

Original Contribution

The effect of enteral versus parenteral nutrition for critically ill patients: A systematic review and meta-analysis

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ABSTRACT

Study objective: To analyze the effect of enteral nutrition compared with parenteral nutrition in critically ill patients.

Design: Systematic review and meta-analysis of randomized controlled trials.

Setting: Intensive care unit.

Patients: 23 trials containing 6478 patients met our inclusion criteria.

Intervention: A systematic literature search was conducted to identify eligible trials in electronic databases including PubMed, Embase, Scopus, EBSCO and Cochrane Library. The primary outcome was mortality, the secondary outcomes were gastrointestinal complications, bloodstream infections, organ failures, length of stay in ICU and hospital. We performed a predefined subgroup analyses to explore the treatment effect by mean age, publication date and disease types.

Main results: The result showed no significant effect on overall mortality rate (OR 0.98, 95%CI 0.81 to 1.18, $P = 0.83$, $I^2 = 19\%$) and organ failure rate (OR 0.87, 95%CI 0.75 to 1.01, $P = 0.06$, $I^2 = 16\%$). The use of EN had more beneficial effects with fewer bloodstream infections when compared to PN (OR 0.59, 95%CI 0.43 to 0.82, $P = 0.001$, $I^2 = 27\%$) and this was more noteworthy in the subgroup analysis for critical surgical patients (OR 0.36, 95%CI 0.22 to 0.59, $P < 0.0001$, $I^2 = 0\%$). EN was associated with reduction in hospital LOS (MD -0.90 , 95%CI -1.63 to -0.17 , $P = 0.21$, $I^2 = 0\%$) but had an increase incidence of gastrointestinal complications (OR 2.00, 95%CI 1.76 to 2.27, $P < 0.00001$, $I^2 = 0\%$).

Conclusion: For critically ill patients, the two routes of nutrition support had no different effect on mortality rate. The use of EN could decrease the incidence of bloodstream infections and reduce hospital LOS but was associated with increased risk of gastrointestinal complications.

1. Introduction

When nutrition support was first introduced decades ago, its purpose was to provide the body with essential nutrients, to promote physical development, and to improve clinic outcomes for critically ill patients when oral feeding fails. For critically ill patients, the provision of nutrition is internationally recognized as the standard of care and integral parts of clinical therapies in intensive care unit (ICU), and it is increasingly accepted as a benchmark for the quality care in ICU [1–3]. There are two routes of nutrition support, namely, enteral nutrition (EN) and parenteral nutrition (PN), which is considered as an important determinant of clinical outcomes [4,5]. Use of EN is thought to be more approaching to physiological conditions. Besides providing required nutrients, EN could help maintain

intestinal structure and function, prevent bacterial translocation and stress ulcer. The shortcoming of EN is potential lower nutritional adequacy and gastrointestinal intolerances like diarrhea or vomit. By contrast, PN could better provision of goal calories with fewer gastrointestinal (GI) complications, but is associated with more complications of infection [1,6–8]. During the past decade, EN has been presented as a prior method of nutrition support, both the joint guidelines by the ESICM [9] and ASPEN [10] recommend to use EN in critically ill adult patients immediately after the admission to the ICU rather than PN. Enteral nutrition feeding protocol highlighting the importance of EN has been recommended and widely used [11,12]. However, these recommendations were based on low quality evidence, more high-quality and large-scale randomized controlled trials (RCTs) were needed to confirm or overturn these

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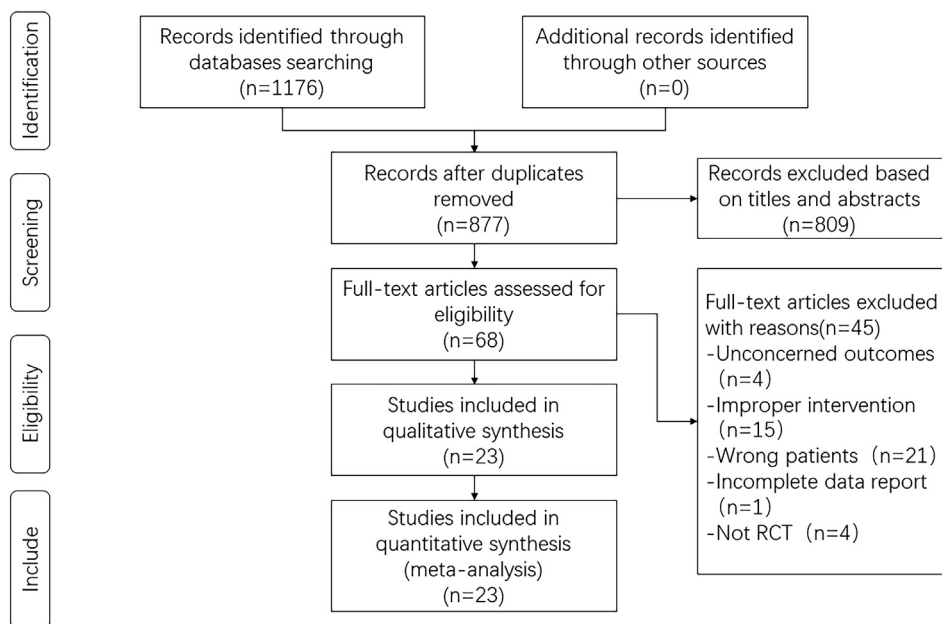


Fig. 1. Flow chart of database search and study selection.

existing conclusions [9,10,13,14].

Previously, five meta-analyses contrasting the two nutrition support routes in critical illness patients reported no different mortality effect but did find a reduction in infectious complications with EN versus PN [4,15–18]. Elke and coworkers [4] found a significant treatment effect difference between dissimilar caloric intake groups, considered high caloric intake was related to a negative treatment effect of PN on mortality and infectious complications. However, many included studies of above-mentioned meta-analyses were outdated and published twenty years ago. More recent studies with large sample size should be aggregated to explore the effect of EN and PN in the ICU setting. Recently, Reignier and coworkers completed the largest RCT to compare the effect of two routes of nutrition support on critically ill patients [19]. In the multicenter and pragmatic study concerning 2410 patients, as compared with PN group, the EN therapy did not reduce the mortality or the risk of infections but increase the risk of digestive complications. This conclusion has challenged the common view that enteral route is clinically superior to the parenteral route in critically ill patients. Therefore, we tend to accomplish an updated systematic review and meta-analysis to further evaluate the effect and compare clinical outcomes between EN and PN for critically ill patients. In addition, we have registered the study in PROSPERO with a registration number CRD42018085907.

2. Methods and materials

2.1. Selecting criteria

Trials included in our meta-analysis should fulfill the following criteria: (1) population should be adult patients (at least 18 years old) who were critically ill. If population was unspecified, we deemed the patient population met one of the following criteria to be critically ill patients: the patients enrolled and study concluded in

any types of ICU; the patients received therapies which is normally delivered in ICU (e.g. invasive mechanical ventilation); the patients' illness required intensive care (e.g. severe trauma that needed urgent laparotomy, brain injury with GCS score ≤ 8 at admission); the patients had been transferred into ICU during study period or had ICU LOS; (2) the study type should be RCT; (3) the intervention should be standard EN versus standard PN, the nutrition support in different routes should start at the same time; (4) the studies should report concerned outcomes. Mortality (including hospital, ICU, 28-day mortality or other. If several mortality rates were reported in one study, we used the mortality at hospital charge in our analysis) was the primary outcome for the meta-analysis. Secondary outcomes were the GI complications (diarrhea and vomiting), bloodstream infections (bacteremia, sepsis, septicemia, catheter-related infection), organ failures (all kinds of organ failures recorded in included studies, including single or multiple organ failure, multiple organ dysfunction syndrome, necessary organ replacement therapy), length of ICU and hospital stay.

2.2. Search strategy and study selection

Five electronic databases were systematically searched (PubMed, Embase, Scopus, EBSCO and Cochrane Library) for eligible RCTs published from the earliest available date until February 2018 without language restriction. And reference lists from studies identified by the research were examined as well. We designed a comprehensive search strategy using the terms “intensive care units”, “critical care”, “enteral nutrition”, “parenteral nutrition”, “randomized controlled trial” and their derivative words, the PubMed and Embase search strategy were recorded in Appendix 1.

The search and selection were conducted by two authors and the process of identifying eligible RCTs was summarized in Fig. 1. Our review authors proceeded searches and reviewed the full text of eligible studies independently. Any disagreement was resolved by a third

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