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Reply to Peçanha Antonio *et al.*

From the Authors:

Dr. Peçanha Antonio and colleagues write that administration of at least 70% of estimated energy requirements to critically ill patients provides a survival advantage. However, randomized clinical trials are the gold-standard method for drawing causal inferences about therapies (1), and there is evidence from three well-conducted multicenter randomized trials involving 1,000, 894, and 3,957 patients, respectively, that mortality is unaffected by targeting a specific energy delivery during the acute phase of critical illness (2–4).

The letter also raises concerns that our study compared "overfeeding" with usual feeding practice, particularly given the proportion of patients with obesity in our cohort. The body mass index of our study participants (29.2 kg/m^2) reflects the adult body mass index in our region (5). Those assigned the energy-dense formula received a mean (SD) of 29.1 (6.2) kcal/kg of ideal body weight/d and 23.2 (7.1) kcal/kg of actual body weight/d from the enteral route (*see* Table E4 in the online supplement of Ref. 5). We are not aware of any published data establishing that this dose of energy delivered via the enteral route represents overfeeding and/or is a risk factor for increased death. Moreover, for our primary outcome (Day 90 mortality), body mass index was a predefined subgroup of interest, and the relative risk of death (energy-dense formula vs. standard nutrition for the 1,423 participants with a body mass index $\geq$ 30 kg/m^2) was 0.94 (95% confidence interval, 0.77–1.14) (4). Finally, as there is no consensus definition for overfeeding or how to diagnose it, the belief that it has occurred in the subgroup with obesity is speculative at best.

Dr. Peçanha Antonio and colleagues also suggest that our study provides limited additional information, given the 6-month outcome data provided by a previous trial (6). We agree that the EAT-ICU (Early Goal-directed Nutrition in ICU Patients) trial was well conducted but assert that a single-center open-label trial providing 6-month outcome data from 105 survivors does not diminish the information obtained from analyzing data from 2,492 survivors randomly assigned to receive a blinded intervention at 1 of 46 ICUs across two countries.

We agree that future trials of nutritional therapy, particularly focused on the time after the first 5–7 days, are warranted. However, the conduct of an adequately powered randomized trial to evaluate the effect on patient-centered outcomes of an intervention commencing after 5–7 days of admission to an ICU represents substantial challenges. We maintain that our trial has provided valuable insights into the current population-level effects of acute energy delivery on longer-term outcomes. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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