**INTRODUCTION**

Acute kidney injury (AKI) is common in intensive care unit (ICU) patients, with an incidence ranging from 20 to 50%, but with relatively lower incidence in postsurgical patients and higher incidence in those with sepsis and shock. Loss of kidney function affects the metabolism of all macronutrients in this hypermetabolic state where hypertriglyceridemia and hyperglycemia are common. Malnutrition in AKI may increase complications and impact outcome including hospital length of stay (LOS) and mortality. Nutritional status assessment is, therefore, essential in AKI patients to prevent further nutritional depletion (Table 1).

**NUTRITIONAL MARKERS AND MEASUREMENTS IN AKI**

Anthropometric measurements such as body mass index (BMI), skinfold thickness, and mid-arm circumference may become difficult to assess and interpret due to fluid shifts and edema that may be associated with AKI. Subjective global assessment (SGA), nitrogen balance, and markers such as serum albumin, insulin-like growth factor-1 (IGF-1), and cholesterol have been considered as options while evaluating nutritional status and outcome in patients with AKI. The uses and limitations of the markers are summarized in Table 2.

**Albumin**

Obialo et al., in a retrospective study, evaluated 100 AKI patients and found that in the absence of multiorgan failure, serum albumin levels less than 3.5 g/dL had a relative risk of death, irrespective of the presence of sepsis. They concluded that in AKI, patient’s albumin levels less than 3.5 g/dL had a relative risk of death, irrespective of

**Table 1: Goals of nutritional therapy in acute kidney injury (AKI)**

- To reduce negative protein balance and prevent protein-energy malnutrition
- To retain lean body mass and maintain normal body composition
- To avoid metabolic derangements and improve biochemical parameters
- To improve respiratory function capacity and healing
- To improve kidney function
- To improve overall outcomes and reduce mortality

**Prealbumin**

Perez et al. in a longitudinal study evaluated 161 patients and observed that prealbumin level below 11 mg/dL was associated

**Table 2: Markers used in acute kidney injury (AKI) and their limitations**

<table>
<thead>
<tr>
<th>Markers</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prealbumin, albumin, and cholesterol</td>
<td>May be decreased irrespective of PEW</td>
</tr>
<tr>
<td>Leukocyte count</td>
<td>Less specificity</td>
</tr>
<tr>
<td>Modifications in body weight</td>
<td>Total body water is elevated in AKI</td>
</tr>
<tr>
<td>Anthropometry (skinfold, triceps, arm circumference, etc.)</td>
<td>Hypervolemia and edema can mask the changes in muscle mass</td>
</tr>
<tr>
<td>Protein catabolic rate or protein equivalent of nitrogen emergence</td>
<td>Affected by edema</td>
</tr>
<tr>
<td>Energy expenditure</td>
<td>Measurements require calculations based on urea kinetics during RRT + collection of dialysates</td>
</tr>
<tr>
<td>Nutritional score (SGA and its changes)</td>
<td>Prediction formulas are not constantly accurate in critically ill patients (they are generally based on body weight)</td>
</tr>
</tbody>
</table>

**Other prospective tools**

- Growth hormone or IGF-I levels: Only limited data in AKI
- Inflammatory markers [C-reactive protein (CRP), serum interleukins]: Nonspecific and nonnutritional parameters which may have limitations in specific assessment of nutritional risk
- Bioelectrical impedance analysis: No data available on AKI

Adapted from Fiaccadori et al.
with increased mortality in AKI patients. They also demonstrated that an increase in prealbumin of 5 mg/dL was associated with a decreased mortality rate (29%). Another randomized controlled study of 120 critically ill patients, which used prealbumin as an indicator of nutritional status, showed that patients who were given high calorie of 25 × 11 kcal/kg had a significant increase in prealbumin levels at the end of a 7-day follow-up. However, the study did not look into the usage of prealbumin as an indicator of nutritional support in AKI.

**Insulin-like Growth Factor-1 (IGF-1)**
IGF-1 is a peptide analogous to insulin whose production is affected by nutritional status, and its reduction was associated with a lower survival in patients with AKI. Analyzing 56 AKI patients, Guimarães et al. found that IGF-1 levels less than 50.6 ng/mL were independently associated with reduced survival rates, regardless of the presence of sepsis. At the end of a 28-day follow-up, patients with lower levels of IGF-1 had 80% reduction in survival rate. The serum stability, short half-life, and good correlation with nutritional status make IGF-1 an early and sensitive indicator of mortality in AKI patients.

**Cholesterol**
Low-cholesterol level and extremely low levels of low-density lipoprotein have been noted in critically ill patients with sepsis, trauma, and liver dysfunction and may be predictors of morbidity and mortality. Obialo et al. in their study observed that cholesterol levels less than 150 mg/dL in AKI patients were associated with low survival rates. Similar observations were made by Guimarães et al. in their study of 56 AKI patients admitted to ICU, in whom reduced cholesterol levels (<96 mg/dL) were associated with significant reduction in survival rate. The ISRNM now recommends cholesterol levels be included for biochemical assessment of PEW in AKI.

**Anthropometry**
Anthropometry is a simple inexpensive tool used to evaluate nutritional status. Measurements such as skinfold thickness and mid-arm circumference are used as representatives of muscular and adipose tissue compartments. However, the usage of anthropometry in the critically ill has its limitations, as it reflects total body water, rather than alterations in body composition. Standardization of anthropometric measurements in critically ill may be difficult, which makes it an unreliable tool in ICU.

In general population increase in BMI is associated with increased morbidity and mortality. However, in patients with conditions such as AKI, congestive heart failure, CKD, and chronic obstructive pulmonary disease (COPD), the reverse is noted, with increased BMI being associated with better outcome including survival, the reasons for which remain unclear.

**Bioelectrical Impedance Analysis (BIA)**
BIA is a noninvasive tool to evaluate body composition that is easy to use and inexpensive. The analysis is based on the body’s resistance to the flow of low-amplitude (800 mA) and high-frequency (50 kHz) electrical current. The BIA presumes that the human body is identical to a cylinder that conducts electricity in a similar manner, so the hydration status of bodily tissues remains the same in all the individuals. This could be a potential limitation in patients with AKI who frequently are noted to have fluid shifts and volume changes relating to edema, intravascular fluids, and diuretics.

**Subjective Global Assessment (SGA)**
SGA is based on symptoms such as weight loss, gastrointestinal (GI) symptoms, mobility, and signs of loss of fat and muscle mass on physical examination. This is one of the most frequently used tools for nutritional screening and assessment and helpful in predicting the outcomes.

Fiaccadori et al. evaluated the prevalence and outcome of the preexisting malnutrition in patients with AKI. In this prospective study, they identified malnutrition by SGA and anthropometric measurements at admission. They found that the anthropometric, immunologic, and biochemical nutritional indices were significantly decreased in the malnutrition group that was identified by SGA, when compared with those having normal nutritional status. Patients identified with SGA-C status exhibited the lowest of these parameters. The study also showed that diagnostic accuracy of traditional methods (anthropometric, biochemical, or immunologic) was negatively affected by several nonnutritional factors, specifically, in those with impaired renal functions. Severely malnourished patients had significantly increased morbidity for sepsis, septic shock, cardiogenic shock, acute respiratory failure, hemorrhage, and intestinal occlusion and also increased hospital LOS and in-hospital mortality.

**Nutritional Requirements**
In patients with AKI, nutritional requirements should be assessed, considering the degrees of stress and complex metabolic abnormalities affecting not only the water, acid–base balance, and electrolytes but also carbohydrate, protein, and lipid utilization. Hypercatabolism, which occurs due to insulin resistance, acute phase reaction, and increased circulation of catabolic hormones, is one of the main determinants of nutritional status and requirements in AKI patients.

To estimate the catabolic stress in AKI, Druml proposed the measurement of excretion of urine urea nitrogen and variation in body urea nitrogen. In patients requiring dialysis, dialysate losses should be included in the total nitrogen loss.

Druml’s proposed calculation in combination with the clinical assessment helps to profile patient categories as mentioned below:

- **Patients with lower catabolism**
  - loss of nitrogen up to 5 g of ingested dietary nitrogen
  - nephrotoxicity is the most common reason for AKI
  - have low mortality rates (approximately 20%)
  - rarely require dialysis

- **Patients with moderate catabolism**
  - nitrogen loss of 5–10 g/day
  - acute kidney injury caused due to surgeries and infections
  - have higher mortality rates (approximately 60%)
  - may require dialysis.

- **Patients with marked catabolism**
  - patients with sepsis or severe injuries
  - high mortality rates (80%)
  - frequently require dialysis.

Scheinkestel et al. found that the nitrogen balance was inversely associated with clinical outcomes. More importantly, survival rate increased to 20%, with increase in nitrogen balance.
Nutrition Support in AKI

Nutrition Therapy in AKI

Prescription of nutritional support is quite a challenge and the following aspects should be kept in mind:

- In malnourished and hypercatabolic patients, adequate nutrients should be provided to the patients on renal replacement therapy (RRT).
- In patients with a high-residual glomerular filtration rate (who are often nonoliguric), large amount of nutrients may be provided, as there is little risk of water and electrolyte disorders.
- For patients recovering from AKI, the quantity of water, amino acids, and electrolytes should be appropriately limited to delay the need for dialysis until the renal function restores.
- Fluid overload and hyponatremia should be avoided and sufficient calories and nitrogen should be given with minimal amount of water.
- High biological value protein may be given in adequate amounts in patients with AKI.

The loss of amino acids associated with various RRTs is outlined in Table 3.

Enteral Nutrition

Enteral nutrition (EN) should be preferred whenever possible as it helps in maintaining gut integrity and preventing bacterial translocation. Studies suggest that trophic feeding even with small amounts can have protective effect on intestinal mucosal tissue. Studies suggest that trophic feeding even with small amounts can have protective effect on intestinal mucosal tissue.20

Continuous feeding is preferred, widely used, and well tolerated.21

Another study of EN in patients with AKI, Fiaccadori et al.22 studied adequacy and complications of nutrient administration in 247 patients who received nutrition support exclusively through the enteral route. Gastrointestinal complications were the most common reason for suboptimal delivery of nutrition. However, no significant difference in GI complications was noted between those with AKI and normal renal function patients. High gastric residual volumes occurred in both the group of patients; however, it was significantly high in AKI patients who were on RRT. The study concluded that EN was safe and effective in AKI and that parenteral amino acid supplementation deserves consideration in those requiring RRT.

Parenteral Nutrition

Parenteral nutrition (PN) should be given for patients with significant gut dysfunction or those who are intolerant to enteral feedings. The combination of EN and PN when required to achieve nutritional goals has been shown to be safe, but it is highly recommended to make every attempt to feed enterally before pursuing options to include PN.

Parenteral nutrition is customized and prepared under sterile conditions in hospitals in countries such as the United States of America, while the standard premixed parenteral formulas are available in Europe and Asia. All-in-one solution is available as a single bag with glucose, amino acids (essential and nonessential), lipids, vitamins, trace elements, and electrolytes. Caution should be exercised on closely monitoring and correcting electrolytes while using premixed ready-to-use parenteral solutions.

To ensure maximum utilization of nutrients and to avoid metabolic derangements such as hyperglycemia and rise in blood urea nitrogen, it is recommended that the infusion be started at a low rate and gradually increased to achieve goals over a period of time.

Intradialytic Parenteral Nutrition

Intradialytic parenteral nutrition (IDPN) is an option for provision of intravenous nutrition support to patients during hemodialysis. To meet all energy, protein, and other nutrient requirements, IDPN alone is not sufficient, but it provides a considerable amount of energy and protein with each dialysis session to supplement the patient's oral or enteral intake.26

Intradialytic PN is suggested for patients whose oral intake is unable to meet their nutritional requirements. Many studies using IDPN have failed to show the efficacy convincing this mode of nutrition provision. Intradialytic PN can be provided during dialysis by which the fluid balance can be maintained and nutrients can be supplied in a shorter duration of time. The use of IDPN has primarily been studied in patients with CKD on hemodialysis and still remains controversial. It’s role in patients with AKI remains unclear.

Criteria (2009) for Initiating IDPN with Functional GI Tract29,30

Following are the criteria to initiate IDPN in patients with functional GI tract

- Poor oral food intake and nutritional supplements
- Intolerance to tube feeds
- Subjective global assessment rating of C
- Weight loss >10%
- Serum albumin <3.4 g/dL
- History of any of the following:
  - Anorexia caused by uremic state
  - Anorexia nervosa due to higher levels of urea and creatinine
  - Change in the taste of food
  - Recurrent illness

Table 3: Loss of amino acids in various dialysis techniques23–25

<table>
<thead>
<tr>
<th>S. no</th>
<th>Type of dialysis</th>
<th>Protein/amino acid loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hemodialysis with low flux, cuprophane membrane</td>
<td>Loss of 10–13 g amino acid per dialysis</td>
</tr>
<tr>
<td>2</td>
<td>Hemodialysis with high-flux dialyzers</td>
<td>8 g of free amino acid per session</td>
</tr>
<tr>
<td>3</td>
<td>Continuous RRT</td>
<td>Protein loss of 1.3 g/L of output. For 50 L of output per day the loss is up to 65 g/day</td>
</tr>
<tr>
<td>4</td>
<td>Peritoneal dialysis</td>
<td>Average loss of 9.6 g protein per 24 hours in peritoneal fluid</td>
</tr>
<tr>
<td>5</td>
<td>Peritoneal dialysis with peritonitis</td>
<td>Average loss of 15.1 g protein per 24 hours in peritoneal fluid</td>
</tr>
</tbody>
</table>
Nutrition Support in AKI

Table 4: Guidelines for nutritional requirements in acute kidney injury

<table>
<thead>
<tr>
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<th></th>
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</thead>
<tbody>
<tr>
<td>Energy</td>
<td>20–30 kcal/kg body weight/day</td>
<td>25–30 kcal/kg/day</td>
<td>20–30 kcal/kg body weight/day</td>
<td>1.2–1.7 g/kg actual body weight/day</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>3–5 g (max 7)/kg body weight/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat</td>
<td>0.8–1.2 (max 1.5) g/kg body weight/day</td>
<td>1.2–2 g/kg/day</td>
<td>Noncatabolic state: 0.8—1 g/kg body weight/day</td>
<td>On RRT 1.0–1.5 g/kg body weight/day</td>
</tr>
<tr>
<td>Protein (essential and nonessential amino acids)</td>
<td>0.6–0.8 (max. 1.0) g/kg body weight/day</td>
<td></td>
<td>On RRT 1.0–1.5 g/kg body weight/day</td>
<td>On CRRT 1.7 g/kg body weight/day</td>
</tr>
<tr>
<td>Conservative therapy</td>
<td>1.0–1.5 g/kg body weight/day</td>
<td>Frequent hemodialysis or CRRT 2.5 g/kg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extracorporeal therapy</td>
<td>Up to maximum 1.7 g/kg body weight/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous renal replacement therapy (CRRT), in hypercatabolism</td>
<td>Extracorporeal treatment causes increased loss of micronutrients which should be supplemented. Excessive supplementation may result in toxicity. Micronutrient status should therefore be monitored</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronutrients</td>
<td>PN to be considered when requirements cannot be met via EN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preferred route of feeding</td>
<td>Nasogastric (NG) route is a standard method of access for EN administration</td>
<td>EN preferred</td>
<td>Low potassium and low phosphate levels can be implemented where the corresponding serum levels are high</td>
<td></td>
</tr>
</tbody>
</table>

- Mental stress
- Hypercatabolism
- Not dialyzed adequately
- Gastroparesis
- Constipation

Recommendations from various guidelines on nutrition support in patients with AKI are summarized in Table 4.

Conclusion

Nutritional screening, assessment, and support are essential but challenging in patients with AKI. It needs to be customized based on etiology, severity, comorbidities, and need for RRT. Current guidelines recommend using the gut (oral or EN support) whenever possible and meet the nutritional demands to prevent protein energy malnutrition and micronutrient losses. Parenteral nutrition including IDPN may be considered in specific situations when unable to meet goals with enteral nutrition support.

References


