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A.S.P.E.N. Clinical Guidelines: Nutrition Support in Adult Acute and Chronic Renal Failure

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Background

Renal failure results when the kidneys cannot adequately excrete nitrogenous and metabolic wastes, either acutely, as a part of a clinical illness, or chronically over years of declining renal function. The spectrum of symptoms and outcomes in acute renal injury are highly variable ranging from anuria to adequate urine output, and from a short period of reduced glomerular filtration to the need for prolonged renal replacement therapy. To reflect this diversity of clinical presentation, the Acute Dialysis Quality Initiative Group recommended a change in terminology from acute renal failure to acute kidney injury (AKI).[1] The major causes of AKI include sepsis, trauma, hypotension, intravenous contrast dye, medications, and preexisting chronic kidney disease (CKD). Despite improvements in dialysis therapy and the delivery of nutrition support, the mortality of AKI continues in the range of 50%–60%.[1–4]

The evidence-based National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K-DOQI) guidelines classify CKD into 5 categories (I-V) based on measured glomerular filtration rate (GFR; Table 1).[5] The most common causes of CKD include diabetes mellitus, hypertension, and glomerular disease. Despite advances in dialysis and transplantation, the prognosis of CKD remains bleak. According to the United States Renal Data System, the annual mortality for chronic dialysis patients exceeds 20%, and life expectancy of dialysis patients is 3–11 years shorter than the age-matched general population (range depending on age).[6]

The purpose of these Clinical Guidelines is to evaluate the evidence underlying the provision of nutrition support to patients with AKI and CKD. Chronic nutrition care of these patients beyond the provision of enteral nutrition (EN) or parenteral nutrition (PN) is not addressed by these Guidelines. The data tables focus on citations since 2000, to cover the period since the previous 2002 A.S.P.E.N. Guidelines[7] and to reflect recent advances in dialysis technology.

Methodology

The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) consists of healthcare professionals representing the disciplines of medicine, nursing, pharmacy, dietetics, and nutrition science. The mission of A.S.P.E.N. is to improve patient care by advancing the science and practice of nutrition support therapy. A.S.P.E.N. vigorously works to support quality patient care, education, and research in the fields of nutrition and metabolic support in all healthcare settings. These Clinical Guidelines were developed under the guidance of the A.S.P.E.N. Board of Directors. Promotion of safe and effective patient care by nutrition support practitioners is a critical role of the A.S.P.E.N. organization. The A.S.P.E.N. Board of Directors has been publishing Clinical Guidelines since 1986.[7–9] A.S.P.E.N. evaluates in an ongoing process when individual Clinical Guidelines should be updated.

These A.S.P.E.N. Clinical Guidelines are based upon general conclusions of healthcare professionals who, in developing such Guidelines, have balanced potential benefits to be derived from a particular mode of medical therapy against certain risks inherent with such therapy.

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Table 1. Stages of chronic kidney disease[5]

Stage	Description	GFR (mL/min/1.73 m^2)
I	Kidney damage (protein in the urine) and **normal** GFR	≥ 90
II	Kidney damage and **mild** decrease in GFR	60 – 89
III	**Moderate** decrease in GFR	30 – 59
IV	**Severe** decrease in GFR	15 – 30
V	**Kidney failure** (dialysis or kidney transplant needed)	< 15

GFR, glomerular filtration rate

However, the professional judgment of the attending healthcare professional is the primary component of quality medical care. Because Guidelines cannot account for every variation in circumstances, the practitioner must always exercise professional judgment in their application. These Clinical Guidelines are intended to supplement, but not replace, professional training and judgment.

These Clinical Guidelines were created in accordance with Institute of Medicine recommendations as "systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances."[10] These Clinical Guidelines are for use by healthcare professionals who provide nutrition support services and offer clinical advice for managing adult and pediatric (including adolescent) patients in inpatient and outpatient (ambulatory, home, and specialized care) settings. The utility of the Clinical Guidelines is attested to by the frequent citation of these documents in peer-reviewed publications and their frequent use by A.S.P.E.N. members and other healthcare professionals in clinical practice, academia, research, and industry. They guide professional clinical activities, they are helpful as educational tools, and they influence institutional practices and resource allocation.[11]

These Clinical Guidelines are formatted to promote the ability of the end user of the document to understand the strength of the literature used to grade each recommendation. Each Guideline recommendation is presented as a clinically applicable statement of care and should help the reader make the best patient care decision. The best available literature was obtained and carefully reviewed. Chapter author(s) completed a thorough literature review using Medline, the Cochrane Central Registry of Controlled Trials, the Cochrane Database of Systematic Reviews, and other appropriate reference sources. These results of the literature search and review formed the basis of an evidence-based approach to the Clinical Guidelines. Chapter editors work with the authors to ensure compliance with the author's directives regarding content and format. Then the initial draft is reviewed internally to promote consistency with the other A.S.P.E.N. Clinical Guidelines and Standards of Practice and externally reviewed (either by experts in the field within our organization and/or outside of our organization) for appropriateness of content. The final draft is reviewed and approved by the A.S.P.E.N. Board of Directors.

Table 2. Grading of Guidelines and Levels of Evidence

Grading of Guidelines	
A	Supported by at least two level I investigations
B	Supported by one level I investigation
C	Supported by at least one level II investigation
D	Supported by at least one level III investigation
E	Supported by level IV or V evidence
Levels of Evidence	
I	Large randomized trials with clear-cut results; low risk of false-positive (alpha) and/or false-negative (beta) error
II	Small, randomized trials with uncertain results; moderate-to-high risk of false-positive (alpha) and/or false-negative (beta) error
III	Nonrandomized cohort with contemporaneous controls
IV	Nonrandomized cohort with historical controls
V	Case series, uncontrolled studies, and expert opinion

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The system used to categorize the level of evidence for each study or article used in the rationale of the Guideline Statement and used to grade the Guideline Recommendation is outlined in Table 2.[12] The grade of a Guideline is based on the levels of evidence of the studies used to support the Guideline. A randomized controlled trial (RCT), especially one that is double-blind in design, is considered to be the strongest level of evidence to support decisions regarding a therapeutic intervention in clinical medicine.[13] A systematic review (SR) is a specialized type of literature review that analyzes the results of several RCTs. A high quality SR usually begins with a clinical question and a protocol that addresses the methodology used to answer this question. These methods usually state how the literature is identified and assessed for quality, what data are extracted and how they are analyzed, and whether there were any deviations from the

Table 3. Nutrition Support Guideline Recommendations in Adult Acute and Chronic Renal Failure

Guidelines Recommendation	Grade
1. Patients with renal disease should undergo formal nutrition assessment, including evaluation of inflammation, with development of a nutrition care plan.	D
2. Standard amino acid parenteral nutrition formulations should be used in acute kidney injury.	C
3. Intradialytic parenteral nutrition should not be used as a nutritional supplement in malnourished chronic kidney disease-V hemodialysis patients.	C
4. Patients with renal failure who require nutrition support therapy should receive enteral nutrition if intestinal function permits.	E
5. Energy requirements in patients with renal disease should be evaluated using indirect calorimetry when possible. If indirect calorimetry is not possible, individualized assessment of energy intake goals, as with other nutrition support patients, is recommended.	D
6. To promote positive nitrogen balance in patients with acute kidney injury, protein intake should be adjusted according to catabolic rate, renal function, and dialysis losses.	D
7. Electrolyte intake in patients should be adjusted by monitoring serum concentrations of K, Mg, P, and Ca.	D

protocol during the course of the study. In most instances, meta-analysis (MA), a mathematical tool to combine data from several sources, is used to analyze the data. However, not all SRs use MAs. SRs and MAs are used in these Clinical Guidelines only to organize the evidence but are not used in the grading process.

A level of I, the highest level, will be given to large RCTs where results are clear and the risk of alpha- and beta-error is low (well-powered). A level of II will be given to RCTs that include a relatively small number of patients or are at moderate-to-high risk for alpha- and beta-error (under-powered). A level of III is given to cohort studies with contemporaneous controls, while cohort studies with historic controls will receive a level of IV. Case series, uncontrolled studies, and articles based on expert opinion alone will receive a level of V.

Practice Guidelines and Rationales

Table 3 provides the entire set of guideline recommendations for nutrition support in adults with acute and chronic renal failure.

1. Patients with renal disease should undergo formal nutrition assessment, including evaluation of inflammation, with development of a nutrition care plan. (Grade: D)

Rationale: Cross-sectional cohort observations of patients with AKI[14–19] and Stage V CKD[20–26] link low serum albumin concentration with mortality (Table 4). While it is difficult to separate the impact of inadequate protein intake from acute or chronic illness effects, recent cohort observations have recognized the role of inflammation in renal disease. Patients with AKI have high levels of cytokines[16,27–30] that suggest the hypoalbuminemia may result from a negative acute phase response due to inflammation. Patients with Stage V CKD have higher inflammatory cytokine levels than healthy control subjects.[29] Greater weight loss, lower serum albumin concentrations,[25] and depressed appetite occur with inflammation.[26] The trend in albumin concentration in Stage V CKD predicts mortality over 18 months, even when controlled for nutritional (protein intake, muscle mass, and lymphocyte percentage) and inflammatory factors.[31] While current clinical practice does not include accepted methods of reducing the inflammatory response, evaluation of the serum protein status together with a marker of inflammation, such as C-reactive protein (CRP) may help to identify patients at high risk for mortality and for whom nutrition support should be considered.

While protein and energy wasting are common with both CKD and AKI, cachexia (severe wasting) is not.[32] By Subjective Global Assessment with the addition of albumin <3.8 g/dL to represent inflammation in Stage V CKD patients, 11% of patients had malnutrition alone with no inflammation and 18% had combined malnutrition and inflammation.[33] Since muscle atrophy, appetite, and mortality were worse for patients with inflammation, and inflammation may worsen nutrient intake and nutrition status, evaluation of both nutrition status and inflammation are advised.

Future research is needed to establish agreed-upon inflammatory markers for each stage of renal disease, as well as the best tools for evaluating nutrition status in clinical situations. While low albumin is often a concomitant of inflammation, it is not a specific indicator. The evaluation of inflammation is best carried out using multiple indicators.

Table 4. Nutrition Risk and Clinical Outcomes in Renal Disease

Citation Year Level	Population	Study Groups	Results	Comments
Obialo[15] 1999 Level IV	AKI (N = 100)	Alb < 35 vs > 35 g/L Total chol ≤ 150 vs > 150 mg/dL	Mortality: Low alb RR 5.5 (95% CI, 1.9-13.2; $P = .001$) Low chol RR 7.4 (95% CI, 2.7-20.3; $P < .0001$) Alb not significant predictor in absence of multiple organ failure	No measure of inflammation, authors attribute low alb to inadequate protein intake or excess protein catabolism Small population
Kadiroglu[16] 2007 Level IV	AKI (N = 59)	S (18 M, 28 F), NS (10 M, 3 F)	IL-6: S 40.4 pg/mL, NS 46.3 pg/mL ($P = .016$) TNF-α: S 54.7 pg/mL, NS 94.1 pg/mL ($P = .02$)	Mortality greater with inflammation Small population
Chawla[17] 2005 Level III	ICU pts (N = 194)	Risk factors for development of AKI	In multivariate model, alb predicts AKI, RR = 0.46 (95% CI, 0.25-0.86; $P = .016$)	Some ICU admissions not captured, etiology of AKI not described
Lins[18] 2004 Level III	Consecutive AKI pts from 8 ICUs (N = 293)	S (n = 147), NS (n = 146)	Renal outcomes: CKD V 5%, Renal recovery 35% Alb: S 29 g/L, NS 26 g/L ($P < .001$) APACHE II: S 19, NS 24 ($P = .000$) Organs failed: S 1.3, NS 2.6 ($P = .000$)	APACHE II suggests high acuity
Wang[19] 2006 Level V	Consecutive AKI pts (N = 61)	S (n = 23), NS (n = 38)	Alb: S 2.6 g/L, NS 2.3 g/L ($P = .06$) Fibrinogen: S 378.3 mg/dL, NS 294.7 mg/dL ($P<.01$)	Very small population
Simmons[28] 2004 Level IV	Prospective, observational cohort; Program to Improve Care in Renal Disease (PICARD; N = 98)	S (n = 54), NS (n = 44) CKD V (n = 42), Healthy controls (n = 48)	Mortality 44.9% Odds of death increases 65% for each log unit increase in IL-6 APACHE III: S 72.1, NS 84.3 ($P = .002$) SAPS II: S 49.7, NS 58.7 ($P = .04$)	Cytokine levels predict mortality Small population
Chertow[23] 2005 Level III	CKD-V HD pts (N = 7815)	Prealb values in 1997, mortality observed forward Unclear time period	Overall mortality 22.5% Adjusted RR death 2.41, 1.85, 1.49, and 1.23 for prealb <15, 15-20, 20-25, and 25-30 mg/dL, respectively (relative to prealb ≥40 mg/dL)	Prealb may reflect inflammation

(*continued*)

Table 4. (continued)

Citation Year Level	Population	Study Groups	Results	Comments
Kaizu[24] 1998 Level IV	CKD-V HD pts (N = 45)	IL-6 > 10 pg/mL (n = 11) IL-6 < 10 pg/mL (n = 34)	Alb: Low IL-6 3.96 g/dL High IL-6 3.66 g/dL ($P < .05$) 3 y Wt change: Low IL-6 +0.76% High IL-6 -4.6% ($P < .01$)	Small population
Kalantar-Zadeh[25] 2004 Level III	CKD-V HD pts (N = 331)	Appetite rating, malnutrition, inflammation compared to risk of hospitalization and mortality over 12 mo	Normal appetite (62%) Fair to poor appetite (38%) Odds of poor appetite increased with each log unit of CRP & TNF-α For diminished vs normal appetite: hospitalization rate ratios (adjusted for case mix, alb, BMI, catabolic rate, cardiac history) 1.43 (95% CI,1.23-1.66) Duration of hospitalization rate ratio = 1.95 (95% CI, 1.83-2.08) [$P<.001$ for all rate ratios] Hazard ratio of death 4.74 (95% CI, 1.85-2.16; $P = .001$)	Pts with poor appetite have worse clinical outcomes, appetite related to inflammation
Kalantar-Zadeh[26] 2004 Level II	CKD-V HD pts (N = 58,058)	Alb ≥ 3.8 g/dL (n = 27,757) Alb < 3.8 g/dL (n = 30,244)	Mortality: Alb ≥ 3.8 g/dL, 19% Alb < 3.8 g/dL, 40% ($P < .05$) Multivariate adjusted fraction of death risk due to alb <3.8 g/dL, 19.2%	Declining alb over time predicts mortality, may represent inflammation
Suliman[27] 2005 Level III	CKD-V pts, pre-HD (N = 200)	CRP ≥ 10 mg/L (n = 72) CRP < 10 mg/L (n = 128)	SGA malnutrition: CRP≥10 mg/L, 46%; CRP <10 mg/L, 20% ($P < .001$) Predictors of the sum of all AAs ($r^2 = 0.20$): CRP, sex, alb, GFR predict AA 60-mo mortality: High AA 37%, Low AA 52% ($P<.05$)	Both inflammation and malnutrition independently predict poor AA status and mortality
Carrero[29] 2007 Level III	CKD-V HD pts (N = 223)	Normal appetite (n = 124) Appetite loss (n = 99)	Mortality, poor appetite (hazard ratio for death: 2.72; 95% CI, 1.29-5.72; $P = .008$)	Appetite loss, linked with inflammation, predicts mortality

(continued)

Table 4. (continued)

Citation Year Level	Population	Study Groups	Results	Comments
Carrero[31] 2008 Level III	Two cohorts of CKD-V HD pts (N = 486)	Incident HD (n = 265) MA (n = 80) No MA (n = 185) Prevalent HD (n = 221) MA (n = 86) No MA (n = 135)	Mortality: Incident HR 2.62 (95% CI, 1.34- 5.13; $P = .001$), MA vs no MA Prevalent HR 3.05 (95% CI, 1.61-5.71; $P = .005$), MA vs no MA CRP: No MA 5.5 mg/L MA 25.5 mg/L ($P = .001$) IL-6: No MA 7.4 pg/mL MA 16 pg/mL ($P < .001$) IL-6 >6.5 vs <6.5 pg/mL: Incident OR MA 2.81 (95% CI, 1.33-5.91; $P < .001$) Prevalent OR MA 2.55 (95% CI, 1.37-4.70; $P < .01$)	Overhydration may mask actual MA MA and inflammation with worse outcomes
Honda[30] 2007 Level III	CKD-V HD pts (N = 328)	21 d before 1st HD (n = 227) 9 d after 1st HD (n = 101) BMI < 20 kg/m^2 (n = 44) BMI 20-25 kg/m^2 (n = 143) BMI > 25 kg/m^2 (n = 141)	72 mo survival: BMI <20 kg/m^2, 38% BMI 20-25 kg/m^2, 42% BMI >25, 60% SGA risk reduced survival of each BMI group	Overhydration may have masked degree of wasting

AA, amino acid; AKI, acute kidney injury; alb, albumin; APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; PA, prealbumin; chol, cholesterol; CKD, chronic kidney disease; CRP, C-reactive protein; DXA, dual absorption x-ray absorptiometry; F, female; HD, hemodialysis; HR, hazard rate; ICU, intensive care unit; IL, interleukin; M, male; MA, muscle atrophy; NS, non-survivor; OR, odds ratio; RR, relative risk; S, survivor; SAPS, simplified acute physiology score; SGA, subjective global assessment; TNF, tissue necrosis factor; wt, weight.

2. Standard amino acid parenteral nutrition formulations should be used in acute kidney injury. (Grade: C)

Rationale: Following the marketing of parenteral and enteral products containing essential amino acids (EAA) for use in patients with AKI, 2 small clinical trials compared the use of EAA alone or a combination of essential and non-essential amino acids (EAA/NEAA).[34–35] Mirtallo et al randomized 45 patients who had AKI but were not yet dialyzed to PN with dextrose + EAA or dextrose + EAA/NEAA.[34] Mortality, blood urea nitrogen, creatinine concentrations, and nitrogen balance did not differ between the two PN formulations, though the failure to show a difference may have been due to a lack of statistical power. In a second study,[35] patients were randomized to either hypertonic glucose (n=7), PN with EAA (n=12), or PN with EAA/NEAA (n=11), and some received dialysis. All patients were in negative nitrogen balance with no significant difference between the 2 PN groups, but the dextrose-only group exhibited the greatest degree of negative nitrogen balance.[35] In addition to the limitations presented by small sample size, other factors, including differences in clinical acuity among hospitalized patients, and recent practice changes in dialysis and nutrition support therapy, further reduce the relevance of these studies. There is inadequate evidence at this time to support the use of EAA PN formulations with AKI. Further large RCTs are needed to determine whether EAA solutions are superior to standard solutions in patients with AKI.

3. Intradialytic parenteral nutrition should not be used as a nutritional supplement in malnourished chronic kidney disease-V hemodialysis patients. (Grade: C)

Rationale: Intradialytic PN (IDPN) is limited by the need to complete the entire nutrient infusion during the hemodialysis (HD) treatment, and by the potential for such rapid administration of glucose and lipid to cause adverse effects. Thus, the modality often fails to meet full nutrition requirements for patients with intestinal failure or limited food intake.

While IDPN is associated with increased body weight and serum albumin concentration (Table 5),[36–40] studies have not shown the therapy to reduce mortality.[40] In fact, in a large retrospective medical record review, malnourished patients with normal albumin who received IDPN had a higher rate of mortality than those who received no IDPN.[37] In the same study, however, malnourished patients with serum albumin < 3 g/dL had lower mortality with IDPN. In a large RCT, mortality rates for patients receiving IDPN was no different than that of patients who received oral nutritional supplements without IDPN.[40] Taken together, these studies do not offer strong support for IDPN. However, larger RCTs in malnourished patients are needed to ensure that a clinical benefit of IDPN does not exist.

4. Patients with renal failure who require nutrition support therapy should receive enteral nutrition if intestinal function permits. (Grade: E)

Rationale: Clinical guidelines and reviews support the use of EN in patients with renal failure.[42–43] In patients with AKI (Table 6), delivery of energy and protein by EN was not different from other critically ill patients with normal renal function or healthy controls, even though gastric residuals and tube occlusion occurred more frequently in the AKI patients treated with dialysis therapy.[44] These studies suggest that EN can be delivered effectively in the majority of patients with AKI. In malnourished patients with AKI, patients who received PN had greater mortality and infection rates than those with EN. However the disease acuity score was much higher for the PN group, suggesting that disease severity may have influenced both clinical outcomes and route of feeding.[45] RCTs testing EN vs PN in these critically ill AKI and hospitalized CKD patients are needed.

5. Energy requirements in patients with renal disease should be evaluated using indirect calorimetry when possible. If indirect calorimetry is not possible, individualized assessment of energy intake goals, as with other nutrition support patients, is recommended. (Grade: D)

Rationale: An early study of indirect calorimetry suggested that AKI and sepsis increased energy needs by up to 30% compared to patients with normal renal function and without sepsis.[45] The clinical acuity level of patients at that time, however, was presumably lower than is typical of critically ill patients with AKI today. In addition, this study took place before the current obesity epidemic emerged. In 2005, a random order crossover pilot study compared nitrogen balance in 10 patients with AKI and dialysis who received 1.5 g/kg/d of protein and either 30 kcal/kg/d or 40 kcal/kg/d via PN.[46] Nitrogen balance with both PN regimens was marginally positive, but not different between the 2 regimens. Insulin requirements, serum glucose, and triglyceride concentrations were significantly higher with the 40 kcal/kg/d group. The authors concluded that the minor difference in nitrogen balance was not offset by the increased risk of metabolic complications. The European Society for Clinical Nutrition and Metabolism (ESPEN) Guidelines on Enteral Nutrition in Renal Failure recommend energy intake of 20–30 kcal/kg/d adapted to individual needs in case of underweight or obesity.[42] The ESPEN Guidelines on Parenteral

Table 5. Outcomes Associated with Intradialytic Parenteral Nutrition (PN) in Chronic Kidney Disease (CKD)-V

Citation Year Level	Population	Study Groups	Results	Comments
Capelli[36] 1994 Level IV	CKD-V (N = 81) + IDPN if malnutrition	IDPN (n = 50) No IDPN (n = 31)	12 mo survival: IDPN 64%, 14.7 mo No IDPN 52%, 9.1 mo ($P < .01$)	No randomization to IDPN treatment Small population
Chertow[37] 1994 Level IV	CKD V pts (N = 24,196)	IDPN (n = 1,679) No IDPN (n = 22,517) OR mortality by alb, Cr	Mortality: Alb ≥ 4.0 & Cr >8.0 mg/dL IDPN (n = 26) vs no IDPN (n = 4636); OR 2.6 (95% CI, 1.34-5.04; $P = .005$) Alb ≥ 4.0 & Cr ≤ 8 mg/dL IDPN (n = 24) vs no IDPN (n = 248), OR = 1.65 (95% CI, 0.93- 9.55; $P = .07$) Alb ≤ 3.0 g/dL & Cr > 8 mg/dL: IDPN (n = 276) vs no IDPN (n = 192), OR = 0.64 (95% CI, 0.44-0.92; $P<.01$) Alb ≤ 3.0 g/dL & Cr ≤ 8 mg/dL:IDPN (n = 283) vs no IDPN (n = 271), OR = 0.63 ($P < .01$)	Suggest IDPN be reserved for pts with low alb
Cherry[38] 2002 Level V	CKD-V pts (N = 24)	IDPN > 1 mo	Wt & alb increased (8.8% & 20% respectively) over 9 mo Adverse effects: excess fluid wt, hyperglycemia	Very small population No hard outcomes
Korzets[39] 2008 Level V	CKD-V pts with acute medical or surgical illness (N = 22)	IDPN with 50-85 g AA, 1174-1677 kcal 3x/wk for 6 mo Pre- vs post-IDPN	Alb: Pre 2.8 g/L, Post 3.8 g/L PA: Pre 21.0 mg/L, Post 30.0 mg/L CRP: Pre 77 mg/L, Post 9 mg/L (all $P < .05$)	Changes may reflect reduced inflammation over time after medical/ surgical illness Small population
Cano[40] 2007 Level II	Malnourished CKD-V pts (N = 186)	Oral suppl (n = 93) IDPN (n = 93)	24-mo mortality: Oral suppl 38.7% IDPN 43%	No advantage to IDPN over oral supplement alone Power analysis says 204 pts, but trend not in favor of IDPN

AA, amino acid; alb, albumin; Cr, creatinine; CRP, C-reactive protein; HD, hemodialysis; IDPN, intradialytic parenteral nutrition; OR, odds ratio; PA, prealbumin; suppl, supplement

Nutrition: Adult Renal Failure recommend ≥ 30–35 kcal/kg/d for stable CKD patients.[47]

Resting energy expenditure was measured using indirect calorimetry in 37 non-hospitalized patients with CKD without dialysis, CKD with HD, and CKD with chronic ambulatory peritoneal dialysis (CAPD).[48] Resting energy expenditure was significantly higher in the HD (34.5 ± 4.6 kcal/kg/d) and CAPD (35.3 ± 6.3 kcal/kg/d) patients than in those with CKD not treated with dialysis (28.2 ± 4.2 kcal/kg/d). Clearly, further studies are needed to clarify the optimal energy intake for patients with AKI and CKD, and to evaluate the impact of feeding levels on morbidity and mortality.

6. To promote positive nitrogen balance in patients with acute kidney injury, protein intake should be adjusted according to catabolic rate, renal function, and dialysis losses. (Grade: D)

Table 6. Outcomes Associated with Route of Feeding in Patients with Acute Kidney Injury (AKI)

Citation Year Level	Population	Study Groups	Results	Comments
Fiaccadori[43] 2004 Level IV	ICU pts with AKI (N = 182)	HD (n = 114), No HD (n = 68) Normal controls (n = 65)	APACHE II: HD 24.0, No HD 21.2 Mortality: HD 36.8%, No HD 23.5% Tube obstruction: HD 14%, No HD 6%, $P < .001$ High gastric residual: HD 13.2%, No HD 7.4% ($P = .02$) Energy and protein delivery not different (~20-22 kcal/kg/d and 0.9 g/kg/d protein)	Pts with AKI tolerate EN Worse clinical outcomes in AKI with HD reflect more severe clinical course than when HD not needed
Sezer[44] 2008 Level IV	Pts with AKI + malnutrition (N = 64)	EN (n = 45) PN (n = 19)	APACHE III: PN 75, EN 56 ($P = .05$) Mortality: PN 69%, EN 42% ($P = .05$) Infectious complications: PN 84%, EN 64% ($P = .05$)	Greater mortality, infection with PN may reflect disease process Pts not randomized Small population

APACHE, Acute Physiology and Chronic Health Evaluation; EN, enteral nutrition; HD, hemodialysis; ICU, intensive care unit; PN, parenteral nutrition

Rationale: Patients with AKI require dialysis therapy because of their severely limited intrinsic renal function, but also because AKI is characterized by high rates of catabolism. Several studies suggest that the protein intake during continuous renal replacement therapy (CRRT) should range between 1.8 and 2.5 g/kg/d (Table 7) .[48–50] Patients with AKI treated with HD may demonstrate positive nitrogen balance while receiving 1.5 g/kg/d of protein,[46] but protein intake up to 2.5 g/kg/d may be needed to achieve positive nitrogen balance[50] or normal amino acid profile[46] in patients treated with CRRT. It was also noted that for every 1 g increase in nitrogen balance, patient survival increased by 21%; however, this outcome may also be linked to clinical acuity factors such that sicker patients have more negative nitrogen balance and worse survival.

Because patients with Stage V CKD have essentially no intrinsic renal function, they require 3 or more HD treatments each week or daily CAPD. The recommended protein intake for patients who receive maintenance HD is 1.2 g/kg/d,[42,52] and for those who receive CAPD, recommended protein intake is 1.3 g/kg/d.[53] These doses of protein are recommended to replace albumin and amino acids lost during dialysis treatment, in combination with a catabolic state in patients with CKD, and are based on nitrogen balance measurements.[54–55]

By contrast, patients with stage III or IV CKD have partial renal function and may require restrictions in protein intake to as low as 0.3–0.6 g/kg/d to delay the progression of renal disease (Table 8).[57–59] By intent to treat analysis of the Modification of Diet in Renal Disease (MDRD) trial of 585 patients with CKD observed for 2 years pre-dialysis, progression of renal disease was not slowed by dietary protein restriction to 0.3 or 0.6 g/kg/d when compared to 1.3 g/kg/d.[57] By subgroup analysis according to actual (not prescribed) protein intake, restriction to 0.3 g/kg/d retarded the progression of renal disease.[58] The severity of CKD as well as poor dietary protein adherence impacted the renal function preservation outcomes.[59] The catabolism associated with acute illness or infection most likely raises the protein and energy requirements of these protein-restricted patients, but this issue requires systematic evaluation before recommendations for nutrition support can be made. Thus, individual consideration of needs based on nitrogen balance is indicated. These patients may also receive HD during hospitalization to allow greater protein intake and to remove the toxins produced by their heightened catabolism.

Table 7. Protein Dose Studies in Patients with Acute Kidney Injury (AKI)

Citation Year Level	Population	Study Groups	Results	Comments
Fiaccadori[46] 2005 Level IV	AKI & HD (N = 10)	PN with protein 1.5 g/kg/d, 30 or 40 kcal/kg/d for 3 d in random order crossover, no wash-out between treatment arms	Nitrogen balance: 30 kcal/kg/d +0.67 g 40 kcal/kg/d +1.49 g Triglyceride, glucose, insulin use higher with 40 than 30 kcal/kg/d	Nitrogen balance not improved significantly, but risk of metabolic complications favors 30 kcal/kg/d over 40 kcal/kg/d Pilot study
Scheinkestel[48] 2003 Level IV	AKI & CRRT (N = 11)	PN protein dose escalation 1–2.5 g/kg/d, increase 0.25 g/kg/d every d	AA balance positive with ≥2.5 g/kg/d	AA balance not commonly available Small population Dose escalation data may be impacted by clinical improvement over time
Scheinkestel[49] 2003 Level IV	AKI & CRRT (N = 50)	Protein at 2 g/kg/d (n = 10; 4 PN, 2 EN, 4 PN+EN) Protein dose escalation 1.5, 2 or 2.5 g /kg/d (n = 40; 4 PN, 23 EN, 13 PN+EN) PN (n = 23), No PN (n = 27) EN (n = 42), No EN (n = 8)	Positive nitrogen balance: 2 g/kg/d, 10% Dose escalation, 38% Mortality: PN 8%, No PN 5% EN 21%, No EN 50% Survival improves 21% for each 1 g/d increase in nitrogen balance	Increased protein dose at each stage vs a true randomization Small population
Bellomo[50] 2003 Level V	AKI & CRRT (N = 7)	PN with protein 2.5 g/kg/d	Positive nitrogen balance on 7 of 20 d Median nitrogen balance, −1.8 g/d	Small population

AA, amino acids; CRRT, continuous renal replacement therapy; EN, enteral nutrition; HD, hemodialysis; PN, parenteral nutrition

Table 8. Protein Restriction in Chronic Kidney Disease (CKD)

Citation Year Level	Population	Study Groups	Results	Comments
Klahr[58] 1994 Level I	CKD pts with moderate renal insufficiency – MDRD Study (N = 840)	Prescribed dietary protein 1.3 g/kg/d (n = 294), 0.6 g/kg/d (n = 291), 0.6 g/kg/g (n = 129), 0.3 g/kg/d + keto-acid supplement (n = 126)	Mean decline in GFR not different between groups Very low protein group with marginally slower decline in GFR (P = .07)	Using intention to treat analysis, low protein diet offers little benefit in preserving GFR
Levey[59] 1996 Level I	CKD pts with GFR 13-24mL/min/1.73 m^2 MDRD Study (N = 255)	Actual dietary protein 0.6 g/kg/d (n = 129) 0.3 g/kg/d+keto-acid (n = 126)	0.2 g/kg/d decrease in protein intake results in 1.15 mL/min/y slower decline in GFR (P = .01), ~41% prolongation of time to dialysis Keto acids, no effect	Low protein diet retards progression of CKD
Locatelli[60] 1991 Level I	CKD pts not on dialysis (N = 456)	Dietary protein 1 g/kg/d (n = 230) 0.6 g/kg/d (n = 226)	Renal survival greater for 0.6 vs 1 g/kg/d diet (P < .06) No difference in CKD-V after 2 y	Diet adherence poor on low-protein diet

GFR, glomerular filtration rate; MDRD, Modified Diet in Renal Disease study

Further research with RCTs that control for inflammation, nutrition status, and type of dialysis are needed to delineate protein recommendations at each level of AKI and CKD. The impact of increased protein intake in the context of illness or injury on CKD has not been thoroughly evaluated.

7. Electrolyte intake in patients should be adjusted by monitoring serum concentrations of K, Mg, P, and Ca. (Grade: D)

Rationale: In trauma patients with AKI, those that received PN and CRRT demonstrated profound losses of calcium and magnesium in the dialysate effluent.[61] To maintain calcium and magnesium balance, the patients needed continuous infusion of calcium and magnesium during the dialysis. The incidence of hypokalemia was significantly lower in CRRT than with intermittent HD.[62–64] Selenium, copper, and thiamine balances were all negative in 11 patients with AKI receiving CRRT, raising the potential for deficiency states to develop over time.[64]

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