Supplement Table 51. Summary of studies evaluating protein provision in critically ill adults with acute kidney injury (KQ20)

Study	Design	P (Population)	I (Intervention)	C (Comparator)	O (Outcomes)	Summary
Doig 2015 [308] Zhu 2018 [309]	RCT + post-hoc subgroup analysis	ICU patients with or at risk of kidney dysfunction	Extra IV amino acid (high protein load)	Standard care without IV AA supplementation	Kidney function, mortality	Overall, IV AA did not improve mortality. Post-hoc showed that in patients with baseline kidney injury, higher AA (protein) exposure was associated with worse clinical outcomes, supporting caution with pharmacologic high-protein strategies in renal dysfunction.
EFFORT Protein – AKI post-hoc (Stoppe 2023) [311]	Post-hoc analysis of large international RCT (EFFORT)	312 ICU patients with AKI at enrolment	High protein ≥2.2 g/kg/d (mostly EN ± PN)	Usual protein ≤1.2 g/kg/d	Days alive and out of hospital, 60-day mortality	In AKI patients, high protein (≥2.2 g/kg/d) increased 60-day mortality and delayed discharge vs. ≤1.2 g/kg/d. Harm signal was somewhat attenuated in KRT patients but remained concerning → in AKI (especially non-KRT), very high-dose protein is potentially harmful.
Lee et al. 2024 [313]	Systematic review & meta-analysis of 23 RCTs (n=3,303) with TSA	Adult ICU patients; mixed diagnoses; AKI subgroup explicitly analyzed	Higher protein: mean 1.49 ± 0.48 g/kg/d	Lower protein: mean 0.92 ± 0.30 g/kg/d	Overall mortality, ICU/hospital LOS, MV duration, infections; AKI vs. no-AKI mortality	In all ICU pts, higher protein did not change mortality or other key outcomes. In AKI subgroup, higher protein significantly increased mortality (RR 1.42, 95% CI 1.11–1.82)
Qin et al. 2024 [314]	Systematic review & meta-analysis of 17 RCTs (n=2,965)	Adult critically ill ICU patients (AKI not isolated but AKI incidence reported)	Higher protein ≥1.2–2.0 g/kg/d	Lower protein 0.5–1.1 g/kg/d	Overall mortality, ICU/hospital LOS, MV duration, AKI incidence	High vs. low protein did not improve mortality, LOS, or MV duration. AKI incidence was numerically higher in high-protein group (22.7% vs. 20.3%, RR 1.11), though not statistically significant. Discussion notes concern for high-protein in renal impairment and cites recommendations to restrict to ~0.8–1.0 g/kg/d in acute/chronic renal insufficiency.
NEED Trial – AKI post-hoc (Lv 2024) [316]	Post-hoc analysis of multicenter cluster-RCT	2,552 ICU patients, 567 (22%) with AKI	Higher early protein delivery (3–5-day mean); each +0.1 g/kg/d increase	Lower early protein delivery	28-day mortality	Overall, higher early protein delivery associated with lower 28-day mortality; in subgroup, benefit was confined to Stage 3 AKI, suggesting that in severe AKI, avoiding very low protein and reaching guideline-level doses is important, but not necessarily “high” (≥1.5–2.0 g/kg/d).
ENGINE Trial (Jeerangsapasuk 2025) [106]	Single-center open-label RCT	80 mechanically ventilated ICU patients with AKI	IC + nitrogen balance–guided protein, mostly ≤1.3 g/kg/d (individualized)	Usual nutrition care (non-IC/non-N-balance guided)	28-day mortality, need for RRT, safety labs	Individualized, moderate-dose protein (≤1.3 g/kg/d) reduced 28-day mortality without increasing RRT use or metabolic complications – supports “moderate, monitored dosing” rather than aggressive high-protein in AKI.

RCT, randomized controlled trial; ICU, intensive care unit; AA, amino acid; AKI, acute kidney injury; EN, enteral nutrition; PN, parenteral nutrition; KRT, kidney replacement therapy; TSA, trial sequential analysis; LOS, length of stay; MV, mechanical ventilation; RR, risk ratio; CI, confidence interval; IC, indirect calorimetry; RRT, renal replacement therapy.