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Reply-Letter to the Editor - Timing of PROTein INtake and clinical outcomes of adult critically ill patients on prolonged mechanical VENTilation: The PROTINVENT retrospective study

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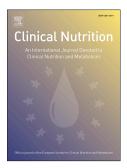
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ACCEPTED MANUSCRIPT

- 1 Reply-Letter to the Editor Timing of PROTein INtake and clinical outcomes of adult critically ill
- 2 patients on prolonged mechanical VENTilation: The PROTINVENT retrospective study
- 3 To the Editor:
- 4 We thank doctors Looijaard, Weijs and Oudemans-van Straaten for their interest in and response to
- 5 the PROTINVENT study we published in Clinical Nutrition. In this study, we studied the association
- 6 between the timing of protein intake and clinical outcomes in critically ill patients on prolonged
- 7 mechanical ventilation and found a time-dependent effect of high protein administration[1]. We are
- 8 honored to answer the questions they have raised.
- 9 We were aware that high energy intake (overfeeding) and severity of illness both might be
- 10 negatively associated with increased mortality and therefore could influence our results. Therefore,
- we performed a multivariate analysis in which we corrected for Body Mass Index, mNUTRIC-score,
- 12 ICU admission year, admission categories (surgical/medical), nutritional route, time to start feeding
- 13 and caloric adequacy. To avoid collinearity, age, the number of comorbidities, APACHE-II and SOFA-
- 14 scores were not corrected for separately as these variables are components of the mNUTRIC score.
- 15 To further clarify this issue the adjusted hazard ratios are depicted in table 1. The presented results
- 16 thus are corrected for the effects of overfeeding and severity of illness amongst other potential
- 17 confounders and do not change the previously published conclusions. The time-dependent effect of
- 18 protein intake persists.
- 19 We agree with the authors of the letter that during the study period a new computerized protocol
- 20 was implemented in our ICU in July 2014 that reduced the numbers of patients being overfed
- 21 according to calculated targets after the implementation [2]. However, we are confident that
- 22 possible confounding was corrected for by adjusting for ICU admission year in the multivariate
- analyses. Neither addition nor replacement of 'ICU admission year' by the covariate 'patients
- 24 included before/after protocol change in July 2014' altered our outcomes significantly. When
- 25 replacing the covariate ICU admission year by 'patients included before/after protocol change in July
- 26 2014' in multivariate analysis the adjusted hazard ratios from table 1 changed from 1.263 (1.055-
- 27 1.513, p=0.011) to 1.266 (1.066 1.519, p=0.011); and from 1.683 (1.206 2.349, p=0.002) to 1.729
- 28 (1.233 2.425, p=0.001); and from 0.751 (0.584 0.965, p=0.025) to 0.742 (0.577-0.954, p=0.020),
- 29 respectively. Moreover, in the study referred to we showed that although the computerized
- 30 protocol reduced overfeeding incidence, this benefit did not translate into differences in mortality
- 31 after the implementation compared with the period before the implementation of the computer
- 32 protocol [2].

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