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The Impact of Preoperative Anti-TNF Therapy on Postoperative Complications in Crohn's Disease: A Systematic Review

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 June 2024 and was last updated on 09 June 2024.

INTRODUCTION

Review question / Objective To investigate whether the use of anti-TNF therapy before surgery affects the incidence of postoperative complications in Crohn's disease. If there is an impact, which types of surgical complications are affected? How long before surgery should the therapy be discontinued to ensure safety?

Rationale Most Crohn's disease patients undergo medical treatment before surgery, often involving one or more medications. Among these, anti-TNF drugs are the earliest and most widely used biologics, typically prescribed for moderate to severe Crohn's disease. Many surgical patients, who generally have severe disease, have used anti-TNF therapy prior to surgery. However, it remains unclear whether preoperative anti-TNF

therapy is associated with the incidence of postoperative complications in Crohn's disease. In clinical practice, there is a lack of effective evidence to guide clinicians on whether to continue or discontinue anti-TNF drugs before surgery. Therefore, this analysis aims to assist clinicians in addressing this issue.

Condition being studied Inflammatory bowel disease, including Crohn's disease and ulcerative colitis, is characterized by chronic inflammation of the intestines and extraintestinal complications. Previous studies have often combined these two conditions without clear differentiation. However, they differ in pathogenesis and treatment approaches, making it seemingly inappropriate to merge them in discussions. The advent of biologics, represented by anti-TNF drugs, has brought new hope for the treatment of Crohn's disease. Research indicates that 70% of Crohn's

disease patients still require surgical intervention during their lifetime. Most patients have undergone various drug therapies before surgery. Existing studies suggest that preoperative steroid use increases postoperative complications in Crohn's disease, but the impact of anti-TNF therapy on postoperative complications remains unclear, with contradictory results from different studies. For elective surgery patients, whether to discontinue anti-TNF therapy before surgery and for how long to discontinue it to reduce postoperative complications remain unclear.

METHODS

Search strategy Relevant studies were retrieved through computerized searches of electronic databases including PubMed, Web of Science, and Embase. When necessary, additional literature and references from key studies were reviewed to include potential related research. The search period was from the establishment of the databases up to May 31, 2024.

Participant or population Adults (age ≥ 18 years) diagnosed with Crohn's disease who have undergone surgery related to Crohn's disease.

Intervention Received anti-TNF therapy (infliximab, adalimumab, golimumab, or certolizumab) within 12 months prior to surgery.

Comparator Did not receive anti-TNF therapy within 12 months prior to surgery.

Study designs to be included Randomized controlled trials, prospective cohort studies, retrospective studies, case-control studies, cross-sectional studies, and case reports with a case series of more than 10 cases.

Eligibility criteria Studies meeting the following criteria were included in the meta-analysis:

1. Adult patients diagnosed with Crohn's disease.
2. Underwent surgery related to Crohn's disease.
3. Received or did not receive anti-TNF therapy within 12 months prior to surgery.
4. Compared the postoperative complications between patients who received anti-TNF therapy before surgery and those who did not.

Exclusion criteria:

1. Inaccessible full-text articles.
2. Studies that did not distinguish between ulcerative colitis and Crohn's disease and discussed them together.

Information sources The electronic databases PubMed, Web of Science, and Embase were

searched. In addition, efforts were made to contact authors for access to full-text articles. Abstracts from conference proceedings were also considered. Manuscripts that have been accepted but not yet published were included in the search. Time to readmission within 30 days of surgery, time to reoperation within 30 days of surgery, and length of postoperative hospital stay.

Main outcome(s) Postoperative complications occurring within 30 days include infectious complications (such as wound infection, intra-abdominal abscess, intra-abdominal leak, and extraperitoneal infections), non-infectious complications (including small bowel obstruction, gastrointestinal bleeding, and venous thromboembolism), and other complications (such as new-onset organ failure and neurological complications).

Additional outcome(s) Time to readmission within 30 days of surgery, time to reoperation within 30 days of surgery, and length of postoperative hospital stay.

Data management Data retrieval and extraction will be independently conducted by two researchers, with disagreements resolved through consensus or with the assistance of a third researcher.

Data retrieval: Relevant literature will be screened by reading titles, abstracts, and full texts, and imported into Endnote or Zotero reference management databases. Duplicate articles will be removed. Cohen's Kappa coefficient will be calculated separately after each selection stage.

Data extraction: A standardized data table will be created to summarize research data. The research table will include the following:

1. Basic information of included studies (first author, publication year, country, study type).
2. Characteristics of the study population (number of patients, age, gender, anthropometric characteristics such as height and weight).
3. IBD classification, disease severity, preoperative treatment, surgical methods, duration of surgery, length of hospital stay, postoperative complications, readmission rate, and reoperation rate.

Quality assessment / Risk of bias analysis Two researchers will independently assess the risk of bias for each included study. The Cochrane Risk of Bias Assessment Tool (ROB2) will be used for randomized trials. The ROBINS-I tool will be used for non-randomized studies, with reasons for decisions recorded in cases where outcomes differ.

Strategy of data synthesis 1. Patients who received anti-TNF- α therapy before surgery will be compared to a control group (no treatment). A random-effects model will be used to summarize the effect size. For dichotomous data, the event rates in both groups will be reported, and odds ratios (ORs) with 95% confidence intervals (CIs) will be calculated. For continuous data, the mean difference (MD) with 95% CIs will be calculated. Statistical tests will be conducted at a significance level of 0.05.

2. Forest plots will be used to display the results.

3. Statistical heterogeneity will be assessed using Cochran's Q and I^2 statistics. If the p-value is < 0.1, heterogeneity will be considered significant. Subgroup or sensitivity analyses may be performed if substantial heterogeneity exists.

4. Publication bias will be evaluated by creating and visually assessing funnel plots.

Subgroup analysis The plan is to conduct subgroup analyses based on different biologic therapies and the time interval from the last use of anti-TNF therapy to surgery, categorized as >12 weeks and <12 weeks.

Sensitivity analysis The sensitivity analysis will be conducted as follows:

1. Trying different analytical models, such as the fixed-effect model, to observe whether the results are influenced by model selection.

2. Gradually excluding each included study and observing whether the point estimate of the pooled effect size falls outside the 95% confidence interval of the overall pooled effect size.

Language restriction Studies published exclusively in English.

Country(ies) involved China.

Keywords Anti-TNF therapy, postoperative complications, Crohn's Disease.

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