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Effect of preoperative oral nutritional supplements on clinical outcomes in patients undergoing surgery for gastrointestinal cancer

A systematic review and meta-analysis

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Abstract

Background: The clinical benefit of preoperative oral nutritional supplements (ONS) in patients undergoing surgery for gastrointestinal cancer remains controversial.

Objective: To evaluate the effect of preoperative ONS on postoperative clinical outcomes in patients with gastrointestinal cancer.

Methods: We searched PubMed, EMBASE, Web of Science, Cochrane Library, Scopus, and the Chinese National Knowledge Infrastructure databases for randomized controlled trials evaluating preoperative ONS in patients undergoing surgery for gastrointestinal cancer from inception until April 2024. Two researchers independently assessed the quality of the included literature and performed statistical analyses using Review Manager 5.4 software.

Results: A total of 12 eligible studies with 1201 patients (600 ONS group and 601 control group) were included in this meta-analysis. Compared with a normal diet, preoperative ONS effectively reduced infectious complications (odds ratio = 0.63; 95% confidence interval [CI], 0.40–0.98; $P = .04$), white blood cell count (mean difference [MD] = –0.66; 95% CI, –1.04 to –0.28; $P = .0007$), C-reactive protein (MD = –0.26; 95% CI, –0.33 to –0.19; $P < .00001$), and markedly improved albumin levels (MD = 1.71; 95% CI, 0.97–2.46; $P < .00001$), prealbumin (MD = 24.80; 95% CI, 1.72–47.88; $P = .04$), immunoglobulin G (MD = 0.86; 95% CI, 0.44–1.28; $P < .00001$), CD4 T lymphocyte cells (MD = 3.06; 95% CI, 2.21–3.92; $P < .00001$), and CD4 T lymphocyte cells/CD8 T lymphocyte cells (MD = 0.33; 95% CI, 0.10–0.56; $P = .004$). However, there were no significant differences between the 2 groups in terms of noninfectious complications (odds ratio = 0.77; 95% CI, 0.39–1.53; $P = .46$), immunoglobulin A (MD = –0.21; 95% CI, –0.44 to 0.02; $P = .08$) or length of hospital stay (MD = –0.04; 95% CI, –0.71 to 0.64; $P = .92$).

Conclusion: Preoperative ONS may effectively reduce postoperative infectious complications, improve postoperative nutritional status and immune function, and relieve the inflammatory response in gastrointestinal cancer patients. Therefore, we recommend that preoperative nutrition could be optimized with ONS in patients undergoing gastrointestinal cancer surgery.

Abbreviations: ALB = albumin, CD4+ = CD4 T lymphocyte cells, CD8+ = CD8 T lymphocyte cells, 95% CI = 95% confidence interval, CRP = C-reactive protein, IgA = immunoglobulin A, IgG = immunoglobulin G, LOS = length of hospital stay, MD = mean difference, ONS = oral nutritional supplements, OR = odds ratios, PA = prealbumin, RCTs = randomized controlled trials, WBC = white blood cells.

Keywords: clinical outcomes, gastrointestinal cancer, meta-analysis, oral nutritional supplements, preoperative nutrition

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1. Introduction

Gastrointestinal cancer is one of the most common cancers, and malnutrition is exceedingly common in patients with gastrointestinal cancer.[1] Malnutrition is an independent risk factor for poor prognosis in surgical patients[2] and can lead to increased postoperative complications, prolonged hospital stay, increased medical costs, delayed recovery of gastrointestinal function, and seriously affect patient quality of life.[3–6] At present, surgical resection remains the main treatment for gastrointestinal cancer. However, relevant studies[4,7] have shown that preoperative malnutrition has a negative effect on the clinical prognosis of patients undergoing gastrointestinal cancer surgery, seriously affecting postoperative rehabilitation. Therefore, it is particularly important to improve the nutritional status of patients through reasonable nutritional support before surgery. Domestic and foreign nutritional guidelines[8,9] suggest that patients with nutritional risks and (or) malnutrition should receive preoperative nutritional support therapy for 7 to 14 days. Oral nutritional supplements (ONS) is preferred for patients that have a functional gastrointestinal tract and can eat orally. ONS refers to nutritional preparations that can provide patients with a variety of macro and micronutrients for the purpose of increasing nutrient intake.[9] ONS is simple, convenient, and compliant with human physiology.[10] It is an effective nutritional treatment for enhancing protein, fat, carbohydrate, mineral, and vitamin intake, and providing a balanced nutrient profile to surgical patients.[10] Intake of ONS can improve patient nutritional status and reduce the occurrence of postoperative adverse outcomes.[7] Several clinical studies and systematic reviews[11,12] 12 to 15 have shown that ONS accelerates wound healing, reduces the incidence of postoperative complications, shortens hospital stay, and improves quality of life. However, Burden et al[13] reported that standard oral nutritional supplements before surgery had no effect on postoperative complications and length of hospital stay (LOS). To date, studies testing whether preoperative ONS can effectively improve the clinical outcome of patients undergoing gastrointestinal cancer surgery have drawn different conclusions, and some have had conflicting results. Therefore, the clinical benefit of preoperative ONS in patients with gastrointestinal cancer remains controversial.

The purpose of this systematic review and meta-analysis was to summarize evidence from the latest randomized controlled trials, comprehensively evaluate the effect of preoperative ONS on postoperative clinical outcomes in patients undergoing gastrointestinal cancer surgery, and provide evidence for clinical practice.

2. Methods

The systematic review and meta-analysis were conducted and are reported based on the statements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[14] The protocol of this study has been registered in the International Prospective Register of Systematic Reviews (PROSPERO, registration no. CRD42023426066).

2.1. Search strategy

We systematically searched electronic databases including PubMed, EMbase, Web of Science, The Cochrane Library, Scopus, and the Chinese National Knowledge Infrastructure to identify all relevant randomized controlled trials (RCTs) published from inception until April 2024. The following combination strategy of Medical Subject Headings (MeSH) and text words were used to retrieve the articles: "Gastrointestinal Neoplasm," "Stomach Neoplasms," "Gastric Cancer," "Colorectal Cancer," "Colorectal Carcinoma, 'Colon Cancer,' 'Colonic Neoplasm,' 'Rectal Tumor,' 'Rectum Cancer,' 'Preoperative Period,' 'Preoperative,' 'Preoperative Care,' 'oral nutritional supplements,' 'ONS,' 'Oral nutrition,' 'Enteral Nutrition,'* 'randomized,' "Randomized Controlled Trial," and "placebo." Lists of references to relevant studies and reviews were manually searched to identify other potential studies. Only articles written in English and Chinese were included in this study.

2.2. Inclusion and exclusion criteria

Two reviewers (ZQH and YZC) independently identified all eligible studies based on the prespecified inclusion and exclusion criteria. Disagreements between the 2 reviewers were resolved by mutual discussion or by recourse to a third-party expert The inclusion criteria of this systematic review were defined according to the acronym "PICOS": Population (P): patients aged 18 years or above and undergoing gastrointestinal cancer surgery, Intervention (I): patients received oral nutritional supplements for at least 5 days before surgery on the basis of a normal diet; Comparison (C): normal diet without other nutritional supplement, Outcomes (O): met at least one of the following relevant clinical outcome indicators: infectious complications, noninfectious complications; nutritional indicators: prealbumin (PA), albumin (ALB); immune indicators: immunoglobulin G (IgG), immunoglobulin A (IgA), CD4 T lymphocyte cells (CD4+), CD4+/CD8 T lymphocyte cells (CD8+); inflammatory indicators: white blood cells (WBC), C-reactive protein (CRP), and LOS. Study design (S): Only RCTs were included in this study. Exclusion criteria included: (1) retrospective study or nonrandomized controlled trial; (2) nutrition was supplemented by enteral tube or parenteral route; (3) studies only reported postoperative nutritional intervention; (4) the full text or experimental data were unavailable; (5) expert consensus, guidelines, case reports, letters to the editor, and review articles were also excluded.

2.3. Data extraction

After reading the full text, 2 researchers (ZQH and YZC) independently extracted data from the eligible articles using predetermined data extraction tables that included author, country, year of publication, disease type, sample size, study design, participant age, type of surgery performed, specific intervention characteristics and duration, and reporting outcome measurement data of interest (infectious complications, noninfectious complications, PA, ALB, WBC, CRP, IgA, IgG, CD4+, CD4+/CD8+, and LOS). The study author was consulted for more information, if necessary. Differences in the extraction of data were mainly resolved by consensus or consultation with third-party experts.

2.4. Quality assessment

Two independent investigators (ZQH and GXJ) were assigned to critically evaluate the methodological quality of all eligible studies according to the Cochrane Handbook for Systematic Reviews of Interventions.[15] The assessed domains were random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcomes assessment, incomplete outcome data, selective reporting, and other biases. The risk of each included study was assessed as "low risk," "unclear risk," and "high risk" according to the match degree between evaluation criteria and extracted information. Review Manager 5.4 software was used to draw the summarized quality evaluation results into Cochrane risk assessment charts. Disagreements were solved by discussion or appeal to the third author.

2.5. Statistical analysis

Statistical analyses were performed using Review Manager 5.4 software (The Nordic Cochrane Centre, Copenhagen, Denmark).

Forest plots were generated to measure the effect of all study combinations on the outcome variables. The dichotomous variables were expressed as odds ratios (OR) with a 95% confidence interval (95% CI), and mean difference (MD) with a 95% CI was applied to evaluate the continuity variables. Heterogeneity was assessed using the Q test and I^2 value. If the heterogeneity was acceptable ($I^2 < 50\%$ or $P > .1$), a fixed-effect model was used for the pooled effect size analysis. However, if there was significant heterogeneity ($I^2 > 50\%$ or $P < .1$), we used the random-effects model or a sensitivity analysis based on exclusion of studies that potentially biased the results. Funnel plots and Egger test for publication bias were performed using RevMan 5.4 and STATA (Stata Corporation, College Station, TX), respectively. A P value < .05 was considered statistically significant.

3. Results

3.1. Study selection and characteristics

A total of 1752 records were obtained in the preliminary literature search. After removing duplicates, 1240 records were further reviewed. Based on screening titles and abstracts, 1138 publications were excluded. The remaining 102 potentially eligible full-text articles were further evaluated, of which 90 were excluded for reasons such as lack of outcomes of interest and ineligible interventions. Eventually, 12 eligible studies[16–27] were included in this systematic review and meta-analysis. The flowchart of literature search and selection is shown in Figure 1.

A total of 12 articles[16–27] involving 1201 patients (600 ONS group and 601 normal diet group) were included in the meta-analysis. Five of the included studies were conducted in China and the others were in England (n = 1), Japan (n = 1), Turkey (n = 1), Australia (n = 1), Spain (n = 1), the Czech Republic (n = 1), and Korea (n = 1). Two studies reported on patients undergoing surgery for all gastrointestinal cancers,[16,20] 6 investigated colorectal cancer surgical patients,[17,19,22–24,26] and 4 were on gastric cancer surgical patients.[18,21,25,27] Among the included studies, 3 studies[23–25] chose immunonutrition that mainly included arginine, omega-3 fatty acids, and RNA as the intervention. In 2 studies,[17,21] both groups received nutritional dietary advice, but only the intervention group received preoperative ONS. In the remaining 7 studies,[16,18–20,22,26,27] control group normal diet, while intervention group received preoperative ONS based on a normal diet. The timing of nutritional support was at least 5 days before surgery. The main characteristics of the included studies are summarized in Table 1.

3.1.1. Infectious complications.

Five studies[17,21,23–25] that included 471 participants compared the incidence of postoperative infectious complications. The pooled event rate of this outcome was 21.5% (51/237 patients) in the ONS group compared with 27.8% (65/234 patients) in the control group. The statistical heterogeneity across studies was low ($I^2 = 23\%$, $P = .27$), and a fixed-effect model was adopted to perform the meta-analysis. The pooled results revealed that the incidence of infectious complications was lower in the ONS group compared

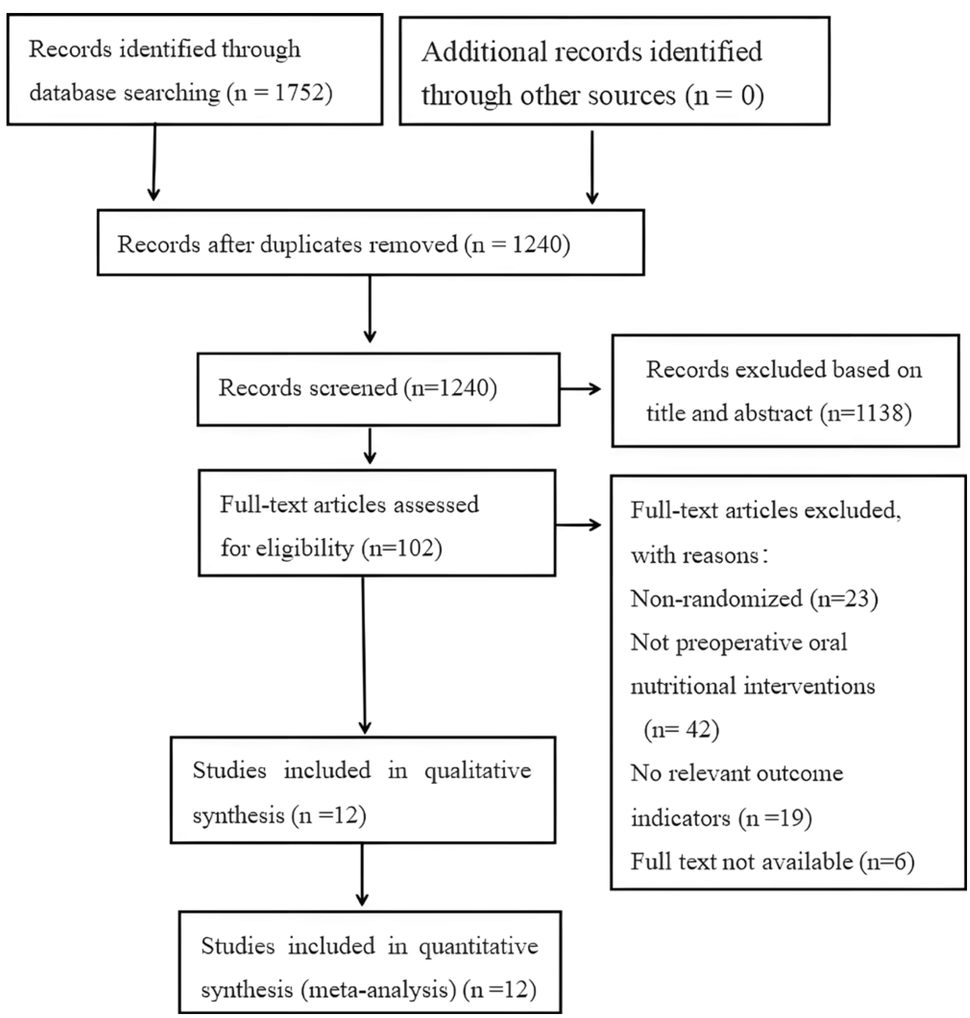


Figure 1. Article selection process.

with the control group (OR = 0.63; 95% CI, 0.40–0.98; P = .04; Fig. 2A).

3.1.2. Noninfectious complications. Three studies[21,23,25] that included 287 participants reported relevant data on noninfectious complications. The incidence of this outcome was 12.1% (17/140 patients) in the ONS group compared with 14.9% (22/147 patients) in the control group. The fixed-effect model was used according to the heterogeneity test (I^2 = 0%, P = .76). The pooled analysis showed that there was no significant difference in terms of noninfectious complications between groups (OR = 0.77; 95% CI, 0.39–1.53; P = .46; Fig. 2B).

3.1.3. Nutritional indicators. A total of 5 studies[18,19,22,26,27] compared postoperative changes in ALB levels, with significant heterogeneity across studies (I^2 = 68%, P = .01). Sensitivity analysis indicated that the high heterogeneity was caused by the paper by Jia,[22] and the heterogeneity was significantly reduced after excluding this article (I^2 = 0%, P = .85). Therefore,

Table 1

Characteristics of the included studies.

Study, year	County	Design	Disease type	Patients number (I/C)	Control	Intervention	Duration of intervention (days)	Reported outcomes
Okamoto et al, 2009[25]	Japan	RCT	Gastric carcinoma	30/30	Normal diet	Normal diet + oral immunonutrition	7	①②⑪
Gunerhan et al, 2009[20]	Turkey	RCT	Gastrointestinal tumors	13/13	Normal diet	Standard enteral nutrition	7	⑦⑧
Barker et al, 2013[16]	Australia	RCT	Gastrointestinal tumors	46/49	Normal diet	Normal diet + ONS	5	⑪
Ding et al, 2015[18]	China	RCT	Gastric cancers	53/53	Normal diet	Normal diet + oral intact protein EN powders	7	③④⑤⑥⑦⑧⑨⑩
Ding et al, 2016[19]	China	RCT	Colorectal cancer	48/48	Normal diet	Normal diet + oral intact protein EN powders	7	③④⑤⑦⑧⑨⑩
Burden et al, 2017[17]	England	RCT	Colorectal cancer	55/46	Dietary advice	Dietary advice + ONS	5	①
Manzanares et al, 2017[24]	Spain	RCT	Colorectal cancer	42/42	Normal diet	Normal diet + oral immunonutrition	8	①⑪
He et al, 2022[21]	China	RCT	Gastric cancer	31/35	Dietary advice	Dietary advice + ONS	7	①②
Tesar et al, 2022	Czech Republic	RCT	Colorectal cancer	60/60	Normal diet	Normal diet + ONS	7	③⑪
Lee et al, 2023[23]	Korea	RCT	Colon cancer	79/82	Normal diet	Normal diet + oral immunonutrition	7	①②⑪
Jia 2023[22]	China	RCT	Rectal cancer	43/43	Normal diet	Normal diet + ONS	7	③④⑥⑦⑧
Wang et al, 2015[27]	China	RCT	Gastric cancer	100/100	Normal diet	Normal diet + ONS	7	③④⑤⑥⑦⑧⑨⑩

① Infectious complications; ② noninfectious complications; ③ albumin; ④ prealbumin; ⑤ immunoglobulin A; ⑥ immunoglobulin G; ⑦ CD4+; ⑧ CD4+/CD8+; ⑨ white blood cells; ⑩ C-reactive protein; ⑪ length of hospital stay.

C = control group, EN = enteral nutrition, I = intervention group, ONS = oral nutritional supplements, RCT = randomized controlled trials.

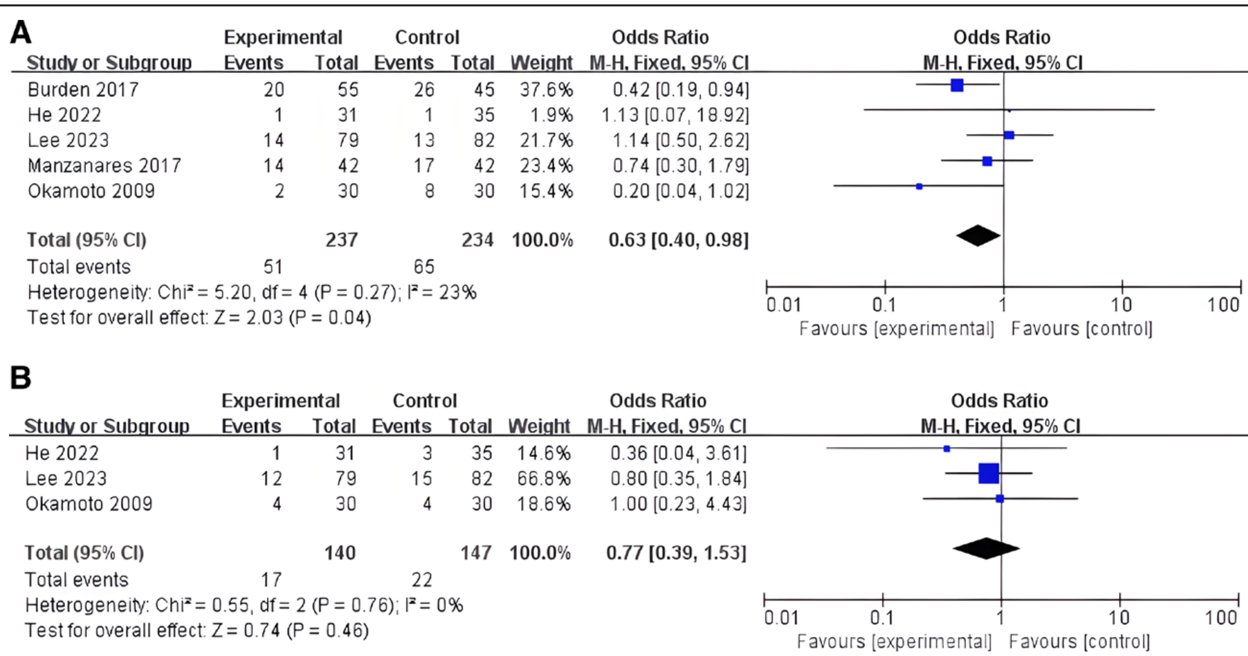


Figure 2. Forest plots of postoperative complications: (A) infectious complications; (B) noninfectious complications.

a fixed-effects model was chosen to analyze the results. Comprehensive evaluation of the remaining 4 studies[18,19,26,27] (522 participants enrolled) found that preoperative ONS effectively improved Alb levels (MD = 1.71; 95% CI, 0.97–2.46; $P < .00001$; Fig. 3A).

Changes in PA levels were reported in 4 studies[18,19,22,27] (488 participants enrolled). Significant heterogeneity among the studies was identified ($I^2 = 97\%$, $P < .00001$). Therefore, a random-effects model was used to calculate the effect size. The combined results showed that PA levels in the ONS group were higher than in the control group (MD = 24.80; 95% CI, 1.72–47.88; $P = .04$; Fig. 3B).

3.1.4. Immune indicators. Three studies[18,19,27] that had included 402 participants and 3 studies[18,22,27] that had enrolled 392 participants reported IgA and IgG levels, respectively. Homogeneity was found in terms of IgA ($I^2 = 0\%$, $P = .37$) and IgG ($I^2 = 0\%$, $P = .51$), therefore, a fixed-effects model was used in the analysis. In the combined meta-analysis, no significant difference in IgA levels (MD = −0.21; 95% CI, −0.44 to 0.02; $P = .08$; Fig. 4A) was found when comparing the pooled results of preoperative ONS with a normal diet. However, IgG levels in the ONS group were significantly higher than in the control group (MD = 0.86; 95% CI, 0.44–1.28; $P < .00001$; Fig. 4B). Five studies[18–20,22,27] that included 517 participants reported data on CD4+ and CD4+/CD8+. There was no statistical heterogeneity in CD4+ ($I^2 = 0\%$, $P = .83$), however, the meta-analysis on CD4+/CD8+ was statistically heterogeneous ($I^2 = 82\%$, $P = .0002$). Therefore, a fixed-effects model was used in the analysis of CD4+, and a random-effects model was used for CD4+/CD8+. The pooled analysis revealed that CD4+ levels (MD = 3.06; 95% CI, 2.21–3.92; $P < .00001$; Fig. 4C) and CD4+/CD8+ (MD = 0.33; 95% CI, 0.10–0.56; $P = .004$; Fig. 4D) were significantly increased in the ONS group.

3.1.5. Inflammatory indicators. Three studies[18,19,27] that included 402 participants assessed changes in WBC levels. The homogeneity across the studies was good ($I^2 = 0\%$, $P = .96$), therefore, a fixed-effect model was used. The pooled results indicated that WBC levels in the ONS group were significantly lower than in the control group (MD = −0.66; 95% CI, −1.04, −0.28; $P = .0007$; Fig. 5A). Additionally, the same studies[18,19,27] reported data on CRP. There was no significant statistical heterogeneity across the studies ($I^2 = 48\%$, $P = .15$), as a result of which we used the fixed-effect model to calculate the results. The pooled analysis suggested that CRP levels were significantly reduced in the ONS group compared to the control group (MD = −0.26; 95% CI, −0.33, −0.19; $P < .00001$; Fig. 5B).

3.1.6. Length of hospital stay. Data on LOS were reported in 5 studies[16,23–26] that had enrolled a total of 520 participants. There was homogeneity across the studies ($I^2 = 0\%$, $P = .59$), therefore, a fixed-effect model was selected to calculate the results. The pooled analysis showed no significant difference between groups in terms of LOS (MD = −0.04; 95% CI, −0.71, 0.64; $P = .92$; Fig. 6).

3.2. Assessment of bias

We identified 12 eligible RCTs and evaluated them according to the Cochrane bias risk assessment tool, as outlined in Figure 7. Most of the studies[16–19,21,23–27] reported the methods for generating random sequences, and three-quarters of the studies[16–19,23,24,26,27] described allocation concealment; the corresponding domain was identified as "low risk." Regarding performance bias, 7 trials[16,17,20–23,27] were identified as "low risk" and the remaining trials were unclear.[18,19,24–26] A quarter of the trials[16,17,21,23] provided information on the assessment of detection bias. All trials were considered to have low risk of reporting and attrition bias and no other biases. Funnel plots and Egger test were used to assess the publication bias, and the results showed no significant publication bias in this study (Fig. 8).

4. Discussion

The systematic review and meta-analysis was based on 12 RCTs that included 1201 patients. The study was designed to evaluate the impact of preoperative ONS on postoperative clinical outcomes in patients with gastrointestinal cancer. The overall meta-analysis found that preoperative ONS reduced infectious complications and levels of inflammatory indicators such as WBC and CRP after gastrointestinal cancer surgery. Results also showed that ONS may improve nutrition indicators (ALB and PA) and immune indicators (IgG, CD4+, and CD4+/CD8+). However, there were no significant differences in noninfectious complications, LOS, or IgA levels between the 2 groups.

Postoperative infectious complications are one of the most common complications of highly invasive abdominal surgery. Surgery of the gastrointestinal system has a high risk of postoperative infectious complications because this type of surgery

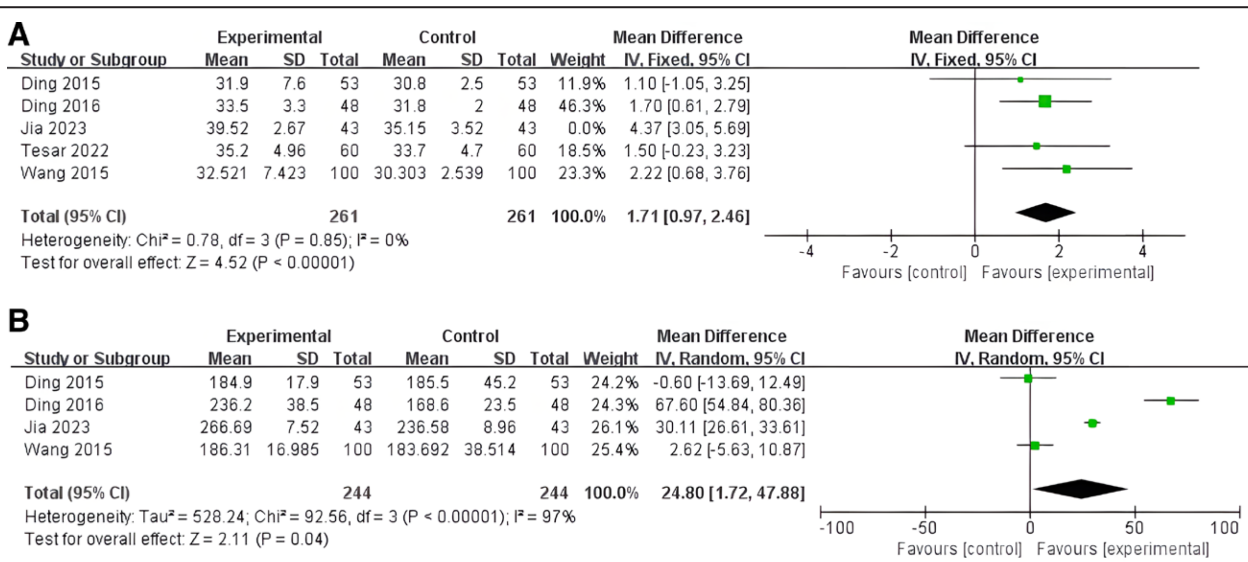


Figure 3. Forest plots of nutritional indicators: (A) albumin; (B) prealbumin.

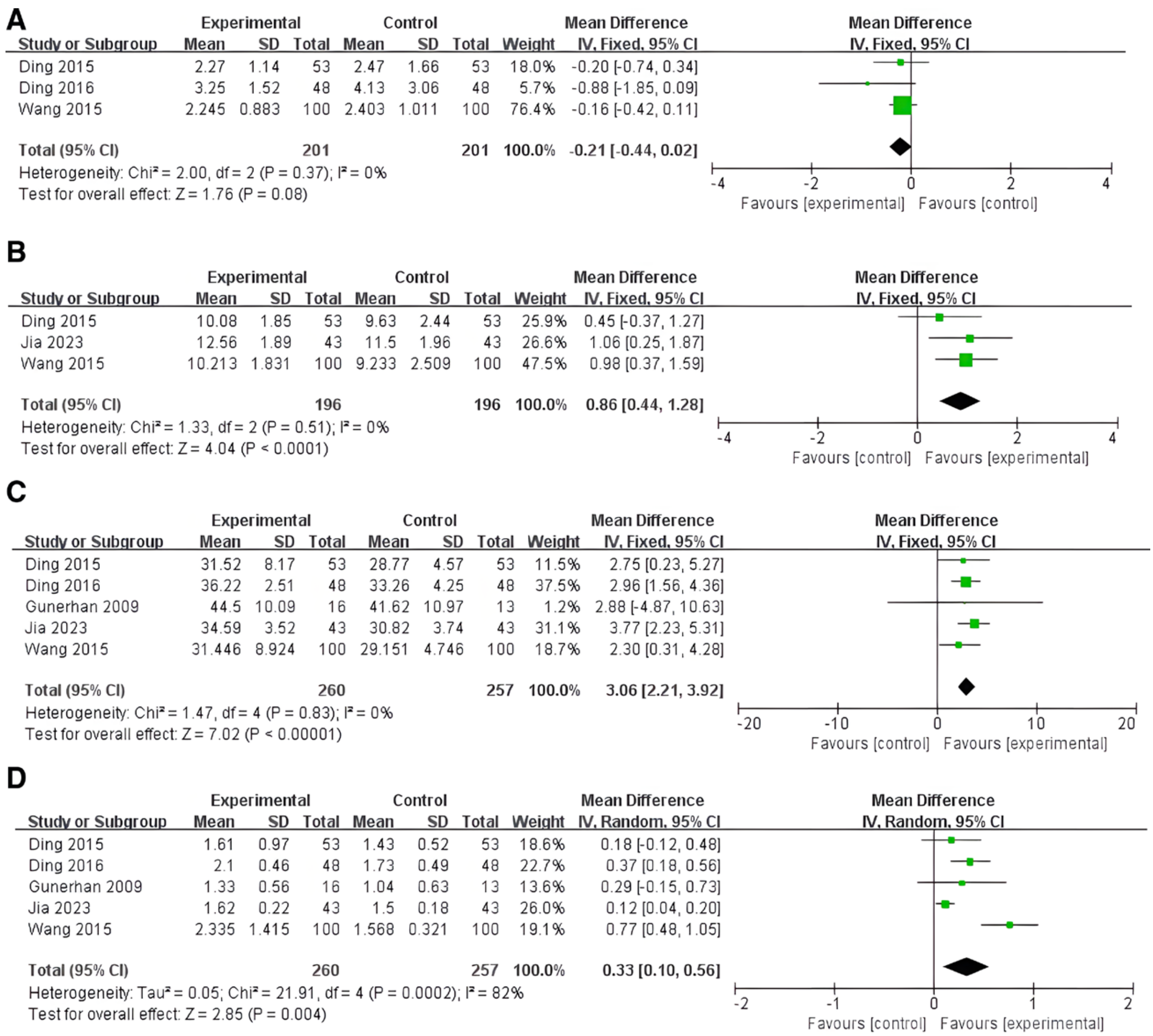


Figure 4. Forest plots of immune indicators: (A) immunoglobulin A; (B) immunoglobulin G; (C) pooled result of CD4+; (D) pooled result of CD4+/CD8+.

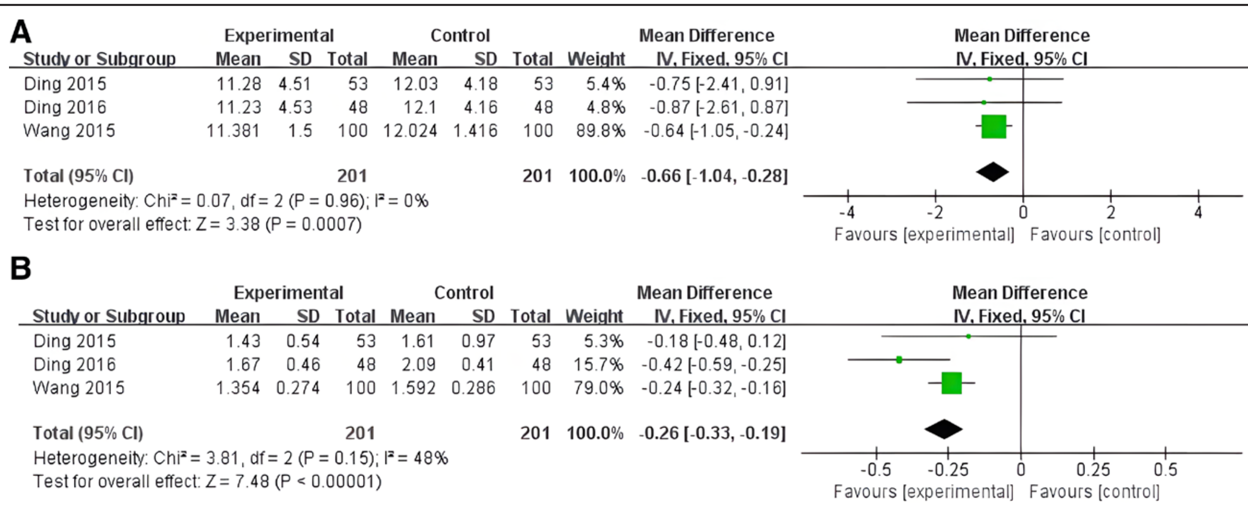


Figure 5. Forest plots of Inflammatory indicators: (A) white blood cells; (B) C-reactive protein.

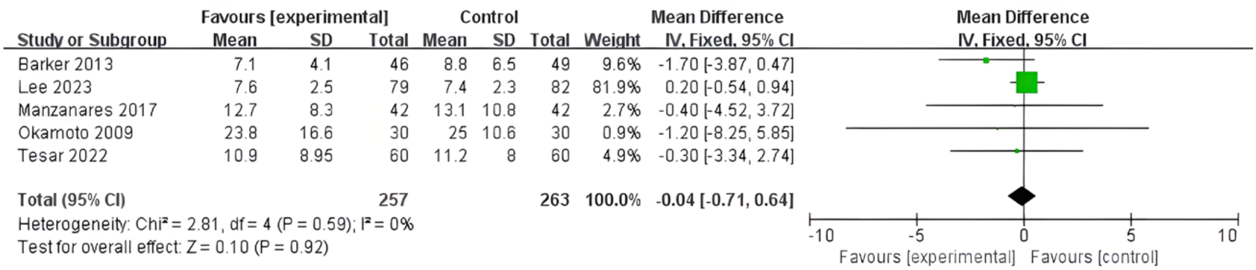


Figure 6. Forest plots of length of hospital stay.

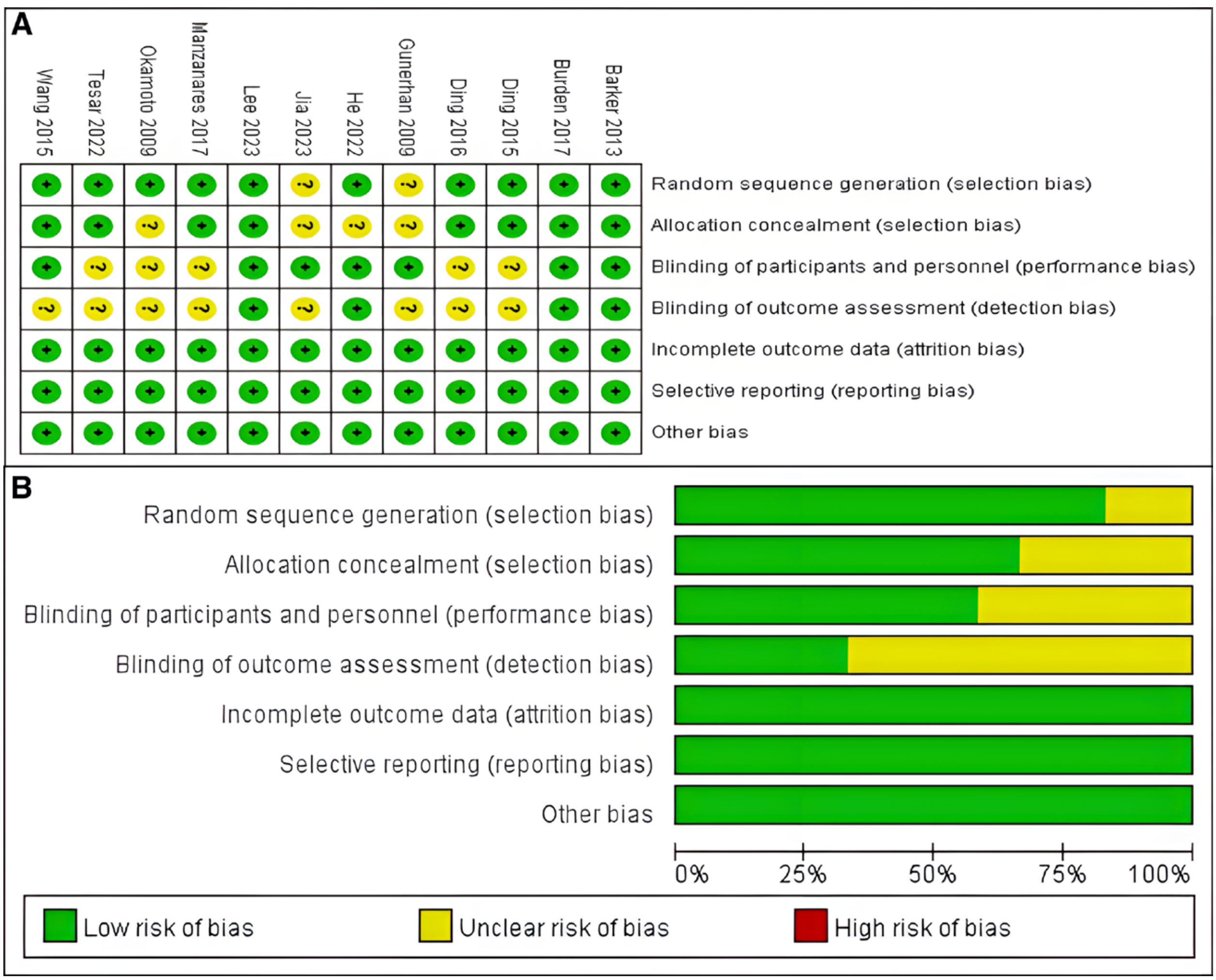
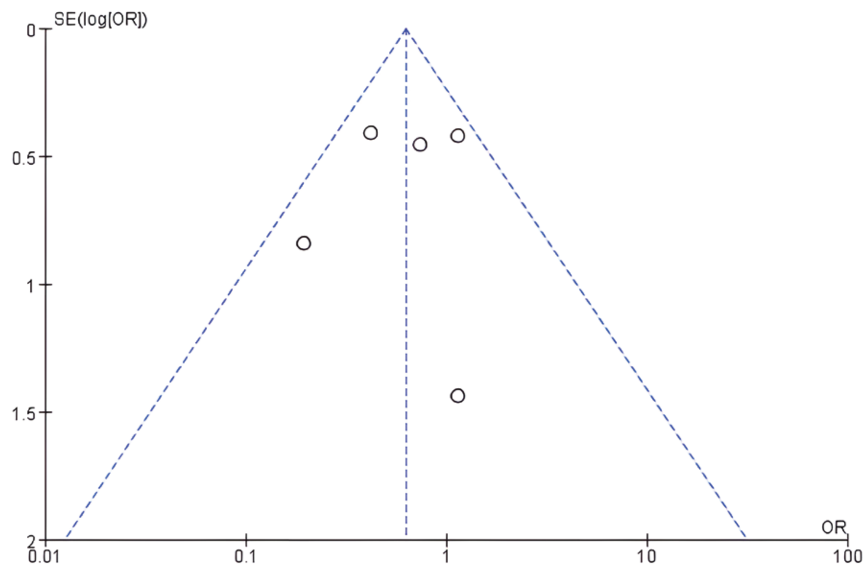


Figure 7. Risk of bias of the included studies using the Cochrane risk of bias tool: (A) risk of bias summary; (B) risk of bias graph.

manipulates the gut, which contains a large quantity of bacteria.[28] Relevant studies[28,29] have shown that surgical stress may lead to impaired intestinal barrier function, and bacteria may be transferred from the intestine to the bloodstream and lymph, increasing the risk of infectious complications such as bacteremia. However, evidence from animal studies suggests that enteral nutritional support can attenuate the stress response, protect the barrier function of the intestinal mucosa, prevent mucosal atrophy, bacterial translocation, and intestinal flora dysregulation, and reduce postoperative infection.[30] Our results revealed that preoperative ONS significantly reduced postoperative infectious complications. Five articles were included in this study, 4 of which suggested a reduction in incision infection, 3 articles suggested decreased urinary tract infection, 3 articles suggested a reduction in lung infections, and one article suggested that it could reduce the incidence of bacteremia and anastomotic fistula. The meta-analysis published by Knight et al[31] also reported that preoperative nutritional support reduced infectious complications. However, the study included only 3 RCTs and was conducted on populations from only 2 regions, which would make the results more susceptible to potential bias. Compared to previous meta-analyses, our study included more RCTs and involved patients from multiple countries and multiple centers, making the results more likely to be generalized. The heterogeneity between the studies was low, so the results were considered reliable.

Before surgery, patients with gastrointestinal cancer often have reduced food intake due to tumor growth, anorexia, obstruction, A



B

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Egger's test for small-study effects:
Regress standard normal deviate of intervention
  effect estimate against its standard error

.
Number of studies =  5                          Root MSE      =   .8169
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Std_Eff	Coefficient	Std. err.	t	P>|t|	[95% conf.	interval]
slope	.7947344	.5199999	1.53	0.224	-.8601373	2.449606
bias	-.139486	.9937519	-0.14	0.897	-3.302048	3.023076

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Test of H0: no small-study effects          P = 0.897
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Figure 8. Funnel plots (A) and Egger test (B) were used to assess publication bias for primary outcome measures: infectious complications.

digestive and absorption disorders, and insufficient nutrient intake leads to malnutrition.[32] In addition, surgical trauma can lead to a stress response, accelerate the catabolism of nutrients in the body, and further increase the risk of postoperative malnutrition.[33] There is considerable evidence that postoperative malnutrition is an independent marker of poor prognosis in patients with gastrointestinal cancer.[34] Therefore, it is particularly important to fill the gap between recommended and actual food intake with reasonable nutritional support prior to surgery to improve the nutritional status and prevent adverse postoperative outcomes. Our meta-analysis showed that oral nutritional support for at least 7 days before surgery significantly improved postoperative serological levels of PA and ALB in patients with gastrointestinal cancer compared with a normal diet. A meta-analysis published by Chen et al[35] produced similar results. However, their study only included patients who underwent surgery for gastric cancer, limiting the scope of application. Compared to previous reviews, our study covered different types of gastrointestinal tumor surgery, and the results were more applicable to patients undergoing elective gastrointestinal surgery. Besides, this study is the latest to systematically compare the effects of preoperative ONS with conventional diet on postoperative nutritional status in patients with gastrointestinal tumors. The results suggest that preoperative ONS may improve nutritional status and reduce the risk of postoperative malnutrition.

Serum immunoglobulin IgG and IgA are important indicators of immune function in humoral immunity and can effectively prevent corresponding diseases. Studies have shown that CD4 T lymphocyte counts are negatively correlated with the risk of incision infection surgery, and an increase in the CD4+/CD8+ ratio indicates that immune function is enhanced.[36] Immune function is an important indicator for evaluating postoperative recovery of tumor patients. Patients with poor immune function have delayed recovery and more postoperative complications.[37] Therefore, it is reasonable to maintain and improve the patient's immune function through effective means during the perioperative period. The results of our meta-analysis showed that preoperative ONS significantly increased the levels of postoperative IgG, CD4+, and CD4+/CD8+ ratio in patients with gastrointestinal cancer. This suggests that preoperative ONS may enhance the immune function of patients compared with a conventional diet. However, there was no statistically significant difference in IgA levels between the 2 groups, which is different from results of the meta-analysis carried out by Chen et al.[35] This difference may be related to differing doses of preoperative oral nutrition and duration of the interventions.

The postoperative systemic inflammatory response caused by surgical stress has attracted the attention of many surgeons. WBC and CRP are commonly used to evaluate the degree of inflammation in clinical practice. CRP level, an extremely sensitive indicator of an acute inflammatory response, begins to rise within 6 hours after the onset of inflammation or tissue damage, peaks within 2 to 3 days, and rapidly declines with the resolution of inflammation.[38] A recent study[39] showed that elevated CRP levels represent more severe systemic inflammation, which is associated with an increased risk of adverse outcomes and worse disease. The results of our meta-analysis found that the levels of postoperative WBC and CRP in the ONS group were significantly lower than in the control group. This indicates that, compared with a normal diet, preoperative ONS may effectively reduce postoperative inflammation and contribute to patient recovery. However, only 3 studies have included this conclusion, and there was limited data to report changes in the levels of inflammatory indicators in detail. Therefore, it is necessary to design large-scale studies in the future to clarify the impact of preoperative ONS on the inflammatory response of surgical patients and elucidate the potential mechanisms for reducing inflammatory response.

However, the 5 articles included in this meta-analysis suggested that preoperative ONS did not shorten patient LOS. This may be because LOS is susceptible to various factors such as physical fitness, disease severity, and surgical trauma, and is not solely controlled by nutritional status. Therefore, determination of whether there is a significant difference between the 2 preoperative nutrition modalities in terms of LOS in patients with gastrointestinal cancer requires further exploration via high-quality randomized controlled trials.

There are some limitations to our study. First, the search strategy of this meta-analysis included only studies published in English and Chinese, which may have created certain limitations. Second, differences in preoperative oral nutrition dose, duration, and composition of nutritional formulations may also have had an impact on the study results. Third, studies with a small sample size that were included in this meta-analysis may limit the generalizability of the findings across a broader population. Finally, the included studies only reported the effect of preoperative ONS on short-term clinical outcomes, not long-term outcomes such as disease-free survival and quality of life. Therefore, it is necessary to consider the impact of preoperative ONS on the long-term clinical prognosis of patients with gastrointestinal tumors in future studies. In addition, high-quality RCTs could be designed in the future to explore the optimal duration of perioperative nutritional interventions, and the optimal type and dose of nutritional interventions could also be determined by comparing the effects of different formulations of oral nutritional supplements.

5. Conclusions

Based on the evidence from these RCTs, this systematic review and meta-analysis showed that preoperative ONS in patients undergoing gastrointestinal cancer surgery may significantly reduce postoperative infectious complications, improve postoperative nutritional status and immune function, and relieve the inflammatory response compared with a normal diet alone. However, more high-quality, large-scale studies are urgently needed to further explore optimal interventions and the duration of preoperative nutritional supplementation.

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