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REVIEW

Enteral versus parenteral nutrition in critically ill patients with severe pancreatitis: a meta-analysis

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Whether enteral nutrition (EN) is superior to parenteral nutrition (PN) in critically ill patients with severe acute pancreatitis remains unknown. The objective of this meta-analysis was to assess the effects of EN versus PN on clinical outcomes in a subgroup of pancreatitis patients. Relevant randomized controlled trials (RCTs) were searched in Scopus, PubMed and Web of Science from inception to August 2016. Ultimately, five RCTs including 348 patients were enrolled in this analysis. Compared with PN, EN was associated with a significant reduction in overall mortality (risk ratio (RR) = 0.36, 95% confidence interval (CI) 0.20–0.65, $P = 0.001$) and the rate of multiple organ failure (RR = 0.39, 95% CI 0.21–0.73, $P = 0.003$). EN should be recommended as the preferred route of nutrition for critically ill patients with severe acute pancreatitis.

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INTRODUCTION

The mortality of acute pancreatitis can approach 20% if it develops into severe necrosis. For the most severe pancreatitis, mortality can vary from 30 to 40%.[1] Increasing evidence suggests that enteral nutrition (EN) helps to maintain the structural and functional integrity of the gut and the diversity of intestinal microbes.[2,3] A recently published meta-analysis of severe acute pancreatitis showed that EN compared with parenteral nutrition (PN) reduced overall mortality, infectious complications, surgical intervention and organ failure.[4] However, we questioned whether EN would benefit critically ill patients, defined as patients admitted to an intensive care unit (ICU) with severe pancreatitis.[5–8] In this study, we performed a meta-analysis of the effect of EN compared with PN on critically ill patients with severe acute pancreatitis.

METHODS

Study collection

A study collection was performed to identify all relevant randomized control trials (RCTs) that compared EN with PN for severe acute pancreatitis patients who were admitted to an ICU. We searched among research reports that were published from inception to August 2016 in Scopus, PubMed and Web of Science. The following terms were used for articles research: 'enteral nutrition OR tube feeding OR artificial feeding OR nasogastric OR nasojejunal' and 'parenteral nutrition OR intravenous', and 'pancreatitis'. No restriction was set for the literature search.

Inclusion criteria

Articles meeting the following characteristics were included: (1) RCT with available data; (2) critically ill adult patients with severe pancreatitis that were enrolled to the ICU; (3) EN versus PN and (4) the relevant outcomes were reported.

Data collection

Two independent reviewers used a standard form for data abstraction. The following clinical outcomes were extracted: first author, trial design, number of participants, year of publication, mortality, multiple organ failure, nutrition routine and the amount of nutrition received by either group.

Quality and bias assessment

Methodological criteria of the *Cochrane Handbook for Systematic Reviews of Interventions* was used to evaluate quality of the included RCTs. 'Yes' represents the use of appropriate methods, 'No' represents the use of inappropriate methods and 'Unclear' means that the methods were not reported.

Statistical analysis

All statistical analyses were performed using STATA 12.0 (Stata Corporation, College Station, TX, USA). Binary variables were combined to estimate the pooled risk ratio (RR) with 95% confidence intervals (CIs) and the overall weighted mean difference with 95% CIs were used for continuous data. A weighted Mantel–Haenszel χ^2 and an I^2-test were performed to examine heterogeneity. When $P < 0.1$ or $I^2 > 50\%$, a random-effects model was used, otherwise a fixed-effects model was preferred. Begg's funnel plots of RR of mortality and multiple organ failure was used to assess publication bias. $P < 0.05$ was considered statistically significant.

RESULTS

Using the above search strategies, 690 articles were obtained. Screening according to the PRISMA flowchart illustrated in Supplementary Figure S1 identified five eligible studies (including 348 patients) that were included in this meta-analysis.[5–9] The characteristics of the included studies and the details of the amount of nutrition received by the EN and PN groups are

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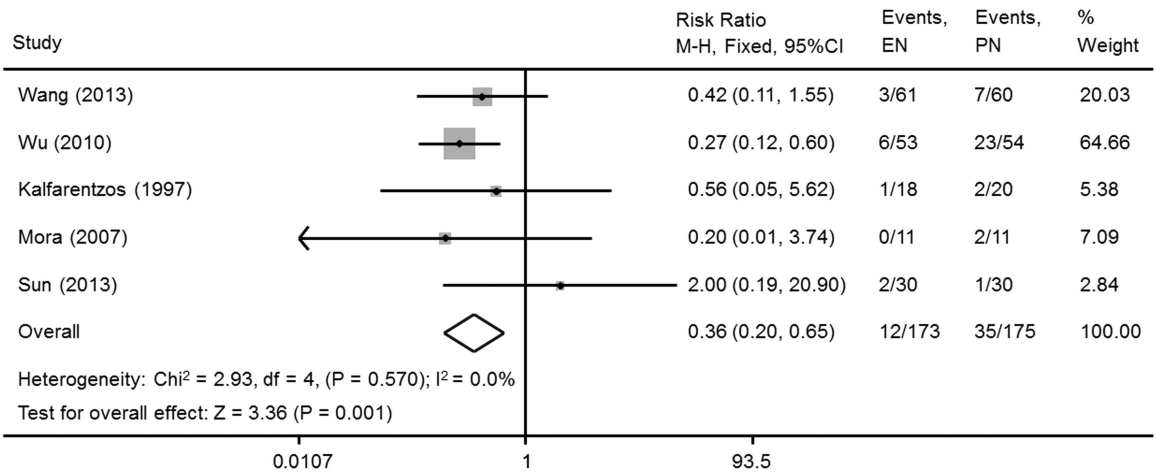

Figure 1. Comparison of the effects on overall mortality of enteral versus parenteral nutrition in critically ill patients with severe acute pancreatitis.

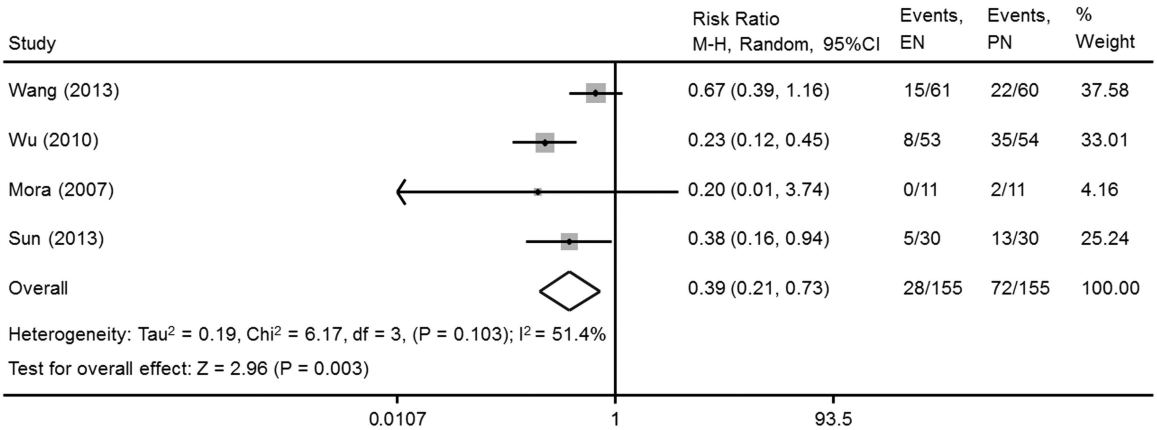

Figure 2. Comparison of the effects on multiple organ failure of enteral versus parenteral nutrition in critically ill patient with severe acute pancreatitis.

shown in Supplementary Table S1a. The quality assessment of these included RCTs is shown in Supplementary Table S1b. After aggregating the available data, there was a significant difference in overall mortality (fixed-effect model: RR = 0.36, 95% CI 0.20–0.65, $P = 0.001$, Figure 1) between the EN and PN groups. The results of multiple organ failure were presented in four studies; the analysis results showed that EN support reduced the frequency of multiple organ failure (random-effect model: RR = 0.39, 95% CI 0.21–0.73, $P = 0.003$, Figure 2). To examine potential publication bias among these included articles, we performed Begg's funnel plots of the RR of mortality and multiple organ failure. No significant publication bias was found (mortality: $Pr > |z| = 0.462$; multiple organ failure: $Pr > |z| = 0.734$).

DISCUSSION

A previous meta-analysis of severe acute pancreatitis showed that EN is superior to PN in terms of mortality and organ failure.[4] However, whether the subgroup of severe pancreatitis patients who are admitted to an ICU could benefit more from EN remains unclear. In this study, we focused on the critically ill patients with severe acute pancreatitis. The selection criteria used in this study, such as critically ill patient, severe acute pancreatitis and a period of ICU management, were designed to take into account the grade of pancreatitis and to reduce heterogeneities as much as possible. In our meta-analysis, EN displayed advantages over PN for critically ill patients with severe acute pancreatitis, such as reduced overall mortality and multiple organ failure, which were similar to a previous study in acute pancreatitis.[4] Many previous human and animal studies on the effects of EN and PN have shown that EN is beneficial in terms of sustaining intestinal immunity and reducing the atrophy of the intestinal mucosa, which lead to improved intestinal barrier function.[2] EN improved the clinical results of critically ill patients with severe acute pancreatitis, which supported the hypothesis that EN maintains the gut barrier function by repairing the mucosal damage of fasting and preserving intestinal epithelial integrity and bacterial flora.[10] However, more studies are warranted to confirm our findings.

There were some limitations to our meta-analysis. First, three full texts and the data concerning multiple organ failure in one of included studies were not available, even upon request. Second, the size of all samples was small. To obtain relatively reliable results, we used a fixed model if the heterogeneity was $< 50\%$; otherwise a random model was used. Finally, there were also limitations regarding differences in the caloric and protein intake; however, the caloric intake between the two groups was similar.

In conclusion, EN can help reduce overall mortality and the rate of multiple organ failure, and should be recommended as the preferred nutritional support for critically ill patients with severe pancreatitis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies the paper on European Journal of Clinical Nutrition website (http://www.nature.com/ejcn)