Nutritional Management of Critically Ill Patients with Acute Kidney Injury

3rd International Conference of European Renal Nutrition Working Group of ERA-EDTA

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Learning Objectives

• Recognize the prevalence and extent of PEW in critically ill patients with acute kidney injury (AKI)

• Understand expert guidelines for nutritional management of critically ill AKI patients to improve outcomes:
  – Prevalence and clinical outcomes of PEW in AKI
  – Causes and pathogenesis of PEW in AKI
  – Understand the nutrient requirements for optimal management of AKI patients
Nutritional Considerations in AKI

• Nutritional status in the setting of AKI is primarily influenced by:
  – Hypercatabolic/hypermetabolic/Inflammatory state
  – Underlying disease process and co-morbidities

• Loss of kidney function further exacerbates/complicates the problem because of associated fluid and electrolyte abnormalities
Nutritional Considerations in AKI

- Renal Replacement Therapy impacts on nutrient balance by losses of macro and micronutrients in the ultrafiltrate/dialyzate as well as glucose exposure.

- Nutritional therapy guidelines are not well established since there are no data from RCTs and clinical practice mostly based on expert’s opinions.
AKI has negative outcomes in hospitalized patients

Presence of PEW on admission in patients with AKI is associated with high mortality

In-hospital mortality according to nutritional status in 309 AKI pts

Nutritional status by SGA (Subjective Global Assessment of Nutritional Status)

**Figure 2.** In-hospital mortality according to nutritional status. □, normal nutritional status; □, moderate malnutrition or risk of malnutrition; ■, severe malnutrition. $\chi^2$ for trend ($P < 0.001$). *$P < 0.001$

Multiple Phenotypes of The Malnutrition Syndrome

Undernutrition
- Chronic starvation without inflammation

Impaired Utilization
- Acute illness with inflammation
- Chronic illness with inflammation

Overnutrition
- Obesity ≥ 30 BMI
- Insulin Resistance

Macro- & Micronutrient deficiency

Loss of Lean Body Mass

Sarcopenic Obesity

Metabolic Syndrome
## Limitations in the assessment of nutritional markers in AKI

<table>
<thead>
<tr>
<th>Nutritional parameters</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Albumin, prealbumin, cholesterol</td>
<td>May be reduced due to inflammation and or volume overload, independently from PEW</td>
</tr>
<tr>
<td>Body weight changes</td>
<td>Total body water is disproportionally increased in AKI</td>
</tr>
<tr>
<td>Anthropometric measurements</td>
<td>Fluid overload can mask changes in body mass changes</td>
</tr>
<tr>
<td>Energy expenditure</td>
<td>Formulas to predict energy expenditure not reliable (often based on body weight)</td>
</tr>
<tr>
<td>Nutritional scoring systems (SGA, etc...)</td>
<td>Limited data in patients with AKI</td>
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<tr>
<td>Body mass and body composition assessments (total body nitrogen, bioimpedance analysis, CT/MRI)</td>
<td>No data on AKI, tools cumbersome, costly, and/or invasive</td>
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</table>

Modified according to Fiaccadori E et al. Sem Dialysis 2011; 24:169-175
The Causes and Consequences of Protein-Energy Wasting in AKI

- Co-Morbid Conditions (Surgery, Critical Illness)
- Infection
- Post-ICU Frailty
- Nutrient Intake
- Uremic Toxins
- Metabolic Derangements (Glucose Intolerance, Metabolic Acidosis, IGF-1/GH Resistance, Hyper/Hypocortisolemia)
- Inflammation

RRT-Associated Catabolism
Protein catabolic rate measured in critically ill patients with AKI on RRT

Macias WL et al, J Parent Ent Nutr 1996; 20:56
Fiaccadori E et al., Nephrol Dial Transpl 2005; 20:1976
Cytokines and Skeletal Muscle Protein Metabolism

Flores et al, JCI, 1989

* p < 0.05 vs Saline
## Loss Of Nutrients in RRT, According to Dialysis Modalities/Dialysis Membranes

<table>
<thead>
<tr>
<th>Nutrient Loss</th>
<th>HD</th>
<th>HDF</th>
<th>CRRT</th>
<th>PD</th>
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</thead>
</table>
| Amino acids   | Cellulose acetate: 6.1 ± 1.5 g/HD  
Low flux PMMA: 7.1 ± 2.6 g/HD  
High Flux PS: 8.0 ± 2.8 g/HD  
High Flux PMMA: 12.0 ± 2.0 g/HD | Not well studied.  
300 to 7000 mg/HDF session!  
Depends on membrane and UF volume  
HDF results in lower serum albumin versus HD | 0.2 g/L, thus 10-15 g/day | 2-4 g/day |
| Proteins      | Minor: 0.5 – 1.5 g/HD due to blood loss  
Major: 5-15 g/HD if reuse of HD membrane | | 5-10 g/day | 5-15 g/day |
| Glucose       | 25 g/HD if use of glucose free dialyzate  
Minor if use of glucose-based dialyzate | Unknown, presumably not significantlky to HD | Not known | Uptake of 100-150 g/day or more |

*References:*  
Chazot C et al. Abstract Congress Société de Néphrologie; Nep Ther 2012; 8: 303  
Hypophosphatemia and phosphate supplementation during continuous renal replacement therapy in children

Maria José Santiago¹, Jesús López-Herce¹, Javier Urbano¹, Jose María Bellón², Jimena del Castillo¹ and Angel Carrillo¹

Figure 1 | Changes in the phosphate levels during the first 72 h of treatment. Comparison between patients with and without phosphorus supplements in the replacement and dialysis solutions. P indicates phosphorus.
Hypophosphatemia During Continuous Veno-venous Hemofiltration Associated with Mortality in Critically Ill Patients with Acute Kidney Injury

Yang Y et al. 2012 e-pub

Cumulative survival rate. The incidence of CRRT-associated hypophosphatemia (left) and frequency (high = > 50% of CRRT-days) (right) increases 28-day mortality of critically ill patients with AKI (p = 0.002).
Carbohydrate and Lipid Metabolism in AKI

- AKI is characterized by hyperglycemia due to peripheral insulin resistance and accelerated hepatic gluconeogenesis. This is primarily driven by concurrent critical illness state.

- Lipid metabolism is affected in AKI due to delayed elimination of fat (triglycerides) infusion and inhibition of lipolysis. In addition fat oxidation is increased.
Lipid Metabolism in AKI

Druml W et al. *Kidney Int* 1983; 24 (Suppl.16): S-139-142

Total post-heparin lipolytic activity (PHLA), hepatic triglyceride lipase (HTGL), and lipoprotein lipase activity (LPL) in AKI
Tight blood glucose control is renoprotective in critically ill patients

Positive impact of IIT versus conventional treatment on the incidence of different renal outcomes in surgical ICU patients.

Measured Resting Energy Expenditure (REE) in AKI

REE in AKI patients
1835 Kcal/69 Kg
= 27 Kcal/Kg/day

Faisy C et al., Am J Clin Nutr 2003; 78:241-249
Artificial nutrition and outcome in AKI: availables studies have many methodological problems!

- Few patients
- Suboptimal selection of patients
- Population and syndrome heterogeneity
- No stratification for severity of illness or nutritional status
- Use of historical controls or no controls at all
- In most cases retrospective studies
- Quantitative and qualitative inadequacy of Kcal and/or N intake
- Inadequate duration of nutritional support
Nutritional Support in Patients with AKI

Cochrane Data Base: 8 studies, n= 257 patients
- 6 studies 1978-1983
- 1 study 2005
- 1 study 2007 (no RRT)

Conclusions:
Not enough (and reliable) data for a systematic review!

The analysis of the data does not provide strong
evidence that nutrition support improves survival and
recovery from AKI in critically ill patients

LI Y et al: Cochrane Database of Systematic Reviews 2010
No Advantage in Increasing Amino Acids/Protein intake in AKI treated with CRRT

3 cohorts of patients with AKI on CRRT:
1) With supplemented Amino acids (AA) 1.2 g/kg/day (n=24)
2) AA 2.5 g/kg/day with non protein calories of 30-35 kcal/kg/day (n= 16)
3) AA 2.5 g/kg/day with non protein calories of > 35 kcal/kg/day (n= 7)

In these retrospective studies, high AA intake resulted in:
- A trend to less negative nitrogen balance
- Similar AA losses
- Higher serum urea requiring more aggressive dialysis
- No effect on outcome

⇒ No clear advantages in increasing AA/protein intake to 2.5 g/Kg/day or more

Bellomo R et al., Ren Fail 1997; 19:111-20
Bellomo R et al., Int J Artif Org 2002; 25:261-8
Recommendations for protein and amino acid intake in AKI patients

- **Protein**: 1.5 – 1.7 g/kg ideal body weight/day
  - Add 0.2 g/kg/day during Parenteral Nutrition and CRRT since 10–15% of infused amino acids are lost in the dialysate/ultrafiltrate

- **Amino acid**:
  - Both EAA + NEAA are necessary.
  - Certain amino acids, such as glutamine are shown to be effective in animal and small pilot studies and can be supplemented in the feeding regimens

Kidney Int Suppl 2012; 2: 37-68*
Recommendations for energy intake in AKI patients

- A total energy intake of 20-30 kcal/kg/d in patients with any stage of AKI
- No more than 25 Kcal/kg/day of non protein calories
- 2/3 of non protein calories as glucose
  - not to exceed 5 g/kg/day according to ESPEN
  - not to exceed 7 g/kg/day according to KDIGO
- 1/3 of non protein calories as lipids
  - 1-1.5 g/Kg/day, 18-24 hour infusion, according to ESPEN
  - 0.8-1.0 g/kg/day according to KDIGO

Kidney Int Suppl 2012; 2: 37-68
Enteral nutrition is the preferred modality in patients with AKI and nutritional support

- Enteral nutrition (oral, if not possible tube feeding) recommended and is safe in patients with AKI
- EN helps maintain gut integrity, decreases bacterial and endotoxin translocation
- No clinically relevant increase in complications
- A combination of enteral and parenteral support often needed to reach the targeted intake of proteins

Fiaccadori E et al. Kidney Int 2004; 65: 999-1008
Benefits of late PN:
- Faster recovery,
- Less complications,
- More cost-savings
- ? Organ sparing
Trace element supplementation

- CRRT results in significant losses and negative balances of selenium, copper and thiamine, which contribute to low plasma concentrations

- In general, daily supplementation with standard doses of parenteral commercial multitrace element preparations results in sufficient trace elements to overcome the amount lost by CRRT

- However, prolonged CRRT is likely to result in thiamine and selenium deficiency despite supplementation at recommended amounts

- Data on optimal dose of multitrace elements in patients on prolonged CRRT are needed

Key points

- PEW is frequent in AKI patients with or without underlying CKD and represents an independent predictor of mortality and morbidity.

- While artificial nutrition is considered as a key component of therapy in AKI patients, there is paucity data that examined the characteristics or efficacy of artificial nutrition in these settings.

- The recommended levels of energy and protein intake for AKI patients is no more than 25-30 Kcal/Kg/day and 1.5 - 1.7 g/Kg/day, respectively.

- Enteral nutrition should be the initial modality for artificial nutrition in AKI; in certain cases it can be integrated with PN to achieve nutrition needs.

- The type of dialysis therapy can dictate the characteristics of nutritional supplementation in AKI and hospitalized CKD patients.