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Letter to the Editor

Identification of sub-groups that may be harmed or benefit from higher energy intake

Dear Editor,

The TARGET [1] investigator should be commended for completing a well-designed critical care nutrition trial. This study was multicentre, double-blinded, adequately powered for mortality, and achieved meaningful differences in energy intake while keeping volume of enteral feed and protein intake similar between two groups. Given the large sample size and robust study design, we believe that further analyses of this study will aid in the refinement of clinical guidelines [2,3].

The TARGET trial demonstrated that higher energy intake did not affect mortality outcomes in unselected critically ill patients. In the subgroup analysis however, we observed that higher energy intake (1.5-kcal group) among older patients (age $\geq$ 65) and those with a higher risk of death had a trend towards increased 90-day mortality. This observation may have clinical implications and in our opinion, should be further explored. The ASPEN guidelines [2], based on expert opinion on the evidence provided by observational studies, endorse the use of the mNUTRIC score and clinicians are encouraged to deliver more calories for patients with high scores. Since older patients and those with a higher risk of death would likely score high on the mNUTRIC, these patients may be recommended to receive higher energy intake. This can potentially cause harm, going by findings from the subgroup analysis described above. Perhaps the TARGET investigator could perform a post-hoc analysis that stratifies patients according to their mNUTRIC scores. Such an analysis will provide better evidence to guide clinical recommendations and practice, since the risk of indication bias (inherent in observational studies) is minimised by randomisation and this strength is naturally maintained in a post-hoc analysis.

We agree with the authors that the association between energy intake and mortality risk may be related to the timing of delivery. Recent studies suggest that energy intake during the initial phase of critical illness is positively associated with mortality, whereas the opposite was observed at the later phase [4,5]. In view of this, the most recent ESPEN guidelines recommend gradual increment of energy delivery at the initial phase of critical illness [3]. However, this is a low-grade recommendation as there is a paucity of data in the literature. Therefore, a post-hoc analysis that explores the effects of timing and dose of energy intake [4] on mortality and infection outcomes may also be enlightening.

Conflict of interest

The authors declare no conflict of interest.

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