

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2024 October 27; 16(10): 3074-3380



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The primary aim of *World Journal of Gastrointestinal Surgery* (WJGS, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

INDEXING/ABSTRACTING

The WJGS is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for WJGS as 1.8; JIF without journal self cites: 1.7; 5-year JIF: 1.9; JIF Rank: 126/292 in surgery; JIF Quartile: Q2; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Zi-Hang Xu, Production Department Director: Xiang Li, Cover Editor: Jia-Ru Fan.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Peter Schemmer

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

October 27, 2024

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Influencing factors and preventive measures of infectious complications after intestinal resection for Crohn's disease

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Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade C

Novelty: Grade B

Creativity or Innovation: Grade B

Scientific Significance: Grade B

P-Reviewer: Ntawuyamara E

Received: March 21, 2024

Revised: August 28, 2024

Accepted: September 13, 2024

Published online: October 27, 2024

Processing time: 190 Days and 23.8 Hours



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Abstract

The incidence of Crohn's disease (CD) has increased in recent years, with most patients requiring intestinal resection. Complications after intestinal resection for CD can lead to poor prognosis and recurrence, among which infectious complications are the most common. This study aimed to investigate the common risk factors, including medications, preoperative nutritional status, surgery-related factors, microorganisms, lesion location and type, and so forth, causing infectious complications after intestinal resection for CD, and to propose corresponding preventive measures. The findings provided guidance for identifying susceptibility factors and the early intervention and prevention of infectious complications after intestinal resection for CD in clinical practice.

Key Words: Crohn's disease; Intestinal resection; Postoperative infectious complications; Influencing factors; Preventive measures

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Core Tip: Infectious complications after intestinal resection for Crohn's disease (CD) can lead to a variety of adverse outcomes such as prolonged hospitalization, increased readmission rates, poor prognosis, and increased health-care burden in these patients. Therefore, identifying the risk factors for infectious complications and their early prevention are essential. This study aimed to investigate the risk factors, such as medications, preoperative nutritional status, and others, causing infectious complications after intestinal resection for CD, and to propose corresponding preventive measures. The findings provided guidance for reducing the occurrence of infectious complications.

Citation: Lv SR, Huang X, Zhou LY, Shi J, Gong CC, Wang MK, Yang JS. Influencing factors and preventive measures of infectious complications after intestinal resection for Crohn's disease. *World J Gastrointest Surg* 2024; 16(10): 3363-3370

URL: <https://www.wjgnet.com/1948-9366/full/v16/i10/3363.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v16.i10.3363>

TO THE EDITOR

Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract caused by complex interactions between genetic susceptibility, environmental factors, and alterations in the intestinal microbiota[1]. The incidence of CD has increased globally due to environmental exposure factors such as urbanization or advances in diagnostic methods[2]. As a progressive disease, most patients with CD develop complications such as strictures, fistulas, or abscesses, and approximately 80% of these patients require intestinal resection surgery[3,4]. Moreover, the incidence of postoperative complications, such as postoperative ileus, bleeding at the anastomosis site, intra-abdominal sepsis, and entero-cutaneous fistula, after surgery for CD is higher than that after other surgeries due to the disease characteristics and the fact that patients with CD are often malnourished[5]. Postoperative complications in patients with CD affect surgical outcomes, length of hospitalization, and prognosis, which are closely related to short- and long-term clinical outcomes of patients[6].

A recent study used an improved machine learning algorithm, specifically the randomized forest analysis model, in patients with CD after intestinal resection to predict the likelihood of short-term major complications, including anastomotic fistula, intra-abdominal septic complication (IASC), bleeding, and intestinal obstruction[7]. Thus, infectious complications after intestinal resection in CD are important risk factors. According to previous studies, the incidence of postoperative complications in patients with all types of CD ranges from 5.7% to 50%, with infectious postoperative complications being the most common[8,9]. The main postoperative infectious complications in CD include surgical site infections (SSIs) and extra-abdominal infections. Further, SSIs encompass superficial wound infections, deep wound infections affecting the fascia, and organ space infections such as IASCs and anastomotic leakage[10]. SSIs are a significant cause of morbidity and mortality and exert a considerable impact on both patients and the health-care system, including discomfort, prolonged hospitalization, increased readmission rates, adverse health outcomes, and increased health-care burden[11-13].

A few studies have reported on the factors influencing infectious complications after intestinal resection for CD, which mainly included preoperative nutritional status, medication, surgical methods, and so forth[14-16]. However, the results of the recent studies are still inconsistent and lack systematization. Therefore, in this study, we discussed the main influencing factors and preventive measures of infectious complications after intestinal resection for CD to provide a certain suggestion and guidance for reducing postoperative infectious complications of CD.

METHODOLOGY

The PubMed databases were searched for studies published in English. The following key terms were used to identify studies related to postoperative infectious complications in CD: CD, intestinal resection, postoperative complications, infectious complications, SSIs, IASCs, and postoperative anastomotic fistula. These key terms were combined and searched using the set operators "AND" and "OR". After removing duplicate studies, 240 studies published between Jan 2000 and Mar 2024 were retrieved. Of these, 45 discussions of testing techniques or surgical options, 11 case reports, 18 reviews, and 29 discussions of postoperative recurrence were excluded. Further, descriptive studies and studies that combined infectious complications with other complications were excluded, and ultimately 59 relevant studies were included for analysis. Further references were added by manually searching the relevant studies. For the studies considered appropriate for inclusion, the available texts were obtained and assessed in detail. The final studies were selected based on discussed consensus among all authors followed by our medical professional knowledge.

PREDICTING METHODS

A few previous studies were conducted to predict factors affecting postoperative complications in CD using various methods. A study used univariate and multiple regression to determine the risk factors for short-term postoperative complications in CD. The findings revealed that elevated preoperative C-reactive protein (CRP) and decreased

postoperative hemoglobin levels increased the possibility of postoperative complications[17]. Another French prospective study also used multivariate logistic regression analysis and found that preoperative corticosteroid treatment within the 4 weeks prior to surgery was significantly associated with an increased incidence of postoperative complications[9]. Several studies also used multivariate logistic regression analysis to explore the risk factors associated with postoperative infectious complications in CD. These studies found that preoperative albumin levels, anemia, and length of surgery were associated with postoperative infectious complications[16,18,19].

Wang *et al*[7], in their retrospective study, used machine learning methods, particularly random forest methods, to predict postoperative complications in CD, including anastomotic fistula, IASC, bleeding, and intestinal obstruction. They found that both nomogram and random forest performed well in predicting short-term major postoperative complications and preoperative CD activity index (CDAI) ≥ 220 reduced preoperative serum albumin levels and prolonged operative time, which were probably the most critical variables. The aforementioned findings might help identify patients at higher risk of complications and provide appropriate perioperative management to improve patient prognosis and reduce the incidence of complications, especially infectious complications.

INFLUENCING FACTORS

Medications

CD can be treated with multiple medications, including steroids, immunosuppressants, biologics, and others, depending on the site and severity of its onset. As the mechanism of aforementioned medicines is immunosuppression, an increased risk of infection in patients is expected[20]. Few studies have been conducted on the effect of medications on infectious complications after intestinal resection for CD. Several studies showed that preoperative or postoperative use of steroids or immunosuppressive medicines was associated with the development of infectious complications after intestinal resection for CD[18,21,22]; on the contrary, some other studies did not report this association[23]. Biologic agents, mainly including anti-tumor necrosis factor [anti-tumor necrosis factor- α (TNF- α)], infliximab, and vedolizumab, are effective treatments for CD. However, some studies demonstrated that preoperative use of anti-TNF- α or infliximab before intestinal resection for CD, especially within 8 weeks before surgery, was associated with an increased incidence of postoperative infectious complications, including intra-abdominal abscesses and anastomotic fistulae[24-27]. Other studies, in contrast, did not find an association between anti-TNF- α , infliximab, vedolizumab, and the development of postoperative infectious complications[15,28,29]. Moreover, one study found that specific classes of biologic therapy did not independently increase the risk of postoperative infectious complications, yet combined immunosuppression increased the overall risk of infectious complications and the incidence of intra-abdominal sepsis[30]. Differences in the results of these studies might be due to the medicine type, dose, timing of medication, endpoint, and other confounding factors.

Preoperative nutritional indicators

CD, as a wasting disease, is often accompanied by malnutrition, with a prevalence ranging from 20% to 85%[30]. Nutritional status is closely related to infectious diseases. Therefore, the association between preoperative nutritional status and postoperative infectious complications in patients with CD undergoing intestinal resection is important to investigate. A Chinese study found that body mass index (BMI) < 17.5 kg/m² was a risk factor for infectious complications after intestinal resection for CD[31]. Although CD is a wasting disease, the obesity rate in its patients is similar to that in the general population[32]. Several studies have found that BMI ≥ 30 kg/m² is also a risk factor for postoperative infectious complications in CD[18,33]. Moreover, subcutaneous fat thickness and fat distribution are important indicators for assessing the nutritional status. Two studies have demonstrated that an increase in subcutaneous fat thickness or increased proportion of subcutaneous fat relative to visceral fat volume distributed more in the thoracic *vs* lumbar spinal regions is a significant predictor of incisional SSI or other infectious complications after intestinal resection for CD[34,35]. Furthermore, although albumin is not a direct indicator of nutritional status, it may reflect systemic inflammation, protein loss, malnutrition, and so forth. Thus, it can indirectly reflect the preoperative nutritional status of patients. Moreover, serum albumin is important for wound healing and collagen synthesis at the anastomotic site, and hypoproteinemia may result in potentially poor wound healing and anastomotic fistulae[3]. A number of studies have shown that preoperative hypoalbuminemia (albumin < 30 g/L) is associated with a higher incidence of IASCs or SSI after intestinal resection for CD[16,22,36-38]. In addition, preoperative anemia has also been found to be a predictor of septic complications. The aforementioned studies suggest that either preoperative malnutrition or obesity is a potential risk factor for infectious complications after intestinal resection for CD.

Surgery-related factors

Besides other factors in the perioperative period, factors directly related to intestinal resections for CD were also associated with postoperative infectious complications, such as emergent surgery, duration of surgery, previous surgery, perioperative drainage, and surgical approach. Urgent surgery was found to be associated with an increased risk of postoperative complications in CD, with wound infection, intra-abdominal abscesses, and anastomotic fistulae being the most common complications[39]. A Japanese study found that a surgery time of more than 180 min was associated with an increased risk of intra-abdominal sepsis after intestinal resection for CD. A Chinese study also showed that prolonged surgery time was a risk factor for SSI[19,38]. Another study explored the impact of various surgery-related factors on the occurrence of SSI after surgery for CD, and found that prolonged surgery was associated with SSI and active drainage was related to a reduced risk of organ/space SSI[40]. Preoperative percutaneous abscess drainage was also found to

significantly reduce the incidence of postoperative severe IASC in patients with CD[41]. In addition, a previous history of intestinal resection was shown to be a risk factor for postoperative complications in patients with CD[42]. A meta-analysis also suggested that a history of previous surgery was associated with an incidence of postoperative IASC in CD[22].

Microorganisms

Intestinal microorganisms play a role in the postoperative recurrence of CD and have been associated with the development of postoperative anastomotic fistulae in colorectal surgery[43,44]. Therefore, a potential relationship may be found between intestinal microorganisms and the development of infectious complications after intestinal resection for CD. A prospective cohort study used random forests to predict the impact factors for infectious complications at the surgical site after intestinal resection for CD. The findings revealed that the intestinal microbiota was the top selected variable, and the model containing 14 genera of microbiota had the largest area under the curve[45]. *Clostridium difficile* (*C. difficile*) is an anaerobic, Gram-positive bacterium detected in the intestines of up to 30% of patients with inflammatory bowel disease (IBD), and its infection or colonization is common in patients with CD. Studies have found that patients with IBD with *C. difficile* infection are at higher risk of worse outcomes than those without *C. difficile* infection[46]. A study on pediatric patients with CD showed that *C. difficile* infection was associated with earlier timing of intestinal resection surgery in patients[47]. For infectious complications, a study used propensity score-weighted analysis to explore the impact of *C. difficile* infection on outcomes in patients with IBD who underwent colon resection and found that *C. difficile* infection was associated with an increased risk of SSI, sepsis, and infectious shock[48].

Lesion type and location

CD involves a wide range of lesions, including upper gastrointestinal tract, ileum, colon, and perianal lesions, and the types of lesions are categorized as stenotic and penetrating. Different lesion locations and types may result in different risks of postoperative complications. Studies found that patients with CD combined with perianal lesions were at higher risk for re-surgery[49], and those involving upper gastrointestinal tract lesions were more likely to have IASCs after intestinal resection[37]. Moreover, a study found that patients with CD who had colonic or ileocolonic involvement were more likely to develop SSIs after intestinal resection than those with only ileal involvement[40]. According to a study, penetrating CD is associated with a higher risk of postoperative complications of intestinal resections[39]. Similarly, a retrospective Japanese study found that penetrating intestinal lesions of CD increased the risk of IASCs after intestinal resection[19]. In addition, the CDAI, which comprehensively assesses the activity level of CD, can also be used as a predictor of postoperative complications in CD. Wang *et al*[7] found that preoperative CDAI of ≥ 220 was a risk factor for postoperative complications after intestinal resection, including infectious complications. Another Chinese study also found that a CDAI of > 150 was a high-risk factor for anastomotic infectious complications after intestinal resection for CD[50].

Other factors

Besides the aforementioned factors, other factors have been found to be associated with infectious complications after intestinal resection for CD; however, related studies are limited. For example, two studies suggested that perioperative blood transfusions could lead to an increased risk of postoperative infectious complications in CD, which might be related to transfusion-induced immunosuppression[51,52]. Moreover, inflammatory markers, including preoperative CRP and postoperative interleukin-6, can be used as infectious predictors of CD after bowel resection[16,53]. Influencing factors of infectious complications after intestinal resection for CD are summarized in Figure 1.

PREVENTIVE MEASURES

Medication management

A few studies have proposed preventive measures for the aforementioned risk factors associated with infectious complications after intestinal resection for CD. The use of immunosuppressive medications within 4 weeks prior to intestinal resection has been associated with a higher incidence of sepsis, infectious shock, and anastomotic leakage in patients with CD. Hence, an appropriate preoperative drug-free interval may be able to reduce the risk of infection[21].

Improving malnutrition

Preoperative poor nutritional status is associated with an increased risk of infectious complications after intestinal resection of CD. Patients should be assessed for malnutrition using the Malnutrition Universal Screening Tool criteria or the Nutrition Risk Screening 2002[54]. Natural dietary supplements, such as vitamins, minerals, and probiotics, should be prescribed to improve nutritional status and antioxidant, antiviral, and anti-inflammatory effects, which benefit immune regulation[55]. A meta-analysis, including multiple studies, demonstrated that preoperative enteral nutrition reduced the incidence of infectious complications after intestinal resection surgery in patients with CD[56].

Surgical conditions

The operating room environment and related equipment should be maintained strict hygiene. Medical staff should pay attention to hand hygiene, environmental disinfection, preoperative skin disinfection, and standardized aseptic operation, as these measures are essential for controlling SSIs[55]. Mechanical bowel preparation procedures could be conducted before surgery[57]. In addition, the use of a dual-ring wound protector during surgery or postoperative active drainage

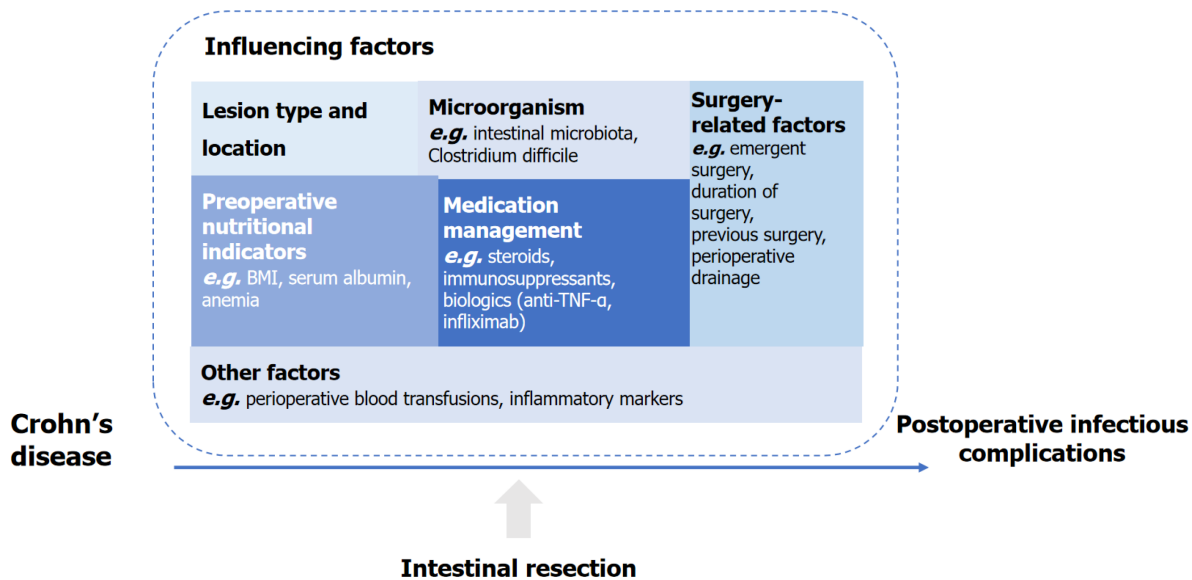


Figure 1 Influencing factors of infectious complications after intestinal resection for Crohn's disease. BMI: Body mass index; TNF- α : Tumor necrosis factor- α .

was a surgery-related factor that reduced infectious complications after intestinal resection[40,58].

Microbial prophylaxis

Intestinal microbiota and microbial infections are associated with postoperative complications in CD. Therefore, therapeutic or prophylactic interventions targeting intestinal microorganisms, especially pathogenic infections such as *C. difficile*, can reduce the risk of postoperative complications. A randomized controlled study demonstrated that appropriate preoperative antibiotic prophylaxis can significantly reduce the incidence of postoperative incisional SSIs[57].

Integrated strategies

Beyond preventive measures targeting an individual risk factor, a retrospective study suggested that individualized prehabilitation, including nutritional support, antibiotic therapy or abscess drainage, and cessation or reduction of corticosteroid therapy, prior to intestinal resection could reduce the incidence of anastomotic complications in patients with high-risk CD[59]. Therefore, implementing personalized pre- and post-surgical preventive measures targeting the aforementioned risk factors for patients with CD with intestinal resection may be an effective way to reduce postoperative infectious complications. The multidisciplinary team can provide patients with nutritional optimization protocols, medication guidance, and so forth to reduce preoperative risk factors, and apply an individualized approach to each situation.

CONCLUSION

Infectious complications after intestinal resection for CD are influenced by a variety of factors, including preoperative nutrition, medication use, microorganisms, surgery-related factors, and others. Medication management, improving malnutrition and surgical conditions, microbial prophylaxis, and integrated strategies could be implemented in clinical practice as preventive measures to reduce the incidence of postoperative infectious complications.

ACKNOWLEDGEMENTS

We thank Xue-Lu Yu and other colleagues, the reviewers, and the editors for improving this manuscript.

FOOTNOTES

Author contributions: Wang MK and Yang JS conceptualized, designed, and revised the manuscript; Lv SR and Huang X drafted the manuscript; Zhou LY, Shi J and Gong CC collected and summarized the literature. All authors have read and approved the final manuscript. Lv SR and Huang X wrote the draft, and contributed equally to this work as co-first authors. Both Wang MK and Yang JS conceptualized, proposed, and supervised the whole process of this manuscript, and played important and indispensable roles in the manuscript preparation and revision as the co-corresponding authors. Wang MK applied for and obtained the funds for this research project. Wang MK conceptualized, designed, and supervised the whole process of the project. He searched the literature, and revised

and submitted the early drafts of the manuscript. Yang JS was instrumental and responsible for the comprehensive literature search, preparation, and submission of the current version of the manuscript. This collaboration between Wang MK and Yang JS is crucial for the publication of this manuscript and other manuscripts still in preparation.

Supported by Scientific Research Foundation of Shanghai Municipal Health Commission of Changning District, No. 20234Y038.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

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S-Editor: Qu XL

L-Editor: A

P-Editor: Zhao S

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