

Intensive Care Nutrition and Postintensive Care Recovery

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KEYWORDS

- Critical illness • Feeding • Parenteral nutrition • Enteral nutrition
- ICU-acquired weakness • Catabolism • Recovery • Autophagy

KEY POINTS

- Critically ill patients are at risk of developing intensive care unit (ICU)-acquired weakness, which aggravates outcome and may persist even years after ICU admission.
- Early full-dose artificial nutrition does not benefit critically ill patients and may even be harmful, especially early parenteral nutrition.
- The ideal timing of artificial nutrition for critically ill patients as well as the optimal dose and composition remain unclear.
- There is no benefit of adding specialized “immunonutrients” to the feeding mixture of critically ill patients, and glutamine administration may be harmful.
- The harmful impact of early parenteral nutrition seems explained by the inability to inhibit muscle wasting and by feeding-induced suppression of autophagy.

INTRODUCTION

Intensive care unit (ICU)-acquired weakness is a devastating complication of critical illness. With time in ICU, the incidence increases and its presence is associated with increased short-term and long-term mortality.^{1,2} In ICU survivors, ICU-acquired weakness often does not recover completely, even years after ICU admission.³ Persistent ICU-acquired weakness is considered to be part of the postintensive care

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syndrome, which encompasses a spectrum of persistent physical, mental, and cognitive impairment seen in survivors of critical illness, especially after prolonged and/or severe critical illnesses.⁴ The mechanisms underlying ICU-acquired weakness are complex and involve structural and functional alterations in both muscles and nerves.⁵ Attributed myofibers show signs of atrophy, which may be triggered by inflammation, immobilization, endocrine and metabolic alterations, impaired microcirculation, denervation, and certain drugs.⁵ Apart from that, relative starvation may also play a role. Indeed, a considerable number of patients have a nutritional deficit on ICU admission and/or cannot receive normal feeding. In healthy volunteers, prolonged underfeeding mimics the severe muscle atrophy as typically observed in prolonged critically ill patients. In these otherwise healthy people, this condition obviously can be reversed by giving nutrition.⁶

TO FEED OR NOT TO FEED?

Several observational studies have associated the accumulation of a caloric and/or protein deficit in critically ill patients with an increased risk of ICU-acquired weakness and mortality. Hence, for a long time, early full nutritional support has been recommended for critically ill patients.⁷ However, whether the relationship between feeding deprivation and ICU-acquired weakness and decreased survival is causal or not cannot be deduced from observational studies. Indeed, because tolerance of feeding, especially of enteral nutrition (EN), is affected by the severity of illness, the association of enhanced feeding with improved outcome could be explained by a better feeding tolerance in less sick patients.⁸ Establishing a causal relationship can only be done by a randomized controlled trial (RCT). Because of the long-lasting dogma of starvation harming critically ill patients and the resultant ethical constraints, RCTs randomizing patients to artificial feeding or no feeding have not been performed. Instead, in the last years, several large RCTs have investigated the impact of different doses (and routes) of artificial feeding.^{9–17} These studies have substantially changed the insights in the effects of nutritional support in critical illness (**Table 1**). Indeed, recent RCTs have not confirmed the hypothesized benefit of early, enhanced artificial feeding of critically ill patients and several trials have indicated potential harm.^{9,10,15} This article reviews the evidence obtained from these studies, the underlying mechanisms potentially explaining the results, and the remaining questions.

IS EARLY SUPPLEMENTATION OF INSUFFICIENT ENTERAL NUTRITION WITH PARENTERAL NUTRITION BENEFICIAL?

In patients unable to eat by mouth, early EN has been recommended over early parenteral nutrition (PN).¹⁸ Often, however, full EN is not tolerated or even contraindicated. Hence, the question arises when to initiate or associate PN to ensure the intended nutritional target. Because of the lack of adequately powered RCTs, clinical practices have varied widely. Proponents of early PN have referred to the avoidance of a caloric and protein deficit by this approach, whereas opponents referred to the potentially increased risk of complications, especially infectious complications.⁸

In the last years, several RCTs have investigated whether early supplementation of insufficient or failing EN with PN offers clinical benefit.^{9–13} In contrast to the expectations, none of these RCTs showed benefit on the primary endpoint and the 2 largest RCTs, the Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically Ill Patients (EPaNIC) and Early versus Parenteral Nutrition in the Pediatric Intensive Care Unit (PEPaNIC) trial, demonstrated harm.^{9–13,19} Indeed, as compared with withholding PN until 1 week after ICU admission, early supplementation of insufficient EN

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