

The effect of higher versus lower protein delivery in critically ill patients: a systematic review and meta-analysis of randomized controlled trials

ABSTRACT

Background: The optimal protein dose in critical illness is unknown. We aim to conduct a systematic review of randomized controlled trials (RCTs) to compare the effect of higher versus lower protein delivery (with similar energy delivery between groups) on clinical and patient-centered outcomes in critically ill patients. **Methods:** We searched MEDLINE, EMBASE, CENTRAL and CINAHL from database inception through April 1, 2021. We included RCTs of (1) adult (age ≥ 18) critically ill patients that (2) compared higher vs lower protein with (3) similar energy intake between groups, and (4) reported clinical and/or patient-centered outcomes. We excluded studies on immunonutrition. Two authors screened and conducted quality assessment independently and in duplicate. Random-effect meta-analyses were conducted to estimate the pooled risk ratio (dichotomized outcomes) or mean difference (continuous outcomes). **Results:** Nineteen RCTs were included ($n = 1731$). Sixteen studies used primarily the enteral route to deliver protein. Intervention was started within 72 h of ICU admission in sixteen studies. The intervention lasted between 3 and 28 days. In 11 studies that reported weight-based nutrition delivery, the pooled mean protein and energy received in higher and lower protein groups were 1.31 ± 0.48 vs 0.90 ± 0.30 g/kg and 19.9 ± 6.9 versus 20.1 ± 7.1 kcal/kg, respectively. Higher vs lower protein did not significantly affect overall mortality [risk ratio 0.91, 95% confidence interval (CI) 0.75-1.10, $p = 0.34$] or other clinical or patient-centered outcomes. In 5 small studies, higher protein significantly attenuated muscle loss (MD -3.44% per week, 95% CI -4.99 to -1.90; $p < 0.0001$). **Conclusion:** In critically ill patients, a higher daily protein delivery was not associated with any improvement in clinical or patient-centered outcomes. Larger, and more definitive RCTs are needed to confirm the effect of muscle loss attenuation associated with higher protein delivery. PROSPERO registration number: CRD42021237530.

Keyword: Critical illness; Muscle; Nutrition support; Protein; Systematic review