Protein-Energy Wasting: Acute Kidney Injury

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Acute kidney injury is a heterogeneous group of conditions characterised by a sudden decrease in glomerular filtration rate, manifested by an increase in serum creatinine concentration or oliguria.

Protein energy wasting is a state of decreased body stores of protein and energy fuels.

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1. Introduction

Protein-energy wasting (PEW) was proposed by the International Society of Renal Nutrition and Metabolism (ISRNM) to define a state of decreased body stores of protein and energy fuels (body protein and fat masses) in patients with chronic kidney disease (CKD) and acute kidney injury (AKI) [1]. PEW is prevalent in AKI patients and a meta-analysis of two studies reported that the prevalence of PEW in patients with AKI was ~66.7% [2]. The pathogenesis of PEW in AKI is multifactorial, including metabolic alterations and impaired homeostasis responses due to sudden loss of kidney function [3], intrarenal and systemic inflammation associated with AKI [4], hypercatabolic state from the underlying comorbidity and critical illness [5], and amino acid loss in KRTs [6].

2. Assessment of PEW in Patients with AKI

Nutritional status assessment is critical to identify patients who are PEW and at risk of mortality. The ISRNM expert panel recommends that clinical diagnosis of PEW requires at least three out of four main categories, namely serum biochemistry; low body weight, reduced total body fat, or weight loss; a decrease in muscle mass; low protein or energy intakes [1]. Subjective global assessment (SGA) has also been used for assessment of PEW [2].

a. Serum Biochemistry

Serum albumin is frequently used to assess nutritional status, as it is relatively inexpensive and widely available, though serum pre-albumin is considered more sensitive due to its shorter half-life (2–3 days) than serum albumin (20 days) [7]. Although the synthesis of albumin and pre-albumin is influenced by dietary protein intakes, non-nutritional factors such as inflammation, overhydration, physiological stress, and infection, which are commonly experienced by patients with AKI, are also implicated in low levels of serum albumin or pre-albumin [7]. Therefore, the serum albumin and pre-albumin levels may be reduced independent of PEW. In fact, serum albumin and pre-albumin are not included in the standardized diagnostic criteria for malnutrition proposed by the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition [8], while the Global Leadership Initiative Malnutrition suggests that serum albumin and pre-albumin may be used as a supportive proxy measure of inflammation [9].

Serum cholesterol is a parameter of malnutrition that has been included in several nutritional screening and assessment tools. A meta-analysis demonstrated that serum cholesterol was associated with the risk of malnutrition in older adults with or without acute diseases [10]. Hypocholesterolemia is paradoxically associated with reduced risk of mortality in patients on maintenance hemodialysis [11], attributed to the cholesterol-lowering effect of systemic inflammation and malnutrition [12]. Similar to other visceral proteins, hypocholesterolemia had been documented in critically injured patients, which was correlated with organ dysfunction and presence of infections [13].

b. Body Mass

Evaluation of body mass and muscle mass using anthropometric measures and physical examination are important diagnostic criteria of PEW [1]. BMI is the most widely used indicator of body mass and has been shown to be paradoxically associated with mortality in CKD patients on dialysis [14]. The obesity paradox observed in patients with renal insufficiency may be explained by higher plasma levels of protective mediators, a greater hemodynamic stability during KRT, and adipose tissue acting as a “buffer” for uremic toxins [15]. Schiffl [16] reviewed eight retrospective studies, which showed conflicting findings on the association between BMI and mortality in critically ill patients with AKI, and the author

suggested that the obesity paradox observed in patients with AKI could be attributed to statistical fallacy and the result of chance, bias, and residual confounding variables in retrospective cohort analyses. Essentially, PEW occurs at any BMI and unintentional weight loss should also be considered as an important indicator of PEW [1]. In the context of acute illness, unintentional weight loss of more than 1% within a week should be suggestive of PEW [8], but assessment of weight loss in patients with AKI is challenging as weight changes are often masked with fluid retention.

c. Muscle Mass

Muscle wasting is a fundamental feature of PEW. Objective and feasible assessment of muscle mass is essential for diagnosis of PEW. Mid-arm muscle circumference is a measured surrogate of lean body mass that has been shown to be a significant predictor of survival in patients on maintenance hemodialysis [17]. Measurement of arm circumference is not sensitive to identify muscle wasting during acute illness [18], and the accuracy and practicability of this anthropometric measurement in sedated or bed-ridden patients with edema is uncertain. Sabatino et al. [19] proposed that ultrasound imaging of quadriceps muscle is a reliable and non-invasive method for evaluation of skeletal muscle in patients with AKI, and this method had been validated against the computerized tomography scan [20]. Further studies investigating the potential utility of this muscle assessment method in patients with AKI are warranted.

d. Dietary Intake

Suboptimal nutritional intake is one of the contributory factors to development of PEW. The nutritional requirements of patients with AKI are affected by disease severity, pre-existing nutritional status, underlying co-morbidities, and KRT modality. The clinical practice guidelines have recommended energy and protein intakes of 20–30 kcal/kg/day and 1.2–2.0 g/kg/day for patients with AKI, respectively [21][22]. However, our systematic review showed that the means of energy and protein intake among patients with AKI were much lower than the recommended amount, which were 11.0–13.5 kcal/kg/day and 0.50–0.64 g/kg/day, respectively [23]. There was inconclusive evidence on the association between energy and protein intake with clinical outcomes in patients with AKI, and those studies that reported higher mortality risk in patients with low energy and protein intakes had limitations with the statistical models that were not fully adjusted [23]. Meta-analyses of randomized controlled trials have demonstrated that energy and protein provisions were not associated with clinical outcomes in critically ill patients [24][25], though data specific to AKI patients was lacking. Hypocaloric nutrition is suggested at the early phase of critical illness to avoid overfeeding as substantial energy is produced endogenously via substrate mobilization [26]. In preclinical studies, energy restriction has been shown to exert renoprotective effects during AKI [27]. Although a greater amount of protein provision is recommended to achieve positive nitrogen balance, particularly in AKI patients undergoing KRTs [22], high protein intakes are potentially associated with negative metabolic complications and poorer clinical outcomes [28][29]. Future work is required to determine optimal energy and protein provision to patients with AKI.

e. Subjective Global Assessment

SGA is a scoring tool consisting of five components of medical history (weight change, dietary intake, gastrointestinal symptoms, functional capacity, and metabolic requirement) and three components of physical examination (loss of body fat, loss of muscle mass, and presence of edema/ascites). A SGA rating is derived based on these components, which "A" indicates well-nourished/normal, "B" indicates mildly/moderately malnourished, while "C" indicates severely malnourished [30][31]. Our systematic review observed a high prevalence of PEW (ranging from 67.9 to 82.1%) assessed via SGA in patients with AKI and the meta-analysis showed that PEW diagnosed based on SGA B or C was associated with increased risk mortality by almost twofold (Risk ratio: 1.99, 95% CI: 1.36–2.91) [23].

3. Conclusions

SGA is a valid tool for assessment of PEW in patients with AKI, as it has been demonstrated to be associated with increased mortality risk. Standard nutrition parameters have been widely used for diagnosis of PEW in patients with CKD, however these parameters in isolation have limited prognostic validity with clinical outcomes in patients with AKI, who are often presented with fluid accumulation and deranged metabolic profile. The cut-off values of these standard nutrition parameters may not be relevant for patients with AKI experiencing drastic deterioration in nutritional status. There is a critical need to explore other novel and validated nutrition parameters for PEW assessment in patients with AKI. Further studies are also warranted to examine whether AKI patients diagnosed with PEW will be benefited from aggressive nutrition therapy.

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