DOI: 10.1002/ncp.11231

INVITED REVIEW

Nutrition support for patients with renal dysfunction in the intensive care unit: A narrative review

Joanna L. Otis MS, RDN[1] | **Nicholas M. Parker PharmD, RPh**[2] | **Rebecca A. Busch MD**[3]

[1]Department of Clinical Nutrition, University of Wisconsin Hospital and Clinics, Madison, Wisconsin, USA

[2]Department of Pharmacy, University of Wisconsin Hospital and Clinics, Madison, Wisconsin, USA

[3]Division of Acute Care and Regional General Surgery, Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

Correspondence
Rebecca A. Busch, MD, Division of Acute Care and Regional General Surgery, Department of Surgery, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave. CSC H4/360, Madison, WI 53792, USA.
Email: busch@surgery.wisc.edu

Abstract

Providing optimal nutrition support in the intensive care unit (ICU) is a challenging and dynamic process. Energy, protein, fluid, electrolyte, and micronutrient requirements all can be altered in patients with acute, chronic, and acute-on-chronic kidney disease. Given that renal dysfunction occurs in up to one-half of ICU patients, it is imperative that nutrition support providers understand how renal dysfunction, its metabolic consequences, and its treatments, including renal replacement therapy (RRT), affect patients' nutrition needs. Data on nutrient requirements in critically ill patients with renal dysfunction are sparse. This article provides an overview of renal dysfunction in the ICU and identifies and addresses the unique nutrition challenges present among these patients, including those receiving RRT, as supported by the available literature and guidelines.

KEYWORDS

acute renal failure, adult, critical care, fluids-electrolytes/acid-base, minerals/trace elements, renal disease, vitamins

INTRODUCTION

Aberrations in a single-organ system—the renal system—can introduce a litany of metabolic and therapeutic nuances to providing nutrition support to the critically ill. Given the high prevalence of renal dysfunction in intensive care units (ICUs), it is necessary for nutrition support providers to appreciate the kidney's role in nutrient homeostasis as well as the potential pitfalls associated with common medical strategies for managing renal failure, including renal replacement therapy (RRT). In the setting of limited clinical data, it is imperative that providers have a keen understanding of the impact of renal dysfunction and its treatments on nutrient needs so that they can appropriately individualize nutrition support in these complex and dynamic patients to prevent nutrition deficiencies, malnutrition, and their associated complications.

RENAL DYSFUNCTION IN THE ICU

Renal dysfunction is one of the most common conditions seen in ICUs worldwide. Although rarely the primary reason for ICU admission, the presence of renal dysfunction complicates care, increasing patient morbidity, mortality, and costs.[1,2] Renal dysfunction typically presents

in the ICU as an acute, chronic, or acute-on-chronic group of syndromes.

Definition of renal dysfunction

Renal dysfunction broadly encompasses a continuum of disease with a variety of etiologies and staged severity. Acute kidney injury (AKI) is defined by the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) criteria as an abrupt decrease in kidney function occurring over ≤7 days as represented by increased creatinine values or decreased urine output (Table 1).[3] Chronic kidney disease (CKD), on the other hand, is defined as persistent alterations in kidney function or structure lasting >3 months with implications for health according to the KDIGO 2024 Clinical Practice Guideline.[4] CKD is classified by cause, glomerular filtration rate (GFR), and markers of kidney damage (eg, albuminuria), (Tables 2 and 3). AKI on CKD represents an acute decline in kidney function in a patient with baseline CKD, whereas acute kidney disease and disorders is a term reserved for patients not meeting criteria for AKI or CKD but who are still at risk for poor outcomes potentially amenable to intervention.[5] Finally, end-stage renal disease (ESRD) refers to patients with an estimated GFR (eGFR) <15 ml/min, often requiring chronic RRT.

TABLE 1 Staging of acute kidney injury when occurring over ≤7 days.[3]

Stage	Serum creatinine	Urine output
1	1.5–1.9 × baseline OR ≥0.3 mg/dl increase	<0.5 ml/kg/h for 6–12 h
2	2.0–2.9 × baseline	<0.5 ml/kg/h for ≥12 h
3	3.0 × baseline OR Increase in serum creatinine to ≥4.0 mg/dl OR Initiation of renal replacement therapy	<0.3 ml/kg/h for ≥24 h OR Anuria for ≥12 h

Epidemiology

Reports on the incidence and prevalence of renal dysfunction in the ICU vary based on developing consensus definitions. For AKI, the most complete recent estimate comes from the AKI-Epidemiologic Prospective Investigation (EPI) study.[6] This study sought to evaluate the incidence of AKI in ICU patients through a multicenter, international cross-sectional evaluation that included >1800 patients from 97 ICUs across 33 countries. Researchers found that 57% of patients developed AKI of any severity within the 1-week study period, and AKI stages 2 or 3 occurred in 39% of patients. RRT was ultimately required in 13.5% of the patients evaluated, including 23.5% of patients with AKI. This incidence of AKI appears relatively consistent with other studies.[7,8]

The true prevalence of underlying CKD is difficult to estimate among ICU patients given the perennial lack of

TABLE 3 Albuminuria categories in chronic kidney disease.[4]

Albuminuria category	ACR, mg/g	Comment
A1	<3	Normal to mildly increased
A2	3–300	Moderately increased
A3	>300	Severely increased

Abbreviation: ACR, albumin-to-creatinine ratio.

TABLE 2 Glomerular filtration rate categories in chronic kidney disease when present for >90 days.[4]

GFR category	GFR, ml/min per 1.73 m^2	Comment
G1	>90	Kidney damage with normal kidney function
G2	60–89	Kidney damage with mild loss of kidney function
G3a	45–59	Mild to moderate loss of kidney function
G3b	30–44	Moderate to severe loss of kidney function
G4	15–29	Severe loss of kidney function
G5	<15	Kidney failure

Abbreviation: GFR, glomerular filtration rate.

baseline laboratory values. The paucity of data likely underestimates the incidence of AKI on CKD; however, some studies report the prevalence of underlying CKD in upward of 30% of patients who develop AKI in the ICU, whereas others report it to occur at rates similar to AKI in patients without CKD.[8–10] Although a fair number of patients with CKD will not develop a component of AKI, CKD predisposes patients to AKI on CKD as demonstrated in a nested case-controlled study of >600,000 patients.[8,11] Of the 1764 patients who required RRT, most had evidence of underlying CKD. Further, the prevalence of CKD and ESRD is globally increasing, owing to escalating rates of hypertension, diabetes, and an overall aging population.[12] To this end, patients with ESRD are more likely to require ICU beds than the general population, highlighting the importance of this topic.

Etiology

There are multiple causes of renal dysfunction that can be broadly classified into three categories: prerenal (due to decreased renal blood flow), intrinsic (due to pathology of the kidney vessels, glomeruli, or tubules), or postrenal (due to obstruction).[13]

In the ICU, the most frequent cause of AKI is prerenal, due to decreased renal blood flow in the setting of shock. Indeed, distributive shock from sepsis, hypovolemic shock from hemorrhage, and cardiogenic shock from heart failure are some of the most common causes of AKI seen in the ICU, accounting for >50% of cases.[2] Drugs or nephrotoxic agents can also induce prerenal injury by altering intraglomerular hemodynamics, leading to ischemic insult, or by direct glomerular or tubular cell injury, consistent with an intrinsic injury.[5] Nephrotoxic drugs were reported in 14.4% of patients with AKI in the AKI-EPI study.[6] Causes of acute intrinsic renal injury include but are not limited to acute tubular necrosis, acute interstitial nephritis, and acute glomerulonephritis, which can be precipitated by prolonged prerenal injury, nephrotoxic agents, rhabdomyolysis, infection, and autoimmune conditions, among others.[13] Postrenal AKI results from acute obstruction of the urinary system at the level of the renal calyx, renal pelvis, ureter, bladder, or urethra most often because of calculi, malignancy, blood clots, or prostatic enlargement.

The duration of dysfunction helps to differentiate between acute and chronic disease. Repeated acute insults of any variety can lead to progressive loss of renal function and, ultimately, CKD or ESRD.[14] The most common primary diseases responsible for CKD include diabetes mellitus, hypertension, primary glomerulonephritis, chronic tubulointerstitial nephritis, and hereditary or cystic diseases.[14]

Outcomes

Clinical outcomes for AKI and CKD are intimately related, yet they may also act as distinct entities. Patients with AKI are at increased risk for progression to CKD, and patients with CKD are at increased risk of AKI on CKD when critically ill.[5,15] However, some studies report poorer prognosis in patients with normal kidney function before AKI in the ICU compared with those who experienced AKI on CKD or CKD alone,[16,17] whereas others note increased morbidity and mortality in patients with CKD compared with those with AKI alone.[18–20] Still others found no difference in outcomes for patients with ESRD requiring ICU admission and RRT compared with matched patients with AKI requiring RRT.[21] These mixed findings may be the result of different patient populations, evolving consensus definitions, or perhaps differences in disease stratification, as detailed by Neyra et al, wherein they found that in the presence of underlying CKD, AKI stages 2 or 3 were independently associated with increased risks of progressive CKD and mortality,that was not seen with stage 1 AKI on CKD.[8]

For patients *without* pre-existing CKD, however, Neyra et al and others found the risk of developing CKD or mortality to increase incrementally in accordance with the stage of AKI severity.[8,22] Patients with AKI requiring RRT have in-hospital mortality rates ranging from 40% to 55%[2] and a 2.3-fold increase in mortality after controlling for numerous confounders.[23] Even mild cases (stage 1 KDIGO AKI) are linked to decreased survival at 10 years[24] in comparison with the increased risk of mortality associated with patients with CKD requiring ICU admission only lasting 6 months beyond discharge.[19] The duration of AKI also influences survival. One study found that patients whose AKI reversed within 7 days had only a 10% mortality rate at 1 year compared with nearly 60% after adjusting for age in patients who did not have quick renal recovery.[25] These findings emphasize the significant social and economic impact of AKI.

OVERVIEW OF RENAL REPLACEMENT THERAPY

Indications

RRT acts as a substitute for failing kidneys by removing excess fluid volume, uremic toxins, electrolytes, and other small molecules, such as amino acids. RRT can additionally assist with maintaining the acid-base balance. In a patient with renal dysfunction, the indications for RRT may be summarized with the mnemonic AEIOU: metabolic **a**cidosis; **e**lectrolytes (especially hyperkalemia); **i**ngestion (of dialyzable toxins like methanol, salicylates, or lithium);

volume **o**verload refractory to diuretics; and **u**remia causing platelet dysfunction and/or encephalopathy.[26]

Modalities and components

The central component of all RRT modalities is the semipermeable filter membrane.[26,27] This selective membrane allows the passage of water, electrolytes, and small molecules but restricts the passage of larger molecules, such as proteins and blood cells.[26,27] During hemodialysis, blood flows along one side of the semipermeable membrane, and a dialysate solution flows along the other.[27] Small molecules cross the membrane from high concentration to low, thereby moving excess solutes from the blood to the dialysate by diffusion.[27,28] In ultrafiltration, hydrostatic pressure is applied to the blood within the machine, forcing water and solutes across the membrane.[26–28] In most cases, RRT consists of simultaneous hemodialysis and ultrafiltration.[27,28]

The three major modalities of RRT are intermittent hemodialysis (HD or iHD), continuous RRT (CRRT), and peritoneal dialysis (PD). Although a valuable treatment for some patients, PD is the least efficient RRT modality and is rarely suitable for critically ill patients, so it will not be discussed here. iHD is performed a few hours at a time, typically three times weekly for chronic maintenance, or as often as daily in the acute setting.[27] Fluid removal during iHD can reach 1000 ml/h which may not be tolerated by hemodynamically unstable patients or adequate enough for patients receiving large fluid volumes from medications and blood products.[27,28] Conversely, CRRT operates continuously at a slower, steadier rate. This helps to avoid fluctuations in blood pressure while still achieving a significantly higher total volume of fluid and solute removal.[26,28] The most common method of CRRT is continuous venovenous hemodialysis (CVVH or CVVHD), but other configurations are also used.[28]

The surface of the semipermeable filter membrane promotes coagulation by activating platelets. This leads to an increased risk of blood clotting on the membrane. To prevent this complication, anticoagulation with either citrate or heparin is usually required.[27] Citrate works locally as an anticoagulant by chelating calcium in the blood, preventing it from activating the coagulation cascade. In addition to chelating calcium, citrate also readily binds to magnesium. Thus, while receiving citrate anticoagulation, calcium and magnesium infusions are necessary to maintain serum levels.[29] Citrate can also affect the acid-base balance because citrate metabolizes to bicarbonate; however, it does not tend to increase the risk for metabolic alkalosis.[30] Compared with citrate, heparin carries a higher risk of bleeding but otherwise has fewer systemic effects.[27,30]

EFFECTS OF RENAL DYSFUNCTION AND RRT ON NUTRIENT NEEDS IN THE ICU

Patients with renal dysfunction are at high risk of malnutrition because of a complex interplay of factors. In the acute setting, increased protein catabolism, insulin resistance, and impaired nutrient metabolism contribute to malnutrition.[31] Chronically restricted diets, taste changes, poor appetite, hormonal derangements, systemic inflammation, and nutrient losses caused by RRT exacerbate the risk of malnutrition.[2]

Impaired waste, electrolyte, and fluid removal, as well as metabolic alterations, create significant challenges in the nutrition management of patients with renal dysfunction. Despite such complexities, ensuring adequate nutrition in the ICU is crucial to preventing nutrition deficiencies, malnutrition, and their complications. Please see Table 4 for a summary of recommendations.

Energy

Renal impairment alone does not have a significant impact on a patient's energy needs. Rather, energy needs depend more on the patient's comorbid conditions, medical therapies, surgical interventions, wounds, age, sex, body composition, and level of physical activity. Energy needs can change quickly and substantially in hospitalized patients with AKI or AKI on CKD, especially in the ICU setting and even more so with the initiation of RRT. Thus, energy targets should be re-evaluated routinely and any time there is a significant change in clinical status. There are three primary methods used to estimate daily energy needs: indirect calorimetry (IC), simple weight-based calculations, and predictive equations. The use of one method over another is dependent on patient-specific and/or institutional factors.

IC is considered the gold standard for determining energy needs in hospitalized patients, but its use can be limited by availability, cost, and clinical circumstances. When available, IC is recommended for critically ill and medically complex patients as a strategy to prevent overfeeding and underfeeding, both of which can have deleterious effects.[56] Patients with severe renal impairment can be either hypermetabolic or hypometabolic, so estimating needs accurately is a challenge. In fact, a study of 124 ICU patients with severe AKI revealed that

TABLE 4 Energy and nutrient recommendations in the setting of renal dysfunction.

Category	Recommendations
Energy[31–37]	AKI or AKI on CKD: 20–30 kcal/kg/day ◦ Catabolic phase ± RRT: 20–25 kcal/kg/day ◦ Anabolic phase ± RRT: 25–30 kcal/kg/day CKD ± RRT: 30–35 kcal/kg/day • Obtain IC if possible, especially for medically complex patients or extremes in body composition
Protein[31–36,38,39]	Stable CKD ◦ Stages 3–5 not on RRT: 0.55–0.6 g/kg/day (or 0.3–0.4 g/kg/day with keto analogs) ◦ Stages 3–5 not on RRT with DM: 0.6–0.8 g/kg/day AKI: 0.8–1 g/kg/day for uncomplicated AKI; 1.2–2 g/kg/day if metabolically stressed Stable ESRD on maintenance iHD: 1–1.2 g/kg/day AKI or AKI on CKD receiving iHD: 1.5 g/kg/day; or receiving CRRT: 1.5–2.5 g/kg/day • High- and low-protein renal enteral formulas are available; however, protein restrictions are generally inappropriate for hospitalized patients with CKD because of the increased catabolism • Protein modulars may be required to meet high protein requirements while receiving EN support • Custom PN formulas are able to meet protein requirements; premixed PN formulas may not meet protein needs
Fluid[2,27,32,36]	AKI: unrestricted unless significant volume overloaded or hyponatremia CKD ± RRT: unrestricted if oliguric; restrict to 1–1.2 L/day if anuric ◦ Concentrated EN formulas often required ◦ Restrict PN volume if anuric and/or fluid overloaded CRRT: often unrestricted but dependent on the modality of CRRT and patient factors, including fluid and hemodynamic status ◦ Standard EN formulas may be appropriate ◦ May or may not need to restrict PN volume
Electrolytes	
Sodium[32,36,40–42]	CKD ± iHD: restrict to <2300 mg/day ◦ Renal-specific EN formulas have reduced sodium concentrations ◦ Minimize the sodium concentration of PN AKI or CRRT: restriction not generally indicated ◦ Standard EN formulas usually appropriate ◦ Sodium concentration of PN dependent on fluid status/serum sodium levels

(Continues)

TABLE 4 (Continued)

Category	Recommendations
Potassium[27,32,36,40–43]	AKI or CKD ± iHD: Restrict intake to <2000–3000 mg/day only if hyperkalemic; restriction should be individualized to maintain normal serum levels ◦ Renal-specific EN formulas have reduced potassium concentrations ◦ May need to minimize/remove potassium from PN CRRT: Supplementation may be required ◦ Standard EN formulas may be appropriate ◦ Potassium concentration of PN is dependent on serum levels; may not need to restrict • Potassium is added to dialysate (1–4 mEq/L) to help manage serum levels • Excessive potassium intake/hyperkalemia can contribute to metabolic acidosis
Magnesium[29,31,32,40–42]	AKI or CKD ± iHD: meet DRI for the general population ◦ Renal-specific EN formulas have reduced magnesium concentrations CRRT: supplementation may be required ◦ Standard EN formulas often appropriate ◦ Magnesium concentration of PN is dependent on serum levels • Magnesium is added to dialysate
Phosphorus[29,32,36,40–42,44,45]	AKI or CKD ± iHD: restrict only if hyperphosphatemic ◦ 800–1000 mg/day (standard low-phosphorus diet) ◦ Restriction should be individualized to maintain serum levels ◦ Renal-specific EN formulas contain reduced phosphorus concentrations; may need to restrict phosphate amounts in PN CRRT: ◦ Phosphate may or may not be present in dialysate ◦ Aggressive phosphate supplementation required if using phosphate-free dialysate ◦ Standard EN formulas often appropriate ◦ Phosphate concentration of PN is dependent on serum levels; maximize phosphate in PN if receiving phosphate-free dialysate
Calcium[29,32,36,40–42]	CKD stages 3–4: restrict to 800–1000 mg/dl iHD: restrict to <2000 mg/day ◦ Renal EN formulas contain reduced calcium concentrations ◦ Decrease PN calcium concentration if ionized calcium level is elevated CRRT: Supplementation may be required ◦ Standard EN formulas often appropriate ◦ Standard calcium concentration of PN usually appropriate • Consider all sources of calcium, including diet, supplements, and phosphate binders • May be added to dialysate versus supplemented if receiving citrate anticoagulation while receiving CRRT
Bicarbonate[4,27,32,36,40–42]	• Supplement if serum bicarbonate <22 mmol/L or as needed to maintain acid/base balance • Added to dialysate, often at supraphysiologic concentrations to rapidly correct metabolic acidosis

TABLE 4 (Continued)

Category	Recommendations
	• Increase acetate concentrations in PN if metabolic acidosis present • Avoid using bicarbonate or adjustments to PN acetate to attempt to correct a respiratory acid-base imbalance • Avoid overfeeding with either EN or PN; overfeeding can cause a respiratory acidosis
Vitamins	
Thiamine[31,32,40–42,46–48]	AKI or CKD ± iHD: no specific recommendations CRRT: 100 mg/day • High-protein renal-specific enteral formulas contain 2–4 mg thiamine per liter • Adult parenteral MVI often contain 6 mg thiamine per dose; additional thiamine may be added to the PN formula • TPP is the preferred assay to assess for deficiency because it is unaffected by the acute phase response
Pyridoxine[32,37,40–42,46,47,49]	AKI or CKD ± iHD: no specific recommendations CRRT: 100 mg/day • High-protein renal-specific enteral formulas contain ~8 mg pyridoxine per liter • Adult parenteral MVI often contain 6 mg pyridoxine per dose; additional pyridoxine may be added to the PN formula • Red cell PLP most reliable assay during the acute phase response
Folic acid[31,32,40–42,46]	AKI or CKD on RRT (iHD or CRRT): 1 mg/day High-protein renal-specific enteral formulas contain 750–1000 mcg folic acid per liter • Parenteral MVI often contains 600 mcg folic acid per dose; additional folic acid may be added to PN formula • RBC folate and homocysteine levels are the preferred assays
Ascorbic acid[32,40–42,46,50,51]	AKI or CKD on iHD: 75–100 mg/day CRRT: 250 mg/day • High-protein renal-specific enteral formulas contain 90–100 mg ascorbic acid per liter • Parenteral MVI often contain 200 mg ascorbic acid per dose; additional ascorbic acid may be added to PN formula • Plasma vitamin C levels decrease during the acute phase response
Vitamin D[32,36,38,40–42,46,52]	AKI or CKD ± RRT: Supplement with ergocalciferol, cholecalciferol, or calcifediol if deficient • Consider calcitriol (active form) in severe renal impairment • High-protein renal-specific enteral formulas contain 10–30 mcg vitamin D per liter • Parenteral MVI preparations often contain 5 mcg vitamin D (ergocalciferol or cholecalciferol) per dose; additional vitamin D supplementation may be given separately from PN • 25D levels decrease during acute phase response
Minerals	
Copper[31,40–42,46,53,54]	AKI or CKD ± iHD: no specific recommendations CRRT: 3 mg/day if receiving CRRT for ≥2 weeks

(Continues)

TABLE 4 (Continued)

Category	Recommendations

	• High-protein renal-specific enteral formulas contain ~2 mg copper per liter
	• Parenteral trace minerals often contain 0.3 mg copper per dose as cupric sulfate; additional copper may be added to PN formula[54]
	• Serum copper increases during acute phase response
	  ◦ Low levels support deficiency
	  ◦ Normal levels do not exclude deficiency

Selenium[40–42,46,47,51,54,55]	AKI or CKD: no specific recommendation CRRT: 50–200 mg/day • Renal-specific enteral formulas contain 60–100 mg selenium per liter • Parenteral trace minerals often contain 60 mg selenium per dose as selenious acid; additional selenium may be added to PN formula[54] • RBC selenium is unaffected by the acute phase response

Abbreviations: 25D, 25-hydroxyvitamin D; AKI, acute kidney injury; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; DM, diabetes mellitus; DRI, dietary reference intake; EN, enteral nutrition; ESRD, end-stage renal disease; IC, indirect calorimetry; iHD, intermittent hemodialysis; MVI, multivitamin; PLP, pyridoxal 5-phosphate; PN, parenteral nutrition; RBC, red blood cell; RRT, renal replacement therapy; TPP, thiamine pyrophosphate.

62% of patients were hypermetabolic, 34% were normometabolic, and 14% were hypometabolic when resting energy expenditure (REE) was measured by IC.[57] Further, IC is especially valuable for patients with obesity, abnormal muscle mass (either high or low), or severe fluid overload because predictive equations for energy needs become much less reliable in these populations.[32] The ability to tailor nutrition regimens for critically ill patients with renal dysfunction allows for targeted nutrition therapy while mitigating metabolic complications such as protein catabolism, electrolyte imbalances, glucose dysregulation, metabolic acidosis, and malnutrition.[32,33]

Historically, CRRT was a barrier to obtaining accurate IC results owing to its assumed influence on carbon dioxide removal.[58] However, recent research, including the MECCIAS trial, demonstrates that changes in carbon dioxide levels during CRRT have limited impact on REE (only about 3%–4%), which is considered a reasonable margin of error. It is now recommended to obtain IC for patients who are hemodynamically stable on CRRT.[31,59] IC can also be successfully used to assess energy needs in patients undergoing iHD. Studies have shown no significant difference in IC measurements between patients receiving iHD compared with those who are not.[31,57] Limitations to IC do exist, so it may not be possible to perform IC on all patients who would benefit. Several clinical situations can invalidate IC results, including supplemental oxygen in spontaneously breathing patients, air leaks, or high ventilator requirements (ie, fraction of inspired oxygen >60% or positive end-expiratory pressure >12 cm H_2O).[56,58] In such situations, or when IC is unavailable, weight-based and predictive equations are an option.

A common and simple method for estimating energy requirements in the ICU is to assign a target number of kilocalories per kilogram per day. Energy targets using this method have been provided by several authors and guidelines. The KDIGO 2012 guidelines recommend patients with AKI receive 20–30 kcal/kg/day.[38] This aligns well with the American Society for Enteral and Parenteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM) guidelines published in 2016 that recommend estimating energy needs for critically ill adults at 25–30 kcal/kg/day.[33,34] For patients requiring RRT, KDIGO, the European Society for Enteral and Parenteral Nutrition (ESPEN), and the International Society of Renal Nutrition and Metabolism (ISRNM) all recommend between 30 and 35 kcal/kg/day for patients with CKD managed with or without RRT. Others recommend that critically ill patients, including those with severe AKI or receiving CRRT, receive 20–25 kcal/kg/day while in a catabolic stage of disease and 25–30 kcal/kg/day once in an anabolic phase.[31,32,35–37,60]

Predictive equations, such as Mifflin-St. Jeor, Ireton Jones, and Harris-Benedict with appropriate stress factors applied, as well as the Penn State equations for those mechanically ventilated in the ICU, can be used for patients with AKI or AKI on CKD, although none have been proven to be particularly accurate. In fact, predictive equations tend to underestimate energy needs in patients with severe AKI. Predictive equations are also unreliable in patients receiving maintenance iHD; and although disease-specific predictive equations have been proposed for patients on iHD, they have yet to be validated.[61,62]

Approximating energy needs with weight-based or predictive equations relies on a dependable reference weight. Critically ill patients with renal dysfunction often experience significant fluid shifts secondary to resuscitation efforts, intravenous fluids, and medications. If a patient's weight is confounded by altered fluid status, an alternative reference weight should be employed. This could be a prehospital weight, usual body weight, estimated dry weight, or ideal body weight. Energy needs for patients with overweight and obesity should be based on an ideal body weight to avoid overfeeding when using simple kilocalories per kilogram per day calculation methods.[32,35] It is also crucial to consider all sources of energy when developing a nutrition support plan for patients in the ICU. Patients frequently receive additional calories from medications such as propofol or dextrose-containing fluids.[32,37] Attention should be given to the potential energy gains and losses from the RRT dialysate as well.[31,63,64]

Dextrose and lipids

CRRT is a potential source of significant exogenous calories from dextrose in the dialysate, regional citrate anticoagulation, and/or lactate used as a buffering agent. The energy delivered through CRRT is dependent on dialysate composition and flow rate; it can be minimal or substantial. Dialysate solutions can contain dextrose at physiologic concentrations that can cross the filter membrane and contribute 3.4 kcal/g. Dialysate may also contain lactate, which provides 3.62 kcal/g. Citrate anticoagulation, when used, provides another 3 kcal/g. One study found that patients had a net uptake of ~500 kcal/day from dextrose and citrate while receiving CRRT, whereas others have found that patients can receive up to 1300 kcal/day from citrate alone.[31,50,63–65] Glucose-free dialysate, on the other hand, may lead to a loss of glucose, which could cause a net loss of energy and increase the risk for hypoglycemia. However, this effect is usually not substantial enough to warrant an increase in carbohydrate delivery.[27] Unlike glucose, lipids are not dialyzed to a great extent, so the impact on energy balance is negligible.[37]

Protein

Optimal protein intake for patients with renal dysfunction is a debated issue and is dependent on several factors, including stage and chronicity, modality of RRT, underlying comorbid conditions, nutrition status, and presence of acute illness.[31,32] For community-dwelling, stable patients with CKD stages 3–5 who are not yet receiving dialysis, the KDOQI 2020 guidelines recommend a protein intake of 0.55–0.6 g/kg/day (or 0.3–0.4 g/kg/day with the addition of keto analogs) to reduce the risk of progressive kidney failure and death. Patients with diabetes and CKD stages 3–5 have slightly higher protein recommendations at 0.6–0.8 g/kg/day.[36] The rationale for a protein restriction is based on the concept that a lower protein intake decreases renal hyperfiltration and azotemia, which would otherwise lead to a more rapid decline in renal function.[33] There is evidence, however, that a protein intake of 0.8 to >1 g/kg/day is not associated with increased risk of kidney failure or death in patients with CKD stage 3 and may have little effect on slowing the progression of CKD or decline in eGFR.[33,66] Furthermore, with advancements in medical therapy within this realm, including renin-angiotensin system blockade and mineralocorticoid inhibitors, protein restrictions may prove to be even less beneficial and may inadvertently contribute to malnutrition.[66,67]

Protein restriction is generally inappropriate for hospitalized patients with CKD owing to the increased catabolism frequently observed during acute illness and systemic inflammation.[31] Similarly, patients with AKI do not benefit from protein restriction, especially in the ICU setting, and traditionally protein should never be restricted in an effort to avoid or delay the need for RRT.[31,32,34] Protein requirements for hospitalized patients with renal dysfunction are primarily dependent on the underlying disease and level of metabolic stress. For instance, elevated levels of protein catabolism occur in the setting of sepsis, severe injury, and/or metabolic acidosis. The recommendations for protein intake for metabolically stressed patients with AKI range between 1.2 and 2 g/kg/day. Conversely, protein needs for hospitalized patients with noncatabolic, uncomplicated AKI from dehydration, a urinary blockage, or contrast-induced nephropathy, are suggested to be 0.8–1 g/kg/day.[31–34,39] The optimal protein dosing for critically ill patients is an area of active research. Although past guidelines recommended a high protein intake, particularly for those receiving RRT, the recent EFFORT trial suggests that high-protein doses may potentially cause harm.[68] Further

investigation in this area is required to determine the ideal protein goals for this patient population, especially for those with renal dysfunction with and without RRT.

Once initiated on RRT, protein needs increase because of the loss of amino acids to the dialysate. Amino acids, small peptides, and other low molecular weight substances are efficiently removed with dialysis via convective and diffusive transport. Larger proteins generally do not pass through the filter membrane.[31,32,37] It has been found that all amino acids are lost in the effluent during CRRT.[65] Achieving a positive nitrogen balance may not be feasible in the setting of a critically ill patient needing RRT, but ensuring adequate energy and protein intake can help to mitigate nitrogen loss. Amino acid losses are modest during iHD, about 10–13 g per session.[32] Patients receiving chronic iHD require a minimum of 1–1.2 g/kg/day of protein to maintain a neutral or positive nitrogen balance, with needs increasing to as high as 1.5 g/kg/day in the setting of increased catabolism, such as with critical illness.[31,32,35,60]

Because patients receiving CRRT are continuously dialyzed, amino acid losses exceed those observed during iHD; studies have shown that patients can lose anywhere from 5 to 20 g/day of amino acids while receiving CRRT, with most suggesting losses toward the upper end of this range.[53] ASPEN and SCCM guidelines recommend that patients receiving CRRT receive up to 2.5 g/kg/day of protein to achieve a positive, or near positive, nitrogen balance.[31,32,34] ESPEN guidelines recommend a slightly lower protein intake of 1.5–1.7 g/kg/day for patients receiving CRRT but note that a higher protein intake of 2–2.5 g/kg/day may be necessary for patients receiving prolonged CRRT.[31] The 2012 KDIGO guidelines recommend a maximum intake of 1.7 g/kg/day in hypercatabolic patients with AKI and for those receiving CRRT.[31,38]

There has been recent interest in the need for carnitine supplementation in patients receiving RRT owing to a high prevalence of measured carnitine deficiency in these patients. Carnitine is important for fatty acid metabolism, cell membrane stabilization, and cellular repair. Carnitine deficiency can result in cardiomyopathy, muscle weakness, erythropoietin-resistant anemia, and intradialytic hypotension.[32,69] Although several authors recommend supplementing carnitine in deficient patients, a recent Cochrane systematic review did not find sufficient evidence to support the use of carnitine supplements to treat dialysis-related carnitine deficiency.[70]

Fluid and electrolytes

Fluid and electrolyte fluctuations are common in patients with renal dysfunction, especially in the ICU. Clinicians must balance resuscitative needs and efforts to maintain kidney perfusion against evidence of developing AKI and volume overload. Impaired renal function often leads to imbalances in sodium, potassium, magnesium, and phosphate homeostasis. These disturbances may be exacerbated by medications such as diuretics as well as autodiuresis of renal recovery. Tissue breakdown also releases intracellular stores of potassium, phosphate, and magnesium, which can further contribute to electrolyte derangements. Additionally, the specific RRT chosen can significantly impact electrolyte requirements.[32] It is therefore vital for providers prescribing nutrition support to anticipate these potential fluctuations in fluids and electrolytes and proactively adjust their prescriptions accordingly; specific strategies are detailed below.

Patients with renal impairment often benefit from specialized enteral nutrition (EN) support. Renal formulas contain reduced levels of sodium, potassium, magnesium, and phosphorus, compared with standard formulas, to manage electrolyte imbalances common in kidney disease. These formulas are concentrated to prevent fluid overload, but may be either high in protein content to counteract dialysis-related amino acid losses or low in protein content when used chronically to reduce the risk of uremia in patients not yet receiving dialysis. However, the optimal enteral formula varies based on individual patient needs. Standard formulas may be appropriate or even necessary for some patients, such as those receiving CRRT who experience significant electrolyte losses. A low-electrolyte formula could be detrimental in these cases because of the risk of severe electrolyte depletion.[32]

Parenteral nutrition (PN) is crucial for patients with renal disease when enteral feeding is inadequate. PN formulations must also be tailored to the specific metabolic demands with renal dysfunction, and the electrolyte composition of the PN should align with the patient's dialysis status. For patients not receiving dialysis or those undergoing intermittent hemodialysis, electrolyte doses in PN may be minimal. However, electrolyte doses while receiving CRRT can vary, because serum concentrations are controlled by electrolyte levels in the dialysate. Depending on the dialysate used, supplemental electrolyte needs can be elevated (eg, phosphorus if using a phosphate-free dialysate); specific considerations for each electrolyte are discussed in detail below. To prevent fluid overload, PN volume may require restriction as well, although again, not necessarily for patients receiving CRRT.[32]

Fluid and sodium

Fluid and sodium are often restricted in patients with CKD. Patients receiving iHD are prone to volume

overload, and sodium intake <2300 mg/day is recommended for patients with CKD, with or without dialysis, to aid with blood pressure control and edema.[36] The fluid allowance for patients receiving maintenance dialysis is based on residual urine output and the degree of ultrafiltration during dialysis, with the goal of minimizing interdialytic weight gain while avoiding dehydration. This may amount to only 1–1.2 L/day in anuric patients.[27,32] In the hospital setting, patients with nonoliguric AKI do not require a sodium or fluid restriction unless they are volume overloaded.[2,32]

Each iHD session may remove up to 3–4 L of fluid, but in the absence of residual kidney function or other significant fluid losses, fluid volume from nutrition support, medications, and blood products may accumulate quickly. Fluid removal with CRRT is quite different than with iHD and can be substantial (up to 20 L/day).[32] The prescribed fluid removal rate is the *net* rate and accounts for all fluid inputs each hour. For example, if CRRT is prescribed to remove 100 ml/h and the patient is receiving PN at 75 ml/h, the CRRT will remove 175 ml/h in total. CRRT allows for relative freedom with fluid administration, with the caveat that CRRT may be interrupted for filter replacement or procedures. Prolonged interruptions may quickly lead to excess fluid accumulation if fluid administration is not adjusted during CRRT downtime.

The sodium concentration of RRT dialysate is usually set close to physiologic concentrations or 140 mEq/L.[27,29] During treatment, the patient's serum sodium level will gradually trend toward the sodium concentration of the dialysate solution.[27,29] The amount of sodium and fluid a patient receives through medications and nutrition support are often trivial compared with the impact of sodium and fluid exchange between the blood and dialysate.[29] As an example, a patient receiving CRRT using a dialysate with a sodium concentration of 140 mEq/L will likely have a serum sodium level around 140 mEq/L regardless of fluid composition and medications.

Patients exhibiting fluid overload or hyponatremia should generally receive a concentrated EN or PN formula; however, more dilute formulas or additional fluid resuscitation can be required to account for nonurinary losses (eg, gastrointestinal losses or burns). The optimal sodium concentration in the PN ranges from 0 to 154 mEq/L depending on patient-specific factors. Derangements in serum sodium may warrant increased fluid administration, fluid restriction, diuresis, or other interventions instead of, or in concert with, adjustments to the sodium dose and volume of the PN. The patient's volume status and etiology of hyponatremia or hypernatremia should be evaluated carefully before attempting to "fix" a serum sodium with adjustments to the PN formula.[32]

Potassium

Hyperkalemia is a common electrolyte abnormality in patients with impaired renal dysfunction. Cardiac arrhythmias represent the most feared consequence of hyperkalemia, so prompt action is often warranted. If a potassium restriction is warranted, ASPEN recommends an intake of <40 mg/kg/day (or <1 mEq/kg/day), although most guidelines consider a low potassium diet to fall within the range of 2000–3000 mg/day (~51–77 mEq/day).[32,43] Potassium should not be restricted in the absence of hyperkalemia or worsening renal dysfunction.[36]

For patients receiving nutrition support, a low-electrolyte or renal-specific enteral formula may be required to reduce the risk of severe hyperkalemia, and individually compounded PN solutions can be adjusted to reduce or remove the potassium additives.[32,43] In severe cases of hyperkalemia, or when potassium restriction is not feasible, medications and/or RRT may be necessary interventions.

For patients already receiving RRT, it is also important to note that the potassium concentration in dialysate solutions can be adjusted to create a gradient to correct either hyperkalemia or hypokalemia. Potassium concentrations in dialysate range between 1 and 4 mEq/L, with the most common concentrations being 3–4 mEq/L.[27,29] RRT cannot remove potassium below the concentration present in the dialysate solution, so potassium supplementation is usually modest in the absence of refeeding syndrome or significant extrarenal potassium losses. However, using dialysate low in potassium (ie, <2 mEq/L) or rapid correction of acidosis can lead to a significant drop in potassium levels, necessitating more aggressive supplementation and/or an increase in potassium content of EN or PN.[27,29,71] Daily monitoring of potassium levels in hospitalized patients with CKD, AKI on CKD, or renal failure, especially if they are receiving RRT, is prudent. Levels can fluctuate dramatically and frequently depending on potassium intake, medications, tissue catabolism, residual renal function, and RRT needs.[32,36]

Magnesium

Magnesium levels may rise in the presence of renal dysfunction owing to impaired excretory function; however, patients are not typically advised to restrict magnesium intake. Hypermagnesemia is less common than hyperkalemia and hyperphosphatemia, occurring in only 10%–15% of hospitalized patients with renal failure.[72] The current recommendations are for patients with CKD stages 3–5 with or without dialysis to consume enough

magnesium to meet the dietary reference intake (DRI).[32] RRT dialysate typically contains magnesium at slightly less than physiologic concentrations.[29] This leads to gentle correction of hypermagnesemia but may necessitate some magnesium replacement.[29] In systems using citrate anticoagulant, however, magnesium is sequestered along with calcium; thus, postfilter replacement is required to avoid severe hypomagnesemia.[29,31] Magnesium levels should be monitored and magnesium supplemented as needed. Magnesium concentrations in PN solutions can be adjusted to maintain normal serum levels.[32] Renal-specific enteral formulas are low in magnesium content, although switching to a renal-specific formula based solely on hypermagnesemia, especially if mild, is not usually necessary.

Phosphorus

Serum phosphate levels are affected by dietary intake, residual renal excretory function, and bone-mineral metabolism. Phosphorus excretion is usually impaired when eGFR decreases to <45 ml/min/1.73 m^2, and the prevalence of hyperphosphatemia is as high as 50% for patients with anuria receiving maintenance dialysis.[36] Dietary phosphorus intake should be restricted only if phosphate levels are above the reference range. A typical phosphorus restriction is 800–1000 mg/day, and phosphate binders are prescribed when dietary interventions are insufficient. That said, the optimal serum phosphate level and phosphorus intake in patients with impaired renal function is not known. The updated KDOQI guideline recommends an individualized approach to managing hyperphosphatemia.[32,36] The goal of therapy is to minimize the deleterious effects on bone-mineral metabolism and the cardiovascular system.[73] Sources of phosphorus should be considered because bioavailability varies between animal- and plant-based foods and food additives, with the latter having the most profound effect on serum levels because of near 100% intestinal absorption.[36]

Patients requiring RRT may or may not require a dietary phosphorus restriction. Phosphate is traditionally not present in dialysate, so it is rapidly removed from blood during RRT, although the degree of removal is much less with iHD compared with CRRT.[29] Whereas patients receiving iHD usually require EN and PN formulas with low phosphorus concentrations, patients receiving CRRT frequently need aggressive supplementation to offset the significant losses. Thus, standard EN and PN formulations with high phosphate concentrations are typically indicated during CRRT.[32,44] However, CRRT dialysate *with* phosphate is also available, and, if this is used, additional phosphate requirements are minimal.[45] Close attention is therefore needed for the phosphate content of EN and PN formulations when CRRT is initiated, discontinued, or interrupted—or when the phosphate content of the dialysate is changed—to prevent derangements in serum phosphate.

Calcium

Calcium homeostasis is frequently dysregulated in AKI and CKD. Hypocalcemia can occur in response to reduced calcium resorption by the kidneys; decreased renal conversion of inactive vitamin D to the active form (1,25-dihydroxyvitamin D or calcitriol), which reduces intestinal calcium absorption; and decreased release of calcium from bone. Hyperphosphatemia also leads to hypocalcemia because of phosphate readily binding and sequestering calcium in the blood.[52,74] If left untreated, hypocalcemia will eventually result in secondary hyperparathyroidism and metabolic bone disease. In AKI, severely low calcium levels can have harmful effects on the cardiovascular system, including hypotension caused by a decrease in systemic vascular resistance. Hypocalcemia should therefore be treated with calcium supplementation to maintain normal levels. Because calcium is bound to albumin in the blood, measured total calcium levels will be falsely low when albumin levels are low, such as during the acute phase response. Calcium levels may be "corrected" to account for hypoalbuminemia, although this method has been found to be unreliable; directly measuring ionized calcium levels is the preferred method of assessment.[52]

Hypercalcemia is occasionally seen in AKI and CKD. Although rarely severe, hypercalcemia can be detrimental by promoting vascular calcification and is associated with worse clinical outcomes, including increased mortality.[52,75] The KDOQI guidelines recommend a calcium intake of 800–1000 mg/day for CKD stages 3–4, taking into account all potential sources of calcium including from the diet, supplements, and calcium-based phosphate binders.[36] Maintaining a neutral calcium balance is important for patients receiving maintenance iHD as well, although achieving this balance can be complicated. This is especially true for patients taking vitamin D analogs or calcimimetic agents, which can affect calcium absorption and metabolism. ASPEN recommends <2000 mg calcium per day for patients receiving maintenance iHD.[32] Calcium levels should be monitored daily and repleted if low for patients receiving CRRT.

The presence of calcium in dialysate will depend on which anticoagulant is being used. In systems using citrate anticoagulant, the anticoagulant effect relies on

sequestering calcium from the blood before reaching the filter, so a calcium-free dialysate is used. To avoid severe hypocalcemia, patients receiving CRRT with citrate anticoagulant therefore also receive a calcium infusion postfilter, the rate of which is adjusted to normalize serum levels. In RRT circuits using heparin for anticoagulation (or no anticoagulation), the dialysate will contain physiologic concentrations of calcium. This generally protects against both hypocalcemia and hypercalcemia.[29]

Bicarbonate

The kidney plays an important role in maintaining the acid-base balance by neutralizing and eliminating acid from the body. This is done through the resorption of bicarbonate or excretion of hydrogen ions. Consequently, renal impairment can significantly disrupt the acid-base balance, leading to metabolic acidosis. Muscle wasting, bone reabsorption, and hormonal derangements (eg, insulin resistance) are all consequences of metabolic acidosis, and metabolic acidosis itself can also lead to a further decline in kidney function or AKI.[36,76] From a nutrition perspective, hyperkalemia inhibits the kidney's ability to excrete ammonia, which can worsen metabolic acidosis.[32,77] Tissue catabolism can also lead to the release of protein-bound acids, which, when accumulated, can worsen metabolic acidosis; thus, providing adequate energy and achieving a neutral protein balance is recommended to decrease the extent of muscle protein breakdown. Overfeeding should be avoided to prevent respiratory acidosis, because excessive energy intake can induce hypercapnia.[32] Nutrition support, whether EN or PN, must be carefully considered in these contexts to avoid exacerbating the problem; however, the correction of acidemia with bicarbonate is often necessary.[4,32,36]

Bicarbonate is the only electrolyte routinely added to RRT dialysate in supraphysiologic concentrations to help rapidly correct metabolic acidosis. Lower, more physiologic bicarbonate concentrations may alternatively be used for patients who are prone to metabolic alkalosis.[27] Because critically ill patients often have respiratory failure, respiratory and metabolic acid-base derangements may occur simultaneously.

When formulating a PN prescription, sodium and potassium are each provided as salts of chloride and/or acetate. Acetate is metabolized to bicarbonate in the liver, so increasing the acetate dose will counteract a metabolic acidosis and vice versa.[32] The relative amounts of chloride and acetate in the PN may range from 100% chloride to 100% acetate as needed to maintain the acid-base balance.[78] However, avoid attempting to use PN acetate dose adjustments to correct a primary respiratory acid-base derangement (or a secondary metabolic acid-base derangement that is compensating a primary respiratory acidosis or alkalosis), because doing so may worsen rather than improve the final blood pH.[79] EN formulas are not meaningfully different with respect to the acid-base balance.

Micronutrients

Patients with renal dysfunction, especially in the ICU, are at increased risk for vitamin and trace mineral deficiencies. These deficiencies can occur secondary to inadequate dietary intake, impaired absorption, altered metabolism and nutrient utilization, and/or increased losses, either in urine or to the dialysate.[49,51,53,80] Preexisting malnutrition, comorbid conditions, and medications may also impact micronutrient needs.[46,51] Micronutrients are vital for normal metabolic function, so ensuring adequate intake is important. Routine assessment of micronutrient status in patients with kidney disease is crucial; however, assessing micronutrient status can be challenging in the ICU setting. Systemic inflammation is associated with a redistribution of micronutrients that affects circulating levels, making laboratory assessment less reliable.[36,46,49] Thus, nutrition-focused physical examinations should be performed in conjunction with laboratory tests to evaluate for signs and symptoms of micronutrient deficiencies.[36]

There is a paucity of high-quality evidence regarding micronutrient status of nondialysis-dependent patients with CKD, so the prevalence of deficiencies in this population is not well-known.[33] The KDOQI guideline recommends that patients with CKD stages 3–5 consume a balanced diet that meets the recommended dietary intake for all vitamins and minerals. The guideline also recommends the routine assessment of micronutrient intake and status and to consider supplementation with a multivitamin if intake is suboptimal.[36] It has also been recommended that patients following renal diet restrictions may benefit from water-soluble vitamin supplementation to prevent deficiency because intake of many nutrient-rich foods is limited on renal-restricted diets.[32] The supplementation of individual micronutrients beyond a multivitamin should be individualized based on clinical evidence or suspicion for deficiency.[33,36] Caution should be taken to avoid excessive intake of fat-soluble vitamins in patients with CKD to avoid toxicity.[32,33] High doses of vitamin C supplementation (≥500 mg/day) are also not typically recommended because of an increased risk of oxalate crystal formation.[36] Little is known about trace mineral levels in patients with CKD, but toxicity is

rare despite impaired urinary excretion because losses also occur via the gastrointestinal tract.[32,33]

ICU patients with renal impairment are at risk for developing additional micronutrient deficiencies, especially if initiated on RRT.[49,53] Furthermore, critical illness is associated with a redistribution of micronutrients because of alterations in absorption, excretion, and utilization.[31,49,50,65] For patients with AKI or AKI on CKD not receiving RRT, there is little evidence to recommend routine supplementation of micronutrients beyond what is required to meet the DRI unless deficiencies are identified.[32] Standard multivitamin preparations are appropriate for patients with AKI or AKI on CKD who do not require RRT.[31,32,34] For those receiving RRT, enteral formulas and parenteral vitamins and trace minerals may be inadequate to meet the heightened demands of various micronutrients, so additional supplementation may be required.

RRT significantly increases micronutrient needs because of losses into the effluent or adsorption by the dialysis tubing and membranes.[31,51,53] Water-soluble vitamins and trace minerals have been measured in dialysis effluent, including thiamine, pyridoxine, folic acid, ascorbic acid, chromium, copper, manganese, selenium, and zinc.[50,81] Fat-soluble vitamins have not been found in dialysis effluent because of a higher degree of protein binding and distribution into tissues, so supplementation beyond standard doses is rarely required.[51,53] RRT modality, dose, and duration can all have an effect on the extent of micronutrient losses. CRRT has the highest solute removal among the RRT modalities, and convection-based RRT causes greater loss compared with diffusion-based RRT.[31,51,53] The risk for micronutrient deficiency increases with the duration of CRRT and may occur within 7 to 10 days after CRRT initiation.[51] Studies have identified thiamine, pyridoxine, folic acid, vitamin C, copper, and selenium as the most frequent micronutrient deficiencies among patients undergoing CRRT.[31,50,51,81]

Thiamine

Thiamine, or vitamin B_1, has been found to be deficient in up to 20% of ICU patients with incidence increasing for patients receiving RRT.[81] Berger et al reported that patients undergoing CRRT lose a significant amount of thiamine (~4 mg/day). This rate of depletion is of concern because body stores are limited (only ~30 g), so deficiency can develop quickly.[53,82] It is recommended that patients on CRRT receive 100 mg of thiamine daily while undergoing CRRT.[31,47] Monitoring of thiamine status is an option, although the reliability of blood levels decreases in critical illness. Whole-blood thiamine diphosphate is the most common blood test for assessing thiamine status; however, it is affected by recent dietary intake and inflammation.[48] A more reliable measure that is unaffected by the acute phase response and is representative of total body stores is thiamine pyrophosphate, but this test is less readily available in practice.[46] Physical signs and symptoms of thiamine deficiency include ataxia, peripheral neuropathy, muscle weakness, confusion, and peripheral edema.[83] High-protein renal enteral formulas contain only ~2–4 mg of thiamine per liter.[40–42] The standard parenteral multivitamin preparation contains 6 mg thiamine per dose.[84] Additional thiamine may be added to PN formulas. Thiamine may also be supplemented separately, either enterally or intravenously.[32]

Pyridoxine

The prevalence of pyridoxine, or vitamin B_6, deficiency is estimated between 24% and 56% of patients with ESRD receiving maintenance iHD, and dialysis has been shown to decrease blood levels of pyridoxine by 28%–48%.[85] CRRT has a more dramatic effect on pyridoxine levels compared with iHD. A study on 106 ICU patients found deficiency occurred in 69.2% of patients after 20 days receiving CRRT.[49] Pyridoxine loss was ~0.02 mg/day (13.6%) after only 3 days receiving CRRT in another study that assessed both serum and effluent samples of 10 critically ill patients receiving CVVH or CVVHD. Although the amount of pyridoxine found in effluent was minimal compared with the recommended daily intake (1.3–1.9 mg/day for most adults), serum levels were frequently low in the study patients. This led to the theory that vitamin B_6 deficiency might be linked more to disease severity rather than losses during dialysis.[32,50,81,86] Oh et al also analyzed effluent in patients undergoing various forms of RRT and noted an absence of vitamins B_1, B_6 and B_{12} in effluent. They and others speculate that B vitamins are unmeasurable in effluent owing to a potential dilutional effect with the effluent, adsorption by the hemofilter, and/or conversion to undetected metabolites.[87] Multiple authors have suggested a dose of 100 mg pyridoxine daily for patients undergoing CRRT.[37,47,49] Plasma or red cell pyridoxal 5-phosphate can be used to monitor vitamin B_6 status, with the latter assay being more reliable in the setting of inflammation.[32,46] Signs and symptoms of pyridoxine deficiency include seborrheic dermatitis, angular stomatitis, cheilosis or glossitis, confusion, depression, and microcytic anemia.[32] High-protein renal formulas provide ~8 mg pyridoxine per liter.[40–42] PN multivitamin preparations contain 6 mg per dose.[32,84] Additional pyridoxine may be added to PN formulations or may be supplemented outside of EN or PN formulas, either enterally or intravenously.

Folate

The incidence of folate deficiency in the critically ill is thought to be between 2% and 19%. Folate deficiency is also common in patients requiring RRT because folic acid is easily dializable.[81] Gundogan et al found a significant reduction in both serum concentrations of pyridoxine and folic acid after 72 h receiving CRRT, and Fortin et al found that patients lose ~0.3 mg/day of folic acid while receiving this therapy.[86–88] Ensuring an intake of 1 mg folic acid daily is recommended for patients receiving iHD or CRRT.[31,32] Folate status can be assessed by serum folate, red blood cell (RBC) folate, or plasma homocysteine levels. The latter two assays are preferred because they are more reliable indicators of folate status and do not require a patient to be fasting; however, their levels can be affected by other factors. RBC folate can be reduced in patients with a vitamin B_{12} deficiency owing to the shorter life span of their RBCs. Homocysteine levels can be affected by age, renal function, and other B vitamin deficiencies.[46] Physical evidence of deficiency includes glossitis, paresthesia, unsteady gait, altered mental status, depression, and megaloblastic anemia.[32] High-protein renal formulas contain between 750 and 1000 mcg (0.75–1 mg) folic acid per liter. PN multivitamin solutions contain ~600 mcg folic acid per dose.[84] Additional folic acid may be added to PN formulas. Folic acid can also be supplemented independent of nutrition support.

Vitamin C

Vitamin C losses are significant in patients receiving RRT. Low vitamin C levels are also frequently found with critical illness in part because of increased oxidative stress and a lack of body stores. In fact, vitamin C deficiency has been found in up to 80% of critically ill patients receiving CRRT. One study measured ascorbic acid losses of 68 mg/day, whereas another study measured losses of 93 mg/day.[49,81] Supplementation with 100 mg ascorbic acid daily has been suggested to prevent deficiency, but doses in excess of 200 mg/day have been historically cautioned against owing to an increased risk for oxalate crystal formation and deposition within the heart, kidneys, blood vessels, skin, and bones.[32,50,81] However, a recent review conducted by Honore et al found that doses of up to 2 g/day may be required to maintain normal plasma concentrations in patients receiving CRRT and that such high doses in the short term do not pose an increased risk for oxalate crystal production.[89] Accordingly, several authors recommend patients receiving maintenance HD to aim for an intake of 75–100 mg ascorbic acid per day and for those receiving CRRT to receive 250 mg ascorbic acid daily.[32,50,51] Plasma vitamin C levels may be obtained to assess for deficiency, but, similar to other micronutrients, levels will be affected by inflammation and may not accurately reflect body stores.[46] Signs and symptoms of vitamin C deficiency include scorbutic gums, corkscrew hairs, petechiae, muscle pain and weakness, normocytic anemia, and delayed wound healing.[32] High-protein renal enteral formulas provide 90–100 mg vitamin C per liter.[40–42] Parenteral multivitamins contain 200 mg per dose.[84] Additional ascorbic acid may be added to PN solutions. Separate ascorbic acid supplementation enterally or intravenously is also an option.[32]

Vitamin D

Vitamin D deficiency is common in CKD. In fact, one study found ~70%–85% of patients with CKD stages 3–5 to be deficient in vitamin D as 25-hydroxyvitamin D (25D or calcifediol).[90] Because vitamin D has effects on both calcium absorption in the intestine and parathyroid hormone production, chronic deficiency can lead to the development of secondary hyperparathyroidism and metabolic bone disease, both of which can be complex disorders to manage.[32,91] Patients with CKD should aim for a vitamin D intake similar to the general population unless deficient. If deficient, supplementation should be prescribed to achieve a 25D level of ≥30 ng/ml.[36] In AKI, circulating levels of calcitriol (1,25D) have universally been low when studied.[52,92] This is thought to be a result of either decreased circulating levels of 25D or decreased conversion of 25D to 1,25D by the damaged kidneys. Decreased levels of 25D may be due to inadequate dietary intake or sequestration in response to inflammation, as plasma 25D levels can drop significantly during the acute phase response.[46] Supplementation with vitamin D in severe AKI has shown some benefit in studies, including a decrease in mortality in those who were found to be severely deficient. In AKI and CKD, patients may be prescribed either ergocalciferol (vitamin D_2) or cholecalciferol (vitamin D_3). Alternatively, patients may be supplemented with 25D (calcifediol) itself, if available, which has been shown to increase circulating levels of 25D within hours as opposed to several days as with ergocalciferol or cholecalciferol. Finally, vitamin D analogs or the active form 1,25D can be prescribed. The benefit of providing 1,25D is that it does not require activation by the kidneys. This is often prescribed to patients with renal failure and may have potential utility in severe AKI.[52] Nevertheless, studies have not found a relationship in AKI between 25D or 1,25D levels and mortality. Because vitamin D enhances both calcium and phosphorus absorption, vitamin D supplementation may be hindered by hypercalcemia and/or hyperphosphatemia. To prevent complications, close monitoring of calcium and phosphate

levels is essential for patients with renal disease receiving vitamin D supplementation.[38] High-protein renal enteral formulas provide 10–30 mcg vitamin D per liter.[40–42] Parenteral multivitamins contain 5 mcg of either ergocalciferol or cholecalciferol per dose.[84] Supplementation beyond this amount, if needed, may be given enterally in various forms or intravenously as calcitriol.[93]

Copper

Copper is also readily lost in effluent, and deficiency can occur quickly for patients receiving CRRT. Kamel et al reported that, among 75 patients receiving CRRT, 60% had a copper deficiency. Multiple studies have found copper present in effluent in varying amounts.[51,53,82,94] Patients should have copper levels monitored routinely when receiving this therapy, especially if the duration is for ≥2 weeks.[31] Recently, there was a fatal case of copper deficiency in a patient with severe burns requiring CRRT.[95] It has been suggested that patients be supplemented with 3 mg/day of copper to maintain serum levels while receiving CRRT.[31] Unlike most other micronutrients, serum copper levels increase in the presence of inflammation because ceruloplasmin, its transport protein, is a positive acute phase reactant. Thus, a normal serum copper in the setting of inflammation does not necessarily rule out deficiency.[46,53,55] Microcytic anemia, leukopenia, neutropenia, ataxia, spasticity, paresthesia, and myeloneuropathy are possible signs and symptoms of a copper deficiency.[32] High-protein renal formulas provide ~2 mg copper per liter.[40–42] Parenteral trace element formulations contain 0.3 mg copper per dose in the form of cupric sulfate.[54] Additional copper can be added to PN formulas or given enterally or intravenously, if preferred.[32,96]

Selenium

Selenium is also vulnerable to depletion in patients receiving RRT. Patients receiving maintenance HD have been found to have lower serum selenium levels when compared with controls. Ostermann et al found that 68%–84% of selenium is depleted during CRRT. Studies have also assessed selenium loss in the effluent with varying results.[32,65,88] Supplementation is therefore suggested for patients receiving CRRT with recommendations ranging from 50–70 mg/day to 150–200 mg/day.[47,51,55] Selenium levels should be routinely monitored for patients receiving prolonged RRT of any modality. RBC selenium is the recommended assay because levels are not affected by the acute phase response.[46] Physical signs and symptoms of selenium deficiency are few but can be serious. These include congestive cardiomyopathy secondary to Keshan disease, thyroid dysfunction, neurological disorders, and muscle weakness.[32,97] High-protein renal formulas provide 60–110 mg selenium per liter.[40–42] Parenteral trace element solutions contain 60 mcg of selenium per dose as selenious acid; and more selenium can be added to the PN using a standalone preparation.[32,54,98] Enteral and intravenous options are also available.[32,98]

CONCLUSIONS

Providing adequate nutrition support for the critically ill patient is an important, yet often challenging, therapy. The complexity of caring for these patients is further heightened by the high prevalence of renal dysfunction in this population and the attention required to adapt nutrition care plans to changing kidney function and the use of RRT. Nutrition interventions should be tailored to the patient's overall clinical picture, considering all the comorbid conditions and therapies that can impact a patient's nutrition needs. Because the kidneys are responsible for both excretory and hormonal functions, as well as acid-base balance, a decrease in renal function can significantly alter the demand for various nutrients. RRTs also affect nutrient requirements. Feeding individuals with AKI or renal failure, especially in the critical care setting, can be a dynamic process. As such, these patients require close monitoring and frequent reassessment of nutrition status and needs.

AUTHOR CONTRIBUTIONS

Joanna L. Otis, Nicholas M. Parker, and Rebecca A. Busch all contributed to the conception and design of the manuscript, drafted the manuscript, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ORCID

Rebecca A. Busch http://orcid.org/0000-0002-3462-9515

REFERENCES

1. Hoste EAJ, Kellum JA, Selby NM, et al. Global epidemiology and outcomes of acute kidney injury. *Nat Rev Nephrol*. 2018;14(10):607-625. doi:10.1038/s41581-018-0052-0
2. Griffin BR, Liu KD, Teixeira JP. Critical care nephrology: core curriculum 2020. *Am J Kidney Dis*. 2020;75(3):435-452. doi:10.1053/j.ajkd.2019.10.010
3. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):c179-c184. doi:10.1159/000339789

4. Stevens PE, Ahmed SB, Carrero JJ, et al. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2024;105(4s):S117-S314. doi:10.1016/j.kint.2023.10.018
5. Ostermann M, Bellomo R, Burdmann EA, et al. Controversies in acute kidney injury: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) conference. *Kidney Int*. 2020;98(2):294-309. doi:10.1016/j.kint.2020.04.020
6. Hoste EAJ, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. *Intensive Care Med*. 2015;41(8):1411-1423. doi:10.1007/s00134-015-3934-7
7. Schiefer J, Bernardi MH, Lichtenegger P, et al. Incidence and outcomes of AKI in postoperative patients admitted to ICU using full KDIGO criteria—a cohort study. *J Clin Anesth*. 2023;89:111156. doi:10.1016/j.jclinane.2023.111156
8. Neyra JA, Mescia F, Li X, et al. Impact of acute kidney injury and CKD on adverse outcomes in critically ill septic patients. *Kidney Int Rep*. 2018;3(6):1344-1353. doi:10.1016/j.ekir.2018.07.016
9. Kane-Gill SL, Sileanu FE, Murugan R, Trietley GS, Handler SM, Kellum JA. Risk factors for acute kidney injury in older adults with critical illness: a retrospective cohort study. *Am J Kidney Dis*. 2015;65(6):860-869. doi:10.1053/j.ajkd.2014.10.018
10. Doi K. Role of kidney injury in sepsis. *J Intensive Care*. 2016;4(1):17. doi:10.1186/s40560-016-0146-3
11. Hsu CY, Ordoñez JD, Chertow GM, Fan D, McCulloch CE, Go AS. The risk of acute renal failure in patients with chronic kidney disease. *Kidney Int*. 2008;74(1):101-107. doi:10.1038/ki.2008.107
12. Arulkumaran N, Annear NMP, Singer M. Patients with end-stage renal disease admitted to the intensive care unit: systematic review. *Br J Anaesth*. 2013;110(1):13-20. doi:10.1093/bja/aes401
13. Goyal A, Daneshpajouhnejad P, Hashmi MF, Bashir K. Acute kidney injury. In: *StatPearls*. StatPearls Publishing; 2024.
14. Vaidya SR, Aeddula NR. Chronic kidney diseaseIn: *StatPearls*. StatPearls Publishing; 2024.
15. Tejera D, Varela F, Acosta D, et al. Epidemiology of acute kidney injury and chronic kidney disease in the intensive care unit. *Rev Bras Ter Intensiva*. 2017;29(4):444-452. doi:10.5935/0103-507X.20170061
16. Akbaş T, Karakurt S, Tuğlular S. Renal replacement therapy in the ICU: comparison of clinical features and outcomes of patients with acute kidney injury and dialysis-dependent end-stage renal disease. *Clin Exp Nephrol*. 2015;19(4):701-709. doi:10.1007/s10157-014-1028-4
17. Khosla N, Soroko SB, Chertow GM, et al. Preexisting chronic kidney disease: a potential for improved outcomes from acute kidney injury. *Clin J Am Soc Nephrol*. 2009;4(12):1914-1919. doi:10.2215/CJN.01690309
18. Abdalrahim MS, Khalil AA, Alramly M, Alshlool KN, Abed MA, Moser DK. Pre-existing chronic kidney disease and acute kidney injury among critically ill patients. *Heart Lung*. 2020;49(5):626-629. doi:10.1016/j.hrtlng.2020.04.013
19. Ngu K, Reid D, Tobin A. Trends and outcomes of chronic kidney disease in intensive care: a 5-year study. *Intern Med J*. 2017;47(1):62-67. doi:10.1111/imj.13231
20. Pannu N, James M, Hemmelgarn BR, Dong J, Tonelli M, Klarenbach S. Modification of outcomes after acute kidney injury by the presence of CKD. *Am J Kidney Dis*. 2011;58(2):206-213. doi:10.1053/j.ajkd.2011.01.028
21. Uchino S, Morimatsu H, Bellomo R, Silvester W, Cole L. End-stage renal failure patients requiring renal replacement therapy in the intensive care unit: incidence, clinical features, and outcome. *Blood Purif*. 2003;21(2):170-175. doi:10.1159/000069156
22. Hoste EAJ, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. *Intensive Care Med*. 2015;41(8):1411-1423. doi:10.1007/s00134-015-3934-7
23. Lo LJ, Go AS, Chertow GM, et al. Dialysis-requiring acute renal failure increases the risk of progressive chronic kidney disease. *Kidney Int*. 2009;76(8):893-899. doi:10.1038/ki.2009.289
24. Bihorac A, Yavas S, Subbiah S, et al. Long-term risk of mortality and acute kidney injury during hospitalization after major surgery. *Ann Surg*. 2009;249(5):851-858. doi:10.1097/SLA.0b013e3181a40a0b
25. Kellum JA, Sileanu FE, Bihorac A, Hoste EAJ, Chawla LS. Recovery after acute kidney injury. *Am J Respir Crit Care Med*. 2017;195(6):784-791. doi:10.1164/rccm.201604-0799OC
26. Muaddi L, Ledgerwood C, Sheridan R, Dumont T, Nashar K. Acute renal failure and its complications, indications for emergent dialysis, and dialysis modalities. *Crit Care Nurs Q*. 2022;45(3):258-265.
27. Golper TA, Fissell R, Fissell WH, Hartle PM, Sanders ML, Schulman G. Hemodialysis: core curriculum 2014. *Am J Kidney Dis*. 2014;63(1):153-163. doi:10.1053/j.ajkd.2013.07.028
28. Claure-Del Granado R, Clark WR. Continuous renal replacement therapy principles. *Sem Dialysis*. 2021;34(6):398-405. doi:10.1111/sdi.12967
29. Baeg SI, Lee K, Jeon J, Jang HR. Management for electrolytes disturbances during continuous renal replacement therapy. *Electrolyte Blood Press*. 2022;20(2):64-75. doi:10.5049/EBP.2022.20.2.64
30. Jacobs R, Verbrugghe W, Dams K, et al. Regional citrate anticoagulation in continuous renal replacement therapy: is metabolic fear the enemy of logic? A systematic review and meta-analysis of randomised controlled trials. *Life*. 2023;13(5):1198. doi:10.3390/life13051198
31. Fiaccadori E, Sabatino A, Barazzoni R, et al. ESPEN guideline on clinical nutrition in hospitalized patients with acute or chronic kidney disease. *Clin Nutr*. 2021;40(4):1644-1668. doi:10.1016/j.clnu.2021.01.028
32. Mueller C, ed. *The ASPEN Adult Nutrition Support Core Curriculum*. 3rd ed. American Society for Parenteral and Enteral Nutrition; 2017.
33. MacLaughlin HL, Friedman AN, Ikizler TA. Nutrition in kidney disease: core curriculum 2022. *Am J Kidney Dis*. 2022;79(3):437-449. doi:10.1053/j.ajkd.2021.05.024
34. McClave SA, Taylor BE, Martindale RG, 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.). *JPEN J Parenter Enteral Nutr*. 2016;40(2):159-211. doi:10.1177/0148607115621863
35. Chan W. Chronic kidney disease and nutrition support. *Nutr Clin Pract*. 2021;36(2):312-330. doi:10.1002/ncp.10658

36. Ikizler TA, Burrowes JD, Byham-Gray LD, et al. KDOQI clinical practice guideline for nutrition in CKD: 2020 update. *Am J Kidney Dis*. 2020;76(3suppl 1):S1-S107. doi:10.1053/j.ajkd.2020.05.006
37. Onichimowski D, Goraj R, Jalali R, Grabala J, Mayzner-Zawadzka E, Czuczwar M. Practical issues of nutrition during continuous renal replacement therapy. *Anaesthesiol Intensive Ther*. 2014;49(4):309-316. doi:10.5603/AIT.a2017.0052
38. Palevsky PM, Liu KD, Brophy PD, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. *Am J Kidney Dis*. 2013;61(5):649-672. doi:10.1053/j.ajkd.2013.02.349
39. Stoppe C, Patel JJ, Zarbock A, 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(1):399. doi:10.1186/s13054-023-04663-8
40. Nepro with CARBSTEADY. Abbott Laboratories Inc. Accessed August 6, 2024. https://www.abbottnutrition.com/our-products/nepro-with-carbsteady
41. Renal Support 1.8. Kate Farms Inc. Accessed August 7, 2024. https://shop.katefarms.com/products/renal-support-1-8
42. NOVASOURCE Renal. Nestlé Health Science. Accessed August 6, 2024. https://www.nestlemedicalhub.com/products/novasource-renal
43. Cupisti A, Kovesdy C, D'Alessandro C, Kalantar-Zadeh K. Dietary approach to recurrent or chronic hyperkalaemia in patients with decreased kidney function. *Nutrients*. 2018;10(3):261. doi:10.3390/nu10030261
44. Busch RA, Curtis CS, Kight CE, et al. An institutional change in continuous renal replacement therapy. *Nutr Clin Pract*. 2017;32(2):245-251. doi:10.1177/0884533616662987
45. Prismasol and Phoxillum Label. *Baxter Healthcare Corporation*. Accessed Oct 15, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021703s016-207026s001lbl.pdf
46. Berger MM, Talwar D, Shenkin A. Pitfalls in the interpretation of blood tests used to assess and monitor micronutrient nutrition status. *Nutr Clin Pract*. 2023;38(1):56-69. doi:10.1002/ncp.10924
47. Ostermann M, Lumlertgul N, Mehta R. Nutritional assessment and support during continuous renal replacement therapy. *Sem Dialysis*. 2021;34(6):449-456. doi:10.1111/sdi.12973
48. Frank LL. Thiamin in clinical practice. *JPEN J Parenter Enteral Nutr*. 2015;39(5):503-520. doi:10.1177/0148607114565245
49. Fah M, Van Althuis LE, Ohnuma T, et al. Micronutrient deficiencies in critically ill patients receiving continuous renal replacement therapy. *Clin Nutr ESPEN*. 2022;50:247-254. doi:10.1016/j.clnesp.2022.05.008
50. Fishman G, Singer P. Metabolic and nutritional aspects in continuous renal replacement therapy. *J Intensive Med*. 2023;3(3):228-238. doi:10.1016/j.jointm.2022.11.001
51. Lumlertgul N, Cameron LK, Bear DE, Ostermann M. Micronutrient losses during continuous renal replacement therapy. *Nephron*. 2023;147(12):759-765. doi:10.1159/000531947
52. Leaf DE, Christov M. Dysregulated mineral metabolism in AKI. *Sem Nephrol*. 2019;39(1):41-56. doi:10.1016/j.semnephrol.2018.10.004
53. 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(4):367-377. doi:10.1097/mcc.0000000000000851
54. Tralement. Prescribing information. American Regent Inc.;. Accessed August 21, 2024. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a49ffb90-f307-433e-a86e-aaea6d6a9982
55. Berger MM, Shenkin A, Schweinlin A, et al. ESPEN micronutrient guideline. *Clin Nutr*. 2022;41(6):1357-1424. doi:10.1016/j.clnu.2022.02.015
56. Delsoglio M, Achamrah N, Berger MM, Pichard C. Indirect calorimetry in clinical practice. *J Clin Med*. 2019;8(9):1387. doi:10.3390/jcm8091387
57. Góes CR, Balbi AL, Ponce D. Evaluation of factors associated with hypermetabolism and hypometabolism in critically ill AKI patients. *Nutrients*. 2018;10(4):505. doi:10.3390/nu10040505
58. Schlein KM, Coulter SP. Best practices for determining resting energy expenditure in critically ill adults. *Nutr Clin Pract*. 2014;29(1):44-55. doi:10.1177/0884533613515002
59. 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(12):3797-3803. doi:10.1016/j.clnu.2020.04.017
60. Ikizler TA, Cuppari L. The 2020 updated KDOQI clinical practice guidelines for nutrition in chronic kidney disease. *Blood Purif*. 2021;50(4-5):667-671. doi:10.1159/000513698
61. Ponce D, de Goes CR, de Andrade LGM. Proposal of a new equation for estimating resting energy expenditure of acute kidney injury patients on dialysis: a machine learning approach. *Nutr Metab (Lond)*. 2020;17(1):96. doi:10.1186/s12986-020-00519-y
62. Byham-Gray LD, Parrott JS, Peters EN, et al. Modeling a predictive energy equation specific for maintenance hemodialysis. *JPEN J Parenter Enteral Nutr*. 2018;42(3):587-596. doi:10.1177/0148607117696942
63. 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(6):1559-1563. doi:10.3945/ajcn.116.139014
64. Rogers AR, Jenkins B. Calorie provision from citrate anticoagulation in continuous renal replacement therapy in critical care. *J Intensive Care Soc*. 2021;22(3):183-186. doi:10.1177/1751143720937451
65. Ostermann M, Summers J, Lei K, et al. Micronutrients in critically ill patients with severe acute kidney injury—a prospective study. *Sci Rep*. 2020;10(1):1505. doi:10.1038/s41598-020-58115-2
66. Obeid W, Hiremath S, Topf JM. Protein restriction for CKD: time to move on. *Kidney360*. 2022;3(9):1611-1615. doi:10.34067/kid.0001002022
67. Noce A, Vidiri MF, Marrone G, et al. Is low-protein diet a possible risk factor of malnutrition in chronic kidney disease patients? *Cell Death Discov*. 2016;2(1):16026. doi:10.1038/cddiscovery.2016.26
68. Heyland DK, Patel J, Compher C, 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(10376):568-576. doi:10.1016/S0140-6736(22)02469-2
69. Morgans HA, Chadha V, Warady BA. The role of carnitine in maintenance dialysis therapy. *Pediatr Nephrol*. 2021;36(8):2545-2551. doi:10.1007/s00467-021-05101-z

70. Nishioka N, Luo Y, Taniguchi T, et al. Carnitine supplements for people with chronic kidney disease requiring dialysis. *Cochrane Database Syst Rev*. 2022;2022(12):CD013601. doi:10.1002/14651858.CD013601.pub2
71. Lee J, Mendelssohn DC. Optimizing dialysate potassium. *Hemodial Int*. 2016;20(4):573-579. doi:10.1111/hdi.12422
72. Cascella M, Vaqar S. Hypermagnesemia. In: *StatPearls*. StatPearls Publishing; 2024.
73. Floege J. Phosphate binders in chronic kidney disease: a systematic review of recent data. *J Nephrol*. 2016;29(3):329-340. doi:10.1007/s40620-016-0266-9
74. Hill Gallant KM, Spiegel DM. Calcium balance in chronic kidney disease. *Curr Osteoporos Rep*. 2017;15(3):214-221. doi:10.1007/s11914-017-0368-x
75. Dube P, DeRiso A, Patel M, et al. Vascular calcification in chronic kidney disease: diversity in the vessel wall. *Biomedicines*. 2021;9(4):404. doi:10.3390/biomedicines9040404
76. Noce A, Marrone G, Wilson Jones G, et al. Nutritional approaches for the management of metabolic acidosis in chronic kidney disease. *Nutrients*. 2021;13(8):2534. doi:10.3390/nu13082534
77. Harris AN, Grimm PR, Lee HW, et al. Mechanism of hyperkalemia-induced metabolic acidosis. *J Am Soc Nephrol*. 2018;29(5):1411-1425. doi:10.1681/asn.2017111163
78. Ayers P, Bobo ES, Hurt RT, Mays AA, Worthington PH, eds. *ASPEN Parenteral Nutrition Handbook*. 3rd ed. American Society for Parenteral and Enteral Nutrition; 2020.
79. Achanti A, Szerlip HM. Acid-base disorders in the critically ill patient. *Clin J Am Soc Nephrol*. 2022;18(1):102-112. doi:10.2215/CJN.04500422
80. Jankowska M, Rutkowski B, Dębska-Ślizień A. Vitamins and microelement bioavailability in different stages of chronic kidney disease. *Nutrients*. 2017;9(3):282. doi:10.3390/nu9030282
81. Kamel AY, Dave NJ, Zhao VM, Griffith DP, Connor Jr. MJ, Ziegler TR. Micronutrient alterations during continuous renal replacement therapy in critically ill adults: a retrospective study. *Nutr Clin Pract*. 2018;33(3):439-446. doi:10.1177/0884533617716618
82. Berger MM, Shenkin A, Revelly JP, et al. Copper, selenium, zinc, and thiamine balances during continuous venovenous hemodiafiltration in critically ill patients. *Am J Clin Nutr*. 2004;80(2):410-416. doi:10.1093/ajcn/80.2.410
83. Smith TJ, Johnson CR, Koshy R, et al. Thiamine deficiency disorders: a clinical perspective. *Ann NY Acad Sci*. 2021;1498(1):9-28. doi:10.1111/nyas.14536
84. Infuvite adult multiple vitamins injection. Prescribing information. Sandoz Inc; 2016. Accessed August 21, 2024. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f10e7c39-b9ce-4d3b-98e0-891ccb8d0b1a
85. Corken M, Porter J. Is vitamin B6 deficiency an underrecognised risk in patients receiving haemodialysis? A systematic review: 2000–2010. *Nephrology (Carlton)*. 2011;16(7):619-625. doi:10.1111/j.1440-1797.2011.01479.x
86. Fortin MC, Amyot SL, Geadah D, Leblanc M. Serum concentrations and clearances of folic acid and pyridoxal-5-phosphate during venovenous continuous renal replacement therapy. *Intensive Care Med*. 1999;25(6):594-598. doi:10.1007/s001340050908
87. Oh WC, Mafrici B, Rigby M, et al. Micronutrient and amino acid losses during renal replacement therapy for acute kidney injury. *Kidney Int Rep*. 2019;4(8):1094-1108. doi:10.1016/j.ekir.2019.05.001
88. Gundogan K, Yucesoy FS, Ozer NT, et al. Serum micronutrient levels in critically ill patients receiving continuous renal replacement therapy: a prospective, observational study. *JPEN J Parenter Enteral Nutr*. 2022;46(5):1141-1148. doi:10.1002/jpen.2378
89. Honore PM, Spapen HD, Marik P, Boer W, Oudemans-van Straaten H. Dosing vitamin C in critically ill patients with special attention to renal replacement therapy: a narrative review. *Ann Intensive Care*. 2020;10(1):23. doi:10.1186/s13613-020-0640-6
90. LaClair RE, Hellman RN, Karp SL, et al. Prevalence of calcidiol deficiency in CKD: a cross-sectional study across latitudes in the United States. *Am J Kidney Dis*. 2005;45(6):1026-1033. doi:10.1053/j.ajkd.2005.02.029
91. Brandenburg V, Ketteler M. Vitamin D and secondary hyperparathyroidism in chronic kidney disease: a critical appraisal of the past, present, and the future. *Nutrients*. 2022;14(15):3009. doi:10.3390/nu14153009
92. Zhang H, Jiang Y, Shi N, Lu YQ. Serum vitamin D levels and acute kidney injury: a systemic review and meta-analysis. *Sci Rep*. 2022;12(1):20365. doi:10.1038/s41598-022-24560-4
93. Calcitriol injection. Prescribing information. Akorn; 2022. Accessed August 21, 2024. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4d6046c2-4a28-47b1-9bb4-51fadeded2d2
94. Broman M, Bryland A, Carlsson O. Trace elements in patients on continuous renal replacement therapy. *Acta Anaesthesiol Scand*. 2017;61(6):650-659. doi:10.1111/aas.12909
95. Ben-Hamouda N, Charrière M, Voirol P, Berger MM. Massive copper and selenium losses cause life-threatening deficiencies during prolonged continuous renal replacement. *Nutrition*. 2017;34:71-75. doi:10.1016/j.nut.2016.09.012
96. Copper—cupric chloride injection. Prescribing information. Hospira; 2022. Accessed August 21, 2024. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a84d61a4-8e7f-4be1-aba6-f633b334aafc
97. Shreenath AP, Hashmi MF, Dooley J. Selenium deficiency. In: *StatPearls*. StatPearls Publishing; 2024.
98. Selenious acid injection. Prescribing information. American Regent Inc; 2021. Accessed August 21, 2024. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=49324999-50e3-43ed-a8dd-156d6dbedd9f

How to cite this article: Otis JL, Parker NM, Busch RA. Nutrition support for patients with renal dysfunction in the intensive care unit: A narrative review. *Nutr Clin Pract*. 2024;1-19. doi:10.1002/ncp.11231