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Nutritional Support for Patients with AKI

Etienne Macedo, MD, PhD, FASN

Outline

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- Metabolic and nutritional changes during AKI
- How to evaluate nutritional status in patient with AKI
- What is adequate nutritional support during different phases of AKI

Metabolic Changes During AKI

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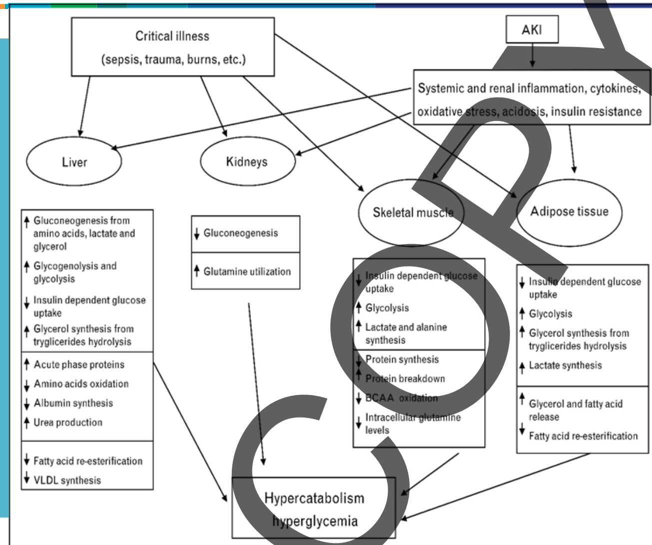
AKI is associated with systemic stress-induced hormonal and metabolic changes

- Increase resistance to anabolic signals and **insulin**
- High glucose concentration
- Increased levels of inflammatory mediators



Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Fiaccadori and Cremaschi, Current Opinion in Critical Care 2009

Metabolic Changes During AKI

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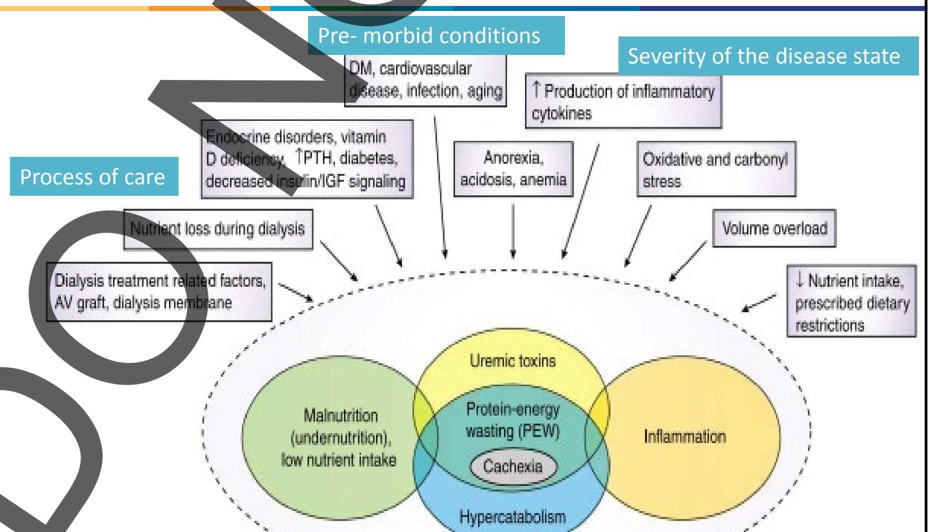


Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Fouque et al, KI 2008

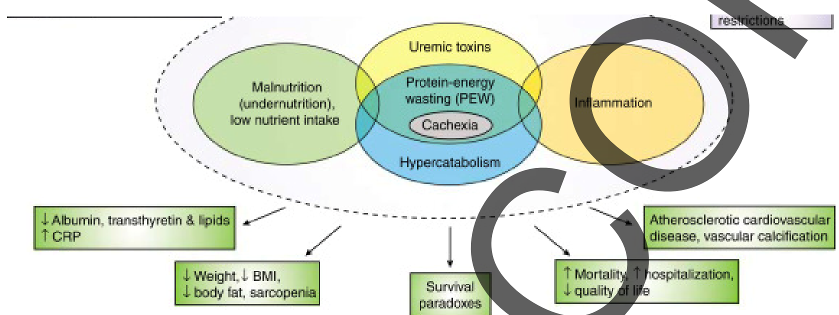
Preiser et al., Critical Care 2015
Cuesta JM et al., Crit Care Med 2012

Malnutrition in Kidney Disease

- Increased inflammation
- Increased energy expenditure (EE)
- Stress hyperglycemia
- Negative nitrogen balance

PEW – protein energy wasting

Term proposed to refer to all the negative metabolic consequences of the acute loss of kidney function on nutritional status



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Fouque et al, KI 2008

Protein Energy Wasting Syndrome Definition

Criteria

Biochemical
- ✓ At least one

Body weight / composition
- ✓ Weight loss independent of BMI

Dietary intake
- ✓ Assessed by diary or interview

Serum chemistry
- Serum albumin < 3.8 g per 100 ml (Bromcresol Green)[a]
- Serum prealbumin (transthyretin) < 30 mg per 100 ml (for maintenance dialysis patients only; levels may vary according to GFR level for patients with CKD stages 2–5)[a]
- Serum cholesterol < 100 mg per 100 ml[a]

Body mass
- BMI < 23[b]
- Unintentional weight loss over time: 5% over 3 months or 10% over 6 months
- Total body fat percentage < 10%

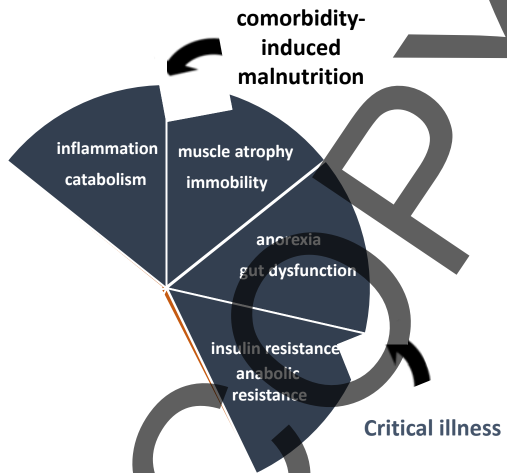
Muscle mass
- Muscle wasting: reduced muscle mass 5% over 3 months or 10% over 6 months
- Reduced mid-arm muscle circumference area[c] (reduction > 10% in relation to 50th percentile of reference population)
- Creatinine appearance[d]

Dietary intake
- Unintentional low DPI < 0.80 g kg^{-1} day^{-1} for at least 2 months[e] for dialysis patients or < 0.6 g kg^{-1} day^{-1} for patients with CKD stages 2–5
- Unintentional low DEI < 25 kcal kg^{-1} day^{-1} for at least 2 months[e]

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Fouque et al, KI 2008

Factors associated with PEW in AKI Critically ill Patients

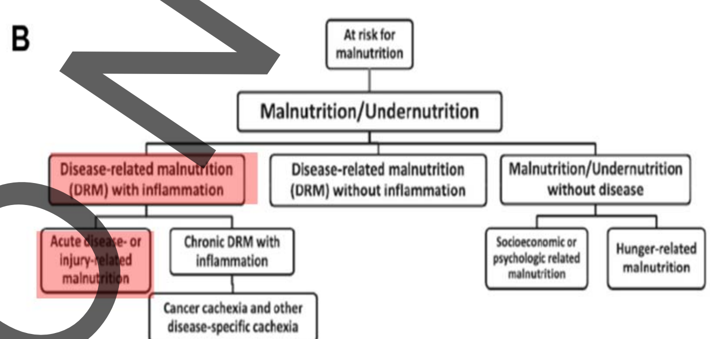


*ESPEN 2009

Osterman et. Al., Intensive Care MedicineJuly 2019, Volume 45, Issue 7, pp 1006–1008

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Factors associated with PEW in Critically ill Patients



Every critically ill patient staying for more than 48 h in the ICU should be considered at risk for malnutrition. Expert

Medical nutrition therapy shall be considered for all patients staying in the ICU, mainly for more than 48 h Good practice

Singer P et al, Clin Nutr 2019;38:48-79

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Factors associated with PEW in AKI Critically ill Patients

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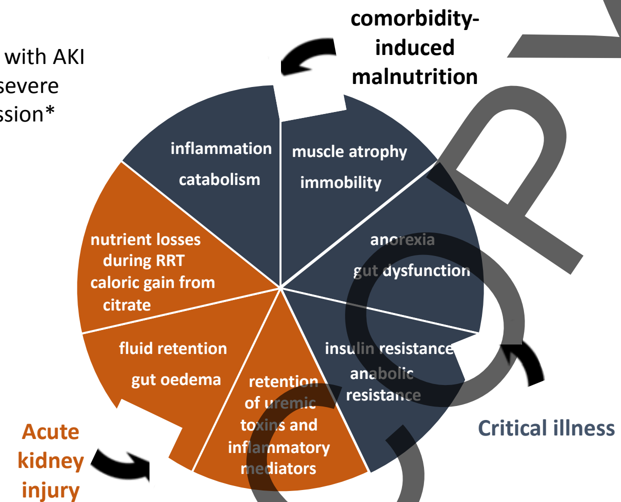
✓ Up to 42% of patients with AKI present with signs of severe malnutrition on admission*



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*ESPEN 2009

Osterman et. Al., Intensive Care Medicine July 2019, Volume 45, Issue 7, pp 1006–1008

Can we avoid PEW in AKI?

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✓ **Worsening of nutritional status** is the result of many mechanisms:
- **inflammatory processes**
- **catabolic factors**

✓ Not a direct effect of nutrient intake

✓ Nutrition can only improve protein and energy balance and possibly protein synthesis but cannot suppress critical illness-induced catabolism.

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Bear DE et al, Critical Care 2017

McClave et al, Journal of Parenteral and Enteral Nutrition 2016

Approach to Diet in AKD

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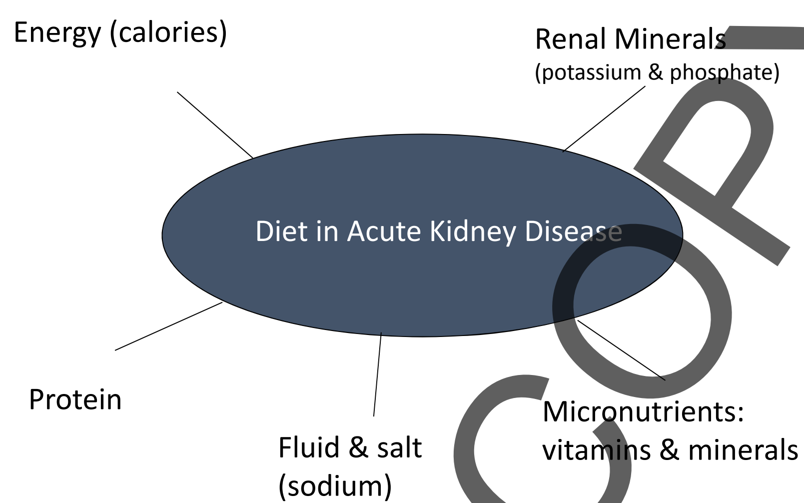

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How much calorie to give?

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- ✓Energy expenditure (EE) tends to be higher during critical illness
- ✓but **both** under- and overfeeding are associated with delayed recovery and increased mortality

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(2019) ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 38(1):48–79

How to measure Energy Expenditure?

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Resting energy expenditure

Indirect calorimetry
(O_2 consumption - CO_2 production)
calculate the total amount of energy produced

"Calculation"
e.g. formula - Harris and Benedikt:
Men (kcal): REE = 66 + (13.7 x BW) + (5 x height) - (6.8 x age)
Women (kcal): REE = 66.5 + (9.6 x BW) + (1.8 x height) - (4.7 x age)

"Estimation"
(based on body weight, ie 25kcal/kg/day)

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Indirect calorimetry: recommendations

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ESPEN Guidelines

In critically ill mechanically ventilated patients, EE should be determined by using indirect calorimetry. **Grade B**

Singer P et al, Clin Nutr 2019;38:48-79

(A.S.P.E.N.)
(SCCM)

A3a. We suggest that indirect calorimetry (IC) be used to determine energy requirements, when available and in the absence of variables that affect the accuracy of measurement.

Taylor BE et al Crit Care Med 2016;44:390-438

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Energy Needs

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Gold standard = indirect calorimetry

Clinical situation requiring careful interpretation of EE measured by indirect calorimetry:

- Agitation or unstable sedation
- Air leaks (10% min volume)
- Unstable body temperature (>1⁰C / 1 h)
- Unstable pH (0.1 +/- /1 h)
- FiO^2 > 60%
- Organ support therapies – RRT, ECMO

Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Oshima T et al JPEN 2016, Jun 22. pii: S0261-5614(16)30142-X

How much calorie to give?

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✓**Indirect calorimetry often not available**

✓Energy expenditure (EE) is difficult to predict

Based on expert consensus, in the absence of IC, we suggest that a predictive equation or a simplistic weight-base equation be used to determine Energy Requirements

-> 25-30kcal /kg/day

✓Equations failed in 80% of patients

-> **equations overestimate calorific requirements**

- risks with over feeding well nourished
- risks with under feeding poorly nourished

Taylor BE et al Crit Care Med 2016;44:390-438

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Bear DE et al, Critical Care 2017

McClave et al, Journal of Parenteral and Enteral Nutrition 2016

Energy Expenditure/Needs

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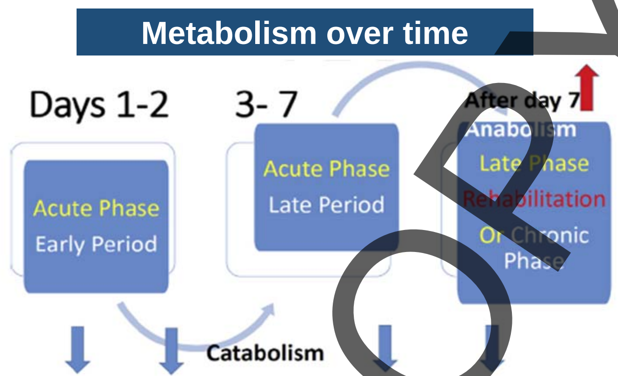
ESPEN Guidelines



Recommendation:

- Hypocaloric nutrition in the early phase of illness -> progressing slowly to full
- Targeted nutrition after day 3 with the aim to achieve more than 70% of EE -> but not more than 100%

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Singer P et al, Clin Nutr 2019;38:48-79

How much calorie to give?

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- ✓There is no evidence that caloric targets should be different in AKI patients with and without RRT.
- ✓In patients on CRRT, citrate contributes to caloric delivery and should be accounted for.

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(2019) ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 38(1):48–79

Caloric Recommendation

Patients with AKI	Level of evidence *	General ICU patients	Level of evidence *
Gradual increase in first week		Gradual increase in first week to	
o **20-30 kcal/kg/day**	5	o 20-25 kcal/kg/day	2C
o **25-30 kcal/kg/day**	5	o up to 70% of EE in first 7 days	2C

1a:	Systematic reviews (with homogeneity) of randomized controlled trials
2a:	Systematic reviews (with homogeneity) of cohort studies
2b:	Individual cohort study or low quality randomized controlled trials (e.g. <80% follow-up)
2c:	**"Outcomes" Research; ecological studies**
5:	**Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"**

Osterman et. Al., Intensive Care MedicineJuly 2019, Volume 45, Issue 7, pp 1006–1008

Calorie Intake and Patient Outcomes in Severe AKI: findings from the RENAL study trial

Analyzed Daily Calorie Intake in 1456 patients from the RENAL trial.

- ✓ Stable calorie intake was only achieved at 4 to 5 days after randomization
- ✓ mean **DCI** was low at ~11 Kcal/Kg/day

(not accounting for the CRRT caloric load from citrate and glucose)

Mean **DCI 867Kcal/day**

Mortality

- Below mean - 46%
- Above mean – 43%

- ✓ **No difference in Mortality based on levels.**
- ✓ **In the multivariable analysis, high DCI levels was not independently associated with a significant decrease in the OR for 90-day mortality.**

Bellomo at al., Critical Care 2014, 18:R45

How much protein to give ?

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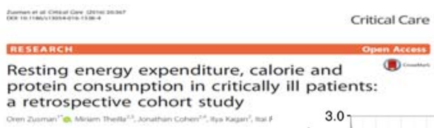
- More protein: beneficial or harmful?

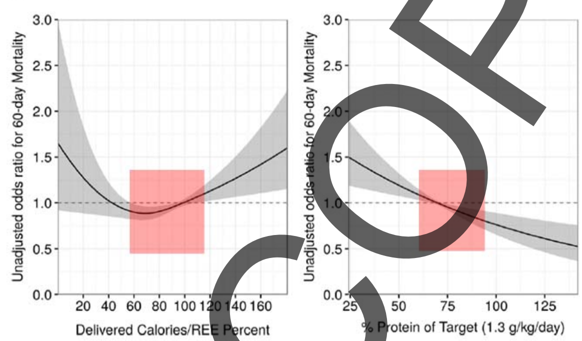

Critical Care

RESEARCH Open Access

Resting energy expenditure, calorie and protein consumption in critically ill patients: a retrospective cohort study

1171 patients

Mortality at D60



Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Zusman O et al Crit Care 2016;20:367

Effects of the nutrition regimen on urea appearance and protein catabolic rate

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- Few studies correlating of amount of nutrition received and the protein catabolic rate (PCR) measured in AKI patients

✓Response to protein intake and restriction in AKI is consistent with the findings reported in other critically ill populations

✓Decreased protein resulted in more muscle protein breakdown with the **same generation of urea as those patients receiving moderate intakes of protein**.

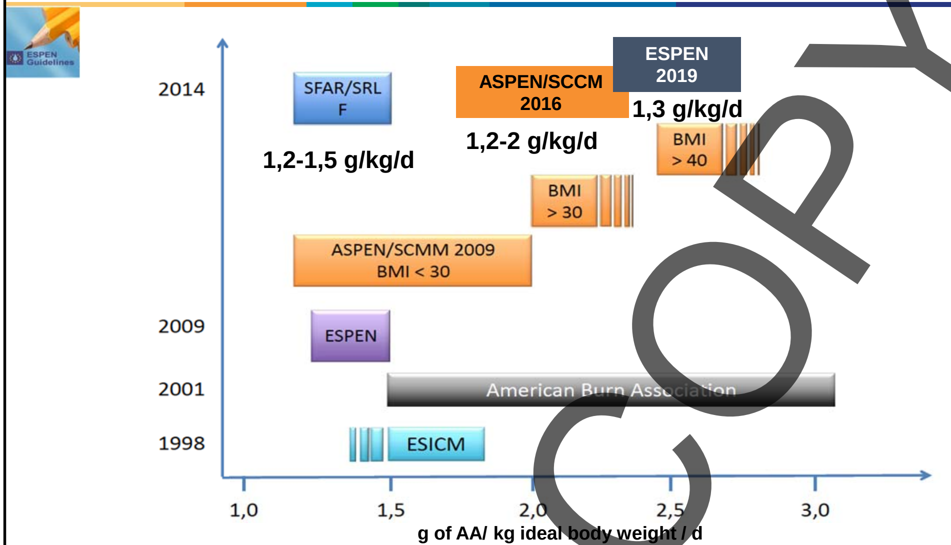
✓Further increases in **protein intake above 1.5 g protein**/kg may lead to increased urea generation

✓Increasing calories beyond energy expenditure may lead to increased protein breakdown and a more negative nitrogen balance.

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Mitchell H. Rosner, Nutritional Support for Patients with Acute Kidney Injury
NUTRITION ISSUES IN GASTROENTEROLOGY, SERIES #96, 2011

Recommendations: Protein Target



Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Singer P Clin Nutr 2019;38:48-79

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.)

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- Suggest that ICU patients with AKI be placed on a standard enteral formulation
  - protein (1.2–2 g/kg actual body weight per day)
  - energy (25–30 kcal/kg/d)
- Consider a specialty formulation designed for renal failure (with appropriate electrolyte profile) if significant electrolyte abnormalities

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

McClave et al, Journal of Parenteral and Enteral Nutrition, February 2016

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.)

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✓Recommend patients receiving frequent hemodialysis or CRRT receive increased protein
  - **Quality of Evidence: Very Low**

- **Rationale:**

o A significant amino acid loss (10–15 g/d) in CRRT

o Based on protein catabolic rate values estimated lean body mass catabolism ~ 1.4–1.8 g/kg/d in patients with AKI on CRRT

o Additional 0.2 g/kg/d **– max 2.5 g/kg/d**

o No advantages have been demonstrated with very high protein intakes (>2.5 g/kg/d)

o Excessively high nitrogen intakes may simply increase the rate of urea production

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

McClave et al, Journal of Parenteral and Enteral Nutrition, February 2016

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.)

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- Protein should **not** be restricted in patients with renal insufficiency as a means to avoid or delay initiating dialysis therapy

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McClave et al, Journal of Parenteral and Enteral Nutrition, February 2016

Protein Recommendation

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Patients with AKI	Level of evidence *	General ICU patients	Level of evidence *
AKI during critical illness and not on RRT: o gradual increase to 1.3 g/kg/day o up to 1.7 g/kg/day	5	o progressive increase to 1.3 g/kg/day	2B
Critically ill patients on intermittent RRT: o 1.0 - 1.5 g/kg/day o 1.5 g/kg/day	5		
Critically ill patients on CRRT: o up to 1.7 g/kg/day	5		

2b:	**Individual cohort study or low quality randomized controlled trials (e.g. <80% follow-up)**
2c:	"Outcomes" Research; ecological studies
5:	**Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"**

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Osterman et. Al., Intensive Care MedicineJuly 2019, Volume 45, Issue 7, pp 1006–1008

Daily Protein Intake and Patient Outcomes in Severe AKI: Findings of the **RENAL** Trial

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Analyzed Daily Protein Intake in 1457 patients from the RENAL trial.

- Mean DPI was low – **0.5g/kg/day**

Only 159 (10.9%) patients received a mean DPI of >1 g/kg

✓ **26.8% of study days**

200 patients received a combination of enteral and parenteral nutrition

✓ **17.1% of study days**

Mortality
- DPI Below mean - 46%
- DPI Above mean – 43%

✓ **Patients with a DPI above the median had similar mortality to patients with a below the median**

✓ **In the multivariable analysis, high DPI was not independently associated with a significant decrease in the OR for 90-day mortality**

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Bellomo at al., Blood Purif 2014;37:325–334

Vitamins and trace elements Recommendation

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Patients with AKI	Level of evidence *	General ICU patients	Level of evidence *
o Supplement micronutrient losses during extracorporeal treatment	5	o Routine supplementation with glutamine or 1b antioxidants not recommended	1B
		o Recommendation to detect micronutrient deficiencies in patient categories at risk	5

1b:	Individual randomized controlled trials (with narrow confidence interval)
5:	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Osterman et. Al., Intensive Care MedicineJuly 2019, Volume 45, Issue 7, pp 1006–1008

Micronutrient Alterations During Continuous Renal Replacement Therapy in Critically Ill Adults: A Retrospective Study

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Retrospective study Emory University Hospital's

Between 2009 and 2012

75 patients receiving nutrition support services and had at least 1 serum micronutrient level measured during CRR

Below normal range in:

- o Thiamin 16% -(9/56)
- o Pyridoxine 67% - (38/57)
- o Ascorbic acid 87% - (13 of 15)
- o Folate 33% - (3 of 9)
- o Zinc 9% (9of24)
- o Copper 60% - (41 of 68)

✓ The incidence of various micronutrient deficiencies in critically ill patients who required CRRT was higher than previously reported.

✓ Prospective studies are needed to determine:

o Is CRRT the main cause oflow micronutrient status -?

o the potential clinical and metabolic efficacy of supplementation in the intensive care unit setting.

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Nutritional Screening post AKI

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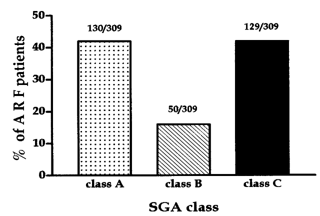
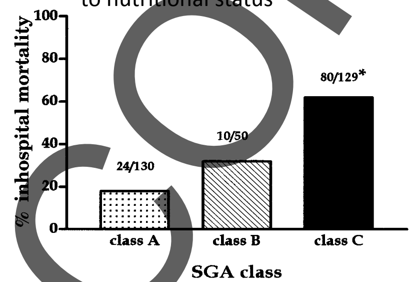
- In the study with 309 ARF patients admitted to the renal ward
- 67% of patients were dialyzed (206 of 309)
- **40% severe malnutrition** by Subjective Global Assessment (SGA)

Nutritional status of ARF patients on admission



In-hospital mortality according to nutritional status



1 normal nutritional status
p ,moderate malnutrition or risk of malnutrition
f severe malnutrition.

patient-Centered Approach

Fiacadori et al., J AM Soc Nephrology, 1999

Nutritional Screening post AKI

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- Nutritional status at admission to renal ward was an independent predictor of in-hospital mortality

✓All AKI patients with **severe AKI should be screened for malnutrition** at discharge and at their first clinic appointment.

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Fiacadori et al., J AM Soc Nephrology, 1999
Fiaccadori and Cremaschi, Current Opinion in Critical Care 2009

Ideal Model for Nutrition Assessment

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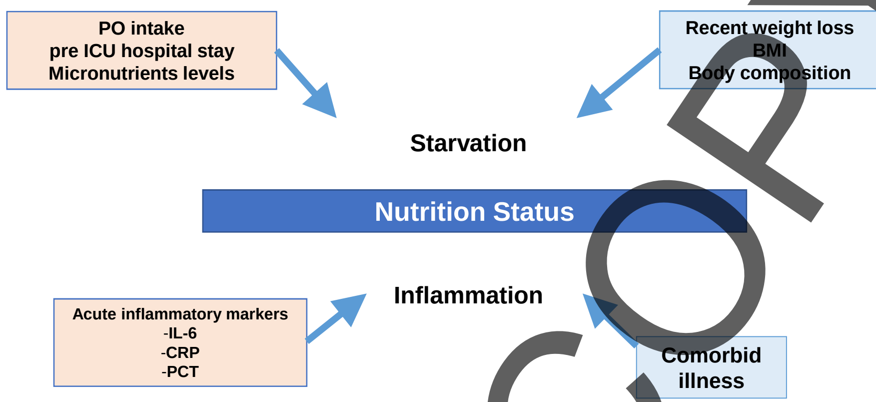

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Tools

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- Malnutrition Universal Screening Tool (MUST)
- Nutritional Risk Screening (NRS 2002)
- Mini Nutritional Assessment (MNA)
- Short Nutritional Assessment Questionnaire (SNAQ)
- Malnutrition Screening Tool (MST)
- Subjective Global Assessment (SGA)

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Malnutrition Universal Screening Tool (MUST)

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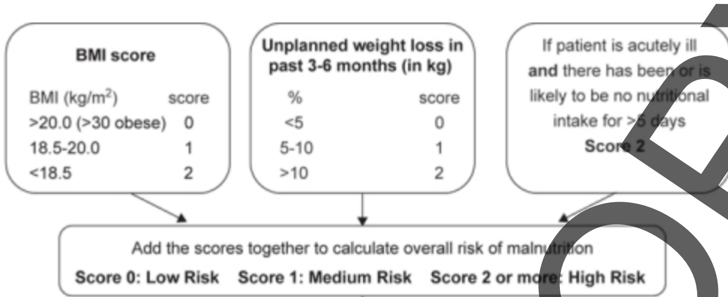

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Nutritional Risk Screening (NRS 2002)

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Table 1 Initial screening

		Yes	No
1	Is BMI < 20.5?		
2	Has the patient lost weight within the last 3 months?		
3	Has the patient had a reduced dietary intake in the last week?		
4	Is the patient severely ill ? (e.g. in intensive therapy)		

Table 2 Final screening

Impaired nutritional status		**Severity of disease (≈ increase in requirements)**	
Absent **Score 0**	Normal nutritional status	Absent **Score 0**	Normal nutritional requirements
Mild **Score 1**	Wt loss > 5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild **Score 1**	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. *Chronic hemodialysis, diabetes, oncology*
Moderate **Score 2**	Wt loss > 5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week	Moderate **Score 2**	Major abdominal surgery* Stroke* *Severe pneumonia, hematologic malignancy*
Severe **Score 3**	Wt loss > 5% in 1 mth (> 15% in 3 mths) or BMI < 18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week in preceding week.	Severe **Score 3**	Head injury* Bone marrow transplantation* *Intensive care patients (APACHE > 10).*

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Kondrup J et al, Clinical Nutrition (2003)

NUTrition Risk in the Critically Ill Score (NUTRIC Score)

Variable	Range	Points
Age	<50	0
	50 to <75	1
	≥75	2
APACHE II	<15	0
	15 to <20	1
	20 to 28	2
	≥28	3
SOFA	<6	0
	6 to <10	1
	≥10	2
Number of comorbidities	0 to 1	0
	≥2	1
Days from hospital to ICU admission	0 to <1	0
	≥1	1
Sum of points	Category	
5–9	High score	
0–4	Low score	

A high score is associated with higher 28-day mortality and longer duration of mechanical ventilation

Heyland Critical Care 2011, 15:R28

Subjective Global Assessment

Most commonly used:
- ✓ Incorporate information on functional status
- ✓ and physical examination

- ❖ Well nourished
- ❖ Moderately malnourished
- ❖ Severely malnourished

Height:______ Admit weight:______ Body mass index:______

A. History

1. *Weight (wt) change:*
   In the past 2 weeks, weight has: increased/decreased/not changed
   Overall weight loss in the past 6 months: ________ kg: ________%.
2. *Change in dietary intake (relative to normal intake): circle*
   No change Borderline/poor Unable to eat
   If intake has decreased, for how long:___________weeks.
3. *Gastrointestinal symptoms (>2 weeks): circle all that apply*
   None Nausea Vomiting Diarrhea Anorexia
4. *Functional capacity: circle*
   No change Decreased activities of daily living Bed ridden
5. *Metabolic stress: circle*
   No stress Low/moderate stress High stress

B. Physical examination: check all that apply

_____Triceps and chest subcutaneous fat loss
_____Quadriceps and deltoid muscle wasting
_____Ankle edema
_____Sacral edema
_____Ascites

Nutritional Evaluation

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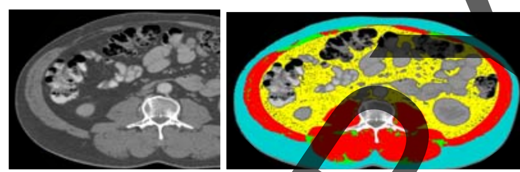
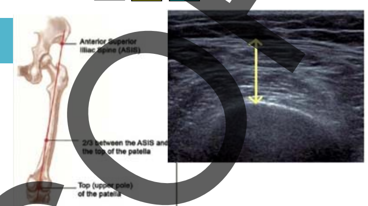
1) **CT Imaging Analysis**



2) **Quadriceps muscle layer thickness**



3) **Bioimpedance**

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Measuring Body Composition

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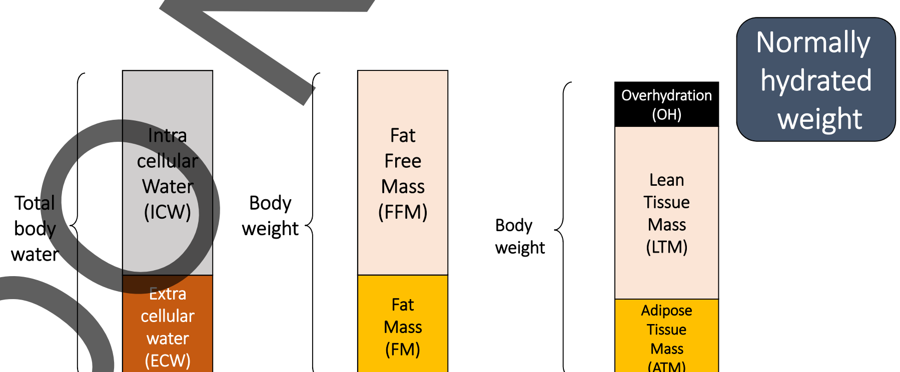
Bioimpedance



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Nutritional Assessment in AKI Limitations

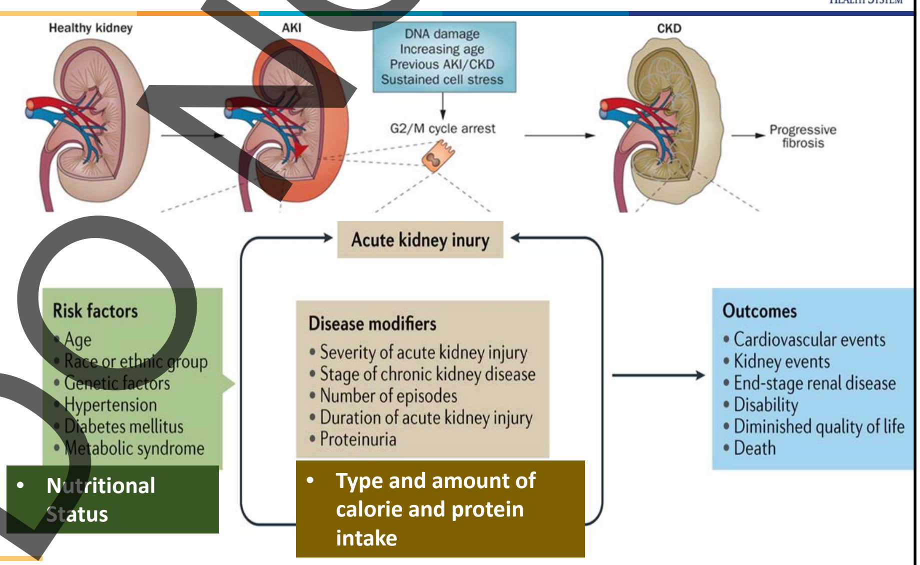
	Problems and limitations
Available bedside tools	
Albumin, prealbumin, cholesterol	May be low as negative markers of inflammation
Lymphocyte count	Lack of specificity
BW changes	Stable or increased BW due to fluid gain can mask lean body mass wasting
Muscle wasting by anthropometry	Less reliable if edema is present
PCR or protein equivalent of nitrogen appearance (PNA)	In patients on RRT must be calculated by urea kinetic methods or directly measured after dialysis fluid collection
Energy expenditure (EE)	Formulas for EE prediction not always reliable in critically ill patients
Nutritional scoring systems (SGA and its modifications)	Most available data in chronic renal failure patients
Potential tools or in development	
Laboratory markers	
Growth-hormone and IGF-1 levels	Few data available in AKI
Inflammatory markers (PCR, serum interleukine levels, etc.)	Lack of specificity
Body mass and composition	
Total body nitrogen	Research tools (cumbersome and/or costly and/or invasive)
Energy-beam-based methods	Research tools (cumbersome and/or costly and/or invasive)
Muscle fiber size and composition	Research tools (cumbersome and/or costly and/or invasive)
Bioimpedence analysis	No data in AKI
CT and/or MRI	No data in AKI

No single nutritional tool is sensitive or specific enough in AKI. Most parameters are influenced by non-nutritional factors: presence of an inflammatory status and fluid overload.

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach

Fiaccadori and Cremaschi, Current Opinion in Critical Care 2009

Factors that May Affect Renal Recovery



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Modified from Chawla, L. S. *et al.* ADQI 16 *Nat. Rev. Nephrol.* (2017)

Acute Kidney Injury: a springboard for progression in chronic kidney disease

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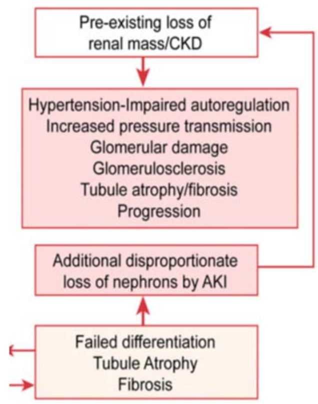

INCOMPLETE RECOVERY POST-AKI

Fibrosis and Maladaptive repair
Vascular drop out as a consequence of endothelial injury
Nephron loss followed by glomerular hypertrophy

REDUCED KIDNEY MASS

Hyperfiltration in remaining nephrons
Increase epithelial transport
Higher oxidative stress

TUBULAR INTERSTITIAL FIBROSIS

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Venkatachalam et al, J Am Soc Nephrol 26: 1765–1776, 2015

Experimental Studies

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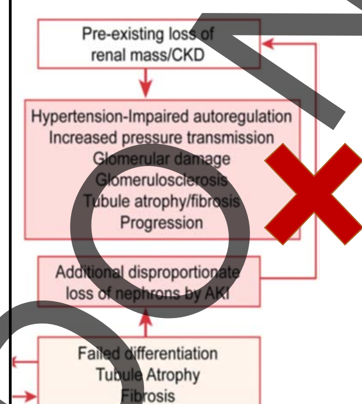

DIETARY PROTEIN RESTRICTION

REDUCE INTRA-GLOMERULAR PRESSURE

CHANGE CYTOKINE EXPRESSION

Reduce glomerular scarring
And matrix deposition

SLOW RATE OF RENAL FUNCTION DECLINE

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Venkatachalam et al, Am J Physiol Renal Physiol 298, 2010
Venkatachalam et al, J Am Soc Nephrol 26: 1765–1776, 2015

Metabolic acidosis may be also implicated in the association of diet and kidney disease progression

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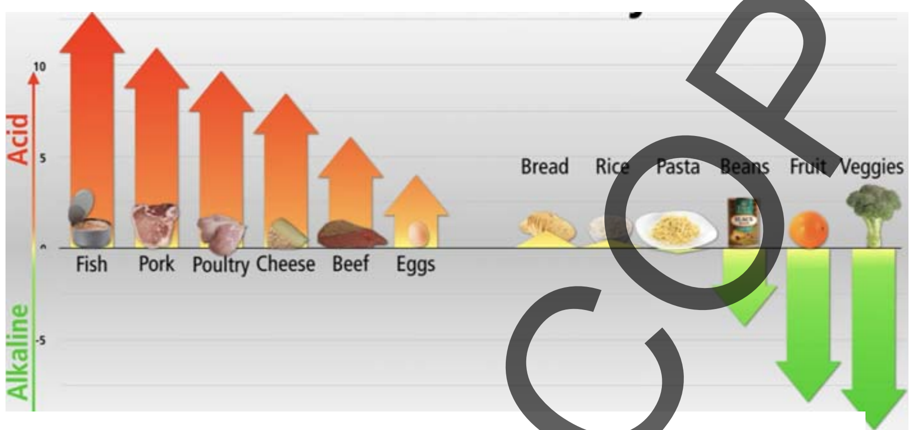
Acid-Load from Different Foods



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Metabolic Acidosis and Progression to Chronic Kidney Disease

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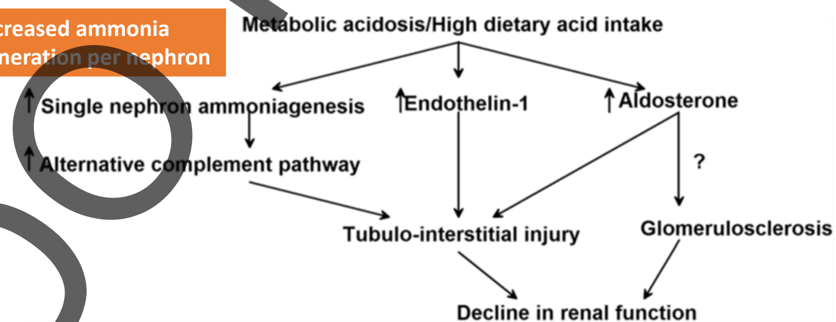
Dietary acid load, even in the absence of overt acidosis, may have deleterious effects

Increased ammonia generation per nephron



Chen and Abramowitz BMC Nephrology 2014, 15:55

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Dietary acid load and chronic kidney disease among adults in the United States

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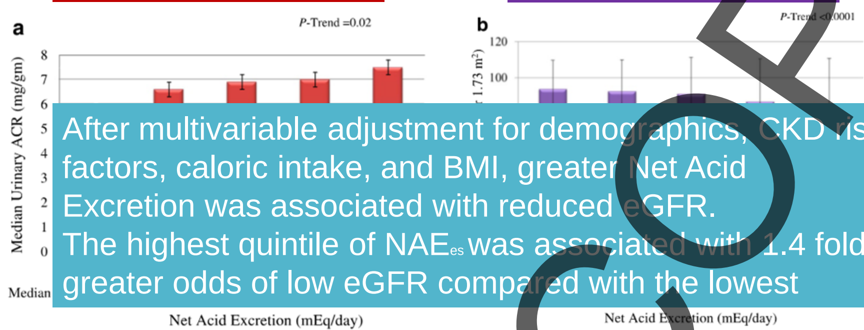
Study cohort (n=12293): cross-sectional analysis of adult participants of the National Health and Nutrition Examination Survey (NHANES) 4.

Albumin Cr Ration - ACR

eGFR



After multivariable adjustment for demographics, CKD risk factors, caloric intake, and BMI, greater Net Acid Excretion was associated with reduced eGFR.
The highest quintile of NAE_{es} was associated with 1.4 fold greater odds of low eGFR compared with the lowest

Higher Net Acid Excretion associated with higher Alb Cr Ratio and lower eGFR

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Banerjee et al. BMC Nephrology 2014, 15:137

Low Protein Diet in the Recovery Phase of AKI

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- Soon!

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Summary

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- Malnutrition is a frequent complication during and post AKI.
- Several factors contribute to the development of malnutrition, mainly the degree of inflammatory status and severity of comorbidities.
- Tools for the assessment of nutritional status need to be validated.
- The amount, type and timing of nutritional support is not defined during or post the AKI episode.
- The effect of nutrition in the recovery of renal function still needs to be established.

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Thank you

Nutritional and Dietary Management of Kidney Disease: A patient-Centered Approach