Comparison of enteral immunonutrition and enteral nutrition in patients undergoing gastric cancer surgery: a systematic review and network meta-analysis of randomized controlled trials

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**Review question / Objective:** The purpose of this study is to evaluate the effects of enteral immunonutrition and enteral nutrition on immune function in patients with gastric cancer surgery, and to provide reference for postoperative nutritional support in patients with gastric cancer.

**Condition being studied:** As a digestive system tumor, patients with gastric cancer often suffer from malnutrition due to poor nutrient absorption and active metabolism of cancer cells. Surgical treatment will further aggravate the degree of malnutrition. Therefore, reasonable nutritional intervention is very important for the prognosis of patients with gastric cancer. At present, the effect of enteral immunonutrition on postoperative patients with gastric cancer is still controversial.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 April 2023 and was last updated on 10 April 2023 (registration number INPLASY202340030).
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METHODS

Participant or population: Patients undergoing gastric cancer surgery.

Intervention: Enteral immunonutrition.

Comparator: Enteral nutrition.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: A population (P), intervention (I), comparator (C), outcome (O), and study design (S) (PICOS) framework was used to describe the eligibility of studies. Specifically, the criteria below were included:- Population (P): patients undergoing gastric cancer surgery; - Intervention (I): enteral immunonutrition; - Comparator (C): enteral nutrition; - Outcomes (O): infectious complication, immune and inflammatory factors, serum proteins, and cellular immunity; - Study design (S): Randomized controlled trials.

Information sources: The PubMed, Embase, Cochrane, Web of Knowledge, and ClinicalTrials.gov databases were searched from inception to March 10, 2023. Articles in all languages were searched.

Main outcome(s): It was found that the CD4+ level, lymphocyte, the transferrin, and systemic inflammatory response syndrome were not statistically different between the enteral immunonutrition and enteral nutrition groups. However, the CD8+ level, IgG, IgM, proalbumin, and infectious complication were statistically different between enteral immunonutrition group and enteral nutrition group.

Quality assessment / Risk of bias analysis: The literature screening was conducted by two researchers (QLX and ARW) independently, through reading the subject, selecting the standard subject, and subsequently reading the abstract and the full text. For randomized controlled studies, the two researchers cross-estimated the quality of the studies using the Jadad scale, including random allocation, randomized hiding, double-blind method setting, exit and loss to follow-up (score out of 7 points: 1-3 for inferior quality and 4-7 points for good quality), while the evaluation of methodological quality used the method recommended by the Cochrane Review handbook. Two researchers independently recorded the necessary information from the publications, including details of the first author, publication date, number of subjects, Enteral immune nutrition formula, nutrition support initiation time, total during time of nutrition support, and mode of feeding for the experimental and control groups. Any differences between the two researchers were decided by discussion with a third researcher (JL).

Strategy of data synthesis: Data were analyzed with Review Manager Version 5.3 (Cochrane Collaboration), with P<0.05 representing statistical significance. We computed the odds ratio (OR) or the MD, and 95% CI with a fixed or random-effect model. Inter-study heterogeneity was evaluated using the I2 statistic and Cochran's Q test, with cut-off values of 25%, 50%, and 75% considered as low, moderate, and high, respectively[27]. If I2 was <50%, the fixed-effects (Mantel-Haenszel) model was used to combine odds ratio (OR) values; otherwise, the random-effect (DerSimonian and Laird) model was used. Sensitivity analysis was performed in relation to the assessed effect sizes and heterogeneity of the studies. The risk of publication bias was assessed using funnel plots, with the asymmetry of the plot indicating potential bias.

Subgroup analysis: No subgroup analyses were performed.

Sensitivity analysis: Sensitivity analysis was performed in relation to the assessed effect sizes and heterogeneity of the studies.
sizes and heterogeneity of the studies. We performed a sensitivity analysis of all the results, and the results indicated no significant differences in the results of the combined analysis after the deletion of individual studies, showing that the overall results were reliable.

**Country(ies) involved:** China.

**Keywords:** enteral immunonutrition, enteral nutrition, gastric cancer, immune function, meta-analysis.

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