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SUMMARIES OF RECENT PUBLICATIONS ON THE BENEFITS OF HIGH PROTEIN IN THE ICU

Table of contents:

The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study

Cathy Alberda, Leah Gramlich, Naomi Jones, Khursheed Jeejeebhoy, Andrew G. Day, Rupinder Dhaliwal, Daren K. Heyland. *Intensive Care Med*, 2009;35;1728–1737

Objectives:

The objective of this study was to examine the relationship between the amount of energy and protein administered and clinical outcomes, and the extent to which pre-morbid nutritional status influenced this relationship.

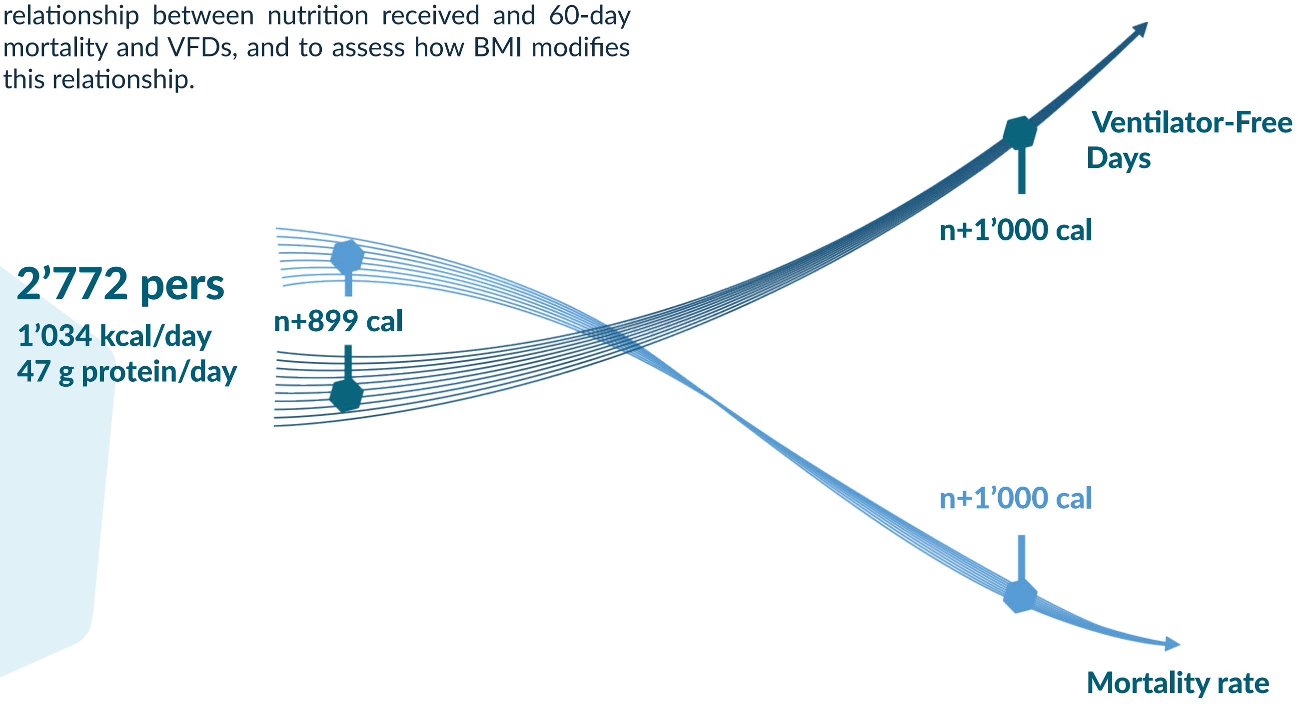
Methods:

An observational cohort study of nutrition practices performed in 167 intensive care units (ICUs) across 37 countries. The collection of patient demographics, the type and amount of nutrition received were recorded daily for a maximum of 12 days.

The follow-up of patients was performed prospectively to determine 60-day mortality and ventilator-free days (VFDs). The body mass index (BMI, kg/m^2) was used as a marker of nutritional status prior to ICU admission. Regression models were used to evaluate the relationship between nutrition received and 60-day mortality and VFDs, and to assess how BMI modifies this relationship.

Results:

2'772 mechanically ventilated patients received an average of 1'034 kcal/day and 47 g protein/day. An increase of 1'000 cal per day was associated with reduced mortality [odds ratio for 60-day mortality 0.76; 95% confidence intervals (CI) 0.61–0.95, p = 0.014] and an increased number of VFDs (3.5 VFD, 95% CI 1.2–5.9, p = 0.003). The authors noticed that the effect of increased calories was associated with lower mortality in patients with a BMI<25 and >or=35 with no benefit for patients with a BMI 25 to <35. Similar results were observed when comparing increasing protein intake and its effect on mortality.



Conclusion:

Increased intakes of energy and protein appear to be associated with improved clinical outcomes in critically ill patients, particularly when BMI is <25 or, > or =35.

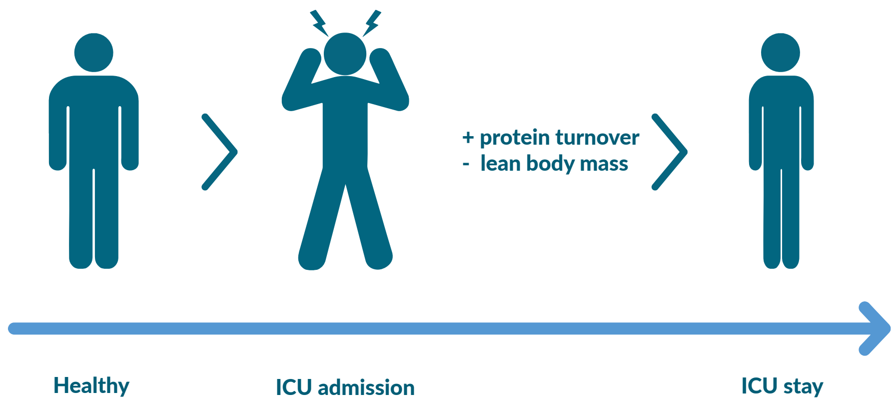
Proteins and amino acids are fundamental to optimal nutrition support in critically ill patients

Peter JM Weijs, Luc Cynober, Mark DeLegge, Georg Kreymann, Jan Wernerman and Robert R Wolfe.
Critical Care. 2014;18:591

Highlights:

Proteins and amino acids are widely considered to be subcomponents in nutritional support. In addition, proteins and amino acids are essential to recovery and survival, not only for their ability to preserve active tissue mass, but also for a variety of other functions.

It is critical to understand that the optimal amount of protein intake during nutritional support is fundamental to appropriate clinical care. Although the body adapts in some ways to starvation, metabolic stress in patients causes increased protein turnover and loss of lean body mass. In this review, the growing scientific evidence is presented on the importance of protein and amino acid provision in nutritional support and their impact on preservation of muscle mass and patient outcomes. Studies identifying optimal dosing for proteins and amino acids are not currently available. The authors discuss the challenges physicians face in administering the optimal amount of protein and amino acids. In addition, protein related nutrition concepts, including adaptation to starvation and stress, anabolic resistance, and potential adverse effects of amino acid provision are presented. They describe the methods for assessment of protein status, and outcomes related to protein nutritional support for critically ill patients. The identification of a protein target for individual critically ill patients is key for outcomes, particularly for specific subpopulations, such as obese and older patients. Additional research is urgently needed to address these issues. In critically ill patients, in parallel with the severity of the injury, increases in proinflammatory cytokines, glucocorticoids, and oxidative stress reinforce the effect of catabolic hormones, and contribute to insulin resistance and muscle wasting.



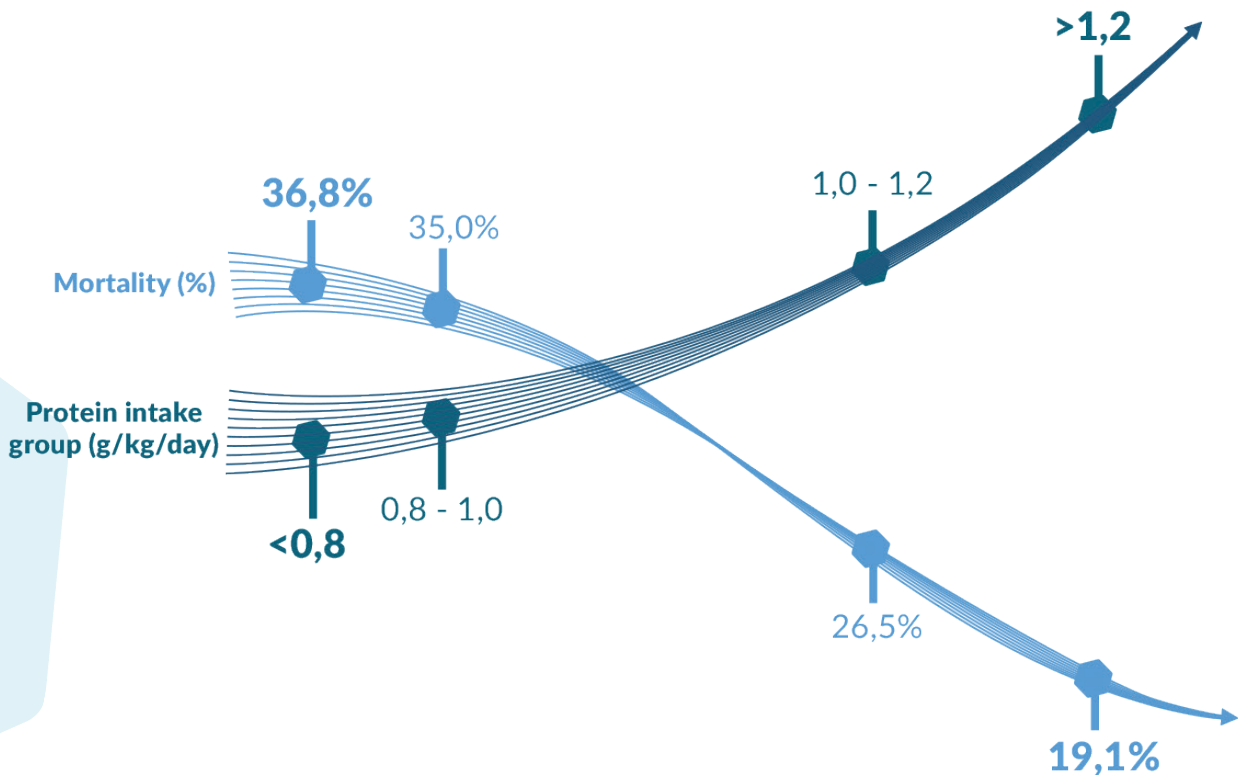
Optimal protein and energy nutrition decreases mortality in mechanically ventilated, critically ill patients: a prospective observational cohort study

Weijs PJ, Stapel SN, de Groot SD, Driessen RH, de Jong E, Girbes AR, Strack van Schijndel RJ, Beishuizen A.
J Parenter Enteral Nutr. Jan 2012;36(1):60-68

Background:
Optimal nutrition for patients in the intensive care unit has been proposed to be the provision of energy as determined by indirect calorimetry and the provision of protein of at least 1.2g/kg/day.

Methods:
A prospective observational cohort study in a mixed medical-surgical intensive care unit in an academic hospital. 886 consecutive mechanically ventilated patients were included. Nutrition was guided by indirect calorimetry and protein provision of at least 1.2 g/kg. Cumulative intakes were calculated for the period of mechanical ventilation. An analysis (Cox regression) of the effect of protein + energy target achieved or energy target achieved versus neither target achieved on 28-day mortality, and adjustments for sex, age, body mass index, APACHE II, diagnosis, and hyperglycemic index.

Results:
The patients' mean age was 63 ± 16 years; body mass index, 26 ± 6; and APACHE II, 23 ± 8. For neither target, energy target, and protein + energy target, energy intake was 75% ± 15%, 96% ± 5%, and 99% ± 5% of target, and protein intake was 72% ± 20%, 89% ± 10%, and 112% ± 12% of target, respectively. Hazard ratios (95% confidence interval) for energy target and protein + energy target were 0.83 (0.67-1.01) and 0.47 (0.31-0.73) for 28-day mortality.



Conclusions:
Optimal nutritional therapy in mechanically ventilated, critically ill patients, defined as protein and energy targets reached, is associated with a decrease in 28-day mortality by 50%; whereas, only reaching energy targets is not associated with a reduction in mortality.

Fundamental determinants of protein requirements in the ICU

Peter J.M. Weijs. *Curr Opin Clin Nutr Metab Care*. 2014;17:183–189

Purpose of review

As feeding the ICU patient is highly discussed, energy feeding has been the topic of randomized studies, however, protein feeding has not been. Study results are contradictory on early feeding; but little is known about early protein requirement. What is this protein requirement based on, and what are the fundamental determinants?

Recent findings

Recent studies addressed the importance of protein feeding and/or muscle (protein) wasting in critically ill patients, targeted feeding has been shown to improve protein balance in one study, and infection rate in one study. In two studies, low muscle mass, which is present in ICU admission, has been shown to be related to higher mortality. Four studies have related muscle wasting to (protein) and feeding strategies showed very diverse results. Two small studies have reported no advantage [n=15, computed tomography] or negative impact (n=62, ultrasound, 50% sepsis patients) of protein on muscle wasting. Two studies, one small (n=33, computed tomography) and one very large (n=1372, Subjective Global Assessment), have reported a positive impact of (early) feeding on muscle wasting.

The key points are:

Understanding of fundamental determinants of protein requirements in critically ill patients is weak, but guidelines of 1.2 g protein/kg per day are currently supported.

Muscle mass is important for both short-term and long-term outcomes in critically ill patients and can be modified by protein feeding.

Tipping the delicate balance between wasting that is beneficial for short-term survival or fatal to long-term physical function remains a matter of debate.

There are no data to support a lower early protein intake; there are data to support a lower early energy intake.

Fundamental determinants of early protein feeding should be biomarkers, functional markers and outcome based.

Conclusions:

Adequate protein feeding in critically ill patients, at least 1.2 g/kg/day and targeted energy feeding using indirect calorimetry are fundamental to nutrition support. The level of protein requirement is related to fat free mass or muscle mass, which makes sex and BMI also relevant. Targeted early protein feeding is found to improve short-term outcome, reduction of muscle wasting and hospital mortality. Long-term outcome of protein feeding has not been studied. However, targeted protein feeding may be harmful in sepsis patients. Until now, it has not been possible to provide protein at the level needed for an individual patient due to a lack of biomarkers that can be used as an indicator of protein required.

Energy deficit is clinically relevant for critically ill patients: no

L. John Hoffer and Bruce R. Bistrian. *Intensive Care Med*. 2015;41:339–341

Highlights:

Many recent randomized clinical trials (RCTs) of nutritional support in critical illness have fallen short of a standard of solid science by focusing only on the benefits of high calorie provision, while ignoring a much more important nutritional requirement[1]. The amount of protein provided in all but two recent clinical trials—both of which indicated better outcomes in the protein-supplemented patients[2]—was far less than what the best available evidence indicates it ought to be.

Experts trained in nutrition agree that critically ill patients need much more protein than normal ones. Thus, while the recommended protein intake for normal people is 0.8 g/kg per day, the commonest recommendation in critical illness is 1.5 g/kg normal dry body weight per day. Most recent RCTs on nutritional support in critical illness provide much less than this.

Frequently obesity and muscle atrophy coexist in the intensive care unit (ICU). Extensive metabolic data, and some limited clinical trial evidence, suggest that the early provision of 1.5–2.5 g protein/kg per day could benefit many critically ill patients[3].

Physiologically based nutritional therapy in protein-catabolic critical illness is a priority. Identifying that patients have borderline/subnormal muscle mass (protein energy malnutrition, cachexia, disuse atrophy, old age or neuromuscular disease) as indicated by history and physical examination, irrespective of the adipose tissue mass is key.

In patients experiencing intense protein catabolism, some precautions have to be taken as in severe liver dysfunction, or in renal insufficiency when renal replacement therapy is unavailable.

Given the imprecision of available methods for estimating energy expenditure, the attempt to match calorie delivery to energy expenditure increases the risk of energy overfeeding and hyperglycemia without any compensating benefit.

The author estimated that prudence dictates erring on the side of safety by limiting calorie provision to 50–70 % of energy expenditure while simultaneously increasing protein provision to compensate for the inefficiency of protein retention created by the hypocaloric state[4].

Many observational studies have shown a relationship between low rates of calorie provision and poor clinical outcomes, but the authors of these studies uniformly failed to appreciate that calorie-deficient diets are even more seriously deficient in protein. The evidence upon which the "not enough calories" hypothesis is based, and which has now been tested with negative results, is more properly interpreted as supporting the "not enough protein" hypothesis, which remains untested.

Recent clinical care guidelines for critically ill obese patients recommend protein provision of 2.0–2.5 g/kg normalized dry body weight per day while limiting calorie provision to 50–70 % of energy expenditure[5]. Lastly, the authors state, "There's no logical reason to restrict this recommendation to patients whose fat store is pathologically expanded".

Protein intake recommendation:

0.8 g/kg per day
Healthy person's protein needs

1.5 g/kg per day
ICU patient's protein needs

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[2]Hoffer LJ, Bistrian BR (2014) What is the best nutritional support for critically ill patients? Hepatobiliary Surg Nutr 3:172–174
[2]Botran M, Lopez-Herce J, Mencia S, Urbano J, Solana MJ, Garcia A (2011) Enteral nutrition in the critically ill child: comparison of standard and protein-enriched diets. J Pediatr 159:27–32
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[4]Hoffer LJ, Bistrian BR (2012) Appropriate protein provision in critical illness: a systematic and narrative review. Am J Clin Nutr 96:591–600
[5]Choban P, Dickerson R, Malone A, Worthington P, Compher C, American Society for Parenteral and Enteral Nutrition (2013) A.S.P.E.N. Clinical guidelines: nutrition support of hospitalized adult patients with obesity. JPEN 37:714–744

Should we increase protein delivery during critical illness?

Van Zanten Arthur R. H. *Journal of Parenteral and Enteral Nutrition*. © 2016 *American Society for Parenteral and Enteral Nutrition*

Rationale for Protein Provision in the Critically Ill

Proteins are synthesized from the pool of free amino acids available from degradation of proteins, denovo synthesis, and nutrition intake provided as oral nutrition, enteral nutrition (EN), or parenteral nutrition (PN). The rate of amino acids is incorporated into newly synthesized proteins, regulation of metabolic pathways, or oxidation and disposal as urea.

Protein Catabolism in Critical Illness

Commonly in critically ill patients, a prolonged and marked catabolic response may be encountered. Reductions in total body protein mass are considered highly relevant as they are associated with many complications such as infectious morbidity[1] and even higher mortality[2].

Muscle Wasting in Critical Illness

Severe protein degradation may lead to unintended and extensive muscle wasting, recently quantified during the first ten days after intensive care unit (ICU) admission by Puthucheary et al[3]. They showed that reductions up to 15%–25% of the muscle mass, as measured by sequential rectus femoris ultrasound, were typical, and the extent of LBM loss was associated with worse outcome. Moreover, loss of muscle mass was more pronounced in patients with multiple-organ dysfunction syndrome (MODS) compared with patients with single-organ failure only.

What Is the Best Protein Target in Critical Illness?

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) guidelines recommend for general ICU patients with a BMI <30 kg/m^2, protein requirements should be in the range of 1.2–2.0 g/kg actual body weight/day, and also that for all classes of obesity where BMI is >30 kg/m^2, protein should be provided in a range ≥2.0 g/ kg actual body weight/d for class I and II patients (BMI 30–40 kg/m^2) and ≥2.5 g/ kg actual body weight/d for class III patients (BMI ≥40 kg/m^2)[4].

Observational Studies on Proteins and Calories in Critical Illness

In a prospective study among 113 severely ill ICU patients in Denmark, a higher provision of protein and amino acids was associated with a lower mortality. This was not the case for the provision of energy[5].

In a large observational study, Weijs et al[6] clearly demonstrated that higher protein intake was associated with better survival. Meeting only caloric targets without meeting protein demands did not confer the same mortality reduction as when also protein targets were reached. In another study, this group showed that in non-septic patients, an almost linear association with mortality reduction was found when protein intake groups from 0.8 g/kg/d were compared with groups ranging from 1.0–1.2 g/kg/d[7]. A strategy to set nutrition targets and to focus on protein intake first was recommended[8].

Consequences of a Primary Protein Strategy

A higher protein intake should be prescribed to the critically ill, or at least it should be tried to achieve better protein targets than has been shown to be delivered in large observational trials, to focus on protein targets and delivery first and subsequently focus on energy delivery. Just prescription and delivery of more enteral or parenteral feeds to achieve better protein intake seems, said the author, a simple solution, but this may come with a price. The author stressed the importance of enteral and parenteral feeds with higher protein content, not by increasing protein content by prescribing more concentrated feeds with more proteins and energy per milliliter with a similar protein to energy ratio, but by developing enteral products with higher protein to energy ratios. Overfeeding in critically ill patients is associated with many complications, such as hyperglycemia due to increased insulin resistance, hepatic steatosis, refeeding syndrome, infectious morbidity, increased ICU length of stay at least partly due to longer duration of mechanical ventilation, and even mortality[9].

Conclusion:

Large RCTs are warranted to study the effects of isocaloric high-protein enteral feeds compared with normal protein enteral feeds as well as parenteral comparators with different amounts of amino acids on relevant clinical end points, including long-term functional outcomes, in survivors. Until this data becomes available, Health Care Professionals should try to optimize protein intake and at least aim to achieve the present recommended targets. At this time, a protein-focused strategy in nutrition support for critically ill patients may help while avoiding overfeeding energy.

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[2] Ali NA, O'Brien JM Jr, Hoffmann SP, et al. Midwest Critical Care Consortium. Acquired weakness, handgrip strength, and mortality in critically ill patients. Am J Respir Crit Care Med. 2008;178(3):261-268.

[3] Puthucheary ZA, Rawal J, McPhail M, et al. Acute skeletal muscle wasting in critical illness. JAMA. 2013;310(15):1591-1600.

[4] McClave SA, Martindale RG, Vanek VW, et al; A.S.P.E.N. Board of Directors; American College of Critical Care Medicine; Society of Critical Care Medicine. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2009;33:277-316.

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[7] Weijs PJ, Looijaard WG, Beishuizen A, Girbes AR, Oudemans-van Straaten HM. Early high protein intake is associated with low mortality and energy overfeeding with high mortality in non-septic mechanically ventilated critically ill patients. Crit Care. 2014;18(6):701.

[8] Weijs PJ, Wischmeyer PE. Optimizing energy and protein balance in the ICU. Curr Opin Clin Nutr Metab Care. 2013;16(2):194-201.

[9] Weijs PJ, Looijaard WG, Beishuizen A, Girbes AR, Oudemans-van Straaten HM. Early high protein intake is associated with low mortality and energy overfeeding with high mortality in non-septic mechanically ventilated critically ill patients. Crit Care. 2014;18(6):701.

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