



Comment on “Efficacy and Safety of a Combination of Enteral and Parenteral Nutrition Support in the Postoperative Period for Patients with Gastrointestinal Cancer: A Systematic Review and Meta-Analysis”

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We read with great interest the systematic review and meta-analysis conducted by Cai et al.,¹ entitled "Efficacy and safety of a combination of enteral and parenteral nutrition support in the postoperative period for patients with gastrointestinal cancer," which evaluates the impact of different nutritional support methods on patient recovery and outcomes. This study provides valuable insights into the potential benefits of combining enteral nutrition + parenteral nutrition (EN + PN) for optimizing postoperative care in patients with gastrointestinal cancer. Although the findings are promising, some areas of the analysis could be strengthened to enhance the robustness and clinical applicability of the outcomes.

The authors have commendably utilized the Cochrane Collaboration Tool for assessing the risk of bias as well as conducted sensitivity analyses through the leave-one-out approach and the exclusion of studies with small sample sizes. However, further stratifying these analyses by the level of bias could enhance our understanding of the impact of study quality on the findings. Particularly, for outcomes such as time-to-first flatus or nutritional indicators, where high or unclear risk of bias in individual studies could disproportionately influence the pooled outcomes, analyzing how the inference shifts with the exclusion of these studies would provide a clearer picture of the robustness of the evidence. Such detailed sensitivity analyses are crucial in systematic reviews with significant heterogeneity and diverse methodological quality.

A sensitivity analysis stratified by the level of bias could have provided a more nuanced understanding of how study quality influenced the findings.² For instance, studies with high or unclear risk of bias may disproportionately affect the pooled results, particularly when assessing subjective outcomes such as the time-to-first flatus or nutritional indicators. Performing sensitivity analyses could have clarified whether the results remained stable after excluding studies with a higher risk of bias. Such analyses are particularly critical in systematic reviews wherein heterogeneity and methodological quality vary significantly across studies.

Although the meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, the certainty of evidence was not evaluated with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework.^{3,4} GRADE provides a transparent approach to rating the quality of evidence and the strength of clinical recommendations. For example, GRADE assesses the key factors such as the risk of bias, inconsistency, indirectness, imprecision, and publication bias. Applying this methodology could have offered a clearer understanding of the reliability and clinical utility of the reported findings. High-quality evidence from GRADE would bolster confidence in recommending EN + PN as the standard postoperative nutritional strategy for gastrointestinal cancer patients, while lower-quality evidence would highlight the need for further trials.

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Although the authors mention that publication bias was not evaluated due to the limited number of included studies for individual outcomes, this remains a significant limitation. Funnel plots and Egger's tests could have been used to assess the likelihood of publication bias, particularly considering the selective reporting of positive results in clinical research. In addition, the search strategy, while comprehensive, may have inadvertently excluded the gray literature (e.g., unpublished studies, conference proceedings). Sources such as OpenGrey, ProQuest Dissertations, and other databases, and conference proceedings available through Scopus or Web of Science can provide valuable unpublished data and research. Including these sources can mitigate publication bias and provide a more balanced representation of the available evidence.

The generalizability of the study's findings to diverse patient populations warrants further consideration. The included studies predominantly focused on gastric and colorectal cancer patients, with limited representation of other gastrointestinal malignancies such as pancreatic or esophageal cancer. Evidently, the nutritional needs and postoperative outcomes can differ significantly among these subgroups, potentially affecting the applicability of the EN + PN strategies. Moreover, subgroup analyses by cancer type could have elucidated whether the observed benefits were consistent across gastrointestinal malignancies or specific to particular conditions.

The authors observed significant heterogeneity in key outcomes, such as immune function markers and time-to-first flatus. The authors used appropriate statistical models (random-effects models for high heterogeneity outcomes). Although random-effects models were appropriately used to account for variability, the sources of heterogeneity remain unclear. Further exploration of heterogeneity through meta-regression or stratified analyses (e.g., by study design, geographical location, or intervention duration) could provide critical insights into factors driving variability in the outcomes. Identifying these factors would not only strengthen

the study's conclusions but also guide future research to optimize nutritional strategies.

The study by Cai et al.¹ represents a valuable contribution to the literature on postoperative nutritional strategies for gastrointestinal cancer patients. By highlighting the advantages of EN + PN in improving recovery, nutrition, and immunity, the authors provide a compelling case for its use in clinical practice. However, addressing these limitations, particularly through sensitivity analyses, GRADE assessments, and better exploration of heterogeneity, would significantly enhance the robustness and applicability of the study findings. We appreciate the opportunity to engage in this important discussion and look forward to future studies that build upon these findings to establish evidence-based guidelines for postoperative nutritional care.

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