best knowledge, few studies highlight L3FI as a significant risk factor in colorectal cancer patients with intra-abdominal infection. Fat tissue can produce several proteins that play important roles in inflammatory processes, including adiponectin and plasminogen activator inhibitor 1.[20,21] Among them, adiponectin can reduce the production of inflammatory factors such as interleukin-6 and tumor necrosis factor-α by inhibiting the proliferation of bone marrow monocytes and the phagocytic activity of macrophages stimulated by lipopolysaccharide, thus playing an anti-inflammatory role.[22,23] A study has

shown that preoperative low adiponectin concentrations significantly increased postoperative infection rates in colorectal cancer, and adiponectin concentrations can predict postoperative infection. Therefore, patients are prone to intra-abdominal infection when there is low L3FI preoperatively.

Low L3MI usually leads to sarcopenia. Sarcopenia is an adverse factor affecting postoperative outcomes. JR Lieffers found a higher overall postoperative infection risk (23.7% vs 12.5%; p=0.025) and longer length of stay (15.9±14.2 days vs 12.3±9.8 days, p=0.038) in colorectal cancer patients with sarcopenia, meanwhile, sarcopenia was an independent risk factor for postoperative infection.[24] At the same time, sarcopenia was also an independent risk factor for postoperative complications in colorectal cancer, and can significantly increase the rate of non-surgical site infection (p=0.03).[25] What's more, sarcopenia can shorten the long-term survival of colorectal cancer after surgery, including overall survival, disease-free survival, and cancer-specific survival.[26] Combined with the results of this study, low L3MI affects postoperative intra-abdominal infection, measures should be taken to screen and reduce this risk factor in clinical practice.

Serum albumin was not only an important parameter of malnutrition but also reflects body composition (such as skeletal muscle mass and density) and systemic inflammatory response, hypoalbuminemia was associated with greater nutritional risk, low skeletal muscle mass, low skeletal muscle density, and the activation of the systemic inflammatory response, so will cause many complications after surgery.[27-29] A large retrospective study by Lai et al concluded that colorectal cancer patients with preoperative hypoalbuminemia experienced a significant increase in postoperative complications, including abdominal infection caused by anastomotic leakage.[30] In addition, preoperative hypoalbuminemia was associated with increased early postoperative mortality and reduced postoperative 5-year overall survival in colorectal cancer.[27,31] Preoperative optimization is needed for this group of patients.

Limitations

This study has the following limitations: 1. The sample size is small and needs to be expanded; 2. This is a retrospective study, we recommend a prospective study to identify more independent risk factors of intra-abdominal infection; 3. Although the model yielded optimal calibration, the generalizability of this nomogram requires additional validation using other large external cohorts.

Conclusions

In conclusion, a nomogram that collectively considers nutritional and immune status (preoperative albumin, the LWR <0.17, low L3FI and low L3MI) preoperatively was created in this study. Our nomogram is a simple and practical predictor that quantifies the individual risk of intra-abdominal infection. Therefore, gastrointestinal surgeons should try to avoid the above-mentioned high-risk factors, regularly monitor and reduce postoperative intra-abdominal infection to shorten the hospitalization time and reduce the hospitalization expenses of patients.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors have declared that no competing interests exist, and no funding was received.

REFERENCES

1. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol. 1992;13:606-8. doi: 10.1016/s0196-6553(05)80201-9.
2. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36:309-32. doi: 10.1016/j.ajic.2008.03.002.
3. Vignali A, Fazio VW, Lavery IC, Milsom JW, Church JM, Hull TL, Strong SA, Oakley JR. Factors associated with the occurrence of leaks in stapled rectal anastomoses: a review of 1,014 patients. J Am Coll Surg. 1997;185:105-13. doi: 10.1016/s1072-7515(97)00018-5.
4. Walker KG, Bell SW, Rickard MJ, Mehanna D, Dent OF, Chapuis PH, Bokey EL. Anastomotic leakage is predictive of diminished survival after potentially curative resection for colorectal cancer. Ann Surg. 2004;240:255-9. doi: 10.1097/01.sla.0000133186.81222.08.
5. Platell C, Barwood N, Dorfmann G, Makin G. The incidence of anastomotic leaks in patients undergoing colorectal surgery. Colorectal Dis. 2007;9:71-9. doi: 10.1111/j.1463-1318.2006.01002.x.
6. Yamaoka Y, Ikeda M, Ikenaga M, Haraguchi N, Miyake M, Yamamoto K et al. Efficacy of skin closure with subcuticular sutures for preventing wound infection after resection of colorectal cancer: a propensity score-matched analysis. Langenbecks Arch Surg. 2015;400:961-6. doi: 10.1007/s00423-015-1347-2.
7. Pickleman J, Watson W, Cunningham J, Fisher SG, Gamelli R. The failed gastrointestinal anastomosis: an inevitable catastrophe? J Am Coll Surg. 1999;188:473-82. doi: 10.1016/s1072-7515(99)00028-9.
8. Korol E, Johnston K, Waser N, Sifakis F, Jafri HS, Lo M, Kyaw MH. A systematic review of risk factors associated with surgical site infections among surgical patients. PLoS One. 2013;8:e83743. doi: 10.1371/journal.pone.0083743.

9. Benson AB, Venook AP, Al-Hawary MM, Cederquist L, Chen YJ, Ciombor KK et al. NCCN Guidelines Insights: Colon Cancer, Version 2.2018. J Natl Compr Canc Netw. 2018;16:359-69. doi: 10.6004/jnccn.2018.0021.
10. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67:93-9. doi: 10.3322/caac.21388.
11. Palmela C, Velho S, Agostinho L, Branco F, Santos M, Santos MP et al. Body Composition as a Prognostic Factor of Neoadjuvant Chemotherapy Toxicity and Outcome in Patients with Locally Advanced Gastric Cancer. J Gastric Cancer. 2017;17:74-87. doi: 10.5230/jgc.2017.17.e8.
12. Eagye KJ, Nicolau DP. Deep and organ/space infections in patients undergoing elective colorectal surgery: incidence and impact on hospital length of stay and costs. Am J Surg. 2009;198:359-67. doi: 10.1016/j.amjsurg.2008.11.030.
13. Schwegler I, von Holzen A, Gutzwiller JP, Schlumpf R, Mühlebach S, Stanga Z. Nutritional risk is a clinical predictor of postoperative mortality and morbidity in surgery for colorectal cancer. Br J Surg. 2010;97:92-7. doi: 10.1002/bjs.6805.
14. Kwag SJ, Kim JG, Kang WK, Lee JK, Oh ST. The nutritional risk is a independent factor for postoperative morbidity in surgery for colorectal cancer. Ann Surg Treat Res. 2014;86:206-11. doi: 10.4174/astr.2014.86.4.206.
15. Lee SY, Jung MR, Kim CH, Kim YJ, Kim HR. Nutritional risk screening score is an independent predictive factor of anastomotic leakage after rectal cancer surgery. Eur J Clin Nutr. 2018;72:489-95. doi: 10.1038/s41430-018-0112-3.
16. Kozak MM, von Eyben R, Pai JS, Anderson EM, Welton ML, Shelton AA, Kin C, Koong AC, Chang DT. The Prognostic Significance of Pretreatment Hematologic Parameters in Patients Undergoing Resection for Colorectal Cancer. Am J Clin Oncol. 2017;40:405-12. doi: 10.1097/coc.0000000000000183.
17. Iseki Y, Shibutani M, Maeda K, Nagahara H, Tamura T, Ohira G et al. The impact of the preoperative peripheral lymphocyte count and lymphocyte percentage in patients with colorectal cancer. Surg Today. 2017;47:743-54. doi: 10.1007/s00595-016-1433-2.
18. Yamamoto M, Saito H, Uejima C, Tanio A, Takaya S, Ashida K, Fujiwara Y. Combined Pre- and Postoperative Lymphocyte Count Accurately Predicts Outcomes of Patients with Colorectal Cancer. Dig Surg. 2019;36:487-94. doi: 10.1159/000492340.
19. Ang JJ, Chia DKA, Chan DKH. Lymphocyte-White Cell Ratio Is a Novel Marker of Morbidity Following Colorectal Cancer Surgery. J Surg Res. 2021;259:71-8. doi: 10.1016/j.jss.2020.11.027.
20. Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease. Circ Res. 2005;96:939-49. doi: 10.1161/01.res.0000163635.62927.34.
21. Lazar MA. The humoral side of insulin resistance. Nat Med. 2006;12:43-4. doi: 10.1038/nm0106-43.

22. Yokota T, Oritani K, Takahashi I, Ishikawa J, Matsuyama A, Ouchi N et al. Adiponectin, a new member of the family of soluble defense collagens, negatively regulates the growth of myelomonocytic progenitors and the functions of macrophages. Blood. 2000;96:1723-32.
23. Wulster-Radcliffe MC, Ajuwon KM, Wang J, Christian JA, Spurlock ME. Adiponectin differentially regulates cytokines in porcine macrophages. Biochem Biophys Res Commun. 2004;316:924-9. doi: 10.1016/j.bbrc.2004.02.130.
24. Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer. 2012;107:931-6. doi: 10.1038/bjc.2012.350.
25. Nakanishi R, Oki E, Sasaki S, Hirose K, Jogo T, Edahiro K et al. Sarcopenia is an independent predictor of complications after colorectal cancer surgery. Surg Today. 2018;48:151-7. doi: 10.1007/s00595-017-1564-0.
26. Trejo-Avila M, Bozada-Gutiérrez K, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M. Sarcopenia predicts worse postoperative outcomes and decreased survival rates in patients with colorectal cancer: a systematic review and meta-analysis. Int J Colorectal Dis. 2021;36:1077-96. doi: 10.1007/s00384-021-03839-4.
27. Almasaudi AS, Dolan RD, Edwards CA, McMillan DC. Hypoalbuminemia Reflects Nutritional Risk, Body Composition and Systemic Inflammation and Is Independently Associated with Survival in Patients with Colorectal Cancer. Cancers (Basel). 2020;12. doi: 10.3390/cancers12071986.
28. Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. Arch Surg. 1999;134:36-42. doi: 10.1001/archsurg.134.1.36.
29. Franch-Arcas G. The meaning of hypoalbuminaemia in clinical practice. Clin Nutr. 2001;20:265-9. doi: 10.1054/clnu.2001.0438.
30. Lai CC, You JF, Yeh CY, Chen JS, Tang R, Wang JY, Chin CC. Low preoperative serum albumin in colon cancer: a risk factor for poor outcome. Int J Colorectal Dis. 2011;26:473-81. doi: 10.1007/s00384-010-1113-4.
31. Haskins IN, Baginsky M, Amdur RL, Agarwal S. Preoperative hypoalbuminemia is associated with worse outcomes in colon cancer patients. Clin Nutr. 2017;36:1333-8. doi: 10.1016/j.clnu.2016.08.023.

Table 1. Patient baseline characteristics and surgery-related factors

Characteristics	Value
Patients (n)	402
Age (years)	59.6±11.3
Gender (n)	
Male/Female	248/154
BMI (kg/m^2)	23.3±3.1
BMI group, n (%)	
<18.5	28 (7.0)
18.5-25	274 (75.1)
>25	100 (24.9)
NRS 2002 score, n (%)	
<3	286 (71.1)
≥3	116 (28.9)
ASA score	
1-2	370 (92.0)
≥3	32 (8.0)
Diabetes, n (%)	
Yes	42 (10.4)
No	360 (89.6)
Disease	
Colon cancer	220 (54.7)
Rectal cancer	182 (45.3)
Preoperative	
Hemoglobin (g/L)	124.5±22.6
Albumin (g/L)	44.3±32.5
CRP (mg/L)	4.0±8.9
WBC (×10^9 cells/L)	7.12±2.41
Lymphocyte (×10^9 cells/L)	1.61±0.83
Neoadjuvant chemotherapy, n (%)	
Yes	144 (35.8)
No	258 (64.2)
Radiotherapy, n (%)	
Yes	82 (20.4)
No	320 (79.6)
Surgery, n (%)	
Laparoscope	78 (19.4)
Laparotomy	324 (80.6)
TNM stage, n (%)	
I	66 (16.4)
II	200 (49.8)
III	136 (33.8)
Intra-abdominal infection, n (%)	
Yes	46 (11.4)
No	356 (88.6)

BMI: body mass index; ASA: American society of Anesthesiologists; CRP: C-reactive protein; WBC: white cell count.

Table 2. The characteristics of participating chefs and cooks (n=90)

Factors	Intra-abdominal infection (n=46)	No intra-abdominal infection (n=356)	*p* value
Age (years)	64.4±8.3	59.0±11.5	<0.001***
Gender, n (%)			0.452
Male	38 (9.5)	210 (52.2)	
Female	28 (7.0)	126 (31.3)	
BMI (kg/m^2)	23.1±3.3	23.3±3.1	0.719
BMI group, n (%)			0.801
<18.5	4 (1.0)	24 (6.0)	
18.5-25	32 (8.0)	242 (60.2)	
>25	10 (2.5)	90 (22.3)	
NRS 2002 score, n (%)			<0.001***
<3	22 (5.5)	264 (65.7)	
≥3	24 (6.0)	92 (22.8)	
ASA score, n (%)			0.845
1-2	42 (10.4)	328 (81.6)	
≥3	4 (1.0)	28 (7.0)	
Diabetes, n (%)			0.541
Yes	6 (1.5)	36 (9.0)	
No	40 (10.0)	320 (79.5)	
Disease, n (%)			
Colon cancer	22 (5.4)	198 (49.3)	0.318
Rectal cancer	24 (6.0)	158 (39.3)	
Preoperative			
Hemoglobin (g/L)	122.7±22.9	138.0±14.3	<0.001***
Albumin (g/L)	34.6±4.3	45.5±6.5	0.132
CRP (mg/L)	3.1±4.3	4.1±9.3	0.481
WBC (×10^9 cells/L)	6.78±2.46	6.95±2.42	0.331
Lymphocyte (×10^9 cells/L)	1.53±0.87	1.86±0.86	0.045*
LWR	0.229±0.12	0.275±0.10	0.042*
LWR <0.17, n (%)	20 (43.5)	70 (19.7)	0.001**
Neoadjuvant chemotherapy, n (%)			0.143
Yes	12 (3.0)	132 (32.8)	
No	34 (8.5)	224 (55.7)	
Radiotherapy, n (%)			0.139
Yes	4 (1.0)	78 (19.4)	
No	42 (10.4)	278 (69.2)	
Type of procedure, n (%)			0.07
Laparoscope	32 (8.0)	292 (72.6)	
Laparotomy	14 (3.5)	64 (15.9)	
Combined multiple organ resection, n (%)			<0.001***
Yes	16 (4.0)	14 (3.5)	
No	30 (7.4)	342 (85.1)	
intestinal obstruction, n (%)			<0.001***
Yes	12 (3.0)	16 (4.0)	
No	34 (8.5)	340 (88.5)	
Blood loss (mL)	79.7±69.7	63.0±20.3	0.001**
TNM stage, n (%)			0.333
I	6 (1.5)	60 (14.9)	
II	20 (5.0)	180 (44.8)	
III	20 (5.0)	116 (28.8)	
L3FI (cm^2/m^2)	44.0±10.8	67.7±23.2	<0.001***
L3MI (cm^2/m^2)	36.5±6.5	44.7±6.3	<0.001***
Remove postoperatively drainage tube (days)	12.8±9.6	7.2±3.1	<0.001***
LOS postoperative (days)	22.5±10.0	9.7±4.0	<0.001***
Total expenses (ten thousand CYN)	22.3±48.6	9.3±8.1	<0.001***

BMI: body mass index; ASA: American society of Anesthesiologists; LWR: lymphocyte-white cell ratio; L3FI: third lumbar spine subcutaneous fat mass index; L3MI: third lumbar spine skeletal muscle mass index; LOS: length of stay; CYN: Chinese Yuan.
*p<0.05, **p<0.01, ***p<0.001.

Table 3. Univariate analysis of the characteristics of the patients with and without intra-abdominal infection

Factors	OR	95% CI	*p* value
Age (years)			
<65	Reference		
≥65	1.85	0.77-4.44	0.169
BMI 18.5-25	Reference		
BMI <18.5	1.2	0.41-3.44	0.748
BMI >25	0.8	0.16-3.87	0.775
NRS 2002 score <3	Reference		
NRS 2002 score ≥3	3.1	1.28-3.58	0.01*
ASA score 1-2	Reference		
ASA score ≥3	1.1	0.24-5.36	0.89
Diabetes			
No	Reference		
Yes	1.3	0.36-4.93	0.666
Albumin (g/L)	1.354	1.21-1.51	<0.001***
LWR			
<0.17	Reference		
≥0.17	3.14	1.27-7.76	0.013*
Neoadjuvant chemotherapy			
Yes	Reference		
No	1.7	0.63-4.45	0.305
Radiotherapy			
No	Reference		
Yes	2.9	0.16-2.9	0.156
Type of procedure			
Laparoscope	Reference		
Laparotomy	1.9	0.76-5.23	0.161
Multiple organ resection			
No	Reference		
Yes	13.0	4.15-40.88	<0.001***
Intestinal obstruction			
No	Reference		
Yes	7.5	2.33-24.17	0.001**
TNM stage			
I	Reference		
II	1.7	0.44-6.74	0.434
III	1.6	0.61-3.96	0.358
Low L3FI			
No	Reference		
Yes	30.4	8.52-108.57	<0.001***
Low L3MI			
No	Reference		
Yes	30.1	10.04-90.42	<0.001***

BMI: body mass index; ASA: American society of Anesthesiologists; LWR: lymphocyte-white cell ratio; L3FI: third lumbar spine subcutaneous fat mass index; L3MI: third lumbar spine skeletal muscle mass index; OR: odds ratio; CI: confidence interval.
*p<0.05, **p<0.01, ***p<0.001.

Table 4. Multivariate analysis

Factors	OR	95% CI	*p* value	*p* for interaction
Albumin (g/L)	1.32	1.16-1.51	<0.001***	<0.001***
LWR				
<0.17	Reference			
≥0.17	5.84	1.08-31.66	0.041*	0.404
Low L3FI				
No	Reference			
Yes	28.48	4.71-172.24	<0.001***	<0.001***
Low L3MI				
No	Reference			
Yes	15.10	2.91-78.35	0.001**	<0.001***

LWR: lymphocyte-white cell ratio; L3FI: third lumbar spine subcutaneous fat mass index; L3MI: third lumbar spine skeletal muscle mass index; OR: odds ratio; CI: confidence interval.
*p<0.05, **p<0.01, ***p<0.001.

Table 5. Area under the curve for predictive factors in the cohort

Factors	AUC	95% CI
albumin	0.897	0.816-0.977
LMR<0.17	0.619	0.489-0.750
Low L3FI	0.845	0.759-0.931
Low L3MI	0.838	0.736-0.940
Nomogram	0.931	0.815–0.971

AUC: Area under the curve; LWR: lymphocyte-white cell ratio; L3FI: Third lumbar paralumbar subcutaneous fat mass index; L3MI: Third lumbar paralumbar skeletal muscle mass index; CI: confidence interval.

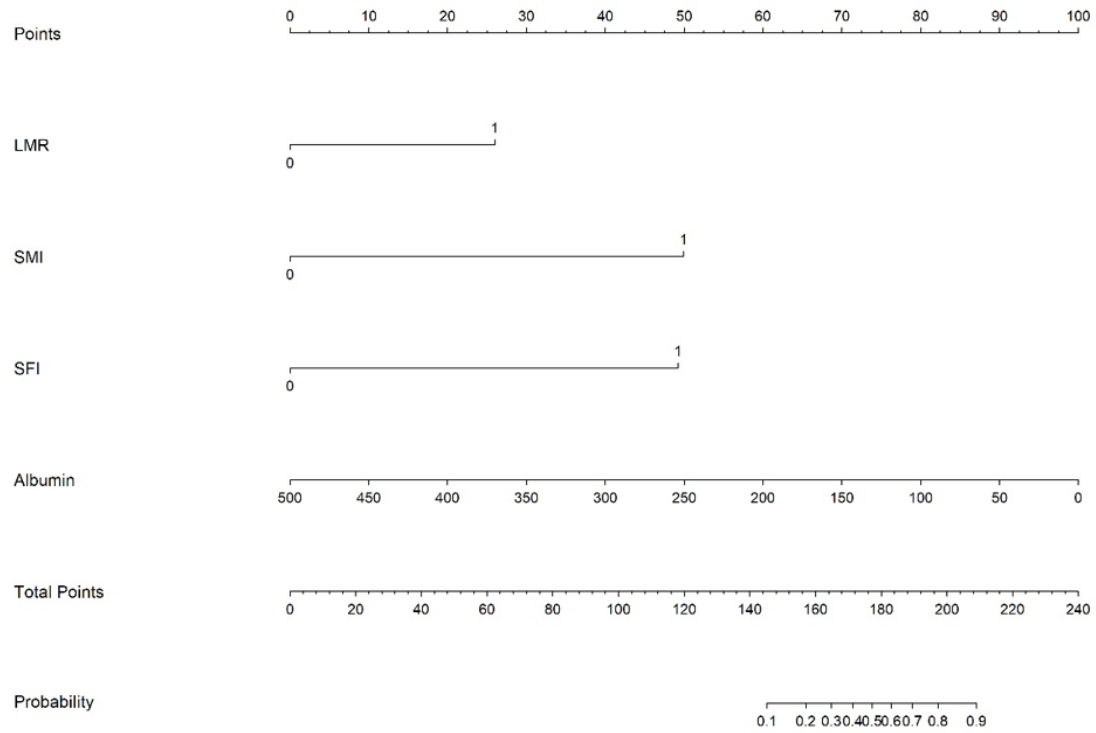


Figure 1. Nomogram for prediction of postsurgical intra-abdominal infection in patients with colorectal cancer. LMR 0: LMR ≥0.17, LMR 1: LMR <0.17; SMI 0: no low SMI, SMI 1: low SMI; SFI 0: no low SFI, SMI 1: low SFI; Albumin: g/dL.

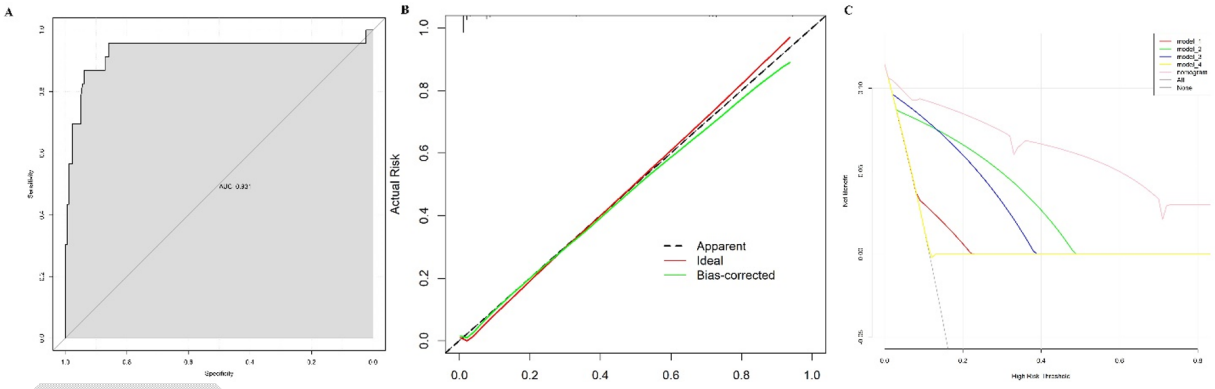
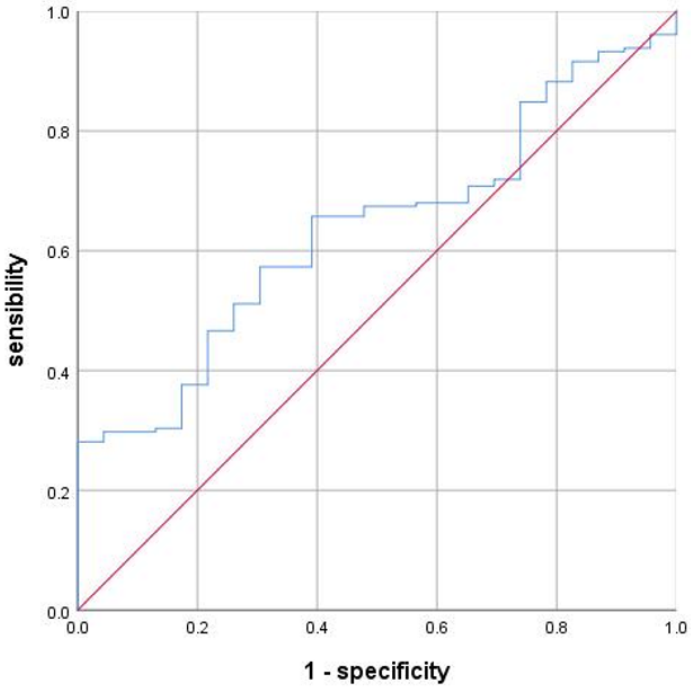


Figure 2. Measures of accuracy of the nomogram for the prediction in the cohort. (A) Discrimination based on ROC with C-index = 0.893 (95% confidence interval 0.815–0.971) in the cohort (B) The calibration curves for the nomogram. The x axis represents the nomogram predicted probability and y axis represents the actual probability of intra-abdominal infection. (C) Decision curve analysis of the nomogram and risk factors alone. Model_1 LMR, Model_1 SMI, Model_3 SFI, Model_4 albumin.

Supplementary Figure and Tables



Supplemental Figure 1. ROC modeling LWR against any intra-abdominal infection. The ROAUC for LWR is 0.635.

Supplementary Table 1. Management of postoperative intra-abdominal infection

Management	Number
Reoperation drainage	8
Image-guided percutaneous drainage	8
Continuous irrigation of double cannula	30
Antibiotics	46
Nutritional support	38

Supplementary Table 2. Frequency of culture of organisms from peritoneal fluid in the patients with intra-abdominal infection

Microorganism	Number (%)
Gram-negative bacteria	36 (75.0)
Escherichia coli	16 (33.2)
Acinetobacter baumannii	2 (4.2)
Enterobacter aerogenes	2 (4.2)
Klebsiella pneumoniae	6 (12.5)
Citrate bacterium floretis	2 (4.2)
Shewanella putrefaciens	2 (4.2)
Enterobacter cloacae	2 (4.2)
Serratia marcescens	4 (8.3)
Gram-positive bacteria	12 (25.0)
Streptococcus pneumoniae	2 (4.2)
Enterococcus faecalis	4 (8.3)
Staphylococcus aureus	4 (8.3)
Enterococcus avium	2 (4.2)