Need for specialized nutrition to prevent accelerated muscle loss in CKD

Prof. Daniel Teta
Head
Service of Nephrology
Hôpital du Valais, Sion

CHUV, Université de Lausanne

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Conflicts of interest, last 5 years

**Speaker fees:**
Abbott Nutrition, Fresenius Medical Care, B Braun, Roche, Amgen, Shire

**Research Grants/Research Financial Supports:**
Baxter/Gambro, B Braun, Fresenius Medical Care,

**Advisory Commitments:**
Abbott Nutrition, Nestlé, Otsuka
CKD Classification - K/DIGO 2012

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012


(red = very poor prognosis)
Incident dialysis patients in Europe: it grows old!

- Austria: 43% under 65, 57% 65 and over
- Belgium: 33% under 65, 67% 65 and over
- Bosnia and Herzegovina: 47% under 65, 53% 65 and over
- Denmark: 44% under 65, 56% 65 and over
- Estonia: 49% under 65, 51% 65 and over
- Finland: 49% under 65, 54% 65 and over
- France: 38% under 65, 62% 65 and over
- Greece: 32% under 65, 68% 65 and over
- Iceland: 44% under 65, 56% 65 and over
- Norway: 45% under 65, 55% 65 and over
- Romania: 41% under 65, 59% 65 and over
- Serbia: 41% under 65, 55% 65 and over
- Slovenia: 41% under 65, 59% 65 and over
- Spain: 44% under 65, 56% 65 and over
- Sweden: 44% under 65, 56% 65 and over
- The Netherlands: 44% under 65, 56% 65 and over
- United Kingdom: 49% under 65, 51% 65 and over

Protein-energy wasting (PEW) is prevalent in CKD

PEW is a state of depletion of body stores
• loss of body/adipose mass
• Loss of muscle mass
• Decline of nutrition biomarkers (e.g. albumin)
• Low energy/protein intake

Fouque D et al. on behalf of the ISRN M, Kidney Int 2008
Prevalence of malnutrition (PEW) in dialysis patients is very high

Accelerated loss of lean body mass in incident dialysis patients with diabetes

N = 142 incident ESRD patients
(91 males, 52.8 ± 1.0 years, 74.2 ± 1.2 kg body weight)
34 with diabetes mellitus
(19 insulin-dependent and 15 non insulin dependent).

Fig. 1. Scatter plots grouped by nondiabetic (non-DM) and diabetic (DM) patients, showing individual lean body mass (LBM) loss in kg during 1 year of renal replacement therapy.

Weight and muscle loss in chronic illness

Etiology and Consequences of Protein Energy Wasting in CKD

Carrero JJ et al on behalf of ISRNM; J Ren Nutr 2013
## Macronutrient requirements in dialysis patients

<table>
<thead>
<tr>
<th></th>
<th>ESPEN (1)</th>
<th>NKF (2)</th>
<th>EBPG (3)</th>
<th>ISRNM (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>Protein g/kg</em>/day</em>*</td>
<td>1.2 – 1.4</td>
<td>1.2</td>
<td>&gt; 1.1</td>
<td>&gt; 1.2</td>
</tr>
<tr>
<td>Prot of HBV 50%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em><em>Energy kcal/kg</em>/day</em>*</td>
<td>35</td>
<td>&lt; 60 y: 35</td>
<td>30-40</td>
<td>30-35</td>
</tr>
<tr>
<td>&lt; 60 y: 30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 60 y: 30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Kg per ideal weight

3 - Fouque D et al. EBPG. Nephrol Dial Transplant 2007
4 - Ikizler TA, Teta D et al. Kidney Int 2013
Recommendations from the PROT-AGE and ESPEN Expert Groups for the older

Bauer J et al. on the behalf of the PROT-AGE Group. J Am Dir Assoc 2013
Deutz NEP et al. Clin Nutr 2014; 33, 929-936;
Protein diets recommendations according to various CKD states

<table>
<thead>
<tr>
<th>Diet</th>
<th>CKD 3-4</th>
<th>Dialysis</th>
<th>Transplant*</th>
<th>Transplant</th>
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<tbody>
<tr>
<td>LPD</td>
<td>0.6-0.8</td>
<td>SPD</td>
<td>HPD</td>
<td>LPD</td>
</tr>
<tr>
<td>30-40</td>
<td>30-40</td>
<td>30-40</td>
<td>30-40</td>
<td>30-(40)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Energy (kcal/kg/d)</th>
<th>Diet Prot (g/kg/d)</th>
<th>Diet Prot (g/kg/d)</th>
<th>Diet Prot (g/kg/d)</th>
<th>Diet Prot (g/kg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. PEW</td>
<td>+</td>
<td>+++</td>
<td>++</td>
<td>+/-</td>
</tr>
<tr>
<td>2. Obese</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>
The older dialysis patient - drop in energy intakes

- 30-50% drops of energy intakes with aging (from 20 to 80 years-old)
- Predilection for energy-diluted foods such as grains, vegetables and fruits, in place of energy-dense and protein-rich nutrients

- Due to:
  - Anorexia
  - Lack of taste
  - Masticatory disability
  - Multiple medications
  - Depression
  - Loneliness
  - Dialysis as a stressor event
  - Frequent hospitalizations
Low physical activity: Steps number measured in 1133 HD patients


Very low active energy expenditure in the elderly HD
Energy expenditure in older dialysis patients

Energy expenditure may decrease in older dialysis patients due to:

- Lower resting energy expenditure (lower muscle mass)
- Lower active energy expenditure (sedentary behavior)

- 20% in elderly dialysis patients vs other patients

However, older dialysis patients may be subjected to more hospitalizations, inflammation, and thus hypermetabolism, which may counteract in part this lower energy expenditure
Older dialysis patients:
Mismatch – actual intakes/ energy requirements
Nutritional management of older CKD patients

- No specific studies looking at nutritional interventions in exclusively in only older CKD patients
- Nutritional interventional studies include many older CKD (mainly on dialysis) patients
- Prevention strategies > Treatment strategies
- Spontaneously lower intakes of energy, protein, calcium, phosphorus
- Spontaneously lower intakes of vitamins and micronutrients
- Protein intake recommendations differ according to CKD status
Prevention of PEW in dialysis patients: effect of renal specific oral supplements

- Randomised, controlled trial, n = 86
- 18 centres (16 France, 1 Germany, 1 Switzerland)
- Inclusion: patients at risk of malnutrition: prot intake (nPNA) < 1.0 g/kg/d, with no PEW

Outcomes:

- Nutritional – dietary intake, dry body weight, BMI, SGA,
- Biochemical – Alb, PreAlb, nPCR, Cr, P, Ca
- Clinical – SF-36, phosphate binder use

Oral supplements enabled HD patients to achieve recommended nutrient intakes

**Total Energy Intake (kcal/kg/d)**

* p < 0.05 between groups

- **Recommended Intake (KDOQI/EDTA)**
  - Baseline
  - Month 3
  - Month 3 - baseline

**Total Protein Intake (g/kg/d)**

- **Baseline**
- **Month 3**
- **Month 3 - baseline**

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Indicators of nutritional status

- **nPCR (g/kg/d)**
  - Baseline: 0.8
  - Month 1: 0.9
  - Month 2: 1.0
  - Month 3: 1.1
  - Renilon (Green line): 34, 34.5, 35, 35.5
  - Standard care (Pink line): 36
  - *p < 0.001

- **Se. Albumin (g/L)**
  - Baseline: 340
  - Month 1: 340
  - Month 2: 350
  - Month 3: 350
  - Renilon (Green line): 280, 290, 300, 310
  - Standard care (Pink line): 320
  - p = 0.06

- **Se. Pre-albumin (mg/L)**
  - Baseline: 60
  - Month 1: 60
  - Month 2: 65
  - Month 3: 65
  - Renilon (Green line): 320, 320, 320, 320
  - Standard care (Pink line): 250, 250, 250, 250
  - †p = 0.06

- **Dry body weight (kg)**
  - Baseline: 60
  - Month 1: 60
  - Month 2: 60
  - Month 3: 60
  - Renilon (Green line): 300, 300, 300, 300
  - Standard care (Pink line): 300, 300, 300, 300
In center provision of intradialytic meals

Rationale
1. In dialysis patients, energy, nutritional « gaps » between requirements and spontaneous intakes
   - gap of Energy: 5-10 kcal/kg/day
   - gap of Protein: 0.2-0.4 g/kg/day
2. Meals during HD may suppress HD-induced catabolic effect

Strategies to close the « nutritional gap »
• In center / intradialytic nutritional intakes

Kalantar Zadeh K, Ikizler TA. J Ren Nutr 2012
Protein metabolism during HD: effect of fasting vs fed state

Fig. 5. Summary of whole body protein breakdown (gray bars), synthesis (open bars), and protein balance (filled bars) under all experimental conditions. *Whole body protein balance significantly different from 0. +Whole body protein balance significantly different between fasting and feeding. #Whole body protein balance significantly different between the HD+ and HD− protocols.

Veeneman Am J Physiol 2003
Plasma aminoacid concentrations decline during a high flux HD session (4h)

The decline in plasma AA is sensed by the muscle cell. Muscle protein synthesis is blocked by a low extracellular AA concentration.

P Deléaval, D Teta, D Fouque et al, 2007
<table>
<thead>
<tr>
<th>Snack Description</th>
<th>Kcal</th>
<th>Prot (g)</th>
<th>Glu (g)</th>
<th>Phos (mg)</th>
<th>K (mg)</th>
<th>Na (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 tartines</td>
<td>360</td>
<td>8,6</td>
<td>60</td>
<td>110</td>
<td>140</td>
<td>550</td>
</tr>
<tr>
<td>Sandwich Ham</td>
<td>380</td>
<td>20</td>
<td>47</td>
<td>215</td>
<td>205</td>
<td>1175</td>
</tr>
<tr>
<td>Sandwich Cheese</td>
<td>490</td>
<td>21</td>
<td>47</td>
<td>380</td>
<td>170</td>
<td>830</td>
</tr>
<tr>
<td>15 g protein powder + 2 tartines</td>
<td>420</td>
<td>22</td>
<td>60</td>
<td>220</td>
<td>145</td>
<td>550</td>
</tr>
<tr>
<td>250 ml (2 x) Renilon 7,5</td>
<td>500</td>
<td>19</td>
<td>50</td>
<td>15</td>
<td>0,8</td>
<td>150</td>
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<tr>
<td>200 ml Resource 2,0 fibre</td>
<td>400</td>
<td>18</td>
<td>44</td>
<td>180</td>
<td>320</td>
<td>120</td>
</tr>
<tr>
<td>200 ml Fortimel</td>
<td>200</td>
<td>20</td>
<td>21</td>
<td>400</td>
<td>400</td>
<td>100</td>
</tr>
</tbody>
</table>
Exercise augments the acute anabolic effects of IDPN in HD patients

Resistance exercise may be more efficient than aerobic exercise to maintain lean body mass in CKD patients
Recommended intakes in micronutrients in dialysis patients: (addition necessary because of losses through dialysates)

**ESPEN 2000 (1)**
- Pyridoxin, mg: 10-15
- Vitamin C, mg: 30-60
- Folic Acid, mg: 1
- Vitamin D, IU: according to [Ca] & [PTH]
- Zinc, mg: 15
- Selenium, µg: 50-70

**EBPG 2007 (2)**
- Thiamine, Riboflavin, cobalaminie, Niacin, Biotine, pentothenic A & tocopherol should be supplemented (expert opinion)

Fouque D et al. EBPG. Nephrol Dial Transplant 2007
If PEW established, use of ONS in HD patients is efficient to treat PEW: summary of RCT

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Days</th>
<th>Nutritional significant effects</th>
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<tbody>
<tr>
<td>Acchiardo et al. (1982)</td>
<td>15</td>
<td>105</td>
<td>↑ albumin, transferrin, bone density</td>
</tr>
<tr>
<td>Allman et al. (1990)</td>
<td>21</td>
<td>180</td>
<td>↑ BW, lean body mass</td>
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<tr>
<td>Tietze et al. (1991)</td>
<td>19</td>
<td>120</td>
<td>↑ BW, arm muscle circumference</td>
</tr>
<tr>
<td>Eustace et al. (2000)</td>
<td>47</td>
<td>90</td>
<td>↑ albumin, grip strength, SF12 mental health</td>
</tr>
<tr>
<td>Hiroshige et al. (2001)</td>
<td>44</td>
<td>180</td>
<td>↑ DEI, DPI, fat mass, fat free mass, albumin</td>
</tr>
<tr>
<td>Sharma et al. (2002)</td>
<td>40</td>
<td>30</td>
<td>↑ albumin</td>
</tr>
<tr>
<td>Leon et al. (2006)</td>
<td>180</td>
<td>365</td>
<td>↑ DEI, DPI, albumin</td>
</tr>
<tr>
<td>Cano et al. (2007)</td>
<td>186</td>
<td>365</td>
<td>↑ nPNA, BMI, albumin, prealbumin</td>
</tr>
<tr>
<td>Fouque et al. (2008)</td>
<td>86</td>
<td>90</td>
<td>↑ DEI, DPI, SGA, QOL</td>
</tr>
<tr>
<td>Moretti et al. (2009)</td>
<td>49</td>
<td>365</td>
<td>↑ nPNA, albumin</td>
</tr>
</tbody>
</table>

Ikizler TA, Teta D et al. on the behalf of the ISRNM Kidney Int 2013
Correction of metabolic acidosis improves protein metabolism and plasma albumin in pre-dialysis patients.

<table>
<thead>
<tr>
<th>Sarcopenia and</th>
<th>Items</th>
<th>Review</th>
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<tbody>
<tr>
<td>Calories</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Energy</td>
<td>147</td>
<td>51</td>
</tr>
<tr>
<td>Protein</td>
<td>282</td>
<td>149</td>
</tr>
<tr>
<td>Amino acids</td>
<td>49</td>
<td>28</td>
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<tr>
<td>Creatine</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>n-3 fatty acids</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Exercise</td>
<td>249</td>
<td>142</td>
</tr>
<tr>
<td>Nutrition</td>
<td>147</td>
<td>42</td>
</tr>
</tbody>
</table>

Clinical effects of vitamin D on muscle, gait and falls in the elderly and in CKD


Prevention of muscle loss in older CKD patients

- Maintain energy requirements: 26-35 kcal/kg/day according to physical activity/clinical condition: individualization!
- Dialysis: High protein requirements: 1.2 - 1.5 g/kg/day
- Enriched-protein meals during dialysis
- If PEW established: ONS and/or IDPN are efficient
- Supplementation of micronutrients necessary
- Individualized prescription of electrolytes/calcium
- Correction of metabolic acidosis
- Non dialysis CKD: low protein diets (with enough calories)
- Other interventions (vitamine D – n-3 fatty acids) - low evidence
Thank you for your attention