Editorial

Issues of energy and protein feeding in critically ill: the permissive underfeeding trial

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In the *NEJM* June 4 Issue, Arabi and co-authors describe a randomized controlled trial of permissive underfeeding or standard enteral feeding in critically ill adults (1).

Nutrition support of the critically ill patient is a highly debated subject, with many unanswered questions on who, what, how much, and when.

Considering only the randomized controlled trials, they have all been performed on total feeding (based on energy). Whether they were guideline oriented trials (2-4), supplemental parenteral nutrition (5-8), or permissive underfeeding or trophic feeding (9-10). Both Arabi trials are in fact the only trials that have tried to differentiate effects of protein intake from the energy feeding intervention (1,9). Just for this simple fact Arabi and co-authors deserve praise.

What is the study about? (1) Who are we feeding? The patients were fairly young with a mean age of 50 years. They also had a mean BMI of almost 30. The study by Alberda and co-authors showed beneficial effects of energy and protein intake up to a BMI of 25 and from BMI 35 upwards (11). They did not observe a mortality benefit by feeding for the BMI group 25-35, which this study by Arabi and co-authors is about. This might be a less vulnerable group of patients, than patients with a low muscle mass (12).

What are we feeding? The patients were included based on the criterium of having started enteral feeding within 48 hours from admission. They were therefore fed by enteral route, which is the preferred route of feeding.

Energy was set at 40-60% of energy target in the permissive underfeeding group and 70-100% for reference group. The achieved mean levels of energy feeding were 46% *vs*. 71% of energy requirement (how much?). As this mean level is obtained from a 14 day intervention (up to discharge, death, or oral feeding), it is also worthwhile to mention that the level of energy intake was around 50% *vs*. 80% from day 2-3 (when?). From recent analysis we obtained that 80% of energy expenditure would be close enough, and good to prevent overfeeding (13). Based on the primary outcome, 90 day mortality, the permissive underfeeding strategy was of no advantage compared to an almost up to target energy feeding strategy. However, the targets are based on the PSU equation for patients with BMI <30, and the Ireton-Jones equation for BMI of 30 and higher. Considering the large level of variation in energy requirement estimation error (14), the targets maybe small to very large overestimations as well as underestimations of the real energy expenditure. Since both feeding strategies were aimed at underfeeding, the level of unknown overfeeding is probably low in this study contrary to other large RCTs (6,8). However, the authors state that on days subsequent to a lower than prescribed energy intake, the energy intake was compensated. This may in fact have resulted in days of overfeeding, which have not been identified as such.

The protein target was set at 1.2-1.5 g/kg body weight. The permissive feeding strategy automatically results in a lower level of protein feeding, for which a cointervention is used in the form of a protein supplement. Since the supplement is used it is strange to use a protein target range, this was an ideal opportunity for individualized protein feeding. The result of this was a protein feeding level of 68% of the protein target for both groups, although it is unknown whether this is 1.2 or 1.5 g/kg target. The actual achieved level of protein feeding from day 2-3 was almost 80% of this target. Well, 80% of 1.5 g/kg is actually 1.2 g/kg, while 80% of 1.2 g/kg is 0.96 g/kg. In comparison to guidelines and other studies, 0.96-1.2 g/kg is a fairly high level of protein feeding. However, in the light of our recent finding that protein feeding should be at a level of intake of more than or equal to 1.2 g/kg to obtain the strongest relationship with decreased mortality, it is of utmost importance to know what the target actually was (13). On the other hand, the same was achieved in both groups; therefore, the equality in protein intake might in fact be highly related to equality in primary outcome. The authors themselves consistently state that protein feeding was at the full recommended level; however this appears to be a gross overstatement (since they state it is 80% of it).

The higher level of protein concentration in the complete feeding during permissive underfeeding was 27.3% *vs*. 18.2% of caloric intake in the reference group. Or in more generally used terms, it was 68 g of protein per 1,000 kcal in permissive underfeeding *vs*. 45 g of protein per 1,000 kcal in the reference group. These levels of feeding, 45-68 g/1,000 kcal are comparable or higher than in our observational study groups with more than 1.0 g/kg; however our patients were fed at a higher energy feeding level (13). This energy may in fact be needed to actually use the protein and amino acids for protein synthesis, which is an energy costly process. The protein balance of the body cannot only be fed by protein, there has to be a certain level of energy feeding to support it. Recently, Liebau and co-authors observed that protein and amino acid feeding did not increase amino acid oxidation at high levels of feeding (15). However, in the Liebau study energy was fed according to individually measured energy expenditure and therefore most likely adequate.

Overall we can conclude from this study that in this group of patients, permissive underfeeding was of no benefit. But apparently also not harmful. Protein intake however was similar in both groups. It is possible that protein intake itself maybe more relevant for outcome than the level of energy fed.

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Footnote

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