Protein intake and clinical and functional outcome in ICU patients
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**Protein intake and clinical and functional outcome in ICU patients: a systematic review as a basis for ESPEN guidelines development**

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**INTRODUCTION**

Metabolic response in critical illness is characterized by an overwhelming protein catabolism, that exceed protein synthesis, rapidly leading to a severe muscle wasting and to a depletion of amino acids required to regulate inflammatory response, immune function and for wound healing. Recent evidence suggests that enhancing protein intake can attenuate catabolic response and improve clinical outcome in critically ill patients. Optimal protein intake is still debated; current guidelines indicate as target 1.2-1.5 g/kg/day and experts suggest even higher intake. Solid data on the effect of protein intake on clinical and functional outcome parameters are lacking.

**METHODS**

- MEDLINE was searched (January 4, 2016) for original articles published between 1946 and 2015. The search was updated on June 2, 2017 to include most recent articles.
- Reference list of the ESPEN, ASPEN, ESICM and the Canadian (international) guidelines for patients on the ICU were checked for additional articles.
- Quality assessment was done according to the guidelines devised by the Nordic Nutrition Recommendations 5 Working Group.
- The grade of evidence was classified as convincing, probable, suggestive or inconclusive.

**RESULTS**

- 28 articles included in the systematic review: 15 clinical trials and 13 prospective cohort studies.
- Overall, protein intake was low, not achieving current recommendations in 72% of the studies.

**Grade of evidence:**

- Higher protein intake and lower mortality risk (19 studies): suggestive
- Higher protein intake and shorter length of mechanical ventilation (10 studies): inconclusive
- Higher protein intake and shorter length of hospital or ICU stay (10 studies): inconclusive
- Higher protein intake and lesser nosocomial infections (6 studies): inconclusive
- From two studies included in the review, a promising positive role of protein on physical performance emerged.

**CONCLUSIONS**

Future RCTs, matching recommended protein target (or even higher target) and comparing different protein intake, are urgently needed to assess the evidence behind protein intake in ICU patients.

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**CHARACTERISTICS of the included studies**

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized Controlled Studies</td>
<td>15 (54%)</td>
</tr>
<tr>
<td>Prospective Cohort Studies</td>
<td>13 (47%)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Quality Rating</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>8 (21%)</td>
</tr>
<tr>
<td>B</td>
<td>20 (72%)</td>
</tr>
<tr>
<td>C</td>
<td>1 (3%)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome Parameter</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>19</td>
</tr>
<tr>
<td>Length of Ventilation</td>
<td>10</td>
</tr>
<tr>
<td>Length of Stay (Hospital and ICU)</td>
<td>10</td>
</tr>
<tr>
<td>Nosocomial Infections</td>
<td>6</td>
</tr>
<tr>
<td>Physical Performance</td>
<td>2</td>
</tr>
</tbody>
</table>

**QUALITY RATINGS of the included studies**

- Grade of evidence:
  - Convincing
  - Probable
  - Suggestive
  - Inconclusive

**FLOWCHART of the selection process (first period: 1946-2015)**

- 1481 abstracts
- 37 full-text articles included
- 542 full-text articles included in the SR
- 359 full-text articles on ICU
- 25 full-text articles on study design
- 1 excluded (on intervention)

**FLOWCHART of the selection process (second period: 2016-June 2017)**

- 69 full-text articles on ICU included
- 6 new full-text articles on ICU
- 7 excluded (on intervention)

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**ABSTRACTS**

1. **A. The role of protein in the prevention of nosocomial infections.**
2. **B. The effect of protein intake on length of stay in ICU.**
3. **C. The impact of protein intake on mortality in ICU patients.**

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**ARTICLES INCLUDED**

- 229 full-text articles
- 214 full-text articles on ICU
- 24 full-text articles on study design
- 4 excluded (on intervention)

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**QUALITY RATINGS**

- **A.** Convincing
- **B.** Probable
- **C.** Suggestive
- **D.** Inconclusive

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**RESULTS**

- **A.** Reduced risk of nosocomial infections (6 studies): convincing
- **B.** Reduced length of hospital or ICU stay (10 studies): suggestive
- **C.** Reduced length of ventilatory support (10 studies): inconclusive
- **D.** No significant difference in mortality (19 studies): inconclusive

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**CONCLUSIONS**

- Higher protein intake and shorter length of hospital or ICU stay recommended.
- Additional studies needed to confirm these findings.

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**FUTURE RCTs**

- Matching recommended protein target (or even higher target).
- Comparing different protein intake.
- Assessing evidence behind protein intake in ICU patients.