Improving Outcomes in Surgery, Trauma and Critical Illness: One Bite at a Time

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Disclosures

• Professor of Surgery and Critical Care U. of Pittsburgh – Leave of Absence

• Medical and Scientific Director – Nestle Health Care Nutrition (Nestle Health Sciences) – North America

• I will not mention or advocate ANY commercial Product

• Nestlé Nutrition Institute
64 year old with Appendicitis

- Female, previously healthy
- March 2011
  - Right lower quadrant pain and urinary tract symptoms.
  - Local hospital – peri-appendiceal abscess
    - Pigtail drain. Sxs. Do not resolve
- June 2011 Continued symptoms
  - Transferred to UPMC - vesico-enteric-cutaneous fistula
  - Colonoscopy – malignancy suspected – bx. adenoma
  - Cystoscopy – tumor eroding into bladder
Why Medical Nutrition Intervention (MNI)?

• It is unavoidable - ALL patients need some form of nutrition
  – Omission – You assume:
    • Patient will do OK on his/her own
    • Nutrition does not make a difference any way
  – Commission – You Know:
    • Your knowledge can guide the patient
    • You can recognize nutrition-related problems
    • You can incorporate Nutrition Intervention akin to other initiatives to provide optimal surgical care
Nutrition intervention must...

• Be easy to implement
  – Require no sophisticated equipment
  – Simple algorithms
  – Incorporated into surgical practice

• Work Neutral
  – Not require more time nor personnel

• Produce a clear benefit
  – Improve clinical outcomes
  – Decrease cost

• How it works (scientific mechanism of action)
64 year old – Adenoca. cecum

- Right hemicolecctomy, partial resection bladder, abdominal wall, iliac vessels?

- Standard
  - 7-11 days
  - 38% complication rate HCUP 2006
  - 10-18% infection rate

- Nutrition
  - Patient has a moderate weight loss
  - Albumin levels are normal
  - Significant disruption of oral intake due to:
    - Testing, anorexia, poor palatability of food, anxiety.
Nutrition Status Predicts Surgical Outcome

- Single Most Important Predictor of Outcome
- Affects all Surgical illnesses
- As important as any other evaluation of risk
- Albumin alone establishes prognosis
- Easy to use, cheap

Nutrition Intervention

• Nutrition Risk is:
  – Low, intermediate, High

• What type of Intervention?
  – None – patient can tolerate moderate starvation
  – Oral Nutrition supplements
    • Specialized Oral Nutrition Supplements
  – Enteral Nutrition
  – TPN

• Any Risks from Nutrition Intervention
  – Complications
  – Cost
  – Disruption in other care
Heyland Meta-analysis - Immune Enhancing Diets and Infectious Complications

Heyland D. JAMA 2001;(286)8:944-953

Figure 2:}

Elective Surgical Patients

- Daly et al, 1992
- Daly et al, 1995
- Braga et al, 1996
- Schilling et al, 1996
- Gianotti et al, 1997
- Senkal et al, 1997
- Braga et al, 1999
- Senkal et al, 1999
- Snyderman et al, 1999

Favors Immunonutrition

Favors Standard Diet
Effect of Arginine, Omega 3 Fatty Acids, Nucleotides on Surgical Infection

Waitzberg et. al. World Journal of Surgery

Overall 17 different studies. Pre-op, Peri-op and Post-operative therapy
Waitzberg et. Al
WJS -30:1592-1604. 2006
Effect of Immunonutrition on Infection

Marik P E, Zaloga G P

JPEN J Parenter Enteral Nutr 2010;34:378-386

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>IMD Events</th>
<th>Total Events</th>
<th>Control Events</th>
<th>Total Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1.1 Arginine</td>
<td>38</td>
<td>39</td>
<td>39</td>
<td>4.2%</td>
<td>0.63 [0.23, 1.73] 2005</td>
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<tr>
<td>de Lusa 2005</td>
<td>10</td>
<td>23</td>
<td>12</td>
<td>3.0%</td>
<td>0.77 [0.24, 2.43] 2005</td>
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<tr>
<td>Casas-Rodera 2008</td>
<td>1</td>
<td>15</td>
<td>3</td>
<td>1.3%</td>
<td>0.29 [0.03, 3.12] 2008</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>38</td>
<td>39</td>
<td>39</td>
<td>4.2%</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>11</td>
<td>15</td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: Chi² = 0.54, df = 1 (P = 0.46); P = 0%</td>
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<tr>
<td>Test for overall effect: Z = 0.90 (P = 0.37)</td>
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</table>

| 3.1.2 FO          |            |              |                |              |                                  |
| Kenzer 1996       | 7          | 18           | 6              | 17%          | 1.17 [0.30, 4.61] 1996           |
| Subtotal (95% CI) | 18         | 24           | 17             | 17%          | 1.17 [0.30, 4.61]                |
| Total events      | 7          | 15           |                |              |                                  |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 0.22 (P = 0.83) |

| 3.1.3 A-F preoperative |            |              |                |              |                                  |
| Xu 2006             | 2          | 30           | 8              | 30%          | 0.20 [0.04, 1.02] 2006           |
| Subtotal (95% CI)   | 30         | 30           | 30             | 30%          | 0.20 [0.04, 1.02]                |
| Total events        | 2          | 15           |                |              |                                  |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.94 (P = 0.05) |

| 3.1.4 A-F postoperative |            |              |                |              |                                  |
| Daly 1992            | 5          | 41           | 13             | 44%          | 0.33 [0.11, 1.03] 1992           |
| Daly 1995            | 1          | 30           | 9              | 30%          | 0.06 [0.01, 0.68] 1995           |
| Schilling 1996       | 3          | 14           | 6              | 14%          | 0.36 [0.07, 1.91] 1996           |
| Braga 1996           | 2          | 20           | 3              | 20%          | 0.63 [0.09, 4.24] 1996           |
| Senkel 1997          | 17         | 77           | 24             | 77%          | 0.63 [0.30, 1.20] 1997           |
| Gianotti 1997        | 13         | 87           | 20             | 87%          | 0.59 [0.27, 1.27] 1997           |
| Braga 1998           | 9          | 55           | 13             | 55%          | 0.63 [0.25, 1.63] 1998           |
| Di Carlo 1999        | 3          | 33           | 6              | 33%          | 0.48 [0.11, 2.12] 1999           |
| Snyderman 1999       | 19         | 82           | 19             | 82%          | 0.44 [0.20, 0.97] 1999           |
| Jiang 2004           | 9          | 60           | 15             | 60%          | 0.53 [0.21, 1.33] 2004           |
| Farreras 2005        | 2          | 30           | 9              | 30%          | 0.17 [0.03, 0.85] 2005           |
| Lob 2005             | 24         | 54           | 24             | 54%          | 1.00 [0.47, 2.14] 2006           |
| Subtotal (95% CI)    | 583        | 553          | 99.2%          |              | 0.52 [0.39, 0.69]                |
| Total events         | 107        | 161          |                |              |                                  |
| Heterogeneity: Chi² = 9.14, df = 11 (P = 0.61); P = 0% |
| Test for overall effect: Z = 4.48 (P = 0.00001) |

| 3.1.5 A-F perioperative |            |              |                |              |                                  |
| Braga 1999            | 14         | 102          | 31             | 104%         | 0.37 [0.19, 0.76] 1999           |
| Senkel 1999           | 10         | 78           | 18             | 78%          | 0.47 [0.20, 1.11] 1999           |
| Tepaske 2001          | 4          | 25           | 12             | 25%          | 0.21 [0.05, 0.78] 2001           |
| Braga 2002            | 5          | 50           | 12             | 50%          | 0.35 [0.11, 1.06] 2002           |
| Helminen 2007         | 7          | 50           | 8              | 50%          | 0.85 [0.28, 2.57] 2007           |
| Subtotal (95% CI)     | 305        | 305          | 305            | 31.5%        | 0.42 [0.27, 0.63]                |
| Total events          | 40         | 81           |                |              |                                  |
| Heterogeneity: Chi² = 2.98, df = 4 (P = 0.68); P = 0% |
| Test for overall effect: Z = 4.10 (P < 0.0001) |

| Total (95% CI)        | 974        | 944          | 100.0%         |              | 0.49 [0.39, 0.62]                |
Figure 4. Results of Subgroup Analyses examining the Effect of Arginine Supplemented Diets on Infection

- GI studies (21)
- Non GI studies (7)
- Lower GI studies (1)
- Upper GI studies (16)
- Lower & Upper GI studies (4)
- Pre Op studies (6)
- Peri Op studies (9)
- Post Op studies (15)
- Infections Overall

Infections Overall

- Arginine Beneficial
- Arginine Harmful

P=0.06
P<0.0001
P=0.03
P=0.03
P=0.28
P=0.03
P<0.0001

Number in parenthesis indicates number of studies
Immunonutrition in gastrointestinal surgery

Y. Cerantola, M. Hübner, F. Grass, N. Demartines and M. Schäfer

157 Patients

IN

Control

Total
Complications
Immunonutrition in gastrointestinal surgery

Infections

Y. Cerantola, M. Hubner, F. Grass, N. Demartines and M. Schafer

38 – 59% ↓↓

Incidence % infections
Specialized Surgical Nutrition in Severely Malnourished Patients with Pancreatic Cancer

Complications

Infection

• Mortality also reduced
  • 1.3% vs 5.9% (p=0.035)

Initial Conclusions - Consensus

- Arginine, omega 3 fatty acids are uniformly beneficial - elective surgery patient
- Best data in GI surgery
- Length of Stay decreased by 2-3 days
- Decreased infections
- Decreased complications
- Decreased severity of infections/complications
- No effect on mortality
Initial Conclusions (2) - Consensus

• All major clinical investigators and Nutrition experts agree.

• Societies and Professional organizations give it High grade of recommendations
  – ASPEN, SCCM, ESPEN

• Can it be adopted into clinical practice?
• How does Immunonutrition work?
• Is it cost-effective?
Arginine Plasma Levels

Arginase Activity After Severe Trauma

Discovery of Myeloid Cells Expressing arginase

• Destroy Arginine
• Suppress Biological Functions (arginine-dependent)
  – Nitric Oxide
  – T lymphocyte Function
  – Wound Healing

Myeloid Cells after Surgery/Trauma
Arginine Deficiency Syndrome
Popovic, zeh, Ochoa 2006 J. Nutr. 137;6(2). 1681-

- Clinically recognizable features (signs, symptoms, biomarkers)
- Arginine deficiency
  - Low arginine
  - T cell markers
  - Decrease Nitric Oxide production
- Mechanism of production of arginine deficiency
  - Arginase in Myeloid cells
- Biological consequences of worsening of disease
  - Increased infection
  - Observed in cancer, leprosy, tuberculosis, other
- A successful treatment
Blocking Arginase improves Rodent’s capacity to reduce infection and improve T cell function

Zhu, Ochoa  Submitted Journal of Immunology
Effect of a SNF on line infections in severely malnourished patients undergoing surgery for Colo-rectal Cancer

![Bar chart showing the percentage of infections with and without SNF.

- WN: No SNF, lowest infection rate.
- MN: Standard nutrition, higher infection rate.
- MN + SNF: SNF added, significantly lower infection rate.

Statistical significance: p=0.013]
Preoperative oral arginine and n-3 fatty acid supplementation improves the immunometabolic host response and outcome after colorectal resection for cancer

Marco Braga, MD, Luca Gianotti, MD, ScD, Andrea Vignali, MD, and Valerio Di Carlo, MD, Milan, Italy

**Fig 6.** Gut oxygen tension, as measured by polarographic implanted microprobes during surgery and throughout the first postoperative week. *P < .007 beginning vs end for control and conventional. †P < .01 pre-op and peri-op vs control and conventional.
Effect of Arginine on % Pedicle Flap Survival

Effect of Arginine and Omega 3 FA on Flap Survival in Surgery for H&N cancer

Effect of ARGOM3 on Microcirculation after Open Heart Surgery
Tepaske - Lancet 2001

Circulating NOx were Increased
Projected Savings from Reduction in Infectious Complications in GI Cancer surg- Perioperative Use of Immunonutrition – Unpublished RTI™ – North Carolina

Sensitivity Analysis** Assumes:

• Meta-analysis outcomes of Waitzberg et al 2006

• Weighted average of additional costs attributed to different types of complications estimated from HCUP

• Oral IMF TID x 5 days pre-op; 1 L TF IMF/d x 7 days post-op

• At baseline infectious complication rate of 15%, projected savings = $1,260 per patient. 100 patients= $126,000

*Arg-n3-nucleotide formula**Example purposes. Not intended to guarantee specific reductions in cost or complications.
Approximate Cost/day of Nutrition Intervention

<table>
<thead>
<tr>
<th>High Protein Drink</th>
<th>SNF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per Unit: $1</td>
<td>Per Unit: $3.33</td>
</tr>
<tr>
<td>Per Day (3 boxes): $3</td>
<td>Per Day (3 boxes): $9.99</td>
</tr>
<tr>
<td>Regimen (3 boxes * 5 days): $15</td>
<td>Regimen (3 boxes * 5 days): $50</td>
</tr>
</tbody>
</table>

Difference for 5 days: $35
Implementing Nutrition Intervention
Inadequate assumptions

• Moderate starvation is well tolerated
• That oral nutrition needs to be controlled to avoid complications
  – NPO for procedures
• Lack of consequences if the patient is kept NPO
• Lack of Policies and Protocols
• Inadequate education of health care workers
• You can “make up for it” later
• *Laissez faire* attitude
Keeping the Patient NPO during illness

The Gas we Pass – Shinta Cho

When you begin to fart after an operation, it means your intestines have started working again.
Optimized Nutrition Intervention
Performance Improvement

• Assess the current state of Nutrition
  – Analyze the prevalence of malnutrition on admission

• Create plans for Intervention
  – Change the Name from Nutrition support service to Medical Nutrition Intervention team
  – Give the MNI the importance that it deserves

• Establish education programs
• Establish protocols
• Establish Carrots and sticks
• MONITOR, MONITOR, MONITOR
Enhancing surgical Outcomes through Process Improvement

Pre-operative Phase
- Can Eat
- Oral Nutrition Supplement
  Arginine, ω- 3FA
  3 /Day for 5 Days

Surgery
- ABX, Avoid Hypothermia, Glucose Control
- NO NG Tube
- Careful IV Fluids
- Pain Control
- Multimodality
- Remove Tubes

Post-operative Phase
- Early Oral /Enteral Intake
- Oral/Enteral Nutrition Supplement
  Arginine, ω- 3FA
  2-3 /Day for 5 - 10 Days
Nutrition Protocol

Surgeon Evaluates Patient

Nutrition Optimization Ordered
Date For Surgery Established

Nutrition Optimization Not Necessary (i.e. minor surgery)

Albumin, Prealbumin and CRP Ordered

Order SNF 3X/Day for 5 days Prior to Surgery

NPO Day of Surgery (Consider High Protein/Carb/No fat liquid diet)

Start Specialized Nutrition Formula 1-3X/Day on POD # 1

Start a Regular Diet. Continue SNF 1-3X/Day for 5-10 Days

CONSIDER (ERAS)
- Enhanced Recovery after Surgery
- Minimize use of NG Tube
- Multimodality pain control (NSAIDS)
- Careful with IVF
- Maintain adequate electrolyte balance
- Do NOT try to Meet Caloric Goals

Patient cannot eat or albumin < 2.8

Consider Nutrition TEAM Consult For TPN
Peri-operative Care

• Pre-op. Oral supplementation of
  – arginine, ω-3 FA, vitamin A
    • 5 days 3 X a day

• SCIP Interventions

• Post-op Early oral Nutrition
  – High Carbohydrate oral drink 6-18 hours
  – arginine, ω-3 FA, vitamin A
    • 5 days 3 X a day

• Adjunct therapy – Enhanced recovery after surgery (ERAS)
  – NO NG
  – NSAIDS
  – Careful use of IVF

• Home in 3-4 days.
Thank you!

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