Jean-Charles Preiser
Yaseen M. Arabi

Be early for enteral, no rush for calories!

Received: 17 November 2015
Accepted: 17 November 2015
Published online: 25 November 2015
© Springer-Verlag Berlin Heidelberg and ESICM 2015

J.-C. Preiser (✉)
Department of Intensive Care, Erasme University Hospital,
Université Libre de Bruxelles, 808 Route de Lennik, 1070 Brussels,
Belgium
e-mail: preiserj@ulb.ac.be
Tel.: +3225554756

Y. M. Arabi
King Abdullah International Medical Research Center, King Saud
Bin Abdulaziz University for Health Sciences, Riyadh, Saudi
Arabia

The recent systematic review and meta-analysis by Marik and Hooper [1] challenges the long-held belief that more calories are better, one of the most controversial areas of discussion in the field of metabolic and nutritional support of the critically ill [2]. This classical statement has been mainly based on observational studies reporting an association between low caloric intakes and higher rate of complications [3, 4], while other retrospective studies have suggested a better outcome with hypocaloric than with normocaloric feeding [5, 6]. Importantly, the thorough and rigorous review of the recent randomized controlled trials [1] revealed no significant outcome difference between groups randomized to “hypocaloric” or “trophic” over “normocaloric” feeding, defined as the provision of energy designed to match the energy expenditure early during the course of critical illness (Fig. 1).

In all retrieved studies, enteral feeding was initiated at an early stage in critical illness, although the studies had several differences in the amount of proteins between the “normocaloric” and the “hypocaloric” or “trophic” groups [6–9], in the management on enteral feeding and in the calculation of caloric intakes. In addition, the degree and duration of caloric restriction differed, by design, between trophic and permissive underfeeding studies (Fig. 1). Nevertheless, the absence of difference in outcome is definitely relevant to contemporary ICUs, as the individual studies were all performed after 2010, the caloric intakes were well separated between groups, and the study populations are reasonably representative of mixed ICUs of the Western world, except for the young age [8–10].

Are these findings surprising? Probably not, when nuancing the potential benefit of early caloric intake with the high risk of inadvertent overfeeding, when the endogenous production of glucose cannot be inhibited by exogenous substrates [11, 12], and considering the non-nutritional calories provided when glucose or lipids are used as maintenance solutions or solvents, which are not always accounted for. As a result, during the early days of critical illness, the excess calories can be stored as adipose tissue within muscles [13] instead of being used to provide energy or to increase muscle mass. Other potential explanations for the lack of benefits or the potential toxicity of normocaloric feeding include the inhibition of autophagy [14]. From a teleological standpoint, the anorexia occurring during the early phase of critical illness could be adaptive to prevent the toxicity of overfeeding, while prioritizing vital functions. This hypothesis is supported by the tight regulation process of appetite by enterohormones released from the gastrointestinal tract.

In contrast to the risk associated with a high caloric intake early during the course of critical illness, the use of the enteral route as early as possible is desirable. Several

Fig. 1 Schematic representation of 3 feeding strategies: normocaloric or full feeding (*green line*) aims to match energy expenditure (EE) as early as possible; hypocaloric or permissive underfeeding aims to match 50–70 % of EE according to individual tolerance; trickle or trophic feeding aims to provide a minimal amount of enteral feeds, resulting in the provision of 10–20 % of EE

lines of evidence support the preferential use of the gastrointestinal tract over the intravenous route for nutrition, even though the final proof of prevention of translocation by enteral nutrition is still lacking in humans. The

proponents of trickle or trophic feeds suggest the infusion of a minimal amount of enteral nutrition, irrespective of the amount of calories infused [9]. Interestingly, the absorption of nutrients itself can be delayed during the acute phase [15], consistent with adaptive changes in digestive physiology to prevent overfeeding.

Several additional issues are raised and left unanswered by the studies analyzed by Marik and Hooper [1], including the selection of the best end-point to assess the efficacy of nutrition. The authors of the meta-analysis reported only the available variables, mortality, length of stay and infectious complications, which could reflect the safety of nutritional interventions, rather than their actual efficacy. Likewise, a global strategy of nutrition associated with physical activity is more likely to preserve muscular function and autonomy, but this assumption needs to be assessed prospectively and rigorously. The frequency of refeeding syndrome, a major safety outcome, could be overlooked in the absence of stratification based on the prior nutrition status, or could also be relevant in patients starving for a few days.

Compliance with ethical standards

Conflicts of interest None.

References

1. Marik PE, Hooper MH (2015) Normocaloric versus hypocaloric feeding on the outcomes of ICU patients: a systematic review and meta-analysis. *Intensive Care Med*. doi: [10.1007/s00134-015-4131-4](https://doi.org/10.1007/s00134-015-4131-4)
2. Preiser JC, van Zanten ARH, Berger MM, Biolo G, Casaer MP, Doig GS et al (2015) Metabolic and nutritional support of critically ill patients: consensus and controversies. *Crit Care* 19:35
3. Villet S, Chiolero RL, Bollmann MD, Revelly J-P, Cayeux RNM-C, Delarue J et al (2005) Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. *Clin Nutr* 24:502–509
4. Alberda C, Gramlich L, Jones N, Jeejeebhoy K, Day AG, Dhaliwal R et al (2009) The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. *Intensive Care Med* 35:1728–1737
5. Crosara ICR, Mélot C, Preiser JC (2015) A J-shaped relationship between caloric intake and survival in critically ill patients. *Ann Intensive Care* 5:37
6. Rubinson L, Diette GB, Song X, Brower RG, Krishnan JA (2004) Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit. *Crit Care Med* 32:350–357
7. Petros S, Horbach M, Seidel F, Weidhase L (2014) Hypocaloric vs normocaloric nutrition in critically ill patients: a prospective randomized pilot trial. *J Parenter Enteral Nutr*. doi: [10.1177/014860711452898](https://doi.org/10.1177/014860711452898)
8. Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP (2011) Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. *Crit Care Med* 39:967–974
9. Rice TW, Wheeler AP, Thompson BT, Steingrub J, Hite RD, Moss M et al (2012) Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *JAMA* 307:795–803
10. Arabi YM, Aldawood AS, Haddad SH, Al-Dorzi HM, Tamim HM, Jones G et al (2015) Permissive underfeeding or standard enteral feeding in critically ill adults. *N Engl J Med* 372:2398–2408
11. Preiser JC, Ichai C, Orban J-C, Groeneveld ABJ (2014) Metabolic response to the stress of critical illness. *Br J Anaesth* 2014(113):945–954
12. Fraipont V, Preiser JC (2013) Energy estimation and measurement in critically ill patients. *J Parenter Enteral Nutr* 37:705–713
13. Casaer MP, Langouche L, Coudyzer W, Vanbeeckvoort D, De Dobbelaer B, Güiza FG et al (2013) Impact of early parenteral nutrition on muscle and adipose tissue compartments during critical illness. *Crit Care Med* 41:2298–2309
14. Hermans G, Casaer MP, Clerckx B, Güiza F, Vanhullebusch T, Derde S et al (2013) Effect of tolerating macronutrient deficit on the development of intensive-care unit acquired weakness: a subanalysis of the EPaNIC trial. *Lancet Respir Med* 1:621–629
15. Deane AM, Rayner CK, Keeshan A, Cvijanovic N, Marino Z, Nguyen NQ et al (2014) The effects of critical illness on intestinal glucose sensing, transporters, and absorption. *Crit Care Med* 42:57–65