Nutrition in the Acute Phase of Critical Illness

Critically ill patient requir vital organ support in ICU have anorexia

- Energy deficit
  - lean-tissue wasting
    - prolonged need for mechanical ventilation and rehabilitation
  - catabolic response
    - immobilization
    - pronounced inflammatory
    - endocrine stress responses
Enteral Nutrition
Timing of initiation

- In observational studies, patients who were fed early through the enteral route have had a better outcome than those who were not.
A meta-analysis of six small trials (total of 234 patients) showed a survival benefit with the immediate initiation of enteral nutrition:
- lower risk of infection
Estimation of energy requirements

- Energy requirements differ per patient and per day in the ICU
- Individually estimated on a daily basis
  - measurements of oxygen consumption and carbon dioxide production
Tight Calorie Control Study (TICACOS)

- 130 patients,
- undergoing mechanical ventilation
- indirect calorimetry to estimate the resting energy expenditure received more nutrition
- calculated energy target

- reduced hospital mortality
- increase in infections and in the length of stay in the ICU
Failure to deliver the prescribed nutrition is the reason that enteral nutrition not improved outcome.

A small, randomized, controlled trial
- traumatic brain injury
- delivering enteral nutrition to reach an estimated energy target immediately
- reach gradually increasing targets over the first week
- reduced rate of infection
Two large, cluster-randomized trials, respectively,
- "increased the amount of nutrition delivered" on clinical outcomes.
- In the smaller study (462 patients)
  - decreased length of hospital stay
  - nonsignificant reduction in hospital mortality
- In the larger study (1118 patients)
  - an earlier initiation of feeding and an increased attainment of caloric goals
  - not provide any benefit either mortality or length of stay in the ICU or hospital
- Trophic vs. Full-Energy Enteral Nutrition in Mechanically Ventilated Patients with Acute Lung Injury (EDEN) trial
  - 1000, relatively young and well-nourished patients
  - acute lung injury
- Small amount of (trophic) enteral feeding for 1 week in the ICU
- Full enteral feeding from the time of admission
  - no between-group difference in acute or long-term functional outcomes
Gastric residual volume

- ICU patient, *gastric empty is often slow or impaired*, resulted in large gastric residual volume
- Since regurgitation of gastric content can lead to *aspiration pneumonia*, enteral feeding is often discontinued in patients who are found to have large gastric residual volumes
The Gastric Residual Volume during Enteral Nutrition in ICU Patients (REGANE) trial (329 patients)
- gastric residual volumes up to 500 ml could be safely tolerated

The Effect of Not Monitoring Residual Gastric Volume on the Risk of Ventilator-Associated Pneumonia in Adults Receiving Mechanical Ventilation and Early Enteral Feeding (NUTRIREA 1) trial (449 patients)
- omission of gastric residual volumes did not increase the incidence of aspiration or related complications
- Improve gastric emptying
  - prokinetic agent such as metoclopramide or erythromycin
  - bypass the stomach to deliver nutrition directly beyond the pylorus
Parenteral feeding
- Rely solely on the enteral route to feed, the numbers of calories often do not meet the calculated targets
  - side effects associated with enteral feeding
  - lack of a functional gastrointestinal tract
European guidelines:
- the *early initiation* (within 48 hours after admission to the ICU) of parenteral nutrition
- nutritional deficit is prevented

American and Canadian guidelines
- allowing *hypocaloric enteral nutrition for 1 week* in well-nourished patients before considering parenteral nutrition.
- observation of complications (e.g., liver-function abnormalities, hyperglycemia, hypertriglyceridemia, and infections) associated with parenteral nutrition and overfeeding
Impact of Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically Ill Patients (EPaNIC) trial (4640 patient) (APACHE II: 23)

- Early PN
  - insufficient enteral nutrition
  - parenteral glucose for 2 days, day 3 delivering on average 40 g of protein per liter per day

- late PN
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<thead>
<tr>
<th>Type of Patients</th>
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Impact of Supplemental Parenteral Nutrition on Infection Rate, Duration of Mechanical Ventilation, and Rehabilitation in ICU Patients (SPN) study

- 305 patients
- not yet receiving 60% of the energy goal on the fourth day in the ICU
- parenteral nutrition or enteral nutrition alone from day 4 to day 8.
### Early PN Trial (N=1372)
- Mixed medical and surgical (N relatively contraindicated)
- Type: short term
- Graph showing Total Energy (kcal) over ICU Day

### EPaNIC Trial (N=4640)
- Mixed medical and surgical (unselected)
- With nutritional risk (NRS, ≥3)
- Graph showing Total Energy (kcal) over ICU Day

### SPN Trial (N=305)
- Mixed medical and surgical (on day 4)
- Eligible for EN but <60% target
- Graph showing Total Energy (kcal) over ICU Day

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Between day 9 and day 28: less with SPN
From randomization to day 28: unaffected
Early Parenteral Nutrition study

- 1372 patients, from 31 ICUs
- early parenteral nutrition within 24 hours after ICU admission
- standard therapy
  - 253 of 686 patients (36.9%) received parenteral nutrition during the first few days in the ICU
  - 27.1% of them receiving parenteral nutrition after a mean of 1.99 days
  - another 7.0% receiving supplemental parenteral nutrition with enteral nutrition after a mean of 5.58 days
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Selection of Macronutrients
Amino Acids

- administration of *exogenous protein* could induce a protein-sparing effect through the stimulation of protein synthesis
**Glutamine** is the most abundant nonessential free amino acid
- synthesized in skeletal muscle
- lower level associated with a poor outcome

A meta-analysis of the early randomized, controlled trials (485 patients)
- glutamine supplementation might decrease the risk of infection, the length of stay in the hospital, and the risk of death
Scottish Intensive Care Glutamine or Selenium Evaluative Trial (SIGNET)
- 500 patients
- a glutamine dose of 0.1 to 0.2 g per kilogram per day
- no benefit of low-dose glutamine administered parenterally to patients receiving parenteral feeding.

Reducing Deaths Due to Oxidative Stress (REDOXS) trial
- 1223 patients
- glutamine dose of 0.6 to 0.8 g per kilogram per day
- an absolute increase of 6.5 percentage in the rate of death at 6 months among patients with organ failure who received early high-dose parenteral nutrition plus enteral glutamine treatment
Arginine

- in the postoperative period
- decrease the rate of infectious complications and the length of stay in the hospital
- current evidence does not support its
Lipids

- n–3 fatty acids that are present in fish oil have been shown to have antiinflammatory effects.
- n–9 fatty acids that are present in olive oil have a more neutral immune effect.
- n–6 fatty acids in soybean oil are proinflammatory.
OMEGA study

- no benefit with the enteral administration of n–3 fatty acids plus antioxidant supplements in 272 patients
- fewer ventilator-free days and longer stays in the ICU among patients in the n–3 group.
Selection of Micronutrients
Micronutrients (consisting of trace elements, vitamins, and electrolytes) prevent deficiencies and associated complications.

Reinitiation of nutrition result in a refeeding syndrome

- deficiencies in thiamine, potassium, and phosphate
- cause fetal complication, such as cardiac failure, lactic acidosis, arrhythmia, respiratory failure
- **trace elements** (selenium, copper, manganese, zinc, and iron) and **vitamins** (E, C, and beta carotene)
  - reduce oxidative cellular damage and organ failure
- **Selenium** supplementation may be beneficial in populations in which selenium deficiency is prevalent
Conclusions
The findings of the EPaNIC and EDEN trials raise concern that targeting full-replacement feeding early in critical illness does not provide benefit and may cause harm in some populations or settings.

The Early Parenteral Nutrition and Supplemental Parenteral Nutrition trials suggest that the use of parenteral nutrition in itself may not increase the risk of infectious complications.
**Table 2. Recommendations for Clinical Nutritional Practice in the ICU and for Future Research.**

**Recommendations for clinical practice**

- Allow hypocaloric enteral feeding in the acute phase of critical illness for up to 7 days in previously well-nourished patients.

- Note that current evidence does not support glutamine supplementation early in critical illness.

- Supply micronutrients to prevent refeeding syndrome.*

**Recommendations for future research**

- Investigate mechanisms underlying benefit or harm from the administration of macronutrients early during critical illness.

- Identify biomarkers of the anabolic recovery phase to guide initiation of more aggressive feeding.

- Validate scoring systems to identify patients who could benefit most from early nutrition.

- Identify the potential role of glutamine as part of parenteral nutrition for critically ill patients after recovery from acute organ failure.
Thans for your attention