



## Editorial

# Optimal amount of calories for critically ill patient



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Clinical nutrition is generally considered in patients unable to eat and is therefore indicated in mechanically ventilated critically ill patients. The recent ESPEN guidelines state that medical nutrition therapy shall be considered for all patients staying in the ICU, mainly for more than 48 h, as every critically ill patient staying for more than 48 h in the ICU should be considered at risk for malnutrition [1] with a low level of supporting evidence. Despite several well-conducted studies recently published, important questions remain matter of debate regarding nutrition practices such as the route of nutrition delivery, timing of nutrition initiation and the exact amount of energy and protein that should be provided. Observational studies performed over the last decades consistently reported an association between a high energy deficit (caloric intake – energy expenditure) and an increased rate of complications (infections, ventilation duration, mortality. . .) [2]. Several interventions can be assessed to compare prospectively different caloric intakes. Controlled trials designed to compare underfeeding or trophic feeding provided by the enteral route failed to demonstrate any benefit of an increased caloric intake to 20–25 kcal/kg/d early during the course of critical illness [3,4]. These findings, together with the increased morbidity found in patients receiving high caloric intakes by early parenteral nutrition [5], support the “baby stomach concept” [6]. Another approach to answer the issue of optimal caloric intakes was assessed by the investigators of the TARGET (The Augmented versus Routine Approach to Giving Energy Trial) study, i.e. a comparison between an energy-dense (1.5 kcal/mL) and a standard enteral formula (1.0 kcal/mL) in mechanically ventilated critically patients. This approach allowed the increase of caloric intakes, without any change in the protein intakes. The tested research hypothesis was a decrease in all-cause mortality within 90 days in patients randomised to the energy-dense formula. The results of this double-blind trial performed in 46 ICUs in Australia and New Zealand were recently published in the *New England Journal of Medicine*. Over the 17 months of the study, 4000 patients were randomised, 3,957 included in the modified intention-to-treat population and 3914 were analysed. The patients from the

energy-dense group and the standard group received a similar average daily volume of enteral nutrition ( $1242 \pm 318$  mL and  $1262 \pm 313$  mL respectively) for a median duration of six days (6, interquartile range from 3 to 11 days; 6, interquartile range 3 to 11 days respectively) corresponding to a total mean calories of 30.2 kcal/kg/day and 21.9 kcal/kg/day respectively. There was no significant difference between the energy-dense group and the routine group in the rate of all-cause 90 days mortality (primary outcome): 26.8% and 25.7% respectively. Similarly, no difference was found in any of the secondary outcome variables measured (death at hospital discharge, death by day 28, use and duration of organ support, rate of infection, electrolyte abnormalities or gastrointestinal events). In seven predefined clinically relevant subgroups of patients classified based on their age, diagnostic (trauma, sepsis, neurological diagnosis), medical or surgical treatment, risk of death, body mass index, the primary outcome did not differ between patients fed with the energy-dense or the standard formula. Regurgitation or vomiting, the use of promotility drugs or insulin was significantly more frequent in patients randomised to the energy-dense arm.

These results are of importance demonstrating similar mortality rate in patients receiving less calories than the energy expended (almost 20 kcal/kg/day) and in those receiving almost an amount of calories close to the energy expenditure (30 kcal/kg/day). In contrast to the study hypothesis, it appears that higher calories did not result in better survival. This result may be discussed in light of the consistency between the intervention and the primary outcome measure chosen, as the clinical plausibility of a link between the short-term intervention and the 90-day mortality is highly debatable. Further nutrition trials exploring patient-centred outcomes such as long-term functional outcomes may promote additional information on the exact role on nutrition in ICU. Although the authors provide useful supplementary analyses on clinically relevant predefined subgroup of patients, this negative result may highlight the patient heterogeneity of the patient response to the intervention: with some positive responses in some patients whereas other patients may have showed negative response resulting in net negative result. Individualised bedside measure of energy expenditure by calorimetry to guide energy delivery, and to minimise the risk of overfeeding during the early phase has recently been recommended [1], although the results of a pilot interventional trial comparing indirect calorimetry-guided nutrition to the standard of care (caloric intake of 25 kcal/kg/day) were mostly inconclusive. Likewise, the effects of other modifications of nutritional interventions including raised amounts of proteins, changes in the composition of amino acids, of fatty acids

or the combination of nutritional interventions with physical activity should be prospectively tested on meaningful outcomes in wisely chosen populations of patients at risk.

#### Disclosure of interest

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