Critical Care Nutrition: Taking Guidelines Directly to the Bedside

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Disclosures

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  Consultant

Metagenics
  Speakers Bureau

What We’re Hearing: Early EN is Bad!

• No “Forced Mandatory Feeds” first week
  1Dellinger (CCM 2013; 41:580)
  2Rice (Crit Care Med 2013; 41:580)
  3Besselink (Lancet 2008;371:651)
  4Heyland (NEJM 2013; 368:1489)
  5Van Zanten (JAMA. 2014;312:514)
  6Harvey (NEJM 2014)

• Trophic feeds are better
  1Dellinger (CCM 2013; 41:580)

• Starve to preserve autophagy
  2Schetz (Crit Care 2013; 17:302)
  3Besselink (Lancet 2008;371:651)

Immunonutrition Kills Patients!

• Arginine (Heyland)
  1Dellinger (CCM 2013; 41:580)

• Probiotics (PROPATRIA)
  2Rice (JAMA 2011; 306:1574)

• Fish oil (Omega)
  3Heyland (JAMA. 2013; 306:1574)

• Glutamine (REDOX)
  4Heyland (JAMA. 2013; 306:1574)

• “End of Era” (Metaplus)
  5Van Zanten (JAMA. 2014;312:514)

We Were Wrong About PN!

• PN is back
• Now PN=EN

Introduction

• Not all patients derive same benefit from nutrition therapy

• Previously well nourished, mild critical illness, short stay ICU
  Less benefit

• Moderate to severe critical illness, long ICU LOS, malnourished
  More likely to benefit
  More likely to be harmed by iatrogenic underfeeding

• Benefit of nutrition Rx depends on:
  Route
  Timing
  Interruptions
  Dosing
  Content
  Mobility

SA McClave, RG Martindale, TW Rice, DK Heyland (CCM 2014;42:2600)

Impact of Clinical Issues

Nutritional Risk
  Disease severity
  Nutritional status

Timing of nutritional intervention
  First week
  Argument to AVOID feeding
    Height of dz process, inflammation, insulin resist, intolerance
    Evidence that full feeds may be harmful
    Importance of preserving autophagy
    Teleologic argument disrupting fight/fright/flight response
    Opposing argument to PROVIDE feeding
    Window of opportunity to attenuate disease severity, SIRS
  Provide non-nutritional benefits of nutrition Rx

Second week
  Change in priorities, less controversial
  Need for nutritional benefits, impact of increasing caloric deficit
  Iatrogenic underfeeding > 7 days bad, catabolism to anabolism
**Value of EN in the Literature: Infection Mortality**

- Early EN vs No Early EN: 
  - Mortality: 14.1% vs 8.7%, *p*=0.05

**EN Benefits: Achieved at Different Doses?**

- **Non-Nutrition benefits** - Lower dose, needed in all patients:
  - Gastrointestinal responses: Trophic on gut integrity, Gut/lung axis of inflammation, Motility/contractility
  - Immune responses: Modulate regulatory cells, Stimulate oral tolerance, Duod colon receptors
  - Metabolic responses: Incretin to insulin sensing, Attenuate stress metabolism

- **Nutrition benefits** - Higher dose, needed in high risk patients:
  - Protein, calories, Micronutrients, anti-oxidants

**Impact of Clinical Issues: Events of First Week May Affect Longterm Outcome**

- **ARDSNet Trials: Mortality Rate Over Time**
  - Implications: Medical care in ICU steadily improving with time. Low TV vent, conserv fluid mgmt, spont breathing, ↓sedation, NIV. As mort drops, harder to show Rx effect, much larger RCTs needed. Aggressive provision of EN presumed part of improved care.

**Question #1**

- Does the literature indicate that underfeeding is BETTER than full feeding in ICU patients?

  **Answer:** No.

  Literature that suggests feeding less is BETTER is flawed.

- **Underfeeding Better than Full Feeds: Flawed!**

<table>
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<th>Hosp Mortality (OR)</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>Signif</th>
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<td>All patients</td>
<td>1.00</td>
<td>1.23</td>
<td>1.99</td>
<td><em>p</em>=0.02</td>
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<tr>
<td>Heyland 2</td>
<td>1.00</td>
<td>1.22</td>
<td>1.42</td>
<td><em>p</em>=0.0005</td>
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<tr>
<td>All pts (no all PO)</td>
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<td>0.77</td>
<td>0.73</td>
<td><em>p</em>&lt;0.0001</td>
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Arabi 1, Heyland 2
Is Underfeeding BETTER than Full Feeding? Plausibility and Type 1 Error

- **Braunschweig INTACT Study**
  - Intens Rx (n=40) vs Stand Rx (n=38)
    - %Goal cal: 84.7% vs 55.4% (p<0.0001)
    - Mortality: 40.0% vs 16.0% (p=0.02)
  - Hosp LOS, ICU LOS, infections, duration MV no different
  - Power analysis indicated (n=200) needed to complete study
  - Cause of death no plausible mechanism (% died withdrawn of care)

- **Ziegler Example of Type 1 Error: PN/Glutamine vs PN in post-op pts**
  - First 50 pts - Less infections with Glutamine
  - Next 50 pts (100 total) - More infections with Glutamine
  - Last 50 pts (150 total) - No difference between groups

- **Arabi 2011 Single Center Study**
  - Under 60-70% (n=120) vs Full 90-100% (n=120)
    - Received: 59.0% vs 71.4%
    - Hosp Mort: 30.0% vs 42.5% (p<0.05)

**Does Underfeeding EQUAL Full Feeding?**

- **Arabi 2015 Multicenter**
  - Demographics
    - Mixed ICU
    - AP II 21.0
    - Age 50.2-50.9
    - SOFA 9.9
    - BMI 29.0
  - Intended
    - 40-60% (n=894) vs 70-100% (n=446)
  - Received
    - 46% vs 71%
  - Infection
    - 35.9% vs 37.9%
  - ICU LOS
    - 13d vs 13d
  - ICU/90d Mort
    - 16.1/27.2% vs 19.1/28.9%

**Concept of Nutritional Risk**

- Components: Impaired nutrition status and disease severity
- J Kondrup (Curr Opin Clin Nutr Metab Care 2014;17:177)
**Concept of Nutritional Risk: Nutric Score**

Six factors for Nutric Score:
- Disease severity:
  - Age
  - Initial APACHE II score
  - Initial SOFA score
  - Interleukin-6
- Comorbidities
- Poor nutritional status:
  - Hosp LOS prior to ICU

**Paradigm Shift: Assess Risk → Therapy → Response**

**Observational Studies**
- NRS-2002 Jie Study1 - High Risk patients (n=120) with NRS Score >5
  - Insufficient (n=77) Sufficient Nutr Rx (n=43)
  - Overall complications 51% → 25%
  - Nosocomial infection 34% → 16%
  - Nutric Score Heyland Study2 (n=1199) (no Interleukin-6 used)

**Randomized Controlled Trials**
- Starke Study (NRS Score ≥3) (n=132)
  - Energy
    - Intervent (n=66) 24 kcal/kg
    - Controls (n=66) 18 kcal/kg
  - Protein
    - Intervent (n=66) 1.0 gm/kg
    - Controls (n=66) 0.7 gm/kg
  - Complic
    - Intervent (n=66) 6.0%
    - Controls (n=66) 18.7%
  - Re-Hosp
    - Intervent (n=66) 25.7%
    - Controls (n=66) 42.4%
- Johansen Study (NRS Score on all pts) (n=212)
  - Complic
    - Intervention (n=18) 3.4
    - Controls (n=14) 3.6
  - NRS Score
    - Intervention (n=18) 14.07d
    - Controls (n=14) 19.67d

**Dosing of EN**
- Low nutritional risk - (NRS 2002 ≤ 3 or Nutric Score ≤5)
  - Low dose EN (trophic or none) for first week
- Moderate risk - ALI/ARDS, MV ≥ 72 hrs
  - Low or high dose EN (Trophic or full feeds)
- High nutritional risk (NRS 2002 ≥5, Nutric ≥6)
  - High dose EN
    - Advance to goal as tolerated over 24-48 hrs
    - Attempt to provide > 80% goal

**Nutritional Assessment**
- Caloric requirements
  - 25-30 Kcal/kg/d
  - Published predictive equations no more accurate
  - Indirect calorimetry
- Protein requirements
  - Greater emphasis
  - Higher doses
  - 1.2-2.0 gm/kg/d
  - Fewer restrictions

**Do Interventional RCTs Support Emphasis on Protein?**
- Doig Nephro-Protect Trial1
  - Unblinded multicenter RCT
  - Pts expected on MV 48 hrs; excluded patients with AKI
  - Short-term IV AAs QD (n=474)
  - Max protein 2.0 gm/kg/d
  - 20 endpoints, 4 subsets
  - No difference in mort, others
- Heyland Protein Top-Up Trial2
  - Multicenter RCT adding PN vs placebo to enteral tube feeding
  - Five centers in Europe, US, Canada (n=167)
  - Primary endpoint = 90d mortality; Secondary = LOS, infect, MOF
  - Results from pilot trial – No difference in outcomes between groups

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1 B Jie (Clin Nutr 2012) 2 DK Heyland (Crit Care 2011;15:R268) (Clin Nutr 2015 Jan)

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1 J Starke (Clin Nutrit 2011;30:194) 2 N Johansen (Clin Nutrit 2004;23:539) *p=0.05

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1 Jallingstrup (Clin Nutr 2012;31:462) 2 P Willis (JPEN 2012;36;S07)
**Initiate Enteral Feeding**

- EN preferred over PN for nutrition support therapy
- Initiate EN within 24-48 hrs of onset of illness
  - Overt signs of contractility not required to start
  - Absent BS predict intolerance, dz severity, need for vigilance
- Initiate EN in the stomach
  - Divert lower if intolerant, high aspiration risk
- Withhold EN with hemodynamic instability
  - Restart with caution if requiring low dose vasopressor support

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**Need for EN in High Risk Patients:**

Utilize Strategies to Increase EN Delivery

- Compensatory Strategies
  - Over-order calories
  - Timed over 18-20 hrs
  - Volume-based feeding
  - Set catch-up rate
- Multi-Strategy De-escalation (Top-Down or PEP-up)
  - Start at goal
  - Volume-based feed
  - Caloric balance
  - SB infusion
  - Start with prokinetics
  - Probiotics (oropharynx and tube)
  - Small peptide formula
  - Elevate HOB
- Nurse-driven protocols for EN (Set ramp up, vol, GRV, NPO, etc)
- Alter NPO status for diagnostic tests, procedures, surgery
- Bundle nutrition elements (set of action statements)

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**Formula Selection in the ICU**

- Start with standard polymeric isotonic formula (most ICU pts)
- Consider use of specialty formulas
  - Obesity formulas (Class II and III)
- Cannot recommend certain formulas
  - Organ-failure formulas
  - Rarely use hepatic, renal failure
  - Don’t use pulmonary failure
  - Disease-specific (diabetic)

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**Monitor Tolerance and Adequacy**

- GRVs should not be used as part of routine care
  - Montejo Multicenter RCT
    - 500cc GRV (n=160)
      - 47.8% * Mortality
      - 89% * Deficit
    - 200cc GRV (n=169)
      - 63.6%
      - 83%
- VAP
  - Deficit
  - No GRV used (n=227)
    - 16.7%     26.4%     27.8%
    - 319 kcal
  - Routine GRV (n=222)
    - 15.8%     27.0%     27.5%
  - Focus instead on:
    - Phys exam
    - Passing stool, gas
    - Tracking I&Os
    - Aspirat risk
    - Access site
    - Protein calorie goals

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**ASPEN/SCCM CCN Guidelines:**

Bundle Statements

**Immunonutrition and Anti-Inflammatory Formulas**

- Elective Surgery, SICU – Use arg/fish oil formula
  - Infection ↓ 41% (OR=0.59)
  - Hosp LOS ↓2.38 days
- Crit Care ICU – Don’t recommend arg/FQ formula
  - No difference mortality, infection, LOS
- ALIARDS – No recommendation anti-inflammatory lipid profile formula
  - Gadeg, Singer, Pontes-Arruda, Grau-Carmona
  - Constant infusion – All benefit
  - Rice ARDSNet, Stapleton
  - Bolus infusion – Harm, no benefit
  - Van Zanten Meta-Plus
  - Constant infusion - Harm

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1. JW Drover (JAAC 2011;212(3);385)
2. JE Gadeg (CCM 1999;27:1409)
3. P Singer (CCM 2006;34:1033)
4. A Pontes-Arruda (CCM 2006;34:2325)
5. T Grau-Carmona (Clin Nutr 2011;30:578)
6. T Rice (JAMA 2012;307:795)
7. R Stapleton (CCM 2011;39:1655)
8. A Van Zanten (JAMA 2014;312:514)
Adjunctive Therapy

• Soluble prebiotic fiber – Consider routine use in all pts

• Probiotics – Use for select patient populations
  Where RCTs have shown safety and benefit
  Do not use routinely for general ICU pts

• Antioxidants – Use for all pts requiring Specialized Nutr Support
  Selenium, zinc, copper, Vit C, Vit E

• Enteral glutamine – Do not use

1 Zhang (World J Gastro 2010;16:3970)

What is the Role of PN in the ICU?

Recent trials have changed our perspective

Exclusive PN Can Be Done Safely

Doig Early PN Study ICU Pts with Short Term EN Contraindication

• Early PN in Pts not expected to get EN for 3 days (n=1372)
  Multicenter PRCT PN vs STD

• Results:
  Durat MV shorter in PN by 0.47 d*
  Trend less ICU LOS by 0.8 d
  No different – Mortality, infection, QOL, hosp LOS, function

• Conclusion:
  PN can be given safely early on
  Little benefit realized

Doig GS, Simpson F (JAMA 2013;309:2130)

Supplemental PN Can Be Done Safely

Swiss Supp PN Study: Durat MV, Hosp LOS, ICU LOS no different (n=300)

CP Heiddeger, M Berger, C Pichard (Lancet 2012 Dec 3)

Should Exclusive PN Be Used More in the ICU?

Impact: Under controlled conditions high risk patients, PN can = EN
EN still preferred over PN, but should lower threshold to use PN

SE Harvey CALORIES Trial Group (NEJM Ahead of Print 10-1-14)

Use of Parenteral Nutrition

• Exclusive PN
  Low Risk - Withhold exclusive PN if EN not feasible (NRS 2002 ≤ 3 or Nutric Score ≤ 5)
  High Risk - Initiate exclusive PN ASAP (esp malnourished) if EN not feasible (NRS 2002 ≥ 5, Nutric Score ≥ 6)

• Supplemental PN - Add after 7-10d if EN < 60% goal high or low risk

• Maximize efficacy of PN
  Use Multidisciplinary Nutrition Team, protocols
  Hypocaloric dosing (80%) first week
  Withhold soy-based lipids first week
  Moderate glucose control (140-180 mg/dL)
  Transition off PN when EN provides > 60% goal

1 Heiddeger (Lancet 2012 Dec 3) 2 Jiang (Clin Nutrit 2011;30:736)
Summary

- Benefit of nutrition Rx derived from provision of early EN
- Standard polymeric formula appropriate for majority
- Use PN earlier in high risk than low risk pts when EN not feasible
- Appropriate monitors to assure safety, tolerance
- Interpret guidelines as they apply to institutional pt populations

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