IS THERE A PLACE IN THE ICU FOR PERMISSIVE UNDERFEEDING AND WHERE?

ENGELA FRANCIS RD(SA)
DEFINITION: PERMISSIVE UNDERFEEDING

• No clear definition in literature

• Permissive underfeeding definition prior to PermiT Trail:
  • Suggest the total lower nutritional intake (calories, proteins and micronutrients)
  Van Zanten, 2015

• Permissive underfeeding is defined as (PermiT Trial):
  • Restricting nonprotein calories to 40-60% of target daily calories required
  • In conjunction with meeting full protein requirements
  Arabi et al 2015
CONTROVERSIES: PERMISSIVE UNDERFEEDING

• Controversies:
  • Duration of permissive underfeeding?
  • For all ICU patients?
  • Are there clear benefits?
RATIONALE FOR PERMISSIVE UNDERFEEDING:

AUTOPHAGY
**AUTOPHAGY**

- Important functions of Autophagy in Critical Illness
  - Cellular repair process that is necessary to clear intracellular damage e.g. damaged mitochondria.
  - Provides a survival mechanism in which amino acids are recycled to make ATP for energy and for protein synthesis to maintain cell structure.
- Autophagy ? The reason for Critical Illness associated anorexia.


Patel et al 2018 (JPEN 42: 508-515)
AUTOPHAGY

• Early full feeding in the Acute phase = Feeding-induced suppression of autophagy

• **Time dependent factor** of Autophagy (“Autophagic Switch”)
  • Macrophagic Autophagy – peaks at 4-6 hrs
  • Chaperone-mediated Autophagy – peaks at 24 hrs

• Thus Autophagy **operates very early** in Critical Illness

Patel et al 2018 (JPEN 42: 508-515)
• **Severity dependent factor** of Autophagy
  
  • Mild Critical Illness – Cell repair + Maintaining ATP production
  • Severe Critical Illness – Excessive autophagy + increased cell death

• **Transition point from homeostatic to pathologic** autophagy - unknown

Patel et al 2018 (JPEN 42: 508-515)
Suppression of Autophagy, can potentially lead to poor ICU outcome and

Excessive Autophagy, can potentially lead to poor ICU outcome

Timing and regulating of Autophagy needs more research
CONTROVERSY:
DURATION OF PERMISSIVE UNDERFEEDING?
DURATION OF PERMISSIVE UNDERFEEDING?

- Prevent overfeeding
  - During critical illness endogenous glucose production is a physiological process (proteolysis + gluconeogenesis)
  - This cannot be suppressed by nutritional therapy
- Exogenous glucose + Endogenous glucose in first week = Overfeeding

- Prevent refeeding risk
  - Vast number of critical ill patients at risk for refeeding syndrome
- Exogenous glucose + Endogenous glucose in first week = Refeeding

Patel et al 2018 (JPEN 42: 508-515)
DURATION OF PERMISSIVE UNDERFEEDING?

Unclear in literature: Different RCT’s used different cut offs.

First week or throughout the initial phase of critical illness?

Recommendation: Permissive underfeeding only during the first week of critical illness? – no consensus
CONTROVERSY:
FOR ALL ICU PATIENTS?
PERMISSIVE UNDERFEEDING: PATIENT POPULATION

• Most of the RCT’s in favour of permissive underfeeding
  • were methodologically limited and
  • therefore their results must be interpreted with caution.

• Arabi (2015) – PermiT Trail
  • No differences in 90 day mortality

• Casaer (2011) - EPANIC
  • IV Glucose - Overfeeding

• EDEN (2012)
  • Trophic feeding
PERMISSIVE UNDERFEEDING: PATIENT - BENEFITS

• PermiT (2015) –
  • Associated with lower blood glucose levels
  • Associated with reduced insulin requirements

• PermiT Post Hoc (2017) –
  • Patients with low prealbumin levels = lower mortality
  • Reason ? – Prevention of refeeding Sx
PERMISSIVE UNDERFEEDING: PATIENT - BENEFITS

PermiT Post Hoc (2017)

“Patients with high and low nutritional risk alike, enteral feeding to deliver moderate calories with full protein intake was associated with similar mortality compared with standard caloric feeding with full protein requirements.”
NUTRITIONAL SCREENING

• Nutritional screening is important to determine patient identification for at risk for nutritional intervention:
  • NRS 2002
    • Kondrup et al 2003 (Clin Nutr 22:415-421)
  • NUTRIC score
    • Heyland et al 2011 (Crit Care 15: R268)
The NUTRIC Score is designed to quantify the risk of critically ill patients developing adverse events that may be modified by aggressive nutrition therapy. The score, of 1-10, is based on 6 variables that are explained below. The scoring system is shown in Tables 1 and 2.

Table 1: NUTRIC Score variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;50</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>50 - &lt;75</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥75</td>
<td>2</td>
</tr>
<tr>
<td>APACHE II</td>
<td>&lt;15</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>15 - &lt;20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>20-28</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>≥28</td>
<td>3</td>
</tr>
<tr>
<td>SOFA</td>
<td>&lt;6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>6 - &lt;10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥10</td>
<td>2</td>
</tr>
<tr>
<td>Number of Co-morbidities</td>
<td>0-1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥2</td>
<td>1</td>
</tr>
<tr>
<td>Days from hospital to ICU admission</td>
<td>0 - &lt;1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥1</td>
<td>1</td>
</tr>
<tr>
<td>IL-6</td>
<td>0 - &lt;400</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥400</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2: NUTRIC Score scoring system: if IL-6 available

<table>
<thead>
<tr>
<th>Sum of points</th>
<th>Category</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-10</td>
<td>High Score</td>
<td>Associated with worse clinical outcomes (mortality, ventilation). These patients are the most likely to benefit from aggressive nutrition therapy.</td>
</tr>
<tr>
<td>0-5</td>
<td>Low Score</td>
<td>These patients have a low malnutrition risk.</td>
</tr>
</tbody>
</table>

Table 3. NUTRIC Score scoring system: if no IL-6 available*

<table>
<thead>
<tr>
<th>Sum of points</th>
<th>Category</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-9</td>
<td>High Score</td>
<td>Associated with worse clinical outcomes (mortality, ventilation). These patients are the most likely to benefit from aggressive nutrition therapy.</td>
</tr>
<tr>
<td>0-4</td>
<td>Low Score</td>
<td>These patients have a low malnutrition risk.</td>
</tr>
</tbody>
</table>

*It is acceptable to not include IL-6 data when it is not routinely available; it was shown to contribute very little to the overall prediction of the NUTRIC score.


March 19th 2013
ESPEN Guidelines for Nutrition Screening 2002

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Abstract—Aim: To provide guidelines for nutrition risk screening applicable to different settings (community, hospital, elderly) based on published and validated evidence available until June 2002.

Note: These guidelines deliberately make reference to the year 2002 in their title to indicate that this version is based on the evidence available until 2002 and that they need to be updated and adapted to current state of knowledge in the future.

In order to reach this goal the Education and Clinical Practice Committee invites and welcomes all criticism and suggestions (button for mail to ECPC chairman).
**Nutritional Risk Screening (NRS 2002)**

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Initial screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is BMI &lt; 20.5?</td>
</tr>
<tr>
<td>2</td>
<td>Has the patient lost weight within the last 3 months?</td>
</tr>
<tr>
<td>3</td>
<td>Has the patient had a reduced dietary intake in the last week?</td>
</tr>
<tr>
<td>4</td>
<td>Is the patient severely ill? (e.g. in intensive therapy)</td>
</tr>
</tbody>
</table>

**Yes:** If the answer is ‘Yes’ to any question, the screening in Table 2 is performed.  
**No:** If the answer is ‘No’ to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.
Table 2  Final screening

<table>
<thead>
<tr>
<th>Impaired nutritional status</th>
<th>Severity of disease (≈ increase in requirements)</th>
</tr>
</thead>
</table>
| Absent  
Score 0 | Normal nutritional status                                                                 | Absent  
Score 0 | Normal nutritional requirements                                                            |
| Mild  
Score 1 | Wt loss >5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week | Mild  
Score 1 | Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. Chronic hemodialysis, diabetes, oncology |
| Moderate  
Score 2 | Wt loss >5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week | Moderate  
Score 2 | Major abdominal surgery* Stroke* Severe pneumonia, hematologic malignancy |
| Severe  
Score 3 | Wt loss >5% in 1 mth (>15% in 3 mths) or BMI <18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week | Severe  
Score 3 | Head injury* Bone marrow transplantation* Intensive care patients (APACHE>10). |

Score:

<table>
<thead>
<tr>
<th>+</th>
<th>= Total score</th>
</tr>
</thead>
</table>

Age

| if ≥70 years: add 1 to total score above | = age-adjusted total score |

**Score ≥3**: the patient is nutritionally at-risk and a nutritional care plan is initiated

**Score <3**: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.
WHAT DOES THE NUTRITIONAL GUIDELINES SAY?
Based on expert consensus, we suggest a determination of nutrition risk (eg, nutritional risk screening [NRS 2002], NUTRIC score) be performed on all patients admitted to the ICU for whom volitional intake is anticipated to be insufficient. High nutrition risk identifies those patients most likely to benefit from early EN therapy.

Based on expert consensus, in the absence of IC, we suggest that a published predictive equation or a simplistic weight-based equation (25–30 kcal/kg/d) be used to determine energy requirements.
ASPDEN (2016)

- We recommend that nutrition support therapy in the form of early EN be initiated within 24–48 hours in the critically ill patient who is unable to maintain volitional intake.

- Based on expert consensus, we suggest that patients who are at low nutrition risk with normal baseline nutrition status and low disease severity (eg, NRS 2002 ≤3 or NUTRIC score ≤5) who cannot maintain volitional intake do not require specialized nutrition therapy over the first week of hospitalization in the ICU.
Based on expert consensus, we suggest that patients who are at high nutrition risk (e.g., NRS 2002 ≥5 or NUTRIC score ≥5, without interleukin 6) or severely malnourished should be advanced toward goal as quickly as tolerated over 24–48 hours while monitoring for refeeding syndrome. Efforts to provide >80% of estimated or calculated goal energy and protein within 48–72 hours should be made to achieve the clinical benefit of EN over the first week of hospitalization.
Based on expert consensus, in the patient determined to be at high nutrition risk (eg, NRS 2002 ≥5 or NUTRIC score ≥5) or severely malnourished, when EN is not feasible, we suggest initiating exclusive PN as soon as possible following ICU admission.

We suggest that hypocaloric PN dosing (≤20 kcal/ kg/d or 80% of estimated energy needs) with adequate protein (≥1.2 g protein/kg/d) be considered in appropriate patients (high risk or severely malnourished) requiring PN, initially over the first week of hospitalization in the ICU.
• Recommendation: There are **insufficient data** to make a recommendation on the use of hypocaloric enteral nutrition in critically ill patients.
ESPEN (2006)

- EN: No general amount can be recommended as EN therapy has to be adjusted according to the progression/course of the disease and to gut tolerance. During the acute and initial phase of critical illness an exogenous energy supply in excess of 20–25 kcal/kg BW/day may be associated with a less favourable outcome (C). During recovery (anabolic flow phase), the aim should be to provide 25–30 total kcal/kg BW/day (C).
• PN: Recommendation: During acute illness, the aim should be to provide energy as close as possible to the measured energy expenditure in order to decrease negative energy balance. (Grade B). In the absence of indirect calorimetry, ICU patients should receive 25 kcal/kg/day increasing to target over the next 2–3 days (Grade C).
TAKE HOME MESSAGE

• Should all critically ill patients be undergoing permissive underfeeding during the first week of critical illness?

• The answer is “NO”.

• Critical illness represents a heterogeneous patient population.
  • Some ICU patients may not need early nutrition interventions.
  • Other patients may derive outcome benefit from early aggressive nutrition therapy that meets target goal feeding.
  • Other patients may need permissive underfeeding to prevent overfeeding or refeeding.

Individualised approach
KEEP CALM AND ASK ME A QUESTION
THANK YOU