Cutuli *et al. Critical Care* (2026) 30:589
https://doi.org/10.1186/s13054-026-06245-w

Critical Care

REVIEW Open Access

Acute kidney injury and renal replacement therapy: a critical synthesis of metabolic derangements and nutritional implications

Salvatore Lucio Cutuli[1,2*], Lee-anne S. Chapple[3,4], Silvia De Rosa[5], Melanie Meersch-Dini[6], John R. Prowle[7], Christian Stoppe[8,9,10], Lui Forni[11,12], Marlies Ostermann[13], Claudio Ronco[14,15] and Emily See[16,17]

Abstract

Background Acute kidney injury (AKI) affects up to 50% of critically ill patients and is frequently complicated by severe metabolic derangements, requiring the initiation of replacement therapy (RRT) in 10–15% of cases. Despite substantial progress in the diagnosis of AKI and optimisation of RRT delivery, the nutritional management of these patients remains an underexplored area.

Main body AKI is increasingly recognised as a systemic metabolic disorder extending beyond impaired renal clearance. Key metabolic alterations include mitochondrial dysfunction, dysregulated gluconeogenesis, increased proteolysis and altered amino acid metabolism, with accelerated nitrogen wasting. These abnormalities are further amplified by acute systemic stress states, including sepsis, systemic inflammation, trauma, burns, liver dysfunction and multiorgan failure. RRT introduces additional metabolic consequences through extracorporeal losses of amino acids and micronutrients. Conversely, citrate anticoagulation, glucose-containing dialysate, and lactate-buffered solutions represent sources of clinically relevant calories. Current nutritional recommendations are largely extrapolated from heterogeneous intensive care populations. Available evidence suggests that AKI primarily influences energy balance rather than energy expenditure, which appears broadly comparable to that of other critically ill populations. While evidence specific to AKI is limited, protein provision of approximately 1.2-1.3 g/kg/day is generally recommended during critical illness. However, higher intakes of up to 1.7–2.5 g/kg/day may be considered in patients receiving RRT to offset extracorporeal amino acid losses and increased protein catabolism. In this setting, emerging concepts such as metabolic tolerance and biomarker-guided metabolic phenotyping may facilitate individualised nutritional strategies.

Conclusions AKI, particularly when requiring RRT, is associated with profound and dynamic metabolic disturbances that substantially influence energy and protein requirements, thereby making nutrition an integral component of organ support therapies. Future research should evaluate precision nutrition strategies that tailor nutritional support to the phase of critical illness, measured energy expenditure, metabolic tolerance, and RRT-related nutrient losses and gains. Such studies should prioritise patient-centred outcomes, including physical function and recovery, in addition to nutritional and metabolic endpoints.

*Correspondence:
Salvatore Lucio Cutuli
sl.cutuli@gmail.com

Full list of author information is available at the end of the article

© The Author(s) 2026. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Keywords Acute kidney injury, Nutrition, Renal replacement therapy, Critical care, Intensive care

Background

Acute kidney injury (AKI) [1] affects up to 50% of patients admitted to the intensive care unit (ICU) [2], and is associated with prolonged organ dysfunction, long-term disability, and increased mortality [2, 3]. Beyond impaired solute and fluid clearance, AKI is recognised as a systemic syndrome [4] characterised by profound metabolic, endocrine, and nutritional disturbances [3]. Specifically, AKI promotes hypercatabolism, altered substrate utilisation, mitochondrial dysfunction, insulin resistance, and accelerated skeletal muscle breakdown, all of which contribute to negative nitrogen balance and protein-energy wasting [5]. These metabolic abnormalities are further amplified by acute systemic stress states, including sepsis, systemic inflammation, trauma, burns, liver dysfunction and multiorgan failure, which commonly coexist in ICU patients. Collectively, these metabolic alterations create unique nutritional challenges that are poorly addressed by general ICU nutrition guidelines and may contribute to adverse outcomes if not recognized and managed appropriately [6, 7].

Around 10–15% of critically ill patients with AKI initiate renal replacement therapy (RRT) to manage fluid overload, electrolyte disturbances, acid-base abnormalities, and uraemia [2, 8]. However, RRT does nothing to reverse the underlying catabolic state and may itself contribute to clinically important losses of amino acids, proteins, water-soluble vitamins, and trace elements [8]. In addition, RRT may influence overall energy balance through delivery of unaccounted calories from citrate, glucose, and lactate-containing solutions. Consequently, nutritional management in patients with AKI receiving RRT remains particularly complex and insufficiently supported by high-quality evidence.

In critically ill patients, nutritional management encompasses three complementary concepts [9]. First, nutritional support aims to meet daily physiological requirements through adequate provision of energy, protein, and micronutrients. Second, repletion strategies seeks to correct documented or suspected deficiencies and compensate for increased metabolic demands and treatment-related nutrient losses, which are particularly relevant in patients receiving extracorporeal organ support. Third, pharmaconutrition involves the administration of supraphysiological doses of selected nutrients to modulate biological pathways. This narrative review summarises the metabolic alterations associated with AKI, examines the nutritional implications of RRT, reviews nutritional strategies aimed at meeting daily physiological requirements while ensuring adequate macro- and micronutrient repletion, and highlights key areas where further mechanistic and clinical research is urgently needed. The role of pharmaconutrition is beyond the scope of this review.

Metabolic alterations in acute kidney injury

Profound metabolic and hormonal abnormalities during AKI promote increased amino acid turnover, impaired fatty acid oxidation, altered glucose metabolism, and accelerated skeletal muscle wasting [10–12]. Understanding these metabolic disturbances is important for optimising nutritional support and nutrient delivery during critical illness.

Energy metabolism

Renal energy metabolism is essential for generating sufficient adenosine triphosphate to sustain the high metabolic demands of tubular solute transport, particularly active reabsorption and secretory processes [13]. Despite comprising less than 1% of total body mass, the kidneys are among the most metabolically active organs, receiving 25% of cardiac output and consuming approximately 10% of whole-body energy expenditure [14]. This substantial energy demand is reflected by the high mitochondrial density within renal tubular cells. Under normal conditions, the primary energy sources for the kidneys are fatty acid oxidation and glycolysis [11]. In addition, branched-chain amino acids can act as substrates for the tricarboxylic acid (TCA) cycle (i.e., citric acid cycle or Krebs cycle) [11]. During AKI, ischemia and oxidative stress induce mitochondrial depolarisation and autophagy [15], leading to metabolic reprogramming characterised by depletion of energy substrates and suppression of key bioenergetic pathways [16].

Few studies have directly assessed energy expenditure in critically ill patients with AKI. In an observational study of 80 patients with severe AKI, mean energy expenditure was 2033 kcal/day, although values varied substantially (1548 to 2415 kcal/day) [17]. Similarly, a cohort study of 42 patients with AKI reported a mean energy expenditure of 1724 kcal/day, with no significant differences between patients receiving RRT and those who were not [18]. An earlier study also found no increase in metabolic rate attributable to AKI in the absence of sepsis [19]. Overall, the available evidence suggests that energy expenditure in critically ill patients with AKI is broadly comparable to that of other critically ill populations and is driven more by the underlying clinical diagnosis and its multisystem consequences than by AKI itself [20, 21]. Taken together, these findings suggest that AKI itself does not independently increase resting energy expenditure; therefore, energy targets should be guided

primarily by the patient's underlying critical illness rather than by the presence of AKI alone.

Protein metabolism and nitrogen balance

The kidneys play an important role in whole-body protein metabolism through amino acid handling, protein turnover and urinary excretion of nitrogenous metabolites [22], including ammonia, urea, uric acid, methylarginines and homocysteine [23]. Approximately 50–70 g of amino acids are filtered daily by the glomeruli, of which 97–98% are reabsorbed and returned to the circulation [24].

AKI disrupts amino acid metabolism and alters the circulating amino acid profile [25]. Plasma concentrations of some essential amino acids (e.g. methionine and phenylalanine) are increased, while others (e.g. valine, leucine, threonine, tryptophan, and lysine) are reduced [5, 26]. Amino acids normally synthesised or metabolised by the kidneys, including tyrosine, arginine, cysteine, methionine, and serine, may become conditionally essential during AKI [27]. Specifically, the kidney contributes to systemic arginine availability through *de novo* synthesis from citrulline, and participates in creatine biosynthesis [28], exerting downstream effects on nitrogen metabolism, urea cycle activity, and whole-body protein homeostasis [29]. Impaired oxidation of branched-chain amino acids (leucine, isoleucine, valine) has been observed in both sepsis-associated and ischaemia-induced AKI [12, 30].

Protein metabolism is also profoundly dysregulated during AKI. Increased whole-body proteolysis releases amino acids from skeletal muscle into the circulation, contributing to muscle wasting and negative nitrogen balance despite exogenous protein delivery [12, 31, 32]. Mobilised amino acids are subsequently utilised for energy production and adaptive stress responses. For example, alanine serves as a major substrate for gluconeogenesis via the Cahill cycle (i.e., glucose-alanine cycle), and glycine, glutamine, and cysteine are used for glutathione synthesis [12]. Although the mechanisms of accelerated protein catabolism during AKI remain incompletely understood, proposed contributors include inflammatory cytokine release, metabolic acidosis, insulin resistance, oxidative stress, catecholamine excess, and glucocorticoid exposure [5].

Urea metabolism

Urea is the principal waste product of amino acid catabolism, generated in the liver from nitrogen released during protein breakdown and normally excreted by the kidneys. During AKI, increased skeletal muscle catabolism and alterations in intermediary metabolism (i.e., intracellular pathways that convert nutrients into energy and cellular components) may contribute to enhanced production and accumulation of nitrogenous waste products, including urea [15]. In murine models of AKI, accumulation of nitrogenous waste products and increased concentrations of urea cycle intermediates (e.g., citrulline) have been observed [10, 12, 16]. These findings suggest possible upregulation of urea cycle activity, potentially driven by accelerated skeletal muscle catabolism and increased amino acid turnover.

Lipid metabolism

Patients with AKI also exhibit important alterations in lipid metabolism. Under normal physiological conditions, fatty acids are the preferred substrate for energy production in the renal cortex, undergoing mitochondrial oxidation to produce acyl-coenzyme A (acyl-CoA) for the TCA cycle [30]. However, during AKI, fatty acid synthesis is increased [33], while fatty acid oxidation is downregulated [11]. Lipid clearance is further impaired by an almost 50% reduction in lipoprotein lipase and hepatic triglyceride lipase activity [10, 11]. These alterations promote hypertriglyceridaemia, particularly during prolonged critical illness or following administration of exogenous lipids, including propofol [34].

Glucose metabolism

The kidney is an important site of gluconeogenesis, contributing up to 20% of overall glucose synthesis and playing an important role in glucose homeostasis [35]. Dysregulation of glucose metabolism occurs commonly during AKI. In a retrospective cohort of > 20,000 critically ill adults, AKI was associated with an increased risk of dysglycaemia [36]. Hyperglycaemia is driven by counter-regulatory hormones, including glucagon, catecholamines, cortisol and growth hormone, which increase gluconeogenesis and exacerbate insulin resistance [10]. Moreover, hyperglycaemia has been consistently associated with the development and progression of AKI [37], thereby representing a potentially modifiable risk factor, although it may also serve as a marker of illness severity and stress-related metabolic dysfunction [38]. Although glycolysis is increased, it is insufficient to overcome energy deficits caused by impaired fatty acid oxidation [11, 39]. These abnormalities have direct implications for nutritional tolerance (e.g. physiologic glycaemic control, serum triglyceride and electrolyte concentrations), particularly in patients with high carbohydrate exposure.

Metabolic alterations during renal replacement therapy

RRT has significant metabolic consequences beyond those of AKI, influencing both nutrient balance and energy homeostasis. Through mechanisms of solute clearance and exposure to dialysate or replacement fluids, RRT contributes to clinically relevant losses of

macro- and micronutrients while also introducing non-nutritional caloric substrates [40]. The net effect is an increased risk of protein-energy wasting and micronutrient deficiency. Overall, RRT does not simply replace renal excretory function but also modifies substrate availability, nutrient balance, and energy homeostasis. These metabolic effects should be considered when prescribing nutritional therapy, as they may substantially influence protein requirements, micronutrient supplementation, and overall nutritional adequacy.

Mechanisms of nutrient removal

Nutrient removal during RRT occurs primarily via diffusion, convection, and, to a lesser extent, adsorption (Fig. 1) [41–43]. Unlike the native kidney, RRT does not reproduce tubular functions, including selective reabsorption, secretion, and metabolic processing. As a result, RRT is associated with losses of amino acids, glucose, phosphate and other water-soluble solutes into the effluent [44]. This explains why apparently modest RRT doses may have disproportionate effects on nutrient and electrolyte homeostasis, despite being far lower than normal renal filtration capacity [45].

The extent of nutrient loss during RRT is strongly influenced by treatment modality, membrane characteristics, effluent dose, and treatment duration. Continuous renal replacement therapy (CRRT) results in greater cumulative nutrient losses because of its prolonged duration and higher cumulative solute clearance, whereas intermittent renal replacement therapy (IRRT) achieves higher instantaneous clearance over a shorter period, resulting in lower cumulative solute clearance [46].

During IRRT, rapid extracellular removal of small solutes is followed by redistribution from intracellular and other slowly exchangeable compartments, producing post-dialysis rebound [47]. However, redistribution kinetics differ substantially between solutes. Potassium rapidly re-equilibrates between intracellular and extracellular compartments, whereas phosphate redistributes more slowly because of its larger intracellular stores and more complex compartmental kinetics. Consequently, phosphate rebound is delayed and often incomplete, particularly with repeated or prolonged RRT [48]. Potassium depletion during CRRT is also mitigated by the routine use of potassium-containing dialysate and replacement solutions, whereas phosphate-free CRRT solutions remain common, making hypophosphataemia a more frequent complication.

By contrast, CRRT provides slower but continuous clearance, allowing greater intercompartmental equilibration and minimising rebound, but ongoing phosphate removal may exceed endogenous redistribution during

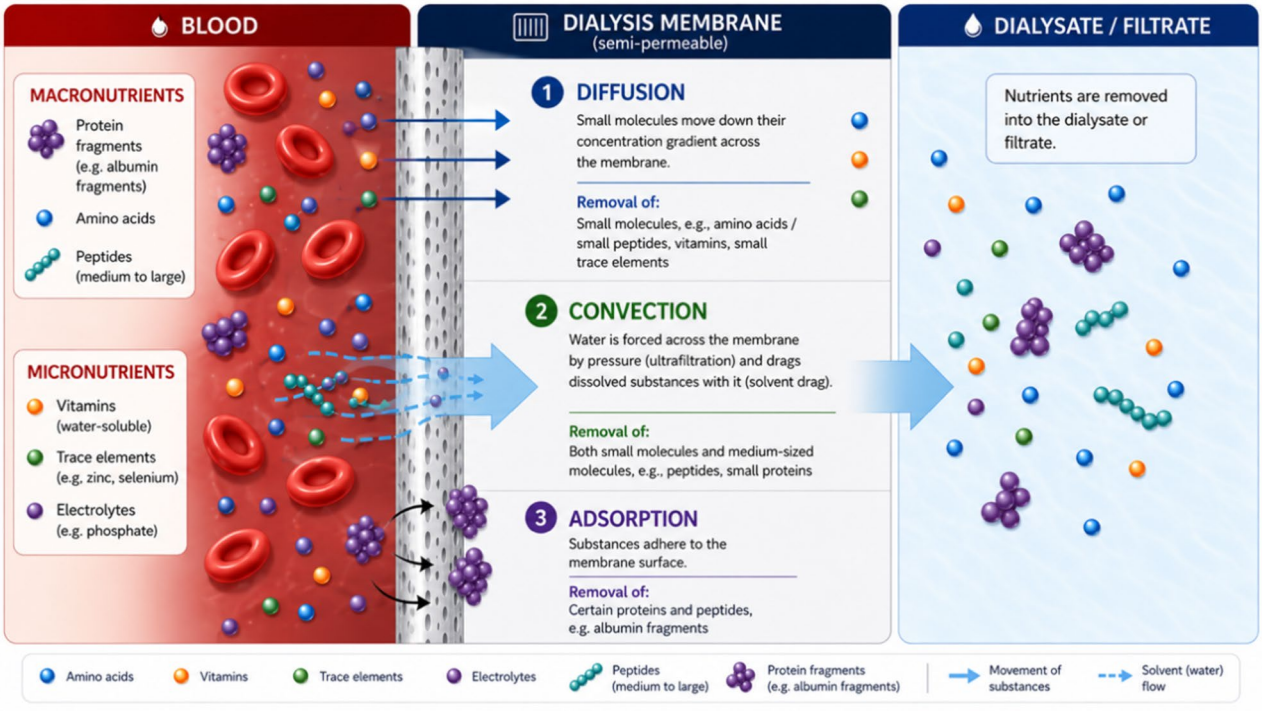


Fig. 1 Mechanisms of nutrient loss during renal replacement therapy. Renal replacement therapy (RRT) removes nutrients through diffusion, convection, and adsorption. Diffusion promotes the movement of small solutes across the semipermeable membrane along a concentration gradient, whereas convection removes dissolved substances through solvent drag during ultrafiltration. Adsorption occurs when molecules bind to the membrane surface. Collectively, these processes may result in the loss of amino acids, small peptides, water-soluble vitamins, trace elements, and electrolytes, while larger proteins are generally retained, although protein fragments and selected peptides may be removed

prolonged treatment [49]. CRRT-associated hypophosphataemia has consistently been associated with adverse clinical outcomes, including prolonged mechanical ventilation [50, 51]. Consequently, nutritional requirements and electrolyte supplementation should be reassessed whenever the RRT prescription changes, particularly during prolonged, high-intensity, or phosphate-free CRRT [1, 52].

Energy balance

RRT influences energy balance through both the delivery and removal of metabolically active substrates, and therefore cannot be considered metabolically neutral [53]. Depending on treatment prescription, patients may receive calories from citrate, glucose, or lactate-containing solutions, whilst simultaneously losing glucose and other energy substrates into the effluent [54]. Regional citrate anticoagulation may provide a substantial treatment-related caloric load, the magnitude of which depends on the citrate protocol and the proportion of citrate ultimately metabolised by the patient. In a prospective study, citrate anticoagulation during CRRT provided approximately 218 kcal/day from citrate and a further 295 kcal/day from glucose-containing solutions [55].

Conversely, transmembrane glucose transfer may result in net glucose losses when glucose-free or low-glucose solutions are used. In patients with limited nutritional intake or increased metabolic demands, these losses may contribute to negative energy balance and, in extreme cases, euglycaemic ketoacidosis [56]. Lactate-containing dialysate or replacement fluids may also contribute to energy delivery, as lactate can be utilised as a metabolic substrate following hepatic and extrahepatic metabolism. However, in patients with severe hepatic dysfunction or circulatory shock, impaired lactate clearance may lead to lactate accumulation [57]. In this setting, elevated lactate concentrations are generally considered a marker of impaired metabolic capacity and disease severity rather than a direct consequence of RRT-related energy delivery.

Protein and amino acid

Protein and amino acid losses during RRT are substantial and clinically important, with free amino acids readily removed into the effluent [40, 58]. During CRRT, amino acid losses average approximately 0.2 g per litre of effluent, corresponding to ~ 10–15 g/day, depending on CRRT dose [1]. IRRT results in comparable losses of approximately 12 g per treatment session and measurable reductions in plasma amino acid concentrations [59]. Direct protein losses of 5–10 g/day may also occur, particularly during high convection volume haemodiafiltration or with highly permeable membranes [60]. Extracorporeal nutrient losses may further exacerbate the negative nitrogen balance resulting from the hypercatabolic state of critical illness and the metabolic alterations in protein metabolism associated with AKI [61]. Consequently, RRT-associated amino acid and protein losses should be considered when determining protein provision, particularly during prolonged or high-intensity RRT.

Vitamins

Water-soluble vitamins (including B-complex vitamins and vitamin C) are particularly vulnerable to depletion during RRT due to their low molecular weight, minimal protein binding and hydrophilicity [46]. Significant losses of folic acid and vitamin B6 have been reported, with measurable declines in serum concentrations over time [62]. Vitamin C depletion is especially pronounced, with a high prevalence of deficiency observed in patients undergoing CRRT and sustained reductions demonstrated even after therapy cessation [63]. Critically ill patients are intrinsically at risk of thiamine deficiency because of reduced nutritional intake, increased metabolic demands, and pre-existing nutritional deficiencies [64]. This risk is particularly pronounced in high risk populations, including patients with previous bariatric surgery, chronic alcohol misuse, or severe malnutrition. During CRRT, thiamine is readily removed because of its small molecular weight and water solubility. Accordingly, extracorporeal losses may aggravate or accelerate the development of deficiency [46]. Although experimental models suggest rapid early losses of B vitamins, clinical detection of certain vitamins, particularly thiamine and vitamin B12, in effluent has been inconsistent [46, 53]. Overall, the risk of micronutrient deficiency is influenced by the cumulative effects of treatment duration and intensity, nutritional adequacy, and the increased metabolic demands associated with critical illness.

Trace elements

Baseline trace element deficiencies are common in critically ill patients and may worsen during RRT [62, 63, 65, 66]. Selenium and copper are among the trace elements most commonly depleted during RRT [67]. However, interpretation of trace element status remains challenging, as serum concentrations are strongly influenced by the acute-phase response and inflammation may reduce circulating selenium and zinc concentrations through redistribution into tissues and changes in carrier proteins, whilst copper concentrations may paradoxically increase owing to elevated ceruloplasmin levels [68, 69]. Consequently, measured concentrations may not accurately reflect total body stores or functional deficiency. In prolonged RRT, cumulative depletion becomes clinically significant, with multiple trace element deficiencies frequently observed [46].

Other nutrients

In contrast, larger and lipophilic molecules are minimally affected by RRT. Lipids and fat-soluble vitamins (A, D, E, and K) are not significantly removed due to their size, limited solubility and ability to bind to other molecules (e.g. lipoproteins) [46, 53, 70]. Proteins larger than approximately 30 kDa are similarly retained. Importantly, even when not directly removed by RRT, nutrient deficiencies may still arise in critically ill patients receiving RRT due to reduced intake, inflammation, altered metabolism, or underlying disease processes.

Nutritional recommendations for patients with AKI and those receiving RRT

Screening for malnutrition using validated tools (e.g., modified Nutrition Risk in Critically Ill [mNUTRIC], Nutritional Risk Screening 2002 [NRS-2002]) to identify patients at risk of refeeding syndrome should be performed at ICU admission, as uniformly recommended for all ICU patients [52]. Patients at high nutritional risk or with prolonged inadequate intake at baseline should receive cautious caloric advancement, thiamine supplementation, and close monitoring of phosphate, potassium and magnesium. Traditional biomarkers of nutritional adequacy (e.g. prealbumin, albumin, urea) are confounded by inflammation, dilution, altered synthesis and extracorporeal clearance, and should not be interpreted in isolation [6, 52].

Enteral nutrition is the preferred route of nutritional support in patients with AKI and should be initiated early in patients who are deemed safe to commence artificial nutrition support. Parenteral nutrition is generally reserved for patients with an absolute contraindication to enteral nutrition or those failing to meet > 60% nutrition targets after 5–7 days [6, 52]. These principles are consistent with current recommendations for critically ill patients without AKI and should not be modified solely on the basis of AKI or RRT (Table 1).

Nutritional prescription during RRT requires integration of illness phase, nutritional risk, metabolic capacity to utilise nutrients, and RRT-related nutrient losses and gains. Particular attention should be paid to patients who are already malnourished, have experienced reduced food intake before or during hospitalisation, or are unable to meet at least 70% of their nutritional requirements through oral intake [52]. Because both AKI and RRT are dynamic, nutrition prescriptions should be frequently reassessed to prevent both under- and overfeeding. A phase-adapted approach to nutritional support in patients with AKI receiving RRT is proposed in Fig. 2.

During the initial phase of critical illness, characterised by marked inflammation, insulin resistance, mitochondrial dysfunction, and impaired substrate utilisation, full nutritional targets may not be achievable or desirable. A gradual advancement of nutritional support may therefore be warranted, particularly in patients with shock, severe metabolic instability, or at risk of refeeding syndrome [71, 72]. As the patient transitions toward recovery and nutrient utilisation improves, nutritional goals may shift toward minimising further skeletal muscle loss and supporting functional rehabilitation.

Table 1 Prescription suggestions according to AKI and RRT

	AKI	RRT
Energy	Estimate energy requirements using indirect calorimetry whenever available. If indirect calorimetry is unavailable, target an energy intake of 20–25 kcal/kg/day achieved gradually	Estimate energy requirements using indirect calorimetry whenever available. Caloric contributions from citrate anticoagulation and from glucose- or lactate-containing dialysate/replacement fluids should be considered when targeting total energy provision of 20–25 kcal/kg/day
Protein	Follow general ICU recommendations, targeting total protein provision of 1.2–1.3 g/kg/day	Consider augmentation to 1.7–2.5 g/kg/day to offset extracorporeal losses
Water soluble vitamins	Follow general ICU recommendations	Water soluble vitamins (thiamine, folate, vitamin B complex, vitamin C) supplementation during prolonged or high-intensity RRT may be beneficial, although evidence-based replacement strategies remain poorly defined
Fat soluble vitamins	Follow general ICU recommendations	Follow general ICU recommendations
Trace elements	Follow general ICU recommendations	Trace elements supplementation during prolonged or high-intensity RRT may be beneficial, although evidence-based replacement strategies remain poorly defined

Acute kidney injury, AKI; renal replacement therapy, RRT; intensive care unit, ICU

Energy requirements

Indirect calorimetry (IC) remains the most accurate method for determining resting energy expenditure (REE) and guiding energy prescription, as it directly measures oxygen consumption and carbon dioxide production [73]. Nevertheless, its use in routine clinical practice remains limited worldwide [74]. Moreover, its application during RRT was historically questioned because extracorporeal carbon dioxide clearance was thought to interfere with the accuracy of the measurement. More recent data, however, indicate that the effect of CRRT on IC-derived REE is small, provided treatment-related nutrient losses and non-nutritional caloric gains are appropriately considered [54]. In the MECCIAS trial [75], CRRT-related variations in carbon dioxide balance altered estimated REE by approximately 3–4%, which is considered

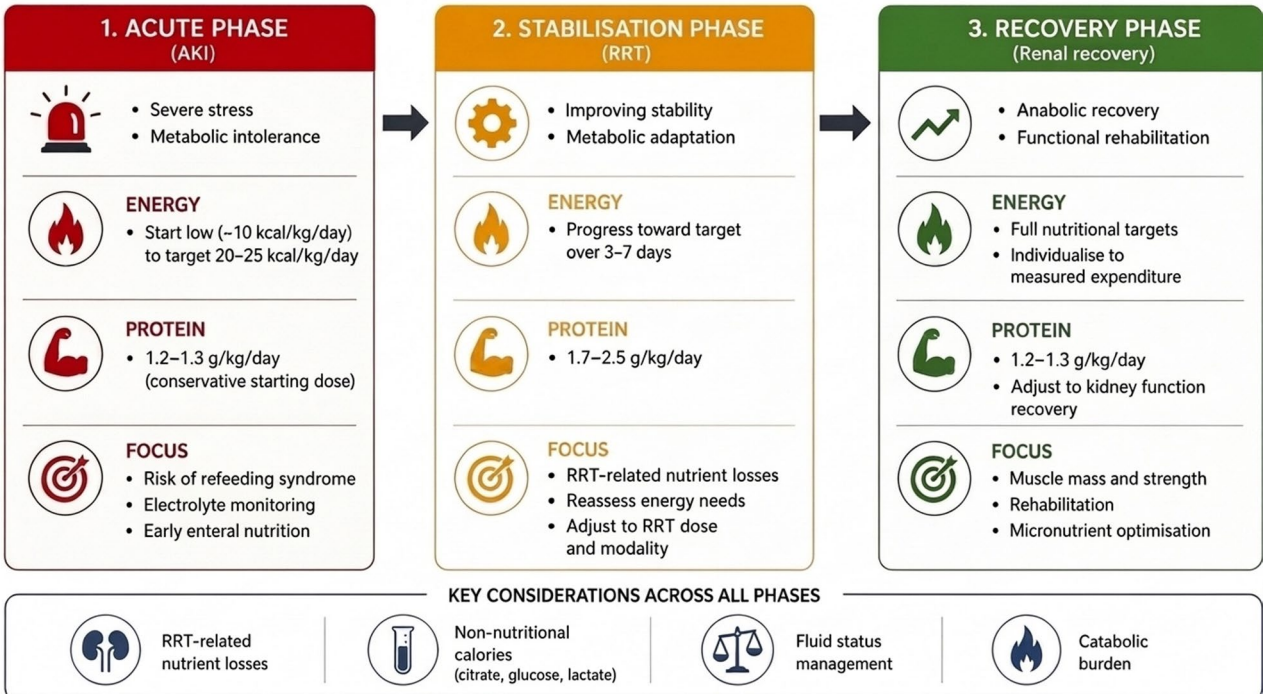


Fig. 2 Phase-adapted nutritional approach in acute kidney injury and renal replacement therapy. Nutritional requirements in AKI evolve throughout critical illness and recovery. Energy and protein provision should be adapted according to illness phase, metabolic tolerance, catabolic burden, and RRT-related nutrient losses and non-nutritional caloric gains, with goals shifting from avoiding overfeeding during acute illness to supporting anabolism and functional recovery. acute kidney injury, AKI; renal replacement therapy, RRT

clinically acceptable. Available evidence also suggests that IRRT does not substantially affect the assessment of REE, with comparable IC measurements reported during and outside dialysis sessions [52, 76]. Nevertheless, technical and clinical factors may still preclude reliable testing. These include oxygen supplementation in non-intubated patients, leaks within the respiratory circuit, and ventilatory settings exceeding the validated range of the device, particularly a fraction of inspired oxygen above 60% or positive end-expiratory pressure above 12 cm H_2O [75, 77]. When IC is not feasible or available, energy requirements in AKI patients may be approximated using pragmatic weight-based targets equal to 20–25 kcal/kg/day or predictive equations, although these approaches are less precise. Energy requirements should ideally be estimated using an adjusted body weight, as actual body weight is often confounded by fluid overload, oedema, capillary leak, and rapid changes in volume status. Therefore, nutritional prescriptions based on actual body weight may overestimate energy requirements and increase the risk of overfeeding in fluid overloaded patients. Importantly, predictive equations are static and demonstrate poor agreement with IC-derived values in this population, particularly in patients with fluid overload or metabolic instability [17, 18, 57].

Energy provision should commence with a lower initial dose of approximately 10 kcal/kg/day followed by gradual advancement towards the nutritonal goal over 3–7 days based on clinical tolerance [52]. Contributions from non-nutritional calories should be accounted for to avoid inadvertent overfeeding. Monitoring strategies include: daily fluid balance; frequent assessment of phosphate, magnesium, potassium, and glucose; and triglyceride measurement (in selected patients).

Current knowledge gaps

Evidence informing energy provision in critically ill patients with AKI, including those receiving RRT, remains limited. Most nutritional recommendations [6, 7] are extrapolated from studies in general ICU populations, in which patients with severe AKI are frequently excluded or underrepresented [78]. Accordingly, nutritional strategies continue to rely more on physiological rationale, post-hoc or sub-group analyses, and expert opinion than on adequately powered randomized controlled trials [79, 80].

A major challenge is the lack of reliable methods to identify which patients are most likely to benefit from specific nutritional interventions. Emerging approaches, such as nitrogen balance assessment and serial evaluation of muscle mass by ultrasound or computed tomography, may provide insights into catabolic burden (e.g. negative nitrogen balance, rapid loss of skeletal muscle mass) and changes in body composition. However, their

role in guiding nutritional prescriptions remains uncertain [81]. Importantly, abnormalities identified by these measures do not necessarily indicate that increasing energy delivery will improve anabolic responses, preserve muscle mass, or enhance clinical outcomes, and therefore require cautious interpretation.

Beyond its effects on kidney function, AKI may contribute to persistent skeletal muscle dysfunction through sustained hypercatabolism, systemic inflammation, endocrine alterations, and accelerated protein breakdown, potentially increasing the risk of ICU-acquired weakness (ICU-AW) [50]. Consistent with this hypothesis, observational studies have demonstrated independent associations between RRT and ICU-AW [82], poorer physical function and health-related quality of life among ICU survivors with AKI [83], and high rates of muscle wasting and ICU-AW in patients receiving CRRT [84]. Although these findings require confirmation in mechanistic and interventional studies, they provide a strong biological rationale for evaluating nutritional interventions using outcomes that reflect muscle preservation, functional recovery, and longer-term quality of life.

Future research should focus on developing precision nutrition strategies that integrate illness phase (acute vs. recovery), metabolic tolerance and biomarker-guided phenotype, measured energy expenditure (e.g. IC), catabolic burden (e.g. nitrogen balance assessment), and RRT-related nutrient losses and gains to better characterise metabolic requirements and treatment responsiveness [79, 80, 85–89]. In parallel, nutritional trials in AKI should adopt standardized and clinically meaningful endpoints for kidney (e.g. RRT discontinuation, major adverse kidney events) and patient recovery (e.g. physical function and recovery), rather than relying solely on biochemical surrogates [90–92].

Protein requirements and urea balance

Traditionally, protein restriction was recommended in critically ill patients with AKI and CKD to limit urea production. However, current protein recommendations for patients with AKI are extrapolated from the broader critically ill population (approximately 1.2–1.3 g/kg/day), reflecting the limited availability of AKI-specific evidence. By contrast, current guidelines advocate higher protein provision for critically ill patients receiving RRT to offset extracorporeal amino acid losses and increased catabolic stress [1, 52, 93–95], with ESPEN [6] advising up to 1.7 g/kg/day and ASPEN [7] up to 2.5 g/kg/day. However these thresholds are largely derived from observational studies, secondary analyses, and expert opinion, such that the optimal protein dose remains uncertain and should be individualised according to metabolic tolerance, catabolic burden, illness phase, and treatment goals.

Recent data have highlighted the uncertainty surrounding optimal protein dosing in AKI. A *post hoc* analysis of the EFFORT Protein trial [25] suggested that higher protein intake (≥ 1.2 g/kg/day) in AKI patients *not* receiving RRT was associated with worse outcomes, potentially mediated by nitrogenous waste generation. Notably, this association was not observed in patients receiving RRT, suggesting that extracorporeal clearance may partially mitigate adverse metabolic consequences associated with higher protein administration. Conversely, a subgroup analysis of the TARGET Protein trial found heterogeneity of treatment effect in patients receiving newly initiated RRT at baseline, favouring usual rather than augmented protein delivery [96]. Collectively, these findings suggest that the optimal protein dose during AKI and RRT remains uncertain.

This uncertainty has renewed interest in the concept of metabolic tolerance and the potential role of urea or the urea-to-creatinine ratio as markers of a patient's capacity to utilise nutritional support [97]. However, elevated blood urea concentrations alone should not routinely prompt reduction of protein delivery, as current evidence is derived primarily from observational studies. Urea concentrations reflect the complex interplay between the underlying catabolic state, amino acid oxidation, kidney and liver dysfunction, RRT prescription, and, in some cases, occult gastrointestinal bleeding [53, 97–99]. Restricting protein solely in response to rising urea concentrations risks exacerbating negative nitrogen balance and accelerating skeletal muscle loss.

From a practical perspective, standard protein enteral formulations are generally appropriate for critically ill patients with AKI receiving RRT. In contrast, disease-specific "renal" formulations are designed for chronic kidney disease and typically contain lower amounts of protein, potassium and phosphate. While insufficient to meet the requirements of critically ill patients with AKI receiving RRT, these formulations may be useful in patients undergoing IRRT who develop hyperkalaemia or hyperphosphataemia, if combined with additional protein supplementation [94].

Current knowledge gaps

Recent studies have renewed interest in intravenous amino acid administration as a potential nephroprotective strategy [100]. Importantly, this approach should not be regarded as a nutritional intervention or as part of the ongoing debate surrounding optimal protein provision in critical illness. Rather, intravenous amino acids are administered as a short-term pharmaconutrition therapy, with proposed effects extending beyond substrate replacement to include modulation of renal haemodynamics, cellular metabolism, and tissue repair pathway [101].

In this context, the proposed renal benefit is that of AKI prevention, rather than treatment. Mechanistically, amino acid infusion increases renal blood flow and glomerular filtration rate through afferent arteriolar vasodilatation, mediated by suppression of tubuloglomerular feedback and enhanced nitric oxide and prostaglandin activity [102]. In addition, amino acids may recruit renal functional reserve, improve cortical and medullary oxygenation, and activate pathways involved in recovery following AKI [103–105].

Vitamin and trace elements requirements

Given the substantial inter-individual variability in vitamins and trace elements losses during RRT, and the confounding effects of inflammation on serum concentrations, routine empiric replacement of water-soluble vitamins is pragmatic, while targeted monitoring (e.g., thiamine, vitamin C, selenium) may be reserved for prolonged CRRT (>7 days) or patients with clinical deficiency syndromes.

Current knowledge gaps

High-quality prospective studies are needed to define optimal monitoring strategies and replacement protocols for vitamins and trace elements during CRRT. Future research should identify which patients benefit from routine biochemical monitoring, establish clinically relevant thresholds for supplementation, and determine whether personalised replacement strategies improve patient-centred outcomes compared with empiric supplementation alone.

Considerations for special AKI populations

Acute systemic stress states

The degree of catabolism during critical illness generally parallels illness severity, with the greatest nitrogen losses observed in sepsis, trauma, burns, and major surgery [6, 106, 107]. Such conditions are common precipitants of severe AKI requiring RRT that have traditionally been considered to warrant aggressive energy and protein supplementation. However, these states are characterised by stress-induced metabolic adaptations, including insulin resistance, hyperglycaemia, accelerated proteolysis, and increased ureagenesis [108–110]. Accordingly, early aggressive nutrition may increase hyperglycaemia, serum insulin levels, and insulin requirements [111]. Moreover, higher protein delivery may increase glucagon secretion and hepatic amino acid metabolism, without clear evidence of improved muscle preservation [112].

Evidence supporting aggressive nutritional strategies in these settings remains limited, being derived from low-quality studies [113] or extrapolated from large randomised trials that have suggested potential harm [114–116]. Balanced energy provision aimed at supporting substrate utilisation while minimising hyperglycaemia may therefore represent a rational approach in patients with acute systemic stress states receiving RRT [117].

Liver dysfunction

Concomitant liver failure presents a unique nutritional challenge in patients with AKI receiving RRT because both organ systems play central roles in substrate metabolism and nitrogen handling. Acute and acute on chronic liver failure are characterised by further disturbances in protein metabolism, glucose homeostasis, ammonia clearance, and metabolic tolerance. Nutritional requirements should be individualised, balancing provision of adequate energy and protein against the risks of hyperammonaemia, hepatic encephalopathy, and metabolic intolerance [118].

Historically, protein restriction was employed to limit ammonia production; however, routine restriction is no longer recommended because inadequate protein provision may worsen negative nitrogen balance and accelerate skeletal muscle wasting [119]. The optimal role of RRT to treat hyperammonaemia in patients with liver disease is unclear but is best established specifically in acute liver failure, in which CRRT is usually preferred as its use is associated with lower risk of aggravating cerebral oedema and lower mortality compared to intermittent RRT [120]. Similarly, in patients with combined liver failure and AKI, RRT may support ammonia removal [121] while permitting ongoing protein provision. These patients may also receive substantial non-nutritional caloric and protein-related inputs, including albumin and glucose-containing infusions, which should be considered when assessing overall nutritional delivery. In patients with hyperammonaemia, CRRT effluent dose often needs to be increased beyond the usually recommended dose range to facilitate ammonia clearance.

Conclusions

AKI in critical illness is increasingly recognised as a systemic metabolic disorder that may contribute to poor clinical and functional outcomes. Although RRT remains essential for the management of severe AKI, it may further aggravate metabolic disturbances through macro- and micro-nutrient losses and alterations in energy balance. Accordingly, nutritional therapy in patients with AKI receiving RRT should be considered an integral component of organ support rather than a secondary supportive measure. Despite growing recognition of the nutritional challenges in this setting, high-quality evidence remains limited. Accordingly, future studies should address: (1) the optimal protein dose in patients with AKI and specifically AKI-RRT through adequately powered randomized trials; (2) the role of amino acid supplementation beyond protein provision; (3) biomarker-guided

approaches to identify patients most likely to benefit from enhanced nutrition; and (4) long-term functional outcomes, rather than biochemical endpoints alone, as primary measures of success.

Such strategies may help identify which patients are most likely to benefit from specific nutritional interventions, thereby improving both kidney-related and patient-centred outcomes.

Abbreviations

AKI	Acute kidney injury
CRRT	Continuous renal replacement therapy
IC	Indirect calorimetry
ICU	Intensive care unit
mNUTRIC	Modified Nutrition Risk in the Critically Ill score
NRS-2002	Nutritional Risk Screening 2002
IRRT	Intermittent renal replacement therapy
REE	Resting energy expenditure
RRT	Renal replacement therapy
TCA	Tricarboxylic acid

Acknowledgements
Ministero della Salute – Ricerca Corrente 2026, Italy. The authors used ChatGPT (OpenAI) to assist in the graphical design of Figs. 1 and 2. All scientific content, interpretation and final editing were performed and approved by the authors, who take full responsibility for the figure.

Author contributions
SLC and ES conceived and designed the study; SLC, LSC, SDR, MMD, JP, CS, ES wrote the first draft of the manuscript; LF, MO, CR critical appraised and reviewed the manuscript. All authors approved the final version of manuscript for submission.

Funding
None to declare;

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
SDR, LF, CR, ES declare no competing interest. SLC was the recipient of the 2025 ESICM – Fresenius Kabi Clinical Nutrition Award. LSC has received lecture fees from Nutricia and Fresenius Kabi unrelated to this review. MMD has received lecture fees from Fresenius Medical Care, Baxter, and Sysmex as well as an unrestricted research grant from Baxter. CS reported receiving grants from Fresenius Kabi and personal fees from Fresenius Kabi, Nestle, Baxter, Nutricia and BBRAUN outside of this work. MO received research funding from Biomerieux and Baxter (paid to institution). JRP reports speaker or consulancy fees from Vantive, BBraun, NorrDia and Paion Pharma.

Author details
[1]Department of Biotechnologies, Intensive Care and Perioperative Medicine, Catholic University of the Sacred Heart, Rome, Italy
[2]Department of Emergency Sciences, Anesthesiology and Intensive Care Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[3]School of Medicine, College of Health, Adelaide University, Adelaide, Australia
[4]Intensive Care Research, Royal Adelaide Hospital, Adelaide, Australia
[5]Centre for Medical Sciences, University of Trento, Trento, Italy
[6]Department of Anaesthesiology, Intensive Care Medicine and Pain Medicine, University Hospital Münster, Münster, Germany
[7]William Harvey Research Institute, Queen Mary University of London, London, UK
[8]Department of Anesthesiology, Intensive Care, Emergency and Pain Medicine, University Hospital Würzburg, Würzburg, Germany
[9]Department of Cardiac Anesthesiology and Intensive Care Medicine, Deutsches Herzzentrum der Charité, Berlin, Germany
[10]German Centre for Cardiovascular Research (DZHK), Berlin, Germany
[11]Department of Critical Care Medicine, Royal Surrey Hospital, Guildford, UK
[12]Department of Clinical and Experimental Medicine, Faculty of Health Sciences, University of Surrey, Guildford, UK
[13]Department of Intensive Care, Guy's & St Thomas' NHS Foundation Hospital, London, UK
[14]Department of Nephrology, Dialysis and Transplantation, San Bortolo Hospital, International Renal Research Institute of Vicenza, Vicenza, Italy
[15]Department of Medicine, University of Padova, Padova, Italy
[16]Department of Critical Care, Melbourne Medical School, University of Melbourne, Melbourne, VIC, Australia
[17]Department of Intensive Care, Royal Melbourne Hospital, Melbourne, VIC, Australia

Received: 25 June 2026 / Accepted: 5 August 2026
Published online: 13 August 2026

References

1. KDIGO Working Group. Work Group Membership. Kidney Int Supplements. 2012;2:2. https://doi.org/10.1038/kisup.2012.2.
2. Hoste EAJ, Bagshaw SM, Bellomo R, Cely CM, Colman R, Cruz DN, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Med. 2015;41:1411–23. https://doi.org/10.1007/s00134-015-3934-7.
3. Ronco C, Bellomo R, Kellum JA. Acute kidney injury. Lancet. 2019;394:1949–64. https://doi.org/10.1016/S0140-6736(19)32563-2.
4. Druml W. Systemic consequences of acute kidney injury. Curr Opin Crit Care. 2014;20:613–9. https://doi.org/10.1097/MCC.0000000000000150.
5. Chua H-R, Puthucheary Z. Critical Care Nephrology: Chap. 74 - Amino Acid Turnover, Protein Metabolism, and Nitrogen Balance in Acute Kidney Injury. Elsevier; 2019.
6. Singer P, Blaser AR, Berger MM, Calder PC, Casaer M, Hiesmayr M, et al. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clin Nutr. 2023;42:1671–89. https://doi.org/10.1016/j.clnu.2023.07.011.
7. Compher C, Bingham AL, McCall M, Patel J, Rice TW, Braunschweig C, et al. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enter Nutr. 2022;46:12–41. https://doi.org/10.1002/jpen.2267.
8. Gaudry S, Palevsky PM, Dreyfuss D. Extracorporeal Kidney-Replacement Therapy for Acute Kidney Injury. Ingelfinger JR, editor. N Engl J Med. 2022;386:964–75. https://doi.org/10.1056/NEJMra2104090
9. Rousseau A-F, Pantet O, Stoppe C, De Man AME, Berger MM. Vitamin C in acute critical illness: don't confuse pharmacotherapy and nutrition! Intensive Care Med. 2026. https://doi.org/10.1007/s00134-026-08546-8.
10. Di Mario F, Sabatino A, Fiaccadori E. Clinical nutrition in patients with Acute Kidney Injury: Traditional approaches and emerging perspectives. Clin Nutr ESPEN. 2025;65:348–56. https://doi.org/10.1016/j.clnesp.2024.12.015.
11. Gupta P, Zhu S, Gui Y, Zhou D. Metabolic Chaos in Kidney Disease: Unraveling Energy Dysregulation. J Clin Med. 2024;13:6772. https://doi.org/10.3390/jcm13226772.
12. Li AS, Baker PR, Park S, Budnick I, He Z, Okamura K, et al. Metabolomic assessment reveals depletion of amino acids and energy metabolites in skeletal muscle after ischemic acute kidney injury in mice. Sci Rep. 2026;16:8823. https://doi.org/10.1038/s41598-026-37424-y.
13. Tang W, Wei Q. The metabolic pathway regulation in kidney injury and repair. Front Physiol. 2024;14:1344271. https://doi.org/10.3389/fphys.2023.1344271.
14. Bhargava P, Schnellmann RG. Mitochondrial energetics in the kidney. Nat Rev Nephrol. 2017;13:629–46. https://doi.org/10.1038/nrneph.2017.107.
15. Scholz H, Boivin FJ, Schmidt-Ott KM, Bachmann S, Eckardt K-U, Scholl UI, et al. Kidney physiology and susceptibility to acute kidney injury: implications for

renoprotection. Nat Rev Nephrol. 2021;17:335–49. https://doi.org/10.1038/s41581-021-00394-7.
16. Baker PR, Li AS, Griffin BR, Gil H-W, Orlicky DJ, Fox BM, et al. Disruption in glutathione metabolism and altered energy production in the liver and kidney after ischemic acute kidney injury in mice. Sci Rep. 2024;14:13862. https://doi.org/10.1038/s41598-024-64586-4.
17. De Góes CR, Berbel-Bufarah MN, Sanches ACS, Xavier PS, Balbi AL, Ponce D. Poor Agreement between Predictive Equations of Energy Expenditure and Measured Energy Expenditure in Critically Ill Acute Kidney Injury Patients. Ann Nutr Metab. 2016;68:276–84. https://doi.org/10.1159/000446708.
18. Sabatino A, Theilla M, Hellerman M, Singer P, Maggiore U, Barbagallo M, et al. Energy and Protein in Critically Ill Patients with AKI: A Prospective, Multicenter Observational Study Using Indirect Calorimetry and Protein Catabolic Rate. Nutrients. 2017;9:802. https://doi.org/10.3390/nu9080802.
19. Schneeweiss B, Graninger W, Stockenhuber F, Druml W, Ferenci P, Eichinger S, et al. Energy metabolism in acute and chronic renal failure. Am J Clin Nutr. 1990;52:596–601. https://doi.org/10.1093/ajcn/52.4.596.
20. Moonen HPFX, Beckers KJH, Van Zanten ARH. Energy expenditure and indirect calorimetry in critical illness and convalescence: current evidence and practical considerations. J Intensive Care. 2021;9:8. https://doi.org/10.1186/s40560-021-00524-0.
21. Zusman O, Theilla M, Cohen J, Kagan I, Bendavid I, Singer P. Resting energy expenditure, calorie and protein consumption in critically ill patients: a retrospective cohort study. Crit Care. 2016;20:367. https://doi.org/10.1186/s13054-016-1538-4.
22. Tessari P, Garibotto G, Inchiostro S, Robaudo C, Saffioti S, Vettore M, et al. Kidney, splanchnic, and leg protein turnover in humans. Insight from leucine and phenylalanine kinetics. J Clin Invest. 1996;98:1481–92. https://doi.org/10.1172/JCI118937.
23. Wu G. Amino Acids in Nutrition and Health. Springer; 2021.
24. Knol MGE, Wulfmeyer VC, Müller R-U, Rinschen MM. Amino acid metabolism in kidney health and disease. Nat Rev Nephrol. 2024;20:771–88. https://doi.org/10.1038/s41581-024-00872-8.
25. Stoppe C, Patel JJ, Zarbock A, Lee Z-Y, Rice TW, Mafrici B, et al. The impact of higher protein dosing on outcomes in critically ill patients with acute kidney injury: a post hoc analysis of the EFFORT protein trial. Crit Care. 2023;27:399. https://doi.org/10.1186/s13054-023-04663-8.
26. Druml W, Bürger U, Kleinberger G, Lenz K, Laggner A. Elimination of amino acids in acute renal failure. Nephron. 1986;42:62–7. https://doi.org/10.1159/000183635.
27. Møller N, Meek S, Bigelow M, Andrews J, Nair KS. The kidney is an important site for in vivo phenylalanine-to-tyrosine conversion in adult humans: A metabolic role of the kidney. Proc Natl Acad Sci U S A. 2000;97:1242–6. https://doi.org/10.1073/pnas.97.3.1242.
28. Edison EE, Brosnan ME, Meyer C, Brosnan JT. Creatine synthesis: production of guanidinoacetate by the rat and human kidney in vivo. Am J Physiol Ren Physiol. 2007;293:F1799–1804. https://doi.org/10.1152/ajprenal.00356.2007.
29. Brosnan ME, Brosnan JT. Renal Arginine Metabolism. J Nutr. 2004;134. https://doi.org/10.1093/jn/134.10.2791S. :2791S-2795S.
30. Gao W, Chen Y, Li B, Liu S-P, Liu X, Jiang Q. Determining the adsorption energies of small molecules with the intrinsic properties of adsorbates and substrates. Nat Commun. 2020;11:1196. https://doi.org/10.1038/s41467-020-14969-8.
31. Macias WL, Alaka KJ, Murphy MH, Miller ME, Clark WR, Mueller BA. Impact of the Nutritional Regimen on Protein Catabolism and Nitrogen Balance in Patients With Acute Renal Failure. J Parenter Enter Nutr. 1996;20:56–62. https://doi.org/10.1177/014860719602000156.
32. Chapple L-AS, Kouw IWK, Summers MJ, Weinel LM, Gluck S, Raith E, et al. Muscle Protein Synthesis after Protein Administration in Critical Illness. Am J Respir Crit Care Med. 2022;206:740–9. https://doi.org/10.1164/rccm.202112-2780OC.
33. Aranda-Rivera AK, Cruz-Gregorio A, Aparicio-Trejo OE, Pedraza-Chaverri J. Mitochondrial Redox Signaling and Oxidative Stress in Kidney Diseases. Biomolecules. 2021;11:1144. https://doi.org/10.3390/biom11081144.
34. Gervasio JM, Garmon WP, Holowatyj M. Nutrition Support in Acute Kidney Injury. Nut Clin Prac. 2011;26:374–81. https://doi.org/10.1177/0884533611414029.
35. Meyer C, Stumvoll M, Dostou J, Welle S, Haymond M, Gerich J. Renal substrate exchange and gluconeogenesis in normal postabsorptive humans. Am J Physiol Endocrinol Metab. 2002;282:E428–434. https://doi.org/10.1152/ajpendo.00116.2001.
36. Zhang C, Ning M, Liang W, Su W, Chen Y, Guo T, et al. The association between acute kidney injury and dysglycaemia in critically ill patients with and without diabetes mellitus: a retrospective single-center study. Ren Fail. 2024;46:2397555. https://doi.org/10.1080/0886022X.2024.2397555.
37. van Vught LA, Wiewel MA, Klein Klouwenberg PMC, Hoogendijk AJ, Scicluna BP, Ong DSY, et al. Admission Hyperglycemia in Critically Ill Sepsis Patients: Association With Outcome and Host Response. Crit Care Med. 2016;44:1338–46. https://doi.org/10.1097/CCM.0000000000001650.
38. Gunst J, Debaveye Y, Güiza F, Dubois J, De Bruyn A, Dauwe D, et al. Tight Blood-Glucose Control without Early Parenteral Nutrition in the ICU. N Engl J Med. 2023;389:1180–90. https://doi.org/10.1056/NEJMoa2304855.
39. Lan R, Geng H, Singha PK, Saikumar P, Bottinger EP, Weinberg JM, et al. Mitochondrial Pathology and Glycolytic Shift during Proximal Tubule Atrophy after Ischemic AKI. J Am Soc Nephrol. 2016;27:3356–67. https://doi.org/10.1681/ASN.2015020177.
40. Oh WC, Mafrici B, Rigby M, Harvey D, Sharman A, Allen JC, et al. Micronutrient and Amino Acid Losses During Renal Replacement Therapy for Acute Kidney Injury. Kidney Int Rep. 2019;4:1094–108. https://doi.org/10.1016/j.ekir.2019.05.001.
41. Claure-Del Granado R, Clark WR. Continuous renal replacement therapy principles. Semin Dial. 2021;34:398–405. https://doi.org/10.1111/sdi.12967.
42. Bellomo R, Ankawi G, Bagshaw SM, Baldwin I, Basu R, Bottari G, et al. Hemoadsorption: consensus report of the 30th Acute Disease Quality Initiative workgroup. Nephrol Dialysis Transplantation. 2024;39:1945–64. https://doi.org/10.1093/ndt/gfae089.
43. Davenport A. The changing face of dialyzer membranes and dialyzers. Semin Dial. 2025;38:25–34. https://doi.org/10.1111/sdi.13161.
44. Zappitelli M, Juarez M, Castillo L, Coss-Bu J, Goldstein SL. Continuous renal replacement therapy amino acid, trace metal and folate clearance in critically ill children. Intensive Care Med. 2009;35:698–706. https://doi.org/10.1007/s00134-009-1420-9.
45. Gonska T, Hirsch JR, Schlatter E. Amino acid transport in the renal proximal tubule. Amino Acids. 2000;19:395–407. https://doi.org/10.1007/s007260070019.
46. Berger MM, Broman M, Forni L, Ostermann M, De Waele E, Wischmeyer PE. Nutrients and micronutrients at risk during renal replacement therapy: a scoping review. Curr Opin Crit Care. 2021;27:367–77. https://doi.org/10.1097/MCC.0000000000000851.
47. Ratanarat R, Brendolan A, Volker G, Bonello M, Salvatori G, Andrikos E, et al. Phosphate Kinetics during Different Dialysis Modalities. Blood Purif. 2005;23:83–90. https://doi.org/10.1159/000082016.
48. Teixeira JP. Continuous Kidney Replacement Therapy-Induced Hypophosphatemia: A Nuisance or a Clinically Meaningful Target? Am J Kidney Dis. 2026;87:615–7. https://doi.org/10.1053/j.ajkd.2026.03.032.
49. Kim SY, Kim YN, Shin HS, Jung Y, Rim H. The influence of hypophosphatemia on outcomes of low- and high-intensity continuous renal replacement therapy in critically ill patients with acute kidney injury. Kidney Res Clin Pract. 2017;36:240–9. https://doi.org/10.23876/j.krcp.2017.36.3.240.
50. Teixeira JP, Mayer KP, Griffin BR, George N, Jenkins N, Pal CA, et al. Intensive Care Unit-Acquired Weakness in Patients With Acute Kidney Injury: A Contemporary Review. Am J Kidney Dis. 2023;81:336–51. https://doi.org/10.1053/j.ajkd.2022.08.028.
51. Neyra JA, Thompson Bastin M, Ghamarian E, Firenzuoli F, Takeuchi T, Bagshaw SM, et al. Hypophosphatemia During Kidney Replacement Therapy and Ventilator-Free Days: A Post Hoc Analysis of the STARRT-AKI Trial. Am J Kidney Dis. 2026;87:654–e6641. https://doi.org/10.1053/j.ajkd.2025.11.012.
52. Fiaccadori E, Sabatino A, Barazzoni R, Carrero JJ, Cupisti A, De Waele E, et al. ESPEN guideline on clinical nutrition in hospitalized patients with acute or chronic kidney disease. Clin Nutr. 2021;40:1644–68. https://doi.org/10.1016/j.clnu.2021.01.028.
53. Fishman G, Singer P. Metabolic and nutritional aspects in continuous renal replacement therapy. J Intensive Med. 2023;3:228–38. https://doi.org/10.1016/j.jointm.2022.11.001.
54. Jonckheer J, Demol J, Lanckmans K, Malbrain MLNG, Spapen H, De Waele E. MECCIAS trial: Metabolic consequences of continuous veno-venous hemofiltration on indirect calorimetry. Clin Nutr. 2020;39:3797–803. https://doi.org/10.1016/j.clnu.2020.04.017.
55. New AM, Nystrom EM, Frazee E, Dillon JJ, Kashani KB, Miles JM. Continuous renal replacement therapy: a potential source of calories in the critically ill. Am J Clin Nutr. 2017;105:1559–63. https://doi.org/10.3945/ajcn.116.139014.

56. Ting S, Chua H-R, Cove ME. Euglycemic Ketosis During Continuous Kidney Replacement Therapy With Glucose-Free Solution: A Report of 8 Cases. Am J Kidney Dis. 2021;78:305–8. https://doi.org/10.1053/j.ajkd.2020.10.014.
57. Garcia-Alvarez M, Marik P, Bellomo R. Stress hyperlactataemia: present understanding and controversy. Lancet Diabetes Endocrinol. 2014;2:339–47. https://doi.org/10.1016/S2213-8587(13)70154-2.
58. Stapel SN, de Boer RJ, Thoral PJ, Vervloet MG, Girbes ARJ, Oudemans-van Straaten HM. Amino Acid Loss during Continuous Venovenous Hemofiltration in Critically Ill Patients. Blood Purif. 2019;48:321–9. https://doi.org/10.1159/000500998.
59. Mafrici B, Viramontes-Hörner D, Gardner DS, Smith K, Taal MW, Selby NM, et al. Amino Acid and Protein Losses in Adult Patients Receiving Maintenance Dialysis: A Literature Review. J Ren Nutr. 2026;36:30–48. https://doi.org/10.1053/j.jrn.2025.07.012.
60. Fournier A, Birmelé B, François M, Prat L, Halimi J-M. Factors Associated with Albumin Loss in Post-Dilution Hemodiafiltration and Nutritional Consequences. Int J Artif Organs. 2015;38:76–82. https://doi.org/10.5301/ijao.5000389.
61. Lumlertgul N, Cameron LK, Bear DE, Ostermann M. Micronutrient Losses during Continuous Renal Replacement Therapy. Nephron. 2023;147:759–65. https://doi.org/10.1159/000531947.
62. Ostermann M, Summers J, Lei K, Card D, Harrington DJ, Sherwood R, et al. Micronutrients in critically ill patients with severe acute kidney injury - a prospective study. Sci Rep. 2020;10:1505. https://doi.org/10.1038/s41598-020-58115-2.
63. Kamel AY, Dave NJ, Zhao VM, Griffith DP, Connor MJ, Ziegler TR. Micronutrient Alterations During Continuous Renal Replacement Therapy in Critically Ill Adults: A Retrospective Study. Nutr Clin Pract. 2018;33:439–46. https://doi.org/10.1177/0884533617716618.
64. Amrein K, Oudemans-van Straaten HM, Berger MM. Vitamin therapy in critically ill patients: focus on thiamine, vitamin C, and vitamin D. Intensive Care Med. 2018;44:1940–4. https://doi.org/10.1007/s00134-018-5107-y.
65. Fah M, Van Althuis LE, Ohnuma T, Winthrop HM, Haines KL, Williams DGA, et al. Micronutrient deficiencies in critically ill patients receiving continuous renal replacement therapy. Clin Nutr ESPEN. 2022;50:247–54. https://doi.org/10.1016/j.clnesp.2022.05.008.
66. Koekkoek KWA, Berger MM. An update on essential micronutrients in critical illness. Curr Opin Crit Care. 2023;29:315–29. https://doi.org/10.1097/MCC.0000000000001062.
67. Gundogan K, Yucesoy FS, Ozer NT, Temel S, Sahin S, Sahin GG, et al. Serum micronutrient levels in critically ill patients receiving continuous renal replacement therapy: A prospective, observational study. JPEN J Parenter Enter Nutr. 2022;46:1141–8. https://doi.org/10.1002/jpen.2378.
68. Duncan A, Talwar D, McMillan DC, Stefanowicz F, O'Reilly DSJ. Quantitative data on the magnitude of the systemic inflammatory response and its effect on micronutrient status based on plasma measurements. Am J Clin Nutr. 2012;95:64–71. https://doi.org/10.3945/ajcn.111.023812.
69. Oakes EJC, Lyon TDB, Duncan A, Gray A, Talwar D, O'Reilly DSJ. Acute inflammatory response does not affect erythrocyte concentrations of copper, zinc and selenium. Clin Nutr. 2008;27:115–20. https://doi.org/10.1016/j.clnu.2007.10.003.
70. Schneider AG, Picard W, Honoré PM, Dewitte A, Mesli S, Redonnet-Vernhet I, et al. Amino acids and vitamins status during continuous renal replacement therapy: An ancillary prospective observational study of a randomised control trial. Anaesth Crit Care Pain Med. 2021;40:100813. https://doi.org/10.1016/j.accpm.2021.100813.
71. Reignier J, Plantefeve G, Mira J-P, Argaud L, Asfar P, Aissaoui N, et al. Low versus standard calorie and protein feeding in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group trial (NUTRIREA-3). Lancet Respiratory Med. 2023;11:602–12. https://doi.org/10.1016/S2213-2600(23)00092-9.
72. Doig GS, Simpson F, Heighes PT, Bellomo R, Chesher D, Caterson ID, et al. Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial. Lancet Respiratory Med. 2015;3:943–52. https://doi.org/10.1016/S2213-2600(15)00418-X.
73. Oshima T, Berger MM, De Waele E, Guttormsen AB, Heidegger C-P, Hiesmayr M, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. Clin Nutr. 2017;36:651–62. https://doi.org/10.1016/j.clnu.2016.06.010.
74. Derouin E, Picard G, Kerever S. Dieticians' practices in intensive care: A national survey. Clin Nutr ESPEN. 2021;45:245–51. https://doi.org/10.1016/j.clnesp.2021.08.017.
75. Schlein KM, Coulter SP. Best Practices for Determining Resting Energy Expenditure in Critically Ill Adults. Nut Clin Prac. 2014;29:44–55. https://doi.org/10.1177/0884533613515002.
76. Góes CRD, Balbi AL, Ponce D. Evaluation of Factors Associated with Hypermetabolism and Hypometabolism in Critically Ill AKI Patients. Nutrients. 2018;10:505. https://doi.org/10.3390/nu10040505.
77. Delsoglio M, Achamrah N, Berger MM, Pichard C. Indirect Calorimetry in Clinical Practice. J Clin Med. 2019;8:1387. https://doi.org/10.3390/jcm8091387.
78. Heyland DK, Patel J, Compher C, Rice TW, Bear DE, Lee Z-Y, et al. The effect of higher protein dosing in critically ill patients with high nutritional risk (EFFORT Protein): an international, multicentre, pragmatic, registry-based randomised trial. Lancet. 2023;401:568–76. https://doi.org/10.1016/S0140-6736(22)02469-2.
79. Otis JL, Parker NM, Busch RA. Nutrition support for patients with renal dysfunction in the intensive care unit: A narrative review. Nutr Clin Pract. 2025;40:35–53. https://doi.org/10.1002/ncp.11231.
80. Alarcón-Fuentes J, Pedreros-Rosales C, Cornejo-Arriagada B, Müller-Ortiz H, Ramírez-Guerrero G. Nutritional support in acute kidney injury requiring continuous renal replacement therapy: from metabolic alterations to clinical recommendations. Int Urol Nephrol. 2026. https://doi.org/10.1007/s11255-026-05164-7.
81. Weimann A, Edel A, Lücke L, Stoppe C, Kreymann KG. Lean mass loss in the intensive care unit and its restoration: A narrative review. Nutr Clin Pract. 2026;41:350–68. https://doi.org/10.1002/ncp.70100.
82. Raurell-Torredà M, Arias-Rivera S, Martí JD, Frade-Mera MJ, Zaragoza-García I, Gallart E, et al. Care and treatments related to intensive care unit-acquired muscle weakness: A cohort study. Aust Crit Care. 2021;34:435–45. https://doi.org/10.1016/j.aucc.2020.12.005.
83. Mayer KP, Ortiz-Soriano VM, Kalantar A, Lambert J, Morris PE, Neyra JA. Acute kidney injury contributes to worse physical and quality of life outcomes in survivors of critical illness. BMC Nephrol. 2022;23:137. https://doi.org/10.1186/s12882-022-02749-z.
84. Mayer KP, Teixeira JP, González-Seguel F, Tran VQ, Gross JM, Horikawa-Strakovsky A, et al. Acute skeletal muscle wasting in patients with acute kidney injury requiring continuous kidney replacement therapy: A prospective multicenter study. J Crit Care. 2025;89:155142. https://doi.org/10.1016/j.jcrc.2025.155142.
85. Shi Y, Duan H, Liu J, Shi X, Zhao M, Fang Y, et al. Prevalence and Prognostic Significance of Malnutrition in Critically Ill Patients With Acute Kidney Injury. J Ren Nutr. 2026;36:58–69. https://doi.org/10.1053/j.jrn.2025.09.006.
86. Martín-Del-Campo F, Sotelo-Anaya R, Castro-Mata PC, García-García G, Martínez Gallardo-González A, Gómez-Fregoso JA, et al. Nutritional Parameters Associated With Hospital Mortality in Patients With Acute Kidney Injury. J Ren Nutr. 2026;36:49–57. https://doi.org/10.1053/j.jrn.2025.07.003.
87. Meersch-Dini M, Joannidis M, De Rosa S, Endre Z, Ostermann M. What new renal biomarkers tell us about renal physiology: Collection: physiology applied to ICU. Ann Intensive Care. 2026;16:100017. https://doi.org/10.1016/j.aicoj.2025.100017.
88. Xu W, Zhang Z, Gu F, Ye T, Zhang Y, Hu W, et al. Integrating metabolomics and machine learning with in silico analysis to identify early biomarkers and molecular interactions in sepsis-associated acute kidney injury. Sci Rep. 2026;16:10963. https://doi.org/10.1038/s41598-026-45255-0.
89. Scott J, See EJ, Kelly YP. Moving beyond the syndrome: how can acute kidney injury phenotypes help? Curr Opin Nephrol Hypertens. 2025;34:491–9. https://doi.org/10.1097/MNH.0000000000001098.
90. Zarbock A, Forni LG, Koyner JL, Bell S, Reis T, Meersch M, et al. Recommendations for clinical trial design in acute kidney injury from the 31st acute disease quality initiative consensus conference. A consensus statement. Intensive Care Med. 2024;50:1426–37. https://doi.org/10.1007/s00134-024-07560-y.
91. Chawla LS, Davison DL, Brasha-Mitchell E, Koyner JL, Arthur JM, Shaw AD, et al. Development and Standardization of a Furosemide Stress Test to Predict the Severity of Acute Kidney Injury. Crit Care. 2013;17:R207. https://doi.org/10.1186/cc13015.
92. Xu Q, Zhou Z, Jin L, Liu C, Li P, Wang F, et al. Novel biomarkers for predicting successful liberation of renal replacement therapy for acute kidney injury: a systematic review. Crit Care. 2025;29:213. https://doi.org/10.1186/s13054-025-05451-2.

93. Heyland DKothers. The effect of higher protein dosing in critically ill patients (EFFORT Protein). Lancet. 2023;401:568–76. https://doi.org/10.1016/S0140-6736(22)02469-2.
94. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N). J Parenter Enter Nutr. 2016;40:159–211. https://doi.org/10.1177/0148607115621863.
95. Bels JLM, Thiessen S, van Gassel RJJ, Beishuizen A, De Bie Dekker A, Fraipont V, et al. Effect of high versus standard protein provision on functional recovery in people with critical illness (PRECISe): an investigator-initiated, double-blinded, multicentre, parallel-group, randomised controlled trial in Belgium and the Netherlands. Lancet. 2024;404:659–69. https://doi.org/10.1016/S0140-6736(24)01304-7.
96. Summers MJ, Chapple L-AS, Karahalios A, Bellomo R, Chapman MJ, Ferrie S, et al. Augmented Enteral Protein During Critical Illness: The TARGET Protein Randomized Clinical Trial. JAMA. 2025;334:319–28. https://doi.org/10.1001/jama.2025.9110.
97. Stoppe C, Hill A, Christopher KB, Kristof AS. Toward Precision in Nutrition Therapy. Crit Care Med. 2025;53:e429–40. https://doi.org/10.1097/CCM.0000000000006537.
98. Stoppe C, Ridley EJ, Lee Z-Y. Rethinking energy and protein provision for critically ill patients. Intensive Care Med. 2025;51:167–70. https://doi.org/10.1007/s00134-024-07726-8.
99. Krinsley JS, Deane AM, Gunst J. The goal of personalized glucose control in the critically ill remains elusive. Intensive Care Med. 2021;47:1319–21. https://doi.org/10.1007/s00134-021-06530-y.
100. Landoni G, Monaco F, Ti LK, Baiardo Redaelli M, Bradic N, Comis M, et al. A Randomized Trial of Intravenous Amino Acids for Kidney Protection. N Engl J Med. 2024;391:687–98. https://doi.org/10.1056/NEJMoa2403769.
101. Abel RM, Beck CH, Abbott WM, Ryan JA, Barnett GO, Fischer JE. Improved Survival from Acute Renal Failure after Treatment with Intravenous Essential L-Amino Acids and Glucose: Results of a Prospective, Double-Blind Study. N Engl J Med. 1973;288:695–9. https://doi.org/10.1056/NEJM197304052881401.
102. Jeppsson A, Ekroth R, Friberg P, Kirnö K, Milocco I, Nilsson F, et al. Renal effects of amino acid infusion in cardiac surgery. J Cardiothorac Vasc Anesth. 2000;14:51–5. https://doi.org/10.1016/S1053-0770(00)90056-9.
103. Furukawa T, Jufar AH, May CN, Evans RG, Cochrane AD, Marino B, et al. Recruitment of renal functional reserve by intravenous amino acid loading in a sheep model of cardiopulmonary bypass. Intensive Care Med Exp. 2025;13:71. https://doi.org/10.1186/s40635-025-00774-4.
104. Jufar AH, Evans RG, May CN, Hood SG, Betrie AH, Trask-Marino A, et al. The effects of recruitment of renal functional reserve on renal cortical and medullary oxygenation in non-anesthetized sheep. Acta Physiol. 2023;237:e13919. https://doi.org/10.1111/apha.13919.
105. Egbujor MC, Olaniyan OT, Emeruwa CN, Saha S, Saso L, Tucci P. An insight into role of amino acids as antioxidants via NRF2 activation. Amino Acids. 2024;56:23. https://doi.org/10.1007/s00726-024-03384-8.
106. Rousseau A-F, Losser M-R, Ichai C, Berger MM. ESPEN endorsed recommendations: nutritional therapy in major burns. Clin Nutr. 2013;32:497–502. https://doi.org/10.1016/j.clnu.2013.02.012.
107. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, et al. Acute skeletal muscle wasting in critical illness. JAMA. 2013;310:1591–600. https://doi.org/10.1001/jama.2013.278481.
108. Casaer MP, Mesotten D, Hermans G, Wouters PJ, Schetz M, Meyfroidt G, et al. Early versus late parenteral nutrition in critically ill adults. N Engl J Med. 2011;365:506–17. https://doi.org/10.1056/NEJMOA1102662.
109. Cehan V-D, Cehan A-R, Pui MC, Lazar A. A New Perspective on Overfeeding in the Intensive Care Unit (ICU): Challenges, Dangers and Prevention Methods. Life (Basel). 2025;15:828. https://doi.org/10.3390/life15050828.
110. Tanaka A, Hamilton K, Eastwood GM, Jones D, Bellomo R. The epidemiology of overfeeding in mechanically ventilated intensive care patients. Clin Nutr ESPEN. 2020;36:139–45. https://doi.org/10.1016/j.clnesp.2019.12.100.
111. Treskes N, Koekkoek WAC, van Zanten ARH. The Effect of Nutrition on Early Stress-Induced Hyperglycemia, Serum Insulin Levels, and Exogenous Insulin Administration in Critically Ill Patients With Septic Shock: A Prospective Observational Study. Shock. 2019;52:e31–8. https://doi.org/10.1097/SHK.0000000000001287.
112. Thiessen SE, Derde S, Derese I, Dufour T, Vega CA, Langouche L, et al. Role of Glucagon in Catabolism and Muscle Wasting of Critical Illness and Modulation by Nutrition. Am J Respir Crit Care Med. 2017;196:1131–43. https://doi.org/10.1164/rccm.201702-0354OC.
113. Hampton V, Hampton T, Dheansa B, Falder S, Emery P. Evaluation of high protein intake to improve clinical outcome and nutritional status for patients with burns: a systematic review. Burns. 2021;47:1714–29. https://doi.org/10.1016/j.burns.2021.02.028.
114. Haines RWothers. The effect of high protein dosing in critically ill patients. Br J Anaesth. 2024;133:1192–200. https://doi.org/10.1016/j.bja.2024.08.033.
115. Haines RWothers. Association between urea trajectory and protein dose in critically ill adults. Crit Care. 2024;28:24. https://doi.org/10.1186/S13054-024-04799-1.
116. Schouteden Eothers. High vs standard enteral protein after ICU admission: Bayesian analysis of PRECISe. Clin Nutr. 2025;48:153–60. https://doi.org/10.1016/j.clnu.2025.03.022.
117. McNelly A, Langan A, Bear DE, Page A, Martin T, Seidu F, et al. A pilot study of alternative substrates in the critically Ill subject using a ketogenic feed. Nat Commun. 2023;14:8345. https://doi.org/10.1038/s41467-023-42659-8.
118. Dong V, Robinson AM, Dionne JC, Cardoso FS, Rewa OG, Karvellas CJ. Continuous renal replacement therapy and survival in acute liver failure: A systematic review and meta-analysis. J Crit Care. 2024;81:154513. https://doi.org/10.1016/j.jcrc.2023.154513.
119. Patel JJ, McClain CJ, Sarav M, Hamilton-Reeves J, Hurt RT. Protein Requirements for Critically Ill Patients With Renal and Liver Failure. Nutr Clin Pract. 2017;32:S101–11. https://doi.org/10.1177/0884533616687501.
120. Cardoso FS, Gottfried M, Tujios S, Olson JC, Karvellas CJ, US Acute Liver Failure Study Group. Continuous renal replacement therapy is associated with reduced serum ammonia levels and mortality in acute liver failure. Hepatol Baltim Md. 2018;67:711–20. https://doi.org/10.1002/hep.29488.
121. Warrillow S, Fisher C, Bellomo R. Correction and Control of Hyperammonemia in Acute Liver Failure: The Impact of Continuous Renal Replacement Timing, Intensity, and Duration. Crit Care Med. 2020;48:218–24. https://doi.org/10.1097/CCM.0000000000004153.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.