Proteins In Clinical Nutrition

QUANTITATIVE NEEDS IN CLINICAL SITUATIONS

T. Rice (US)
Proteins in Clinical Nutrition: Quantitative Needs in Clinical Situations

Todd W Rice, MD, MSc
Associate Professor of Medicine
Vanderbilt University School of Medicine

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Disclosures

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- Cumberland Pharmaceutical, Inc – Director of Medical Affairs
Objectives

• Review data on protein delivery in critically ill patients

• Overview of guidelines for protein delivery in select subpopulations
Proteins: General

• Highly catabolic states result in significant proteolysis
  – Critical illness, cancer, end organ failure (ESRD, cirrhosis)

• Higher protein intake alone may not overcome proteolysis
  – ? Role of resistance exercise
Proteins in Critical Illness
Understanding of Proteins in Critical Illness
Proteins: Critical Illness

• Protein important for:
  – healing wounds
  – immune function
  – maintaining muscle / lean body mass

• Critical Illness = Hypercatabolic state

• Protein requirements >> Energy (kcal) requirements

• Most enteral formulas have high non-protein cal : nitrogen

• May need to use protein supplements
Acute Skeletal Muscle Wasting in Critical Illness

Change in rectus femoris (RF) cross-sectional area (CSA) over 10 d

Time From Admission, d

Percentage Change in CSA

No. of patients

62

57

60

62

Acute Skeletal Muscle Wasting in Critical Illness

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


Retrospective Study: 1171 pts in ICU over 13 yrs all had Indirect Calorimetry
Guidelines

- Sufficient, high dose protein
- 1.2-2.0 g/kg actual body wt / day
- 1.3 g/kg/d delivered progressively

Protein Delivery: Observational Data

- Reduced mortality when 1.2-1.5 g / kg / d delivered \(^1,^2\)
- Improved survival if pts received > 80% of protein target \(^3\)
- Better outcomes of vented ICU pts who receive > 90% target protein \(^4\)
- Odds of death ↓ by 6.6% w/ each 10% ↑ protein \(^5\)
- Gain of 1% survival for each 1 g / d of protein delivered \(^2\)

High protein intake is associated with low mortality and energy overfeeding with high mortality

Weijs et al. Critical Care 2014 – 843 ICU patients

10-20% Energy deficit decreases mortality  
Protein > 1.2 g/kg/d lower mortality

Figure 3 Hospital mortality for cumulative energy deficit over the first 4 days of ICU stay for non-septic patients (n = 726; P = 0.053). Reference is the measured resting energy expenditure of the patient. *P = 0.012.

Figure 4 Hospital mortality for all patients per protein intake group and for all non-septic and non-overfed patients per protein intake group. *P = 0.008; **P = 0.007.
Greater Protein and Energy Intake May Be Associated With Improved Mortality in Higher Risk Critically Ill Patients: A Multicenter, Multinational Observational Study*

Charlene Compher, PhD, RD, CNSC, FASPEN; Jesse Chittams, MS; Therese Sammarco, MS; Michele Nicolo, MS, RD, CNSC; Daren K. Heyland, MD, MSc, FRCPC

Retrospective Study: 2853 MV pts from 202 ICUs INS Database

Protein Delivery: RCT Data

• Improved creatinine clearance, but not clinical outcomes

• Improved SOFA scores (48hrs), but not LOS or mortality

• Slight reduction of ventilator time (1 day over 3 weeks)

• Less fatigue, greater forearm muscle thickness, but no difference in mortality or LOS

EPaNIC Post hoc: Glucose vs Protein & Alive ICU D/C

• EAT-ICU Trial
• Single Center RCT (N=200)
• Early Goal Directed Nutrition (EGDN) vs. Usual Care
• Kcal in EGDN by IC
• Protein in EGDN via Urine Nitrogen

Fig. 2. Mean daily protein and energy intake per trial day 1–7 for the full patient cohort including those who had protein provision reduced because of a plasma urea value above 20 mmol/L. Error bars are SD for means in the two groups at each time point.

Early goal-directed nutrition versus standard of care in adult intensive care patients: the single-centre, randomised, outcome assessor-blinded EAT-ICU trial

Table 3 Primary and secondary outcome measures in the two intervention groups

<table>
<thead>
<tr>
<th>Primary outcome measure</th>
<th>Early goal-directed nutrition (N = 100)</th>
<th>Standard of care (N = 99)</th>
<th>Adjusted mean difference (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCS score at 6 months adjusted for presence of haematologic malignancy, mean (SD)</td>
<td>22.9 (21.8)</td>
<td>23.0 (22.3)</td>
<td>−0.08 (−5.9 to 5.8)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary outcome measures</th>
<th>Early goal-directed nutrition (N = 100)</th>
<th>Standard of care (N = 99)</th>
<th>Relative risk or mean difference (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital status, no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dead at day 28</td>
<td>20 (20%)</td>
<td>21 (21%)</td>
<td>0.94 (0.55–1.63)</td>
<td>0.83</td>
</tr>
<tr>
<td>Dead at day 90</td>
<td>30 (30%)</td>
<td>32 (32%)</td>
<td>0.93 (0.61–1.40)</td>
<td>0.72</td>
</tr>
<tr>
<td>Dead at 6 months</td>
<td>37 (37%)</td>
<td>34 (34%)</td>
<td>1.08 (0.74–1.57)</td>
<td>0.70</td>
</tr>
<tr>
<td>Length of stay among 6-month survivors, median days (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>7 (5–22)</td>
<td>7 (4–11)</td>
<td>NA</td>
<td>0.21</td>
</tr>
<tr>
<td>Hospital</td>
<td>30 (12–53)</td>
<td>34 (14–53)</td>
<td>NA</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Protein Delivery and Mortality

Figure 2. Effect of protein delivery on mortality*

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>OR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keunin (2006)</td>
<td>1.13 (0.29 - 4.44)</td>
<td>3.10</td>
</tr>
<tr>
<td>Goeters (2002)</td>
<td>1.70 (0.57 - 5.10)</td>
<td>4.38</td>
</tr>
<tr>
<td>Ilbicher (2002)</td>
<td>1.45 (0.68 - 3.12)</td>
<td>7.14</td>
</tr>
<tr>
<td>Oggul&amp;kin (2008)</td>
<td>1.11 (0.37 - 3.31)</td>
<td>4.41</td>
</tr>
<tr>
<td>Hou (2009)</td>
<td>0.80 (0.39 - 1.65)</td>
<td>7.58</td>
</tr>
<tr>
<td>Rice (2011)</td>
<td>1.19 (0.60 - 2.35)</td>
<td>8.11</td>
</tr>
<tr>
<td>Singer (2011)</td>
<td>2.33 (1.07 - 5.09)</td>
<td>6.94</td>
</tr>
<tr>
<td>Huang (2012)</td>
<td>0.77 (0.34 - 1.75)</td>
<td>6.50</td>
</tr>
<tr>
<td>Heyland (2013)</td>
<td>0.78 (0.61 - 1.00)</td>
<td>15.09</td>
</tr>
<tr>
<td>Brittenschweig (2014)</td>
<td>0.28 (0.10 - 0.83)</td>
<td>4.51</td>
</tr>
<tr>
<td>Ferrie (2015)</td>
<td>0.69 (0.27 - 1.79)</td>
<td>5.39</td>
</tr>
<tr>
<td>Doig (IV AA) (2015)</td>
<td>1.22 (0.76 - 1.98)</td>
<td>11.04</td>
</tr>
<tr>
<td>Doig (refeeding) (2015)</td>
<td>0.37 (0.19 - 0.70)</td>
<td>8.52</td>
</tr>
<tr>
<td>Qiu (2015)</td>
<td>1.20 (0.57 - 2.54)</td>
<td>7.29</td>
</tr>
<tr>
<td>Overall (I² = 48.2%, P = 0.025)</td>
<td>0.93 (0.72 - 1.22)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

OR 0.93 (0.72-1.22); P=0.62

Guidelines

- **Suggest** sufficient, high dose protein
  - 1.2-2.0 g/kg actual body wt / day
- Higher in trauma and burn pts
- Quality of Evidence: Very Low

- 1.3 g/kg/d can be delivered progressively
- Grade of recommendation: 0
- Strong consensus (91% agreement)


www.espen.org www.espencongress.com
Timing of PROTein INtake and clinical outcomes of adult critically ill patients on prolonged mechanical VENTilation: The PROTINVENT retrospective study

Nutrition in the ICU: new trends versus old-fashioned standard enteral feeding?

Proteins in Special Populations
# Special Populations: General Protein Target

<table>
<thead>
<tr>
<th>Population</th>
<th>Protein Goals / Targets</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Renal Failure</td>
<td>1.2 - 2.0 g / kg actual body wt / day</td>
<td>Expert Consensus</td>
</tr>
<tr>
<td>Hepatic Failure (acute and chronic)</td>
<td>1.2 - 2.0 g / kg ideal body wt / day</td>
<td>Expert Consensus</td>
</tr>
<tr>
<td>High Nutrition Risk (NRS &gt; 5; Nutric ≥ 5)</td>
<td>&gt; 80% of goal protein w/in 48-72 hr</td>
<td>Expert Consensus from observational data</td>
</tr>
<tr>
<td>Sepsis / Septic Shock</td>
<td>1.2 - 2.0 g / kg actual body wt / day 1.2 g / kg / d</td>
<td>Expert Consensus Grade: GPP</td>
</tr>
<tr>
<td>Frail Patients</td>
<td>1.2 – 1.5 g / kg /day (higher if severe illness)</td>
<td></td>
</tr>
</tbody>
</table>

## Special Populations: Higher Protein Targets

<table>
<thead>
<tr>
<th>Population</th>
<th>Protein Goals / Targets</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Failure on HD or CRRT</td>
<td>2.5 g / kg ideal body wt / day (no glutamine)</td>
<td>Very Low (1 RCT demonstrating + N⁺ Balance)</td>
</tr>
<tr>
<td>Trauma</td>
<td>1.5 - 2.0 g / kg actual body wt / day</td>
<td>Very Low</td>
</tr>
<tr>
<td></td>
<td>“Start w/in 24-48 hrs…”</td>
<td>Grade: 0 – strong consensus</td>
</tr>
<tr>
<td></td>
<td>0.2 – 0.3 g / kg / d of glutamine</td>
<td></td>
</tr>
<tr>
<td>Burns</td>
<td>1.5 - 2.0 g / kg actual body wt / day</td>
<td>Expert Consensus</td>
</tr>
<tr>
<td></td>
<td>0.3 – 0.5 g / kg / d of glutamine</td>
<td>Grade: B – strong consensus</td>
</tr>
<tr>
<td>Open Abdomen</td>
<td>1.2 - 2.0 g / kg ideal body wt / day + add’l 15 – 30 g protein per L exudate</td>
<td>Expert Consensus</td>
</tr>
<tr>
<td>Chronic Critical Illness (esp PICS)</td>
<td>2.0 g / kg / day with resistance exercise</td>
<td>Expert Consensus (ASPEN, Moore, et al)</td>
</tr>
<tr>
<td>ECMO</td>
<td>2.0 – 2.5 g / kg / day</td>
<td>de Waele, et al; Pelekhaty, et al; MacGowan et al, etc</td>
</tr>
</tbody>
</table>
Protein Considerations for the Critically Ill Obese Patient

- Provide high protein, hypocaloric enteral feeding (expert consensus)
- Controlled hypocaloric (60-70% target energy requirements) regimens may reduce fat stores, preserve lean body mass, and increase insulin sensitivity. (ASPEN guidelines).

- Attention to protein!!
  - BMI 30-40: ≥ 2 g/kg IBW/day
  - BMI ≥ 40: ≥ 2.5 g/kg IBW/day
  - 1.3 g / kg adjusted BW / day

Quantitative Protein Summary

- Evidence informing optimal protein delivery in most critically ill patients is sparse (EFFORT, TARGET-PROTEIN Trials)
- Current recommendations are for 1.2 – 2.0 g / kg / day for most critically ill patients
  - Do NOT restrict protein in critically ill w/ renal or hepatic failure
  - Higher protein targets for burns, trauma, CRRT, ECMO
  - Conflicting recommendations for obese critically ill patients
Questions