

The effect of higher protein dosing in critically ill patients with high nutritional risk (EFFORT protein): an international, multicentre, pragmatic, registry-based randomized trial

Heyland DK, Patel J, Compher C, Rice TW, Bear DE, Lee ZY, González VC, O'Reilly K, Regala R, Wedemire C, Ibarra-Estrada M, Stoppe C, Ortiz-Reyes L, Jiang X, Day AG; EFFORT Protein Trial team. *Lancet*. 2023 Jan 25;S0140-6736(22)

Objective

Based on low quality evidence, international guidelines recommend a wide range of protein doses. However, the effect of delivering high-protein doses to critically ill patients is unknown. Therefore, the EFFORT study assesses whether a higher protein dose would improve clinical outcome.

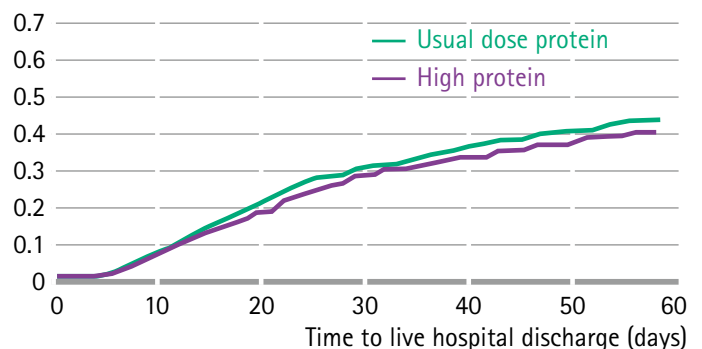
Methods

Study design	Multicenter, randomized, single-blinded, pragmatic, registry-based trial
Patients	Adult critically ill patients with nutritional risk factors and expected to remain ventilated for ≥ 48 h
Study groups	1329 patients were randomized to receive either 2.2g/kg BW/d (n=645, interventional group) of protein or 1.2g/kg BW/d (n=656, control)
Primary outcome	Time to discharge alive from hospital by day 60
Secondary outcome	60-day mortality

Results

- No significant difference in primary endpoint of cumulative incidence of alive hospital discharge to day 60 (46.1% vs. 50.2%) high vs. low protein group (Hazard ratio 0.91, 95% CI 0.77- 1.07; $p=0.27$)
- No significant differences in 60-day mortality (secondary outcome)
- High-dose protein is suggested to be associated with harm in subgroup of patients with AKI and SOFA score ≥ 9 at baseline
- Clinically relevant separation in protein dose was achieved between groups (high-dose group 1.6 [SD 0.5] g/kg/d vs. usual dose 0.9 [SD 0.3] g/kg/d)

Cumulative incidence



Numbers at risk

Deaths (high dose protein)	..	95	162	184	207	218	222
Deaths (usual dose protein)	..	91	142	175	185	198	208
Hospitalisation (high protein)	644	499	353	261	204	165	144
Hospitalisation (usual protein)	653	513	364	261	216	175	145

Fig.1: Cumulative incidence of time to discharge alive from hospital by treatment group (reproduced from Heyland et al.)

Conclusion:

- Prescribing 1.2 g/kg/d of protein in accordance with European and American Guidelines (lower limit) seems to be a reasonable and safe approach in critically ill patients.
- Delivering higher doses of protein to adult critically ill patients with nutritional risk factors does not improve the time to discharge alive from hospital compared with usual dose of protein.
- Higher protein doses might be associated with worsened outcome in patients with AKI and with greater severity of illness.
- **The results of the EFFORT study do not support the notion that severely critically ill patients will benefit from a higher protein dose.**