



Published in final edited form as:

Curr Opin Gastroenterol. 2014 March ; 30(2): 178–181. doi:10.1097/MOG.0000000000000047.

How soon should we start interventional feeding in the ICU?

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Abstract

Purpose of review—Nutrition in the critically ill patient remains a controversial topic. Most clinicians have viewed nutrition as part of patient care but not as a therapeutic intervention. Recent studies have looked at type and timing of nutrition to determine whether they affect important clinical outcomes.

Recent findings—Large-scale, multicentre randomized trials have found that supplemental parenteral nutrition has a deleterious effect in comparison to enteral nutrition alone. Use of early parenteral nutrition in critically ill patients in whom enteral nutrition was contraindicated did not significantly improve clinical outcomes. Also, low-dose or trophic enteral nutrition has similar benefits with less gastrointestinal complications compared with early full dose caloric feedings. The timing of early nutrition has been defined in most large-scale studies as beginning within 48 h of intubation, though some earlier studies used a 24-h cut-off point with some improved outcomes.

Summary—Although not strong, the best available data suggest that critically ill patients should be started on enteral tube feeds within 48 h of intubation whenever possible. The use of parenteral nutrition should be limited within the first 6 days, and not used to augment caloric intake. Finally, similar benefits are seen in patients receiving minimal enteral feeds versus full caloric enteral nutrition.

Keywords

critical care; enteral nutrition; parenteral nutrition; timing; trophic feedings

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Conflicts of interest

Dr Fremont has no conflicts of interest to report. Dr Rice has no conflicts of interest to report with regard to this manuscript. His work on this manuscript is partly funded by NHLBI grant HL 105869. He also receives grant funding from NIH grants RR 032646, HL096504, RR 024975 and HR56174.

INTRODUCTION

Despite numerous recent studies attempting to determine ‘best practice’, the implementation of nutrition in the critically ill patient remains controversial and confusing. As recently as 2009, expert guidelines from North America [1] and Europe [2] disagreed on both type and timing of nutrition. These guidelines are based on expert opinions, but subsequent large multicentre studies have shed some light on determining best practice with regard to optimal timing, type and amount of nutrition in the ICU.

EARLY VERSUS LATE NUTRITION

In the most basic terms, timing of nutrition can be broken down to early versus late. Unfortunately, even this simple dichotomy has problems because the definition of ‘early’ has not been consistent throughout trials. Although early nutrition is often defined as initiating some form of nutrition within 48 h of critical illness, how institutions and studies define the start of critical illness varies from admission to the ICU to time of intubation. Furthermore, in two recent meta-analyses, both showing slight mortality benefits of early nutrition, ‘early’ was defined as the initiation of nutrition within 24 h of critical illness [3,4]. The first study sifted through over 500 randomized controlled trials, eventually finding six, with a combined enrolment of 234 patients. The analysis compared patient-oriented outcomes of infection and mortality, in a heterogeneous group of critically ill patients, randomized to receive early enteral nutrition or not [3]. The use of early enteral nutrition was associated with a 66% reduction in mortality [odds ratio (OR) 0.34; 95% confidence interval (CI) 0.14–0.85] and a 69% reduction in development of pneumonia (OR 0.31; 95% CI 0.12–78). Early enteral nutrition was not associated with a reduction in development of multisystem organ dysfunction. The second study limited the patient population to those who had undergone trauma, finding only three suitable studies and a patient accrual of only 126 [4]. Despite limited power, early enteral nutrition was again associated with a reduction in mortality (OR 0.20; 95% CI 0.04–0.91). Small sample size prevented the evaluation of any other clinical outcomes. Both of these meta-analyses specifically looked at the first 24 h after intubation as their main inclusion criterion, therefore excluding trials that initiated enteral feeds more than 24 h after intubation. Although limited by a small number of patients and weak conclusion, these meta-analyses represent the best available data for the timing of initiating enteral nutrition. However, the results should be confirmed by larger randomized controlled trials.

Subsequent large, multicentre, randomized, controlled trials have defined ‘early’ nutrition as within 48 h [5[■],6[■]]. The EPaNIC trial enrolled over 4500 patients, while the EDEN study enrolled 1000 patients. Both defined early nutrition as starting within 48 h of developing critical illness [5[■],6[■]]. Neither study found the mortality benefit seen in the earlier meta-analyses, more likely due to the limitations of meta-analyses rather than the 24-h discrepancy between definitions of ‘early’ nutrition. However, as no large study has looked at 24 versus 48 h as an initiation of enteral feeds, we can only speculate as to its true significance. Obviously, this fluctuation in timing has also created a wastebasket of what ‘late’ nutrition means in patients.

Keeping these variations in mind, and seeing the trend in the large multicentre randomized controlled trials, it is reasonable to define early nutrition as an intervention occurring within 48 h of the onset of critical illness. A future area of research may look to further elucidate the timing of nutrition within the 48-h range. It is unclear whether nutrition given within 24 h will be more or less beneficial than that given between 24 and 48 h or even later. A confounding factor in this type of research will depend on the comfort level of physicians to enterally feed critically ill patients immediately on arrival to the ICU. Fears about precipitating bowel ischemia in the patient with shock, gastric residual volumes, aspiration, ileus and obtaining enteral access remain prevalent and are probably the largest obstructions to immediate enteral nutrition. Because of these possible complications of enteral nutrition, coupled with the inability to achieve full caloric needs in many patients, the use of parenteral nutrition became a widespread practice in many ICUs. Parenteral nutrition not only became a supplement to enteral nutrition to meet caloric needs, but in many cases also supplanted enteral nutrition and became the sole source of nutrition in critically ill patients [7–9].

SHOULD EARLY ENTERAL NUTRITION BE SUPPLEMENTED WITH PARENTERAL NUTRITION?

The benefits of enteral nutrition have been well established in the literature. Multiple studies have demonstrated that any amount of nutrition administered to the gut has beneficial effects, including stimulating secretion of brush border enzymes, preserving epithelial tight cell junctions, enhancing immune function, preserving intestinal epithelium, mucosal mass and microvilli height and preventing bacterial translocation [10–13]. Initiation of parenteral nutrition to meet the caloric needs of a patient not met by enteral nutrition remains controversial. The European guidelines from 2009 recommended that practitioners consider adding parenteral nutrition to those patients not receiving adequate calories from enteral nutrition by the second day of ICU admission, while the North American guidelines recommended waiting at least a week before starting supplemental parenteral nutrition [1,2]. The EpaNIC trial attempted to answer this question by comparing the use of early (day 2) versus late supplemental parenteral nutrition (day 8) in a heterogeneous group of critically ill adult patients [5[■]]. All patients in the study were managed with a tight glucose control strategy using intravenous insulin and parenteral nutrition was started consisting of only glucose and advanced to protein and lipids over time. Although rates of death in the ICU and hospital and overall survival at 90 days did not differ between groups, the late parenteral nutrition group experienced a 6.3% relative increase in the likelihood of being discharged from the ICU alive, equalling a 1-day shorter median ICU length of stay [5[■]]. Patients in the late parenteral nutrition group also acquired fewer new infections, spent less time on the ventilator and on dialysis [5[■]]. This is the largest study comparing different timing of supplemental parenteral nutrition, when enteral nutrition did not meet full caloric goals. It demonstrated that the addition of parenteral nutrition within the first 48 h in patients only able to tolerate hypocaloric enteral nutrition is detrimental compared with delayed initiation of supplemental parenteral nutrition. A posthoc analysis of the EPaNIC study found that parenteral protein was the likely cause of the detrimental effects in the parenteral arm, and

the more feeding (either enteral or parenteral) a patient received from day 3–7, the less likely that patient would be discharged alive from the ICU [14[■]].

SHOULD PATIENTS UNABLE TO TOLERATE EARLY ENTERAL NUTRITION RECEIVE PARENTERAL NUTRITION?

Despite the results of the EPaNIC study, the question of whether early parenteral nutrition is beneficial in patients unable to receive any enteral nutrition remains largely unknown. EPaNIC could not elucidate this answer because the study only enrolled patients who were able to tolerate at least some enteral nutrition. A recent observational study [8] found that early use of parenteral nutrition may be beneficial if the patient could not receive enteral nutrition. However, a large randomized trial in critically ill patients in which enteral nutrition was contraindicated failed to demonstrate significant benefit of protocolized early initiation of parenteral nutrition compared with standard care [15[■]]. Despite parenteral nutrition being initiated within 24 h of ICU admission in the intervention group compared with a mean of 2.8 days in the control group, 60-day mortality was similar in both groups (21.5 versus 22.8%; $P = 0.60$). Patients started on early parenteral nutrition did experience 0.5 fewer days of mechanical ventilation, but the clinical significance of this remains questionable. Because the control arm was standard of care left to the clinician's discretion, it is difficult to understand the exact differences in nutrition practices between the groups and how these may have affected the clinical outcomes.

HOW MUCH EARLY ENTERAL NUTRITION SHOULD BE PROVIDED?

Although it is well accepted that some enteral nutrition is better than no enteral nutrition, the appropriate amount of calories provided to patients has been a topic of significant debate. Two large studies attempted to answer this question by comparing early low dose enteral nutrition, so-called trophic feeds, versus early full calorie enteral feeds. The first study randomized 200 patients with various causes of acute respiratory failure from a single centre to either trophic feeds (10 ml/h) versus full feeds (25 ml/h with an increase every 6 h until full caloric needs met) for the first 6 days of mechanical ventilation [16]. Enteral feedings were initiated within 48 h of intubation in both groups. The results of this study found no significant difference in clinical outcomes, including days alive and off the ventilator, out of the ICU or survival, between either arms of the study [16]. This study design was repeated in a multicentre randomized controlled study in patients who had lung injury, the so-called EDEN study [6[■]]. One thousand patients were randomized to a similar protocol as the previous study with low-dose trophic feeds versus full feeds for the first 6 days of respiratory failure. Again, this study did not demonstrate any significant difference in clinical outcomes (mortality, ventilator free days, infectious complications) between the two study groups [6[■]]. Not surprisingly, there were more gastrointestinal intolerances in the full feeding arm in both studies, but not severe enough to warrant protocol changes or other significant interventions. Recently, the EDEN investigators published a 1-year outcomes study from their trial, having received data from 525 of the original 1000 patients [17[■]]. At both 6-month and 1-year follow ups after their illnesses, researchers found no significant differences between the low-dose trophic feeding group versus the full dose feeding group in

any meaningful clinical outcome, including cognitive and muscle strength measurements [17[■]].

CONCLUSION

The timing of nutrition for critically ill patients has undergone significant study and change over the last 10 years. The trend now is to initiate nutrition within the first 48 h of mechanical ventilation, to minimize the use of parenteral nutrition and to use some enteral nutrition, though full caloric enteral feedings for at least the first 6 days do not appear to confer significant benefit over low-dose trophic enteral feedings. Continued areas of research will focus on earlier initiation of nutrition, different types of enteral nutrition and supplementation, as well as when, if ever, parenteral nutrition is beneficial.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
 - ■ of outstanding interest
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KEY POINTS

- Early interventional feeding in critically ill patients is variably defined as within 24–48 h from initiation of mechanical ventilation or ICU admission.
- Although sparse, available data suggest early enteral feeding may improve clinical outcomes compared with starvation in critically ill patients.
- Early advancement of enteral feeds to goal caloric rates has not been shown to improve outcomes in a heterogeneous population of mechanically ventilated critically ill patients or in patients with acute lung injury.
- Supplementing enteral nutrition with parenteral nutrition within the first 7 days of critical illness did not improve outcomes in critically ill patients and resulted in higher mortality and longer time to discharge from the ICU alive.