SCCM Critical Care Nutrition Guidelines: Would anything change in a 2013 edition?

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Which Guideline to Follow?
- Canadian
- SCCM
- ASPEN
- ESPEN
- ADA
- EAST
- Aus/NZ
- Am College of Chest Physicians
- ESICM
- Various European Country Guidelines
- Various European Country Guidelines

Introduction: SCCM / ASPEN 2009
- Basic Recommendations
  Not absolute requirements
  Do not project or guarantee outcome or mortality benefits
  Not a substitute for clinical judgment
- Supportive evidence
  Current literature
  National, international guidelines
  Expert opinion
  Clinical practicality
- Target population
  Adult critically ill medical and surgical patients
  Expected to stay in ICU ≥ 2-3 days
  Not a homogeneous population

Model for Guidelines
SCCM Surviving Sepsis Campaign
Development of Guidelines
- List of recommendations compiled by Committee Experts - Action
- PRCTs primary source of support
  Overall strength based on 2 things:
- Level of investigative studies
- Number of supportive studies
  
  Controversy in interpreting literature
  - Resolved by consensus opinion
  - Could result in down-grade

  - Philosophy of this specific guidelines committee:
    - Include patient care recommendations where sole basis was expert opinion
    - Promote recommendations and conditions for use of PN where outcome benefit assured

8  Grading of Literature
9  Grading of Recommendations
• Grade of Recommendation:
  A  Supported by at least two level I investigations
  B  Supported by one level I investigation
  C  Supported by level II investigations only
  D  Supported by at least two level III investigations
  E  Supported by level IV or level V evidence
• Level of Evidence:
  I  Large, randomized trials
  II  Small, randomized trials
  III Non-randomized, contemporaneous controls
  IV Non-randomized, historical controls
  V  Case series, uncontrolled studies, expert opinion

10  Adding Subjectivity to EBM
2013 guidelines would use the Grade System
• Rating of evidence (Rank 1+ to 4+ based on studies)
•
  Strong: We recommend (desirable effects clearly outweigh undesirable)

  Weak: We suggest (desirable effects probably outweigh undesirable)

11  Organizations now using GRADE system
• World Health Organization
• Allergic Rhinitis in Asthma Guidelines (ARIA)
• American Thoracic Society
• British Medical Journal
• American College of Chest Physicians
• UpToDate
• American College of Physicians
• Cochrane Collaboration
• National Institute Clinical Excellence (NICE)
• Infectious Disease Society of America
• European Society of Thoracic Surgeons
• BMJ Clinical Evidence
• Agency for Health Care Research and Quality (AHRQ)
• Over 20 major organizations
Adding Subjectivity to EBM
2013 guidelines would use the Grade System

- Qualifiers
  - Methodologic quality
  - Outcome importance
  - Magnitude treatment effect
  - Therapy risks
  - Burdens of therapy
  - Resource use
  - Precision of estimate
  - Rx effect
  - Varying values

Reasons to exclude some guidelines / consensus papers
- Primary data not evaluated: uses clusters of data or meta-analysis only
- Primary data not graded:
  - Were published as consensus statements without referencing or relying on primary published data
    - No transparency
  - Outdated
    - Caution here as some of published data may be outdated
  - Industry involvement with bias
    - Eli Lilly in 2006 associated Surviving Sepsis with marketing campaign for Xigris

Questions: Are the Guidelines misleading us?
- How can reading the same literature come up with different conclusions?
  - Variations in populations
    - CPG exclude surgical patients (ESPEN, ASPEN, SCCM, ADA) include surgical patients
  - Differences in sample size of RCT
    - ASPEN/SCCM >100, ADA >20, CPG no minimum # criteria
  - Type of data used to make grades/recommendations
    - SCCM, ASPEN, ESPEN, ADA used RCT and observational studies and expert opinion. CPG used RCT and Meta-analyses
  - Language used to give strength of recommendations is variable

Use of observational studies and “expert” opinion (Grade E)
- SCCM/ASPEN: Philosophy; Making a guideline clinically useful at the bedside
  - Example: In setting of hemodynamic compromise, EN should be withheld until the patient is fully resuscitated and/or stable (Grade E).
- CPG: insufficient data
- Note Grade E is expert opinion.
- 29 of 76 in SCCM/ASPEN in 2009 recommendations are Grade E

Use of observational studies and “expert” opinion (Grade E)
- SCCM/ASPEN: Philosophy; Making a guideline clinically useful at the bedside
  - Example: In setting of hemodynamic compromise, EN should be withheld until the patient is fully resuscitated and/or stable (Grade E).
Meta-analysis: should they be used for guidelines?
- Primarily used for hypothesis generation and measuring overall treatment effect:
- Should not be used for hypothesis confirmation
- Using only RCT removes a major bias
- RCT vs meta-analysis
  - Study comparing large RCT to meta-analysis on same subject (studies over 1000 pts) 4 journals (NEJM, Lancet, Annals of Internal Med, JAMA)
  - Agreement between two only fair
  - predicted inaccurately in 35%

Meta-analysis
Advantages
- Generalization to population studies
- Ability to control for between study variation
  - Include monitors to explain variation
- Higher statistical power to detect an effect or signal
Weakness
- Sources of bias not controlled
  - “a good meta-analysis of badly designed studies will still result in bad statistics”
- “Simpson’s paradox”
  - Coding of an effect is subjective, no universally agreed-upon way to weight of risk

Critical Care Guidelines
Areas of common agreement:
ESPERN, ASPEN, SCCM, CPG, ADA
- All agree with:
  - Early enteral feeding
  - Enteral superior to PN
  - Fish oils beneficial (except ADA)
  - Small bowel vs gastric feeding
  - Supplemental antioxidants
  - Use of Glutamine (except ADA)
  - Use of Arginine in Surgery patients
    - Preop in addition to post op when possible

Areas of major differences
- Indirect calorimetry vs predictive equations
- Prokinetics in the ICU
- Arginine in the medical ICU
- Gastric residuals

• A1: Traditional nutrition assessment tools are not validated in critical care... (Grade E) (NO CHANGES)
• A2: EN via feeding tube should be initiated if PO intake not possible. (Grade C)
• A3: EN is preferred over PN... (Grade B) (Changes to Grade A)
• A4a: Start EN within the first 24-48 hours ... (Grade C) (changes to B)
• A4b: Advance to goal over next 48-72 hours. ... (Grade E)
• A5: When patient is hemodynamically compromised EN should be withheld until the patient is fully resuscitated and/or stable (Grade E)
• (Changes to Grade D)

Early Enteral Feeding Meta-analysis

Initiation of EN (cont)
• A6: Bowel sounds, flatus, stools *not* required before feeding initiation ... (Grade B)
  - Based on 1 level one study, 9 level 2 studies
• A7a: Either gastric or small bowel feeding is acceptable... (Grade C)
  • Coming change 2013 would be (Grade B) with added comment to consider starting early gastric and then switch if unsuccessful (not yet confirmed)

Gastric vs Jejunal Feeding

Initiation of EN (cont)
• A6: Bowel sounds, flatus, stools *not* required before feeding initiation ... (Grade B)
  - Based on 1 level one study, 9 level 2 studies
• A7a: Either gastric or small bowel feeding is acceptable... (Grade C)
  • Coming change 2013 will be (Grade B) with added comment to consider starting early gastric and then switch if unsuccessful (not yet confirmed)
• A7b: If repeated high residuals, withhold gastric and switch to jejunal feeding ... (Grade E) (will change to C)
A7c Added: ICU patients can be enterally fed with or without checking residuals (grade TBD, probably C)

Gastric Residual Volumes
“Should we even check GRV?”

C1-C3. Dosing of Enteral Feeding

- Identify target goal calorie requirements of EN defined by predictive equation or indirect calorimetry. ... (Grade: C)

  Predictive equations less accurate than indirect calorimetry for individual patient (worse in obesity). ... (Grade: E)

- Provide >50-65% of goal calories over first week to achieve clinical benefit of EN. ... (Grade: C)

- Add supplemental PN only if unable to meet target goal calorie requirements after 7-10 days by EN alone. ... (Grade: E) (changes to grade C? Based on Ceasar study, ? with Picard study)

- Adding PN prior to 7-10 days does not improve outcome and may increase risk to patient. ... (Grade: C) (changes to B)

G Van de Berge NEJM 2011: EPaNIC study

- Prospective randomized trial 7 ICU’s in Belgium
- 4640’s
  - 2312 early PN (w/in 48h of admissions)
  - 2328 late PN (no earlier than 8 days post admission)
- Both groups received early enteral feeding and insulin to treat hyperglycemia. Attempted to get to goal .lI,SAP
- Group that received late PN
  - Decrease infection risk from 26.2 to 22.8
  - Decrease time on ventilator
  - Decrease number and time on dialysis
  - Decrease LFT abnormality

Was the EPaNIC Study the PN “standard of care”?

- Clearly not the widely applicable !!!!
- All pts started on 20% glucose and got large parenteral glucose load (1200 kcal/2d)
- 90% were surgery patients, mostly cardiac surgery
- Relatively low mortality rates in both groups 8% compared to other ICU studies
- Short term exposure to PN – average ICU LOS only 3-4 days in Early PN group 58% got only 1-2 days of PN in Late PN only 25% received PN
- What was learned from EPaNIC
  - Risk/benefit ratio EN better than PN, kcal not interchangeable
  - Large parenteral glucose load, tight glycemic control, early PN in low risk pts may lead to worse outcome
  - No conclusions on supplement al PN to hypocaloric EN in high risk pts

What about combinations of EN and PN to avoid negative energy?
Not specifically addressed in ASPEN / SCCM 2009

- ESPEN PN Guidelines in Critical Care
  - August 2009 (Clinical Nutrition 28;387-400)
- Supplementary PN with EN
  - All patients receiving less than their targeted enteral feeding after 2 days should be considered for supplementary PN (Grade C)

- SCCM recommendation B1: waiting 5 to 7 days to add supplemental PN will remain the same

D3. Monitor Tolerance
Use of EF Protocols

- D3. Use of enteral feeding protocols increases the overall percentage of goal calories provided and should be implemented. (Grade: C) (will probably change to B, based on PEP-Up protocol, and others in press)

  - Rationale: Use of ICU or nurse-driven protocols which define goal infusion rate, designate more rapid startups, and provide specific orders for handling gastric residual volumes, frequency of flushes, and conditions or problems under which feeding may be adjusted or stopped, have been shown to be successful in increasing the overall percentage of goal calories provided

  - Koszar R J Surg Research 2002

Can We Do Better?
PEP uP protocol

- Pilot project to assess feasibility and safety
- Prospective before and after study
- Design: ventilated ICU patients 3 d Peptamen 1.5®
  - N=20 before
  - N=30 after
- Results: Energy Protein
  - Before: 58.8% 61.2%
  - After: 67.9% 73.6%
  - Full feeds 83.2% 89.4%
- No difference in emesis, regurgitation, aspiration, pneumonia

Doig JAMA Study Dec 2008

- Both groups fed early and relatively effectively
- 95% started feeding within 16 hours
Take home message should not be the Nutrition Guidelines make no outcome difference!

**“Trophic” vs “Full” feeds**

- Investigating mechanism for benefit of enteral feeding
  - Series of in-vivo and in-vitro testing
- Results:
  - Intestinal Alkaline Phosphatase (IAP) can detoxify LPS
  - IAP can protect mucosal barrier
  - IAP is lost with starvation and low flow states and maintained by enteral feeding
- Conclusion
  - IAP partially protects gut in CC/starvation
  - Trophic feeds are adequate to maintain IAP

**DO WE NEED TO DO BETTER?**

Vanderbilt Study:
*Trophic vs Full Feeds:*

% Goal Calories Received Per Day

**Trophic vs Full Feeds**

- Patient Demographics
  - Mean APACHE II 26.9, 38% in shock, P/F Ratio 182

<table>
<thead>
<tr>
<th></th>
<th>Trophic (n=98)</th>
<th>Full (n=102)</th>
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</thead>
<tbody>
<tr>
<td>Vent-free days</td>
<td>17.9 d</td>
<td>17.8 d</td>
</tr>
<tr>
<td>ICU-free days</td>
<td>15.8 d</td>
<td>16.5 d</td>
</tr>
<tr>
<td>Mortality</td>
<td>22.4%</td>
<td>19.6%</td>
</tr>
<tr>
<td>GI intolerance days</td>
<td>27%</td>
<td>40% *</td>
</tr>
<tr>
<td>Survivors to home</td>
<td>51%</td>
<td>68% *</td>
</tr>
</tbody>
</table>

- Difficult to interpret long vs short term benefits?

**E1. Selection of Appropriate Enteral Formulation**

- E1. Immune-modulating enteral formulations (supplemented with agents such as arginine, glutamine, nucleic acid, omega-3 fatty acids, and anti-oxidants) should be used for the appropriate patient population (major elective surgery, trauma, burns, head and neck cancer, and critically ill patients on mechanical ventilation), being cautious in patients with severe sepsis.
  - (For surgical ICU patients ....Grade: A)
  - (For medical ICU patients ....Grade: B) (will change to A)

- ICU patients not meeting criteria for immune-modulating formulations should receive
standard enteral formulations. (Grade: B)

39 Why this difference?
• ASPEN / SCCM:
  • Grade A for Surgery Trauma
  • based on 6 level 1 and 15 level 2 studies (in 2010 9 level 1 and 21 level 2)
  • Grade B for Medicine
    • reviewers concern (purely on data would have stayed A)
• ESPEN:
  • Grade A for elective major Surgery and Trauma
  • Grade B for mild to severe sepsis and ARDS
• CPG:
  • Recommended against use of immune and metabolic modulating
    • 1) surgery patients not included
    • 2) 3 RCT with increased mortality
      • One was never published (ROSS Study: randomization error)
      • one was PN vs enteral (not RCT, not blinded Bertolini)
      • one was post ad hoc analysis (Bower study)
• ADA
  • Did not site specific data but felt some question of safety?
  • Transparency in?

40 E2. Selection of Appropriate Enteral Formulation

• E2. Patients with ARDS and severe acute lung injury (ALI) should be placed on an
  enteral formulation characterized by an anti-inflammatory lipid profile (such as:
  omega-3 fish oils, borage oil, antioxidants)... (Grade: A) (will downgrade to B or C
  with explanation)

41 Clinical Outcomes Using Fish Oil in ARDS/ALI

42 B1. When to Use Parenteral Nutrition
• If early EN not feasible over first 7 days, Standard Therapy (no nutrition support
  therapy) should be provided. (Grade: C) (Changes to B)

• In patient previously healthy, no protein-energy malnutrition, use PN only after first 7
days. (Grade: E) (Changes to ?)

43 B2. When to Use Parenteral Nutrition
• If there is evidence of protein-energy malnutrition (PEM) on admission and EN is not
  feasible, it is appropriate to initiate PN as soon as possible following admission and
  adequate resuscitation. (Grade: C) (Changes to B)

45 G4. Maximize Efficacy of PN
Glycemic control
Use protocol to promote moderately strict glucose control (range of 110-150 mg/dL) (Grade: B) (Grade: E for glucose range) Van den Berghe SICU Study (n=1548)¹

<table>
<thead>
<tr>
<th></th>
<th>Tight Control</th>
<th>Convent Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU mort</td>
<td>5%</td>
<td>8% *</td>
</tr>
<tr>
<td>Hosp mort</td>
<td>7%</td>
<td>11% *</td>
</tr>
</tbody>
</table>

Prieser Unpublished Study ² Hypoglycemia

<table>
<thead>
<tr>
<th></th>
<th>Tight control 80-110 mg/dL</th>
<th>9.8% *</th>
</tr>
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<tbody>
<tr>
<td>Mod control</td>
<td>140-180 mg/dL</td>
<td>2.7%</td>
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(Mortality higher in pts with hypoglycemia)

NICE Sugar Trail ³

Mortality less with target <180 mg/dL

Committee recommended range <100-180 mg/dL (no change for 2013)

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F1. Adjunctive Therapy

- F1. Administration of probiotic agents has been shown to improve outcome (most consistently by decreasing infection) in specific critically ill patient populations involving transplantation, major abdominal surgery, and severe trauma. .. (Grade C)
- No overall ICU recommendation can currently be made for use of probiotics in the general ICU population... Several issues;
  - Species specific effects
  - Heterogeneous populations
  - Gut motility and integrity

Differences in ICU “Clinical Practice Guidelines”

F2. Adjunctive Therapy

- F2. A combination of antioxidant vitamins and trace minerals (specifically including selenium) should be provided to all critically ill patients receiving specialized nutrition therapy. (Grade: B)
- Would change to (Grade A) in 2013, with cautionary statement on giving with concurrent chemotherapy. Statement may state specific populations that may benefit.
- Issues with antioxidants:
  - Various vitamins, doses and combinations included in studies
  - Renal function should be included in consideration
  - Collier BR et al JPEN 2008 was not included in guidelines
• > 4000 patient study + effect on mortality in trauma pts
• Retrospective cohort, Prospective protocol data collection
  - Vit C 1000 mg Q 8h, Vit E 1000 IU Q 8h, Se 200μg QD
  X 7 days
- 4279 patients (2258 with antioxidant, 2021 without
  supplements)
  - Results: no difference in vent days
  - LOS and ICU LOS were decreased
  - Reduced mortality significantly (30% risk reduction)

Collier BR et al JPEN 2008

Disease Specific Formulations in the ICU

• Acute Pancreatitis K1-5
  • Evaluate for disease severity (Grade: E)
  • Nasoenteric access and EN initiated as soon as fluid volume resuscitation is complete (Grade: C) (changes to B or A)
  • Mild to moderate acute pancreatitis does not require nutrition support therapy unless an unexpected complication develops or there is failure to advance to oral diet within seven days) (Grade: C)
  • Severe acute pancreatitis patient may be fed enterally by gastric or jejunal route (Grade: C)
  • Tolerance to EN in severe acute pancreatitis may be enhanced by the following measures:
    • Minimize period of non-use of gut (Grade: D) (changes to C)
    • Feed more distal (Grade: C)
    • Change the content to small peptides, MCT, low fat (Grade: E)
    • PN when EN not feasible (Grade: C)
**Nutrition Guidelines ICU**

**Proposed changes for 2013 summary**

- Start TPN only if enteral attempts have failed or are not possible
  - No change
- Don’t start for at least 7 days unless patient is malnourished prior to admission to ICU
  - No change
- Still in discussion: Van de Berghe (2011) study vs Pichard
  - Based on current trials, just completed may start after 72 hours if EN unsuccessful
  - First 7 days of should be without IV lipids (in USA)
    - No change
  - TPN for short periods (1 or 2 days) is not indicated
    - No change
- If PN started in PN preop continue in the post op setting; Grade B
  - No change

**Specific nutrients**

- Metabolic / immune modulating formulas will be upgraded in Med ICU to A
- More focus and Grade A specifically for the preop use immune modulating formulations

**Route of feeding remains the same**

- EN over PN
- Timing remains the same
  - As early as safe
  - New data supporting within 24 hours is post op and trauma setting

**Conclusion**

- Significant differences in the populations being evaluated accounts for most differences
  - New updated guidelines (2013) will focus more on specific groups in the ICU and use selective recommendation based on ICU diagnosis
- Most current guidelines are in agreement on majority of topics
- Choose a guideline that works for you and stick with it
  - Make sure it has transparency !!!!

**Guidance for Guidelines**

- Good guidelines:
  - Validity, reliability, reproducibility, clinical applicability, flexibility, clarity, transparency, scheduled reviews

**Summary and Conclusion**

- Guidelines are just that, Guidelines
• Not dogma, not absolute, not rules, No guarantees
• Clinical judgment always takes precedent over guidelines
• Guidelines will change with ongoing trials, keep an open mind