Protein in Critically Ill Patients

Ashraf El Houfi. MD
MS(pulmonology) MRCP(UK)
FRCP(London) EDIC
Consultant ICU Dubai Hospital
Proteins

Carbohydrate

Lipid

Electrolytes, Trace Elements

Protein?
Proteins

• **Protein is needed to**
  **Build, Maintain, and Repair body tissue**

• **Protein is also utilized for**
  **Energy in increasing amounts during stress**
Protein Turnover

- Catabolism
- Synthesis
- Amino acids
- Degradation
- Deposition
- Protein
- Gut
Expensive

Requires about 5 ATP per one peptide bond

Amino Acid Structure

Hydrogen

Amino

Carboxyl

R-group (variant)

N terminus

C terminus

Peptides

Metabolic Response to Stress
Abdominal Surgery for Bleeding Crohn’s disease

Post operative ICU Course

NPO for 5 days
Not tolerating when finally started
Gradually started over next 5 days
Not tolerating

Bleeding
Hypotension
Tachycardia
Hypoxia

Intensivist Response
Post operative ICU Course

NPO for 5 days
Not tolerating when finally started
Gradually started over next 5 days
Not tolerating

Bleeding
Hypotension
Tachycardia
Hypoxia

1-2 H

Re-intubate
Resuscitate
Fluid loading
Blood transfusion
Lines
Presser
Correct coagulopathy
Back to surgery

This content may not be amended, modified or commercially exploited without prior written consent.
Energy expenditure in starvation

Nitrogen excretion (g/day)

Days

Partial Starvation

Total Starvation

Normal range


This content may not be amended, modified or commercially exploited without prior written consent.
Metabolic response to stress

## Metabolic response to starvation and stress

<table>
<thead>
<tr>
<th></th>
<th>Starvation</th>
<th>Stress or Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic rate</td>
<td>↓</td>
<td>↑↑</td>
</tr>
<tr>
<td>Body fuels</td>
<td>conserved</td>
<td>wasted</td>
</tr>
<tr>
<td>Body protein</td>
<td>conserved</td>
<td>wasted</td>
</tr>
<tr>
<td>Urinary nitrogen</td>
<td>↓</td>
<td>↑↑</td>
</tr>
<tr>
<td>Weight loss</td>
<td>slow</td>
<td>rapid</td>
</tr>
</tbody>
</table>

The body adapts to starvation, but not in the presence of critical injury or disease


This content may not be amended, modified or commercially exploited without prior written consent.
Metabolic response to stress and trauma


This content may not be amended, modified or commercially exploited without prior written consent.
Metabolic Response to Stress

Muscle

Muscle Synthesis
Muscle Protein
Muscle Breakdown
Amino Acids

Blood

Amino Acids

Demand
Supply

This content may not be amended, modified or commercially exploited without prior written consent.
Critically ill patients!

Can lose as much as 1kg of LBM daily

Loss of LBM accelerates in critical illness

**How Much Protein?**

**Loss of total body protein (in vivo neutron Activation)**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Protein (g/kg/day)</th>
<th>Dextrose (kcal/kg/day)</th>
<th>Lipid (kcal/kg/day)</th>
<th>Nonprotein Calorie Intake (kcal/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n = 7)</td>
<td>1.14 ± 0.13&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>18.3 ± 2.1</td>
<td>8.9 ± 7.9</td>
<td>27.3 ± 8.2</td>
</tr>
<tr>
<td>B (n = 8)</td>
<td>1.47 ± 0.11&lt;sup&gt;b&lt;/sup&gt;</td>
<td>20.4 ± 1.4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7.0 ± 5.4</td>
<td>27.4 ± 5.4</td>
</tr>
<tr>
<td>C (n = 8)</td>
<td>1.86 ± 0.14&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24.7 ± 2.3&lt;sup&gt;c&lt;/sup&gt;</td>
<td>6.6 ± 3.4</td>
<td>31.3 ± 2.5</td>
</tr>
<tr>
<td><em>p</em>&lt;sup&gt;d&lt;/sup&gt;</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

<sup>a</sup>Mean ± SD;  <sup>b</sup><i>p</i> < .001 for all pairwise comparisons;  <sup>c</sup><i>p</i> < .001 for comparison with group A;  <sup>d</sup>analysis of variance.

Effect of high protein enteral nutrition on LBM in ICU

AA administration /kg LBM

-1.8 kg of proteins reflects 9 kg of muscle mass


This content may not be amended, modified or commercially exploited without prior written consent.
- Both groups were fed according to energy expenditure
- Muscle protein turnover was measured using labelled phenylalanine (Phe)
- Bars demonstrate a similar muscle protein synthesis rate, but a different protein degradation rate ($P < 0.05$), resulting in a different protein balance ($P < 0.05$)


This content may not be amended, modified or commercially exploited without prior written consent.
Histological changes in skeletal muscles after ICU admission

Muscle wasting occurred early and rapidly and was more severe among those with multiorgan failure compared with single organ failure.

Lean body mass (CT-scan) and mortality

Low skeletal muscle area, as assessed by CT scan during the early stage of critical illness, is a risk factor for mortality in mechanically ventilated critically ill patients. Further analysis suggests muscle mass as primary predictor.


This content may not be amended, modified or commercially exploited without prior written consent.
<table>
<thead>
<tr>
<th>% Loss of Total LBM</th>
<th>Complications</th>
<th>Associated Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Decreased immunity, increased infections</td>
<td>10</td>
</tr>
<tr>
<td>20</td>
<td>Decreased healing, weakness, infection</td>
<td>30</td>
</tr>
<tr>
<td>30</td>
<td>Too weak to sit, pressure ulcers, pneumonia, no healing</td>
<td>50</td>
</tr>
<tr>
<td>40</td>
<td>Death, usually from pneumonia</td>
<td>100</td>
</tr>
</tbody>
</table>

*Loss of LBM is devastating*
Abdominal Surgery for Bleeding Crohn’s disease

NPO for 5 days
Not tolerating when finally started
Gradually started over next 5 days
Not tolerating

Bleeding
Hypotension
Tachycardia
Hypoxia

Intensivist Response

Post operative ICU Course
Overall performance: Kcals for first 2 weeks in ICU

Who participated in 2011? 221 ICUs
Average Protein Delivery

0.6 g/kg/d for 2 weeks in ICU!

Who participated in 2011? 221 ICUs
The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study

Cathy Alberda, Leah Gramlich, Naomi Jones, Khursheed Jeejeebhoy, Andrew G. Day, Rupinder Dhaliwal, Daren K. Heyland

Point prevalence survey of nutrition practices in ICU’s around the world conducted Jan. 27, 2007

2772 patients from 158 ICUs over 5 continents

Included ventilated adult patients who remained in ICU >72 hours

Relationship of protein/caloric intake, 60-day mortality and BMI


This content may not be amended, modified or commercially exploited without prior written consent.
Extra Protein

Reduces Mortality as well...

Every additional 30 grams/d protein given...

Mortality decreased!

Effect of an increase of 1000 kcal in daily calories or 30g proteins & 60 d mortality risk

<table>
<thead>
<tr>
<th>BMI group</th>
<th>Adj. Odds Ratio</th>
<th>95%CI LCL</th>
<th>95% CI UCL</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>+ 1000 kcal/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>overall</td>
<td>0.76</td>
<td>0.61</td>
<td>0.95</td>
<td>0.014</td>
</tr>
<tr>
<td>&lt;20</td>
<td>0.52</td>
<td>0.29</td>
<td>0.95</td>
<td>0.033</td>
</tr>
<tr>
<td>20 to &lt;25</td>
<td>0.62</td>
<td>0.44</td>
<td>0.88</td>
<td>0.007</td>
</tr>
<tr>
<td>25 to &lt;30</td>
<td>1.05</td>
<td>0.75</td>
<td>1.49</td>
<td>0.768</td>
</tr>
<tr>
<td>30 to &lt;35</td>
<td>1.04</td>
<td>0.64</td>
<td>1.68</td>
<td>0.889</td>
</tr>
<tr>
<td>35 to &lt;40</td>
<td>0.36</td>
<td>0.16</td>
<td>0.80</td>
<td>0.012</td>
</tr>
<tr>
<td>≥ 40</td>
<td>0.63</td>
<td>0.32</td>
<td>1.24</td>
<td>0.180</td>
</tr>
<tr>
<td>N=2729/2728</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteins</td>
<td>+ 30 g proteins/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>overall</td>
<td>0.84</td>
<td>0.74</td>
<td>0.96</td>
<td>0.008</td>
</tr>
<tr>
<td>&lt;20</td>
<td>0.60</td>
<td>0.41</td>
<td>0.87</td>
<td>0.007</td>
</tr>
<tr>
<td>20 to &lt;25</td>
<td>0.81</td>
<td>0.66</td>
<td>0.99</td>
<td>0.036</td>
</tr>
<tr>
<td>25 to &lt;30</td>
<td>0.97</td>
<td>0.79</td>
<td>1.19</td>
<td>0.758</td>
</tr>
<tr>
<td>30 to &lt;35</td>
<td>1.04</td>
<td>0.79</td>
<td>1.37</td>
<td>0.774</td>
</tr>
<tr>
<td>35 to &lt;40</td>
<td>0.62</td>
<td>0.39</td>
<td>0.98</td>
<td>0.039</td>
</tr>
<tr>
<td>≥ 40</td>
<td>0.72</td>
<td>0.51</td>
<td>1.03</td>
<td>0.072</td>
</tr>
</tbody>
</table>


This content may not be amended, modified or commercially exploited without prior written consent.
The tight calorie control study (TICACOS): a prospective, randomized, controlled pilot study of nutritional support in critically ill patients.


- **“High protein study”**
  - Mean protein delivery: 1.0 g/kg/day in supplemental PN group

- **Benefit! Reduced mortality**

  - The primary outcome was hospital mortality
  - Patients in the study group had a higher mean energy (2,086 ± 460 vs. 1,480 ± 356 kcal/day, p=0.01) and protein intake (76 ± 16 vs. 53 ± 16 g/day, p=0.01)
  - There was a trend towards an improved hospital mortality in the ITT group (21/65 patients, 32.3% vs. 31/65 patients, 47.7%, p=0.058) whereas length of ventilation (16.1 ± 14.7 vs. 10.5 ± 8.3 days, p=0.03) and ICU stay (17.2 ± 14.6 vs. 11.7 ± 8.4, p=0.04) were increased
Two-center Swiss RCT

“High protein study”
- Mean protein delivery: 1.0–1.1 g/kg/day in supplemental PN group

Benefit! Reduced infection, LOS

We randomly assigned 153 patients to SPN and 152 to EN.
Mean energy delivery between day 4 and 8 was 28 kcal/kg per day for the SPN group, compared with 20 kcal/kg per day (7) for the EN group.
- Between days 9 and 28, 41 (27%) of 153 patients in the SPN group had a nosocomial infection compared with 58 (38%) of 152 patients in the EN group ($p=0.0338$), the SPN group had a lower mean number of nosocomial infections per patient ($p=0.0248$)
Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: A randomized controlled trial.
Doig GS, Simpson F, Sweetman EA, Finfer SR, Cooper DJ, Heighes PT, Davies AR, O’Leary M, Solano T, Peake S; Early PN Investigators of the ANZICS Clinical Trials Group.


• “High protein study”
  • Mean protein delivery: 1.1–1.2 g/kg/day in early PN group

• Benefit! Reduced time on ventilator, improved QoL!

• The provision of early PN to critically ill adults with relative contraindications to early EN, compared with standard care, did not result in a difference in day-60 mortality.
• The early PN strategy resulted in significantly fewer days of invasive ventilation, less muscle wasting, less fat loss, but not significantly shorter ICU or LOS
Optimal protein and energy nutrition decreases mortality in mechanically ventilated, critically ill patients: a prospective observational cohort study.
Weijs PJ, Stapel SN, de Groot SD, Driessen RH, de Jong E, Girbes AR, Strack van Schijndel RJ, Beishuizen A. 

Netherlands


• 28-day mortality hazard ratio with 95% confidence interval for protein and energy target (PET) group and energy target (ET) group. Model 0 is unadjusted. Model 1 adjusted for sex, age, BMI, diagnosis, hyperglycemic index and Acute Physiology and Chronic Health Evaluation II score. Model 2 additionally adjusted for time to energy target and use of parenteral nutrition.
Original article

Provision of protein and energy in relation to measured requirements in intensive care patients

Matilde Jo Allingstrup a,⁎, Negar Esmailzadeh a, Anne Wilkens Knudsen a, Kurt Espersen a, Tom Hartvig Jensen a, Jørgen Wiis a, Anders Perner a, Jens Kondrup b

a Department of Intensive Care 4131, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, D-2100 Copenhagen, Denmark

b Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen & Clinical Nutrition Unit, Copenhagen University Hospital, Rigshospitalet, Denmark

Copenhagen, Denmark


• 113 select ICU patients with sepsis or burns
• On average, receiving 1900 kcal/day and 84 grams of protein
• No significant relationship with energy intake but…
Prospective observational cohort study of 113 ICU patients

Log-rank test for trend: $P < 0.01$

84.3 g/day (1.06 g/kg/day)

53.8 g/day (0.80 g/kg/day)

114.9 g/day (1.46 g/kg/day)

$P = 0.021$

Increased protein delivery reduces mortality in ICU patients

Protein, energy and mortality

Survival was dependent on provision of protein & AA even when adjusted for APACHE II score, average SOFA score and age. It was unrelated energy balances.

Protein & AA / kg actual body weight : HR 0.31 (95%CI: 0.10-0.96), P=0.043


This content may not be amended, modified or commercially exploited without prior written consent.
Optimizing energy and protein balance in the ICU

Peter J.M. Weijs\textsuperscript{a,b,c,d} and Paul E. Wischmeyer\textsuperscript{e}

\textit{Curr Opin Clin Nutr Metab Care} 2013, 16:194–201

\begin{itemize}
\item NO Benefit in Trials Giving $< 1.0 \text{ g/kg/d}$ Protein
\item Such As: EPaNIC Trial, EDEN Trial, Arabi et al Trial
\item ALL Trials $> 1.0 \text{ g/kg/d}$ Protein Show Benefit!
\item Such As: Early PN Trial, ANZICS 2013, Swiss PN Trial, \textit{Lancet} 2013, TICACOS Trial, \textit{ICM} 2011
\end{itemize}
<table>
<thead>
<tr>
<th>Society</th>
<th>Protein</th>
<th>Energy</th>
</tr>
</thead>
</table>
| SCCM and ASPEPN | Dosage for protein:  
  - 1.2–2.0 g/kg/day in patients with BMI <30  
  - ≥2.0 g/kg ideal body weight for BMI 30–40  
  - ≥2.5 g/kg ideal body weight for BMI ≥40 | Provide >50%–65% of goal calories over the first week of hospitalization (Grade: C) |
| ESPEN | PN  
  1.3–1.5 g/kg ideal body weight plus adequate energy | EN  
  Acute and initial phase: avoid excess of 20–25 kcal/kg body weight/day  
  During recovery: 25–30 total kcal/kg body weight/day (C) |
Adequate protein in acute phase ICU may be the key....

To improve clinical outcomes...

And...post-ICU physical function?

**Recommendation**

Protein Delivery

(1.2-2.0 g/kg/day)
THANK YOU

DR. Ashraf Elhoufi
ICU Dubai Hospital
Questions?