KDOQI Nutrition in Chronic Kidney Disease Guideline Update: Webinar Series

Part 3: Dietary Protein Intake

Agenda

Introduction – Denis Fouque, MD, PhD, FNKF
Protein Energy Intake – Winnie Chan, PhD, RD, FNKF
Protein Type – Winnie Chan, PhD, RD, FNKF
Optimal Protein Intake – Denis Fouque, MD, PhD, FNKF
Conclusion – Denis Fouque, MD, PhD, FNKF
Q & A
Learning Objectives

• Interpret the guideline recommendations and supporting evidence related to dietary protein intake.
• Discuss implementation strategies for best clinical practices.

Disclosures

• Denis Fouque, MD, PhD, FNKF
  Chief, Division of Nephrology-Lyon Sud Hospital, University Claude Bernard, Lyon, France
  Board Member / Advisory Panel
  Fresenius Kabi, Vifor
• Consultant
  Lilly, Sanofi, Astellas
• Research Support
  Fresenius Medical Care
• Speaker’s Bureau
  Nothing to disclose
• Stock / Shareholder
  Nothing to disclose
Disclosures

Winnie Chan, PhD, RD, FNKF
Postdoctoral Research Fellow, University of Birmingham, UK

Board Member / Advisory Panel
National Institute for Health and Care Excellence

Consultant
Nothing to disclose

Research Support
Daphne Jackson Trust
Kidney Research UK

Speaker’s Bureau
Nothing to disclose

Stock / Shareholder
Nothing to disclose

Introduction
Denis Fouque, MD, PhD FNKF
**Nutrition Needs are High:**
PEW is present in 30 to 65% or more of dialysis patients around the world

- Hemodialysis patients, USA, 47% (MIS)
- Hemodialysis patients, Sweden: 30 to 43% (SGA)
- Hemodialysis patients, Netherlands: 28% (SGA)
- Peritoneal dialysis patients, China: 29 to 44% (SGA)
- Peritoneal dialysis patients, Korea: 40% (SGA)
- Peritoneal dialysis patients, Brazil: 36 to 65% (SGA)
- Peritoneal dialysis patients, China: 60% (MIS)

Adapted from TNT Renal

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**Protein intake and phosphate control in renal care: international variations in trends and practice**

Elizabeth Lindley, Maria Cruz Casal, Susan Rogers, Jitka Pancírová, Jennifer Kernc, J Brian Copley, Denis Fouque

1. Leeds Teaching Hospitals NHS Trust, Department of Renal Medicine, Leeds, United Kingdom.
2. Hospital Universitario 12 de Octubre, Department of Nephrology, Madrid, Spain.
3. Codia Waterland, Dialysis Department, Purmerend, the Netherlands.
4. EDTNA/ERCA, Secretariat and Conference Department, Prague, Czech Republic.
5. Shire Pharmaceuticals, Renal Division, Wayne PA, USA.
6. Shire Pharmaceuticals, Clinical Development and Medical Affairs, Wayne PA, USA.
7. Centre Hospitalier Lyon-Sud, Department of Nephrology, Lyon, France.

2012
Methods

- On-line questionnaire developed as part of a collaboration between EDTNA/ERCA and Shire Pharmaceuticals
- Renal care professionals responsible for providing dietary advice to patients in renal units in the Netherlands, Spain, Sweden and the UK completed the questionnaire in Sept–Oct 2012

Renal care professionals

Dietary counselling across countries

Percentage of responders (%)

- UK
- NL
- SW
- SP

- Nurses
- Dietitians
- Physician
Dietary protein intake recommendations

Pre-dialysis patients

Daily protein recommendation (g/kg/day)
- < 1.0
- 1
- 1.1
- 1.2
- 1.3
- > 1.3

Percentage of responders

UK
NL
SW
SP

Dietary protein intake recommendations

Clinical Practice Guideline for Chronic Kidney Disease
Academy of Nutrition and Dietetics and National Kidney Foundation
GRADE Methodology

Assigns separate grades for:
1) Evidence Quality
2) Strength of Recommendation

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
<th>Very low</th>
</tr>
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<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
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<thead>
<tr>
<th>Strength of recommendation</th>
<th>Level 1</th>
<th>Level 2</th>
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Guideline work group decision

Protein and Energy Intake
Winnie Chan, PhD, RD, FNKF
Etiology & Clinical Implications of Protein-Energy Wasting in Chronic Kidney Disease (*Adapted from Chapter 17, Nutrition in Kidney Disease)

Protein-Energy Wasting

- Dietary Restrictions
  - Anorexia
    - ↓ Appetite
    - ↓ Food Intake
  - Peritoneal Dialysis-related Factors
    - Early Satiation with Peritoneal Dialysate Infusion
    - Peritoneal Glucose Absorption
    - Abdominal Discomfort
  - Metabolic & Endocrine Derangements
    - Hyperparathyroidism
    - Hypothyroidism
    - Hypogonadism
    - Growth Hormone Resistance
    - Diabetes / Insulin Resistance
  - Nutrient Losses into Dialysate
  - Metabolic & Endocrine Derangements
  - Inadequate Dialysis
  - Uremic Toxins
  - Loss of Residual Renal Function
  - Metabolic Acidosis
  - Physical Inactivity
  - Nutrient Losses into Dialysate
  - Dialysis Procedure
    - Dialysis-related Hypermetabolism
    - Dialysis-related Inflammation
  - Chronic Low Grade Inflammation
  - Intercurrent Illnesses
  - Metabolic Acidosis
  - Loss of Residual Renal Function
  - Inadequate Dialysis
  - Uremic Toxins

Infection
- Cardiovascular Disease
- Frailty
- Depression

Dietary Intakes of Protein and Energy

- Physical Inactivity
- Nutrient Losses into Dialysate
- Dialysis Procedure
  - Dialysis-related Hypermetabolism
  - Dialysis-related Inflammation
- Chronic Low Grade Inflammation
- Intercurrent Illnesses
- Metabolic Acidosis
- Loss of Residual Renal Function
- Inadequate Dialysis
- Uremic Toxins

Socioeconomic, Psychological & Functional Status
- Low Socioeconomic Status
- Impaired Physical Function
- Depression

Gastrointestinal Abnormalities driven by Comorbid Illnesses

Nutrient Losses into Dialysate

- Metabolic & Endocrine Derangements
  - Hyperparathyroidism
  - Hypothyroidism
  - Hypogonadism
  - Growth Hormone Resistance
  - Diabetes / Insulin Resistance

↓ Dietary Intakes of Protein and Energy

Protein and Energy Intake Recommendations

- Dietary protein intake in maintenance hemodialysis
- Dietary protein intake in peritoneal dialysis
- Energy intake in CKD and post-transplantation
- Protein type

### Intervention Recommendations:
**Dietary Protein Intake in Maintenance Hemodialysis (MHD)**

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<tr>
<td><strong>Dietary Protein Intake in MHD</strong></td>
<td><strong>Dietary Protein Intake in MHD Patients without Diabetes</strong></td>
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</tr>
<tr>
<td>❑ The recommended dietary protein intake for <strong>clinically stable MHD patients</strong> is <strong>1.2 g/kg BW/day</strong> (EVIDENCE &amp; OPINION).</td>
<td>❑ In adults with <strong>CKD 5D on MHD</strong> (1C) or <strong>PD</strong> (OPINION) who are <strong>metabolically stable</strong>, we recommend prescribing a dietary protein intake of <strong>1.0-1.2 g/kg BW/day</strong> to maintain a stable nutritional status.</td>
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<td>❑ At least 50% of the dietary protein should be of high biological value.</td>
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<tr>
<td><strong>N/A</strong></td>
<td><strong>Dietary Protein Intake in MHD Patients with Diabetes</strong></td>
<td>NEW</td>
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<td>❑ In adults with <strong>CKD 5D and who have diabetes</strong>, it is reasonable to prescribe a dietary protein intake of <strong>1.0-1.2 g/kg BW/day</strong> to maintain a stable nutritional status. For patients at risk of hyper- and/or hypoglycemia, higher levels of dietary protein intake may need to be considered to maintain glycemic control (OPINION).</td>
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### Supporting Evidence:
**Dietary Protein Intake Recommendations for MHD Patients**

- **Literature Search**
  - Different levels of protein intakes in patients undergoing MHD
  - No RCTs
  - No Clinical Controlled Studies

- **Recommendation Statement**
  - **Large Cohort Studies**
    - Not designed to investigate protein requirements
    - Contained information on dietary protein intake in pre-existing databases
Summary of Studies Examining Dietary Protein Intake in MHD

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Study Design</th>
<th>Protein Intake Estimation</th>
<th>Relevant Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Mutsert et al.</td>
<td>455</td>
<td>Prospective</td>
<td>nPNA</td>
<td>▪ No relationship between protein intake and mortality after adjustment for inflammation</td>
</tr>
<tr>
<td>Rambod et al.</td>
<td>798</td>
<td>Prospective</td>
<td>nPNA and food diary</td>
<td>▪ ↑ Pre-albumin with mean protein intake = 1.16 g/kg/day</td>
</tr>
<tr>
<td>Segall et al.</td>
<td>149</td>
<td>Prospective</td>
<td>nPNA</td>
<td>▪ ↓ Mortality with protein intake ≥1.2 g/kg/day</td>
</tr>
<tr>
<td>Stojanovic et al.</td>
<td>197</td>
<td>Prospective</td>
<td>nPNA</td>
<td>▪ ↑ SGA score with protein intake = 1.15 g/kg/day</td>
</tr>
<tr>
<td>Araujo et al.</td>
<td>344</td>
<td>Retrospective</td>
<td>3-day food diary</td>
<td>▪ ↑ Survival with protein intake = 1.01 g/kg/day</td>
</tr>
<tr>
<td>Beddu et al.</td>
<td>5059</td>
<td>Retrospective</td>
<td>Urea clearance</td>
<td>▪ ↓ Risk of albumin &lt;33 g/L if protein intake = 1.0 g/kg/day</td>
</tr>
<tr>
<td>Shinaberger et al.</td>
<td>53,933</td>
<td>Retrospective</td>
<td>nPNA</td>
<td>▪ ↑ Mortality with protein intake &lt;0.8 and &gt;1.4 g/kg/day</td>
</tr>
<tr>
<td>Bossola et al.</td>
<td>37</td>
<td>Cross-sectional</td>
<td>3-day food diary</td>
<td>▪ ↑ Albumin with protein intake ≥1.2 g/kg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>▪ ↑ BMI with protein intake ≥1.2 g/kg/day</td>
</tr>
</tbody>
</table>

Consistency in Studies Examining Dietary Protein Intake in MHD

**Most Evidence**
- Protein intake >1.0 g/kg/day
  - Improvements in nutritional markers and survival

**Limited Evidence**
- Protein intake ≥1.2 g/kg/day
  - Improvements in nutritional markers and mortality

**Limited Evidence**
- Protein intake >1.4 g/kg/day
  - Higher mortality
# Intervention Recommendations:
Dietary Protein Intake in Maintenance Hemodialysis (MHD)

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<tbody>
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<td><strong>Dietary Protein Intake in MHD Patients without Diabetes</strong></td>
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</tr>
<tr>
<td>❑ The recommended dietary protein intake for clinically stable MHD patients is 1.2 g/kg BW/day <em>(EVIDENCE &amp; OPINION)</em>.</td>
<td>❑ In adults with CKD 5D on MHD <em>(1C)</em> or PD <em>(OPINION)</em> who are metabolically stable, we recommend prescribing a dietary protein intake of 1.0-1.2 g/kg BW/day to maintain a stable nutritional status.</td>
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<td>❑ At least 50% of the dietary protein should be of high biological value.</td>
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<td><strong>Dietary Protein Intake in MHD Patients with Diabetes</strong></td>
<td>NEW</td>
</tr>
<tr>
<td>❑ In adults with CKD 5D and who have diabetes, it is reasonable to prescribe a dietary protein intake of 1.0-1.2 g/kg BW/day to maintain a stable nutritional status. For patients at risk of hyper- and/or hypoglycemia, higher levels of dietary protein intake may need to be considered to maintain glycemic control <em>(OPINION)</em>.</td>
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# Intervention Recommendations:
Dietary Protein Intake in Peritoneal Dialysis (PD)

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<thead>
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<tbody>
<tr>
<td><strong>Dietary Protein Intake for Chronic Peritoneal Dialysis (CPD)</strong></td>
<td><strong>Dietary Protein Intake in PD Patients without Diabetes</strong></td>
<td>UPDATED</td>
</tr>
<tr>
<td>❑ The recommended dietary protein intake for <em>clinically stable CPD patients</em> is 1.2 – 1.3 g/kg BW/day <em>(EVIDENCE)</em>.</td>
<td>❑ In adults with CKD 5D on MHD <em>(1C)</em> or PD <em>(OPINION)</em> who are metabolically stable, we recommend prescribing a dietary protein intake of 1.0 – 1.2 g/kg BW/day to maintain a stable nutritional status.</td>
<td></td>
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<td>❑ Dietary protein intake should be no less than 1.2 g/kg BW/day.</td>
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<td>❑ Unless a patient has demonstrated adequate protein nutritional status on a 1.2 g protein/kg BW/day diet, 1.3 g protein/kg BW/day should be prescribed.</td>
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<td><strong>Dietary Protein Intake in PD Patients with Diabetes</strong></td>
<td>NEW</td>
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<tr>
<td>❑ In adults with CKD 5D and who have diabetes, it is reasonable to prescribe a dietary protein intake of 1.0 – 1.2 g/kg BW/day to maintain a stable nutritional status. For patients at risk of hyper- and/or hypoglycemia, higher levels of dietary protein intake may need to be considered to maintain glycemic control <em>(OPINION)</em>.</td>
<td></td>
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</tr>
</tbody>
</table>
Supporting Evidence:
Dietary Protein Intake Recommendations for PD Patients

Literature Search

Different levels of protein intakes in patients undergoing PD

No RCTs
No Clinical Controlled Studies

MET INCLUSION CRITERIA

Recommendation Statement

RCTs
Cohort Studies
Cross-sectional Study

Summary of Studies Examining Dietary Protein Intake in PD

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Study Design</th>
<th>Intervention / Protein Intake Estimation</th>
<th>Duration (month)</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al (2008)</td>
<td>89</td>
<td>RCT</td>
<td>1.2 vs 0.8 g protein/kg/day</td>
<td>12</td>
<td>• ↑ Pre-albumin with protein intake of 1.2 g/kg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.3-1.5 g protein/kg/day vs nutrition counseling</td>
<td>6</td>
<td>• No significant differences in TSF and MAMA (exceeded target protein intake)</td>
</tr>
<tr>
<td>Jiang et al (2009)</td>
<td>60</td>
<td>RCT</td>
<td>1.0-1.2 vs 0.6-0.8 g protein/kg/day</td>
<td>12</td>
<td>• No significant differences in albumin, LBM and BMI (target protein intake unmet)</td>
</tr>
<tr>
<td>Sutton et al (2007)</td>
<td>49</td>
<td>RCT</td>
<td>&lt;0.8-1.0 vs 1.2 g protein/kg/day</td>
<td>4</td>
<td>• No significant differences in body weight, BMI, MAC, and SGA (target protein intake unmet)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>1.2 vs 0.9 vs 0.6 g protein/kg/day</td>
<td>&lt;1</td>
<td>• Positive nitrogen balance with protein intake of 1.2 g/kg/day</td>
</tr>
<tr>
<td>Chung et al (2000)</td>
<td>100</td>
<td>Prospective</td>
<td>nPNA</td>
<td>24</td>
<td>• ↑ Survival with protein intake of 1.0 g/kg/day</td>
</tr>
<tr>
<td>Martin-del Campo et al (2009)</td>
<td>29</td>
<td>Prospective</td>
<td>24-hour dietary recall</td>
<td>6</td>
<td>• ↑ BMI, TSF and MMC with protein intake of 1.0 g/kg/day</td>
</tr>
<tr>
<td>Wang et al (2007)</td>
<td>249</td>
<td>Cross-sectional</td>
<td>7-day food frequency questionnaire</td>
<td>-</td>
<td>• ↑ SGA score with protein intake of 1.17 g/kg/day</td>
</tr>
</tbody>
</table>
### Intervention Recommendations:
#### Dietary Protein Intake in Peritoneal Dialysis (PD)

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<tr>
<td>- The recommended dietary protein intake for clinically stable CPD patients is 1.2 – 1.3 g/kg BW/day (EVIDENCE).</td>
<td>- In adults with CKD 5D on MHD (1C) or PD (OPINION) who are metabolically stable, we recommend prescribing a dietary protein intake of 1.0 – 1.2 g/kg BW/day to maintain a stable nutritional status.</td>
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</table>

**N/A**

### Intervention Recommendations:
#### Energy Intake in CKD

<table>
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</thead>
<tbody>
<tr>
<td><strong>Energy Intake for Nondialyzed and Maintenance Dialysis Patients</strong></td>
<td><strong>Energy Intake in CKD</strong></td>
<td>UPDATED</td>
</tr>
<tr>
<td>- The recommended dietary energy intake for individuals with chronic renal failure (GRF &lt;25 mL/min) who are not undergoing maintenance dialysis is 35 kcal/kg BW/day for those who are younger than 60 years old and 30 – 35 kcal/kg BW/day for individuals who are 60 years of age or older (EVIDENCE &amp; OPINION).</td>
<td>- In adults with CKD 1-5D (1C) and posttransplantation (OPINION) who are metabolically stable, we recommend prescribing an energy intake of 25 – 35 kcal/kg BW/day based on age, sex, level of physical activity, body composition, weight status goals, CKD stage, and concurrent illness or presence of inflammation to maintain normal nutritional status.</td>
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<tr>
<td>- The recommended daily energy intake for maintenance hemodialysis and chronic peritoneal dialysis patients is 35 kcal/kg BW/day for those who are less than 60 years of age and 30 – 35 kcal/kg BW/day for individuals 60 years or older (EVIDENCE &amp; OPINION).</td>
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</tbody>
</table>
**Supporting Evidence:**
Energy Intake Recommendations for CKD Patients

- **Non-dialysis-dependent CKD**
  - 10 Controlled Trials
  - 30 – 35 kcal/kg BW/day

- **Hemodialysis**
  - 3 Controlled Trials

Maintain Neutral Nitrogen Balance
Maintain Nutritional Status

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**Supporting Evidence:**
Energy Intake Recommendations for CKD Patients

**Metabolic Study (n = 6)**
- 35 kcal/kg BW/day
  - Maintain neutral nitrogen balance
  - Maintain body composition

**Metabolic Study (n = 6)**
- 38 kcal/kg BW/day
  - Maintain neutral nitrogen balance

---

**Effect of energy intake on nutritional status in maintenance hemodialysis patients**

Larry A. Slomowitz, Francisco J. Monteon, Mary Grosvenor, Steward A. LaDlaw, and Joel D. Koppol.
Supporting Evidence:
Energy Intake Recommendations for CKD Patients

Dietary energy requirements in relatively healthy maintenance hemodialysis patients estimated from long-term metabolic studies

Key Findings:
- Average dietary energy requirement = $31 \pm 3$ kcal/kg/day
- Dietary energy requirement in MHD patients is comparable to adults of similar age, sex and physical activity level
- Clinically stable MHD patients do not have raised dietary energy requirements
- Wide variability in dietary energy requirement (range 26-36 kcal/kg/day)

Intervention Recommendations:
Energy Intake in CKD

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<td></td>
<td>UPDATED</td>
</tr>
</tbody>
</table>
### Implementation Considerations:
**Determination of Body Weight for Protein & Energy Recommendations**

<table>
<thead>
<tr>
<th>Choice of Body Weight (BW)</th>
<th>Method of Assessment (Weight Formula)</th>
</tr>
</thead>
<tbody>
<tr>
<td>*<em>Ideal BW (Hamwi Method</em>)**&lt;br&gt;Hamwi 1964</td>
<td>Women: 100 lb for first 5’0” and add 5 lb for each additional inch &gt; 5’0”&lt;br&gt;Men: 106 lb for first 5’0” and add 6 lb for each additional inch &gt; 5’0”</td>
</tr>
<tr>
<td><strong>Standard BW</strong>&lt;br&gt;KDOQI 2000</td>
<td>Average 50th percentile weights for men and women by age, height, and frame size (Based on NHANES II)</td>
</tr>
<tr>
<td><strong>Desirable BW</strong>&lt;br&gt;Kopple et al 1999</td>
<td>Based on BMI</td>
</tr>
<tr>
<td><strong>Adjusted BW</strong>&lt;br&gt;Karkeck 1984</td>
<td>Adjusted BW = Ideal BW + [(Actual BW – Ideal BW)] x 0.25&lt;br&gt;Adjusted BW should be used if patient’s weight is &lt; 95% or &gt; 115% of Ideal or Standard BW</td>
</tr>
<tr>
<td><strong>Edema-free BW</strong>&lt;br&gt;McCann 2015</td>
<td>Analogous to estimated dry weight in patients undergoing renal replacement therapies</td>
</tr>
<tr>
<td><strong>Percent of Usual BW</strong>&lt;br&gt;Bylam-Gray 2013</td>
<td>Percent Usual BW = [(Usual BW – Current BW)/Usual BW] x 100</td>
</tr>
</tbody>
</table>

*Can subtract 10% for small frame and add 10% for large frame

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### Implementation Considerations:
**Metabolic Status**

**Metabolically Stable Patients**

- Active Inflammation
- Active Infectious Diseases
- Hospitalization within 2 Weeks
- Poorly-controlled Diabetes

- Consumptive Diseases (e.g. Cancer)
- Significant Short-term Weight Loss
- Antibiotic Medications
- Immunosuppressive Medications
Implementation Considerations: Protein and Energy Intake in CKD

Protein intake should not be considered in isolation from energy intake.

Sufficient energy intake is required to support optimal metabolic balance.

Implementation Considerations: Energy Intake in CKD

Stage 5 CKD (Dialysis)
Chronic Inflammation
Infection
Other Intercurrent Illnesses
Hyperparathyroidism
Hyperglycemia
Treatment Goals
Metabolic Stressors
Stage of CKD or Type of Renal Replacement Therapy
Overall Health Status / Health Goals
Acutely vs Chronically Ill
Sex
Age
Physical Activity Level
Weight Status (Maintenance, Repletion, or Loss)
Implementation Considerations: Energy Intake in CKD

Patients’ Overall Metabolic State & Comorbid Conditions

Recommended Range Energy Intake: Personalized to Each Patient

Routine Monitoring and Evaluation
Are energy requirements being met?
Are there any changes in nutritional status?

Adjustment of Dietary Energy Intake Recommendation
Dietary energy intake recommendation may need to be modified accordingly

Protein Type: Plant vs Animal
Winnie Chan, PhD, RD, FNKF
Traditional Concerns of Plant-based vs Animal-based Proteins

➢ Protein and amino acid deficiencies with plant-based proteins precluded the use in CKD

➢ Recommendations persist regarding the use of “high-biological value” protein (i.e., animal-based proteins) in CKD

➢ Animal-based proteins may contribute to common medical problems in CKD:
  - Hypertension
  - Metabolic Acidosis
  - Hyperphosphatemia

Protein Quantity and Quality of Plant-based Protein Diet

**Protein Quantity**  
Meets EAR and RDA  
Avoids protein overload  
Allows adjustment to meet requirements

**Protein Quality**  
More than adequate in a balanced diet

*Adapted from Joshi S et al., Adequacy of Plant-Based Proteins in Chronic Kidney Disease. Journal of Renal Nutrition. 2020; 29(2): 112-17
Potential Effects of Plant-based Protein Diet in CKD

- ↓ Expression of Renin-Angiotensin
  - ↓ Hypertension
- ↓ FGF-23
  - ↓ Hyperphosphatemia
- ↓ Dietary Acid Load
  - ↓ Metabolic Acidosis
- ↑ Potassium (?)

Diabetes
- Improves Glycemic Control
  - ↓ Body Weight

Heart Disease
- Improves Blood Lipid Profile

Plant-based Protein Diet

- ↓ Proteinuria
  - ↓ eGFR Decline
- ↓ Uremic Toxins

↓ Proteinuria
↓ eGFR Decline

Delays CKD Progression

Improves Gut Microbiome

↑ SCFA
- Strengthen Intestinal Barrier
  - ↓ Bacterial Translocation
  - ↓ Inflammation
  - ↑ Overall Immunity

*Adapted from Joshi S et al., Adequacy of Plant-Based Proteins in Chronic Kidney Disease. Journal of Renal Nutrition. 2020; 29(2): 112-17

Health Benefits of Plant-based Protein Diet in CKD

- Diabetes
  - Improves Glycemic Control
    - ↓ Body Weight

- Heart Disease
  - Improves Blood Lipid Profile

- ↑ Potassium (?)

Analysis of Retrospective Data from The National Health and Nutrition Examination Survey III (n = 14,866)

Higher ratio of plant to total protein was associated with lower risk of mortality among adults with eGFR <60 mL/min/1.73m²
# Potential Health Benefits of Plant-based Protein Diet in CKD

**Analysis of Prospective Observational Northern Manhattan Study (n = 900)**

*Plant-based diets were associated with 12% lower risk of decline in eGFR compared with meat-based diets.*

## Intervention Recommendations: Protein Type

<table>
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<tr>
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<tbody>
<tr>
<td>N/A</td>
<td>Protein Type</td>
<td>NEW</td>
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- In adults with **CKD 1-5D (18)** or **posttransplantation (OPINION)**, there is **insufficient evidence** to recommend a particular protein type (plant vs animal) in terms of the effects on nutritional status, calcium or phosphorus levels, or the blood lipid profile.
Supporting Evidence: Protein Type Recommendation for CKD Patients

Literature Search

The impact of plant-based protein vs animal-based protein intake on nutritional biomarkers and health outcomes

3 RCTs (CKD stage 5D)

2 Randomized Crossover Trials (Stages 3-4 CKD)

Systematic Review and Pooled Analysis

Effect of Protein Type in CKD

Study Comparisons:
Duration = 1 week to 6 months
n = 9 to 40

1] Plant-based Protein Diet vs Animal-based Protein Diet
2] Plant-based Protein Diet vs Pre-study Diet (Usual Diet)
3] Animal-based Protein Diet vs Pre-study Diet (Usual Diet)
3] Plant-based Protein Diet vs Control Group

Pre-albumin
1 study

Serum Albumin
4 studies

Lipid Profile
(TC, TG, LDL-C, HDL-C)
3 studies

Inflammatory Markers
(CRP, IL-6, TNF-α)
1 study

Serum, Plasma, and Urinary Calcium Levels
2 studies

Serum and Plasma Phosphate Levels
2 studies
Effect of Protein Type in CKD

Randomized Cross-over Trial:
- n = 15
- Duration = 6 months
- Measurements: Nutritional & Clinical Parameters

Comparisons between:
- Plant-based Protein Diet vs
  1) Animal-based Protein Diet
  2) Pre-study Diet

↓ Protein Catabolic Rate and ↓ Urinary Phosphate Excretion in Plant-based Protein Diet, compared to:
1) Animal-based Protein Diet Group
2) Pre-study Diet

Limitations of Current Literature
Protein Type

- Insufficient Power due to Small Sample Size
- Limitations
- Current Evidence from RCTs is Limited
- Insufficient Intervention Intensity and Duration
### Intervention Recommendations:
**Protein Type**

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- In adults with CKD 1-5D (1B) or posttransplantation (OPINION), there is [insufficient evidence](#) to recommend a particular protein type (plant vs animal) in terms of the effects on nutritional status, calcium or phosphorus levels, or the blood lipid profile.

### Future Research:
**Protein Type**

**Future Research:**
**Effects of Plant-based Protein Diet**

- Adequately Powered RCTs in CKD
  - **Endpoints:**
    - Mortality
    - CKD Progression
    - Proteinuria
    - Markers of Mineral & Bone Metabolism
    - Urinary Phosphate Excretion
    - Lipid Profile (Hyperlipidemic CKD Patients)

- **Mechanistic Studies**
  - Generation of Protein-bound Uremic Toxins and Related Metabolites:
    - P-cresyl Sulfate
    - Indoxyl Sulfate
    - Trimethylamine Oxide
Implementation Considerations:
Protein Type

Animal-based Protein Diet or Plant-based Protein Diet:

➢ Work with patients to meet individualized dietary protein and energy requirements

➢ Ensure diets provide adequate essential amino acids

➢ Monitor adherence to diets:
  1] Use of 3-Day Food Diary
  2] Regularly during first year of intervention
  3] Annually until start of maintenance dialysis
  4] Frequency of monitoring after initiation of dialysis depends on results of nutritional assessment

Optimal Protein Intake
Denis Fouque, MD
The heavy responsibility of protein intake

**Protein intake and kidney function**

**1980s**

Only since the eighties: the mechanic hypothesis

- Hyperfiltration =
  - proteinuria
  - tubular inflammation

- glomerulosclerosis
- interstitial fibrosis
- Kidney failure

*N Engl J Med November 2nd, 2017*
**Protein intake and kidney function**

**the toxicity hypothesis**

**2010s**

*Fig. 6 A schematic model of the generation and toxicity of PS. In gut microbiota, TPL coverts tyrosine to phenol and ammonia. PS is also generated in the liver. PS accumulates in plasma as a metabolite and has deleterious effects on the vasculature and kidneys. In diabetic kidney disease, PS damages podocytes, accelerates GBM thickening, and induces proteinuria. Treatment with TPL inhibitors reduces plasma PS levels and prevents the progression of renal failure in animal models.***

Kikuchi et al, Nature Comm 2019

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**PROTEIN METABOLISM**

*Fig. 7, Han et al., The International Journal of Biochemistry & Cell Biology xxx (2013) xxx–xxx*

**Intake**
- 80 g protein
- 40 g protein

**Urine output**
- 400 mmol urea
- 200 mmol urea
- 20 mmol urea

**Blood**
- 12 mmol urea

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NATIONAL KIDNEY FOUNDATION. Academy of Nutrition and Dietetics
Nutritional safety

Forearm muscle phenylalanine kinetics in CKD patients


The new 2020 guideline
Protein Recommendations 1

Protein Restriction, Non-Dialysis, Non-Diabetic
In adults with CKD 3-5 who are metabolically stable, we recommend, under close clinical supervision, protein restriction with or without keto acid analogs, to reduce risk for ESRD/death (1A) and improve QoL (2C).
- a low protein diet providing 0.55 to 0.60 g dietary protein/kg ideal body weight/day, OR
- a very-low protein diet providing 0.28 to 0.43 g dietary protein/kg ideal body weight/day with additional keto acid/amino acid analogs to meet protein requirements (0.55 to 0.60 g/kg body weight/day)

Protein Restriction, Non-Dialysis, Diabetic
In the adult with CKD 3-5 and who have diabetes, it is reasonable to prescribe, under close clinical supervision, a dietary protein intake of 0.6 - 0.8 g/kg ideal body weight per day to maintain a stable nutritional status and optimize glycemic control (OPINION).

Case report
A patient’s perspective (1)

### Nutritional Status and Dietary intake

<table>
<thead>
<tr>
<th>Month</th>
<th>Weight (Kg)</th>
<th>BMI (Kg/m²)</th>
<th>Ketosteril (pill/d)</th>
<th>Protein intake (g/Kg/d)</th>
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**A patient’s perspective (2)**

### CKD - MBD Status

<table>
<thead>
<tr>
<th>Month</th>
<th>Calcium (mg/dl)</th>
<th>PTH (pg/ml)</th>
<th>Phosphate (mg/l)</th>
<th>Bicarbonates (mmol/l)</th>
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<table>
<thead>
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<td>UN ALFA 0.25 (1 pill/d) + UVEDOSE 100.000 UI (1 ampole every 2 months)</td>
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<td>FEB/2016</td>
<td>PHOSPHOSORB (6 pills/d)</td>
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A patient’s perspective (3)

Recent research
**Nephrotest Paris: Start of dialysis**

1412 patients CKD st 3, follow-up 3.5 yr

*Metzger et al, KI reports 2018*

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**Cochrane systematic review and meta-analysis**

**Start of dialysis**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Very low protein diet</th>
<th>Low-normal protein diet</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
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<td>Events</td>
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<td>MDRD 2 1989</td>
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<tr>
<td>ESCCMCRF 2 1990</td>
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**Total (95% CI)**

<table>
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<tr>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>508</td>
<td>502</td>
<td>100.0%</td>
<td>0.64 [0.49, 0.85]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.09; Chi² = 20.27, df = 9 (P = 0.02); P = 56%
Test for overall effect: Z = 3.10 (P = 0.002)
Test for subgroup differences: Not applicable

158 less with VLP diet

230 less with low-normal diet

-36%

*Hahn et al, Cochrane Database Syst Rev Nov 2020*
A prospective study on total protein, plant protein and animal protein in relation to the risk of incident chronic kidney disease

Sevda Alvirdizadeh, Emad Yuzbashian, Parvin Mirmiran, Shahryar Eghtesadi and Fereidoun Azizi

Conclusion: The results of this study confirmed an inverse association between plant protein intake and the risk of incident CKD, which demonstrates the protective role of plant-based protein in a diet on kidney function.

Alvirdizadeh et al. BMC Nephrology (2020) 21:489

Stay away from this shelf...
Remember that the strongest animals on earth are vegan

Propose a progressive personalized care

- Progressively decrease by 0.2 g/kg/d with the help of 3 dietary encounters
- Coach and measure compliance to reach the prescribed target

Wang et al, Semin Nephrol 2018;4:383
How to implement a guideline

Convincing data
Convince teachers
Convince doctors
Convince dietitians
Convince patients
Convince funding bodies
Conclusion: a precision medicine approach

Thank you!
Questions?