Guidelines for the Adult Critically Ill Patient Webinar Training Series

June 7, 14, 21, and 28, 2016
1:00 – 2:30 pm ET

Exploration of and Application to Practice: Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN)
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Exploration of and Application to Practice: Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN)

Guidelines Introduction
The significance of nutrition in the hospital setting (especially the ICU) cannot be overstated. Critical illness is typically associated with a catabolic stress state in which patients demonstrate a systemic inflammatory response coupled with complications of increased infectious morbidity, multiple-organ dysfunction, prolonged hospitalization, and disproportionate mortality. Over the past 3 decades, exponential advances have been made in the understanding of the molecular and biological effects of nutrients in maintaining homeostasis in the critically ill population. Traditionally, nutrition support in the critically ill population was regarded as adjunctive care designed to provide exogenous fuels to preserve lean body mass and support the patient throughout the stress response. Recently, this strategy has evolved to represent nutrition therapy, in which the feeding is thought to help attenuate the metabolic response to stress, prevent oxidative cellular injury, and favorably modulate immune responses. Improvement in the clinical course of critical illness may be achieved by early EN, appropriate macro- and micronutrient delivery, and meticulous glycemic control. Delivering early nutrition support therapy, primarily by the enteral route, is seen as a proactive therapeutic strategy that may reduce disease severity, diminish complications, decrease LOS in the ICU, and favorably impact patient outcomes.

In response to these recently released guidelines, ASPEN has developed a webinar training series featuring three of the experts who contributed to the guidelines to educate all members of the healthcare team who work in the critical care setting. The webinars will be a rebroadcast of the live in-person course that took place May 10, 2016 in Baltimore, MD.

This webinar training series will involve an exploration of the guidelines and then allow for an in-depth assessment of how the guidelines should be implemented into practice for the provision of optimal nutrition care of the adult critically ill patient. There will be an opportunity to engage in discussion with authors of the guidelines each week.

1. **History of and Introduction to the Current Guidelines and Evaluating the Quality of Evidence**
   June 7, 2016 from 1:00 – 2:30 pm ET

2. **Comparisons of the Current Guidelines to the 2009 Guidelines – What has changed and what has stayed the same?**
   June 14, 2016 from 1 – 2:30 pm ET
3. Application of the Guidelines to Various Patient Scenarios
   CALORIES Trial: Grading the Evidence, Evaluating Strengths and Weaknesses, and Determining Clinical Applications
   June 21, 2016 from 1 – 2:30 pm ET

4. Influence of Publications Since the 2013 Deadline
   June 28, 2016 from 1 – 2:30 pm ET

Individual Webinar Details

1. History of and Introduction to the Current Guidelines and Evaluating the Quality of Evidence
   June 7, 2016 from 1:00 – 2:30 pm ET

   Learning Objectives
   - Describe the history of developing nutrition support guidelines for the adult critically ill patient
   - Interpret Forest plots from a meta-analysis
   - Analyze the differences between observational studies and randomized controlled trials with a focus on strengths and weaknesses of each
   - Summarize the scientific rigor required for the development of societal guidelines

   Faculty
   Robert G. Martindale, MD, PhD, Chief, Division of General Surgery; Medical Director, Hospital Nutritional Services, Oregon Health and Science University, Portland, OR
   Stephen A. McClave, MD, FASPEN, Professor of Medicine, Division of Gastroenterology/ Hepatology, University of Louisville School of Medicine, Louisville, KY

   Discussant
   Todd Rice, MD, Assistant Professor of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University Medical Center, Nashville, TN
   Mary McCarthy, RN, PhD, CNSC, Senior Nurse Scientist, Center for Nursing Science and Clinical Inquiry, Madigan Army Medical Center, Tacoma, WA

   UAN: 0216-0000-16-094-L01-P
   Level: Intermediate
   CE Credits: 1.5

2. Comparisons of the Current Guidelines to the 2009 Guidelines – What has changed and what has stayed the same?
   June 14, 2016 from 1 – 2:30 pm ET

   Learning Objectives
   - Describe which recommendations that were included in the 2009 guidelines were strengthened or weakened by the addition of data to the new guidelines up until December 31, 2013
   - Summarize new supporting literature that reinforces practice concepts that are unchanged from the 2009 guidelines.
   - Discuss new supporting literature that has modified or changed the recommendations from the 2009 guidelines including expanded recommendations for specialized areas of practice (e.g., pancreatitis, trauma, burns, sepsis, post-operative, chronic critically ill, obesity).
3. Application of the Guidelines to Various Patient Scenarios/Incorporating Guidelines into Bedside Practice

**CALORIES Trial: Grading the Evidence, Evaluating Strengths and Weaknesses, and Determining Clinical Applications**

June 21, 2016 from 1 – 2:30 pm ET

**Learning Objectives**

- Identify recommendations included in the nutrition bundle to highlight practice
- Apply guidelines to individual case presentations
- Utilize the guidelines to guide clinical decisions in a variety of complex patient situations

**Faculty**

Stephen A. McClave, MD, FASPEN, Professor of Medicine, Division of Gastroenterology/ Hepatology, University of Louisville School of Medicine, Louisville, KY

Robert G. Martindale, MD, PhD, Chief, Division of General Surgery; Medical Director, Hospital Nutritional Services, Oregon Health and Science University, Portland, OR

Beth Taylor, DCN, RD, LD, CNSC, Nutrition Support Specialist, Surgical ICU, Barnes-Jewish Hospital, St. Louis, MO

**Discussant**

Mary McCarthy, RN, PhD, CNSC, Senior Nurse Scientist, Center for Nursing Science and Clinical Inquiry, Madigan Army Medical Center, Tacoma, WA

UAN: 0216-0000-16-095-L01-P
Level: Intermediate
CE Credits: 1.5

4. Influence of Publications Since the 2013 Deadline

June 28, 2016 from 1 – 2:30 pm ET

**Learning Objectives**

- Summarize the rationale for the deadline date of inclusion for the guidelines
- Analyze the details of six large randomized trials that influenced practice from January 2014 through the present time
- Describe how the guidelines are not obsolete and are in sync with the publication of recent trials.
Faculty
Stephen A. McClave, MD, FASPEN, Professor of Medicine, Division of Gastroenterology/ Hepatology, University of Louisville School of Medicine, Louisville, KY

Discussant
Stephen A. McClave, MD, FASPEN, Professor of Medicine, Division of Gastroenterology/ Hepatology, University of Louisville School of Medicine, Louisville, KY

UAN: 0216-0000-16-097-L01-P
Level: Intermediate
CE Credits: 1.5

Accreditation and Continuing Education Information

Course Details and Target Audience
This course is intended for all healthcare professionals who provide nutrition therapy to critically-ill adult patients – with an emphasis on physicians, nurses, dietitians and pharmacists.

Course Practice Gap and Goal
With newly release guidelines for the provision of nutrition therapy in the critically ill patient population healthcare providers need to be adequately trained on best practices to fully implement the guidelines into practice. The goal of his course is to train healthcare professionals to adequately assess critically ill patients and subsequently provide adequate nutrition therapy to aid with recovery from the illness.

Successful Completion
ASPEN provides continuing education credit to physicians, nurses, pharmacists and dietitians who attend in full each session claimed for credit, and complete the program evaluation. All evaluations and claims for credit must be submitted by August 1, 2016 in ASPEN’s eLearning Center – www.nutritioncare.org/elearning.

Accreditation Statements
Nurses, Pharmacists, Physicians

ASPEN is accredited by the American Nurses Credentialing Center (ANCC), the Accreditation Council for Pharmacy Education (ACPE), and Accreditation Council for Continuing Medical Education (ACCME), to provide continuing education for the healthcare team.

ASPEN designates this [each] live activity for a maximum of 1.5 AMA PRA Category 1 CreditsTM. Physicians should only claim the credit commensurate with the extent of their participation in the activity.

UANs:

<table>
<thead>
<tr>
<th>Tuesday, June 07, 2016</th>
<th>History of and Introduction to the Current Guidelines and Evaluating the Quality of Evidence</th>
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0216-0000-16-097-L01-P
Each activity is available for a maximum of 1.5 contact hours (0.15 CEU). Knowledge activities.

ASPEN is approved by the California Board of Registered Nursing, provider number CEP 3970.

Dietitians:

ASPEN, Provider Number AM005, is a Continuing Professional Education (CPE) Accredited Provider with the Commission on Dietetic Registration (CDR). Registered dietitians (RDs) and dietetic technicians, registered (DTRs) will receive continuing professional education units (CPEUs) for completion of this program / materials. CDR level 2, for 1.5 CPEUs for each individual webinar in the series. Dietitians may post comments on this program on www.cdrnet.org.

Policies

- Any grievances should be addressed in writing to Director of Education and Research ASPEN 8630 Fenton Street Suite 412 Silver Spring, MD 20910.
- Commercialism: ASPEN subscribes to the ACCME Standards for Commercial Support. ASPEN does not provide programs that constitute advertisement or include promotional content. ASPEN does not endorse any products. There will be no discussion of off-label use of products.
- Privacy and Confidentiality: ASPEN respects the privacy of its members and website visitors. Companies that receive personal information from ASPEN in order to execute the business of ASPEN may use personal information only for that purpose.
- Refund Policy: All cancellation requests must be sent to the ASPEN national office, by email to: aspen@nutritioncare.org or by fax to: (301)587-2365. Telephone cancellations will not be accepted.

Requirements for Participation

- Adobe Flash Plugin
- Internet Explorer 7+, Mozilla Firefox, Google Chrome, Safari
- Computer with speakers/headset
- Broadband Internet connection
- Also compatible with iOS and Android based tablets and smartphones.

Faculty Disclosures

In relation to the course being presented, the faculty have the following commercial relationship disclosures and conflicts of interest to report.

- Robert Martindale: while not related to the course content, Dr. Martindale has worked with several commercial entities as listed below. All information presented by Dr. Martindale will be evidence-based. Grant from Metagenics, Consulting fee from Abbott and Nestle

- Stephen McClave: while not related to the course content, Dr. McClave has worked with several commercial entities as listed below. All information presented by Dr. McClave will be evidence-based. Nestle, Metagenics, and Abbott as a member of their speaker’s bureau, and consultant for Metagenics and Covidien. Receives honoraria

- Beth Taylor: nothing to disclose
How to Claim Your Critical Care Series CE Credit

CE Credits for all sessions attended must be claimed by July 30, 2016
(Pharmacy Participants, please see important information below)

Claiming CE for Each Session

- Claim your CE credit by logging into ASPEN's eLearning Center
- Your login for the eLearning Center is the same email and password you use for the main A.S.P.E.N. website
- click on "My Live Events" under the “Your Account” menu on the left hand side of screen
- click “Take Evaluation” below the session you wish to claim credit for. If you have already claimed CE for a session, the “Take Evaluation” option will not appear. The most recent session will be at the bottom of the list.

Obtaining your Course Certificate

- To obtain your course certificate select “CE Transcript” under the “Your Account” menu on the left hand side of screen
- Click the link to complete the “Overall Conference Evaluation”
- Once you complete and submit your overall evaluation, you will have the option to “View Transcript”
- You can print your certificate if you need it, but it will be saved in the eLearning Center so you can easily download it when you need it

Certificate of Training - if you registered for CE for all sessions you will receive a Certificate of Training. The certificate of training will be available with your transcript once you have successfully claimed CE for all four sessions in the series.

Watching Sessions Again

All sessions are recorded and available in the eLearning Center. If you miss a session, the recording will be available about 3 business days following the session. All registered attendees have access to the recordings for 1 year after the course concludes.

You can access session archives through “My Live Events” where you can click “view archive” for any session. You can also access any recordings available to you by visiting “My Library” (the first option under the “Your Account” menu on the left).

IMPORTANT INFORMATION FOR PHARMACY PARTICIPANTS

Pharmacy participants should claim CE as soon as possible following each attended session.

Due to Accreditation Council for Pharmacy Education (ACPE) and National Association of Boards of Pharmacy (NABP) guidelines, A.S.P.E.N. is required to submit CE credits claimed by Pharmacy participants within 60 days of a session. Because this course is over a 4-week period we strongly encourage Pharmacy participants to claim CE immediately follow each session so you do not forget or miss claiming credit within the required 60 day period.

To claim credit, Pharmacy participants will be required to submit their birthdate (MM/DD), NABP ID #, and complete the session evaluation.

For more information or to create your NABP ID, please visit www.nabp.net
A.S.P.E.N. is not responsible for information submitted late or incorrectly by the participant.
Using the Webinar Player

Control Panel is on the left

- The control panel will open to the chat screen by default. To switch between Chat, Questions, or Resources, simply click the header to expend your preferred section.
- Click the “X” on the left side of any header to minimize the interactive elements of the player.
- To reopen the interactive elements, simply click any header which will now be listed along the left side of your webinar screen.
- Chat: Use chat to talk to other attendees.
- Polling: There will be several polls during the session. Click the “polling” icon to submit your answer.
- Resources: Download handouts from today’s session.
- Q&A: Submit your questions to the faculty at any time during the program.
- Notes: On the right side of the screen you can take notes during the program. These notes will be emailed to you following the session.

For Technical support, use the Request Support button at the bottom left corner of the webinar player.

Faculty

Robert G. Martindale, MD, PhD
Chief, Division of General Surgery, Medical Director, Hospital Nutritional Services
Oregon Health and Science University, Portland, OR

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Vanderbilt University Medical Center, Nashville, TN

Mary McCarthy, RN, PhD, CNSC
Senior Nurse Scientist, Center for Nursing Science and Clinical Inquiry
Madigan Army Medical Center, Tacoma, WA
How it started - 2003

- Surviving Sepsis Guidelines 2002
- Lena Napolitano – incoming SCCM President
- Early discussion at SCCM annual meeting

Model for New Guidelines

- Gary Zaloga / Myself
- Nearly no progress
- Gary left for industry
  - Concern for COI
    - SCCM under investigation for Lilly contribution to Surviving sepsis
  - McClave joins

SCCM Guidelines Committee

- Steve McClave, Co-chair
- Vince Vanek
- Juan Ochoa
- Bob Martindale, Co-chair
- Lena Napolitano
- Beth Taylor
- Gail Cresci
- Pam Roberts

ASPEN 2002 Critical Care Guidelines

- Practice Guidelines Critical Care Critical Issues
  - Management
  - Clinical guidelines: Sepsis and critical illness
    - Sepsis guidelines: a critical illness
    - Critical illness care
  - Clinical guidelines: Sepsis and critical illness
    - Sepsis guidelines: a critical illness
    - Critical illness care
  - Clinical guidelines: Sepsis and critical illness
    - Sepsis guidelines: a critical illness
    - Critical illness care
Introduction

- **Basic Recommendations**
  - Not absolute requirements
  - Do not project or guarantee outcome or mortality benefits
  - Not a substitute for clinical judgment (takes precedent)

- **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 2-5 days
  - Not a homogeneous population

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**Process**

- Five year process beginning July 2004 (>45 reviewers)
  - Original manuscript (old style) Peer Review July 2005
  - Voluntary revision Survive Sepsis format
  - Guidelines Committee reorganized format (delay 1 yr)
  - Updated manuscript ASPEN Peer Review Mar 2007
  - ASPEN Board Review Aug 2007
  - SCCM Board and Peer Review Jan 2008
  - CCM Journal Peer Review Nov 2008

- **Final Board Approval**
  - ASPEN Board Jun 2008
  - SCCM Board Jan 26, 2009
  - ASPEN Board Review Aug 2007
  - SCCM Board and Peer Review Jan 2008

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**Development of Guidelines**

- **List of recommendations compiled by Committee Experts**
  - Action statements
  - 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 committee**
  - Include patient care recommendations where sole basis was expert opinion
  - Promote recommendations and conditions for use of PN where outcome benefit assured

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**Grading of Literature**

- Definition of Large trial
  - Fulfill endpoint criteria
  - Size >100 subjects

- Use of Meta-Analysis
  - Organize information
  - Derives overall treatment effect
  - Not to grade recommendation

- Review papers, consensus statements = Expert opinion

- Grade based on level of evidence of individual studies

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**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

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Adapted from Dellinger (CCM 2004;32:858-873)
Summary and Conclusion

• Guidelines are just that, Guidelines
  • No guarantees
• Clinical judgment *always* takes precedent over guidelines  
• Guidelines will change with ongoing trials, keep an open mind
• Protocols incorporating guidelines improves outcome

• Guidelines are just that, Guidelines
  • No guarantees
• Clinical judgment *always* takes precedent over guidelines  
• Guidelines will change with ongoing trials, keep an open mind
• Protocols incorporating guidelines improves outcome
• If anyone asked you to chair a guidelines committee *just say no*
Evaluating the Guidelines and the Quality of Evidence

Stephen A. McClave, MD
Louisville, Kentucky

Disclosures
Nestle
Speakers Bureau
Educational Grant (Fellowship)
Abbott
Speakers Bureau
Medtronic
Consultant
Metagenics
Speakers Bureau

Chicago Dietitian: “Today on SICU rounds, the attending said that the ASPEN guidelines are written by a bunch of people sitting around a desk. Meta-analyses done on the impact of nutrition and the ASPEN/SCCM guidelines themselves are based on poor data.”

RD PhD Former ASPEN Board Member, former AND DNS Chairman: “The ASPEN guidelines aren’t evidence-based. I believe they were developed using ‘expert consensus’ which is a bunch of people sitting around…..We do have to know the difference between expert consensus and a systematic review. I’m not saying they aren’t valuable, they just aren’t evidence-based.”

Two Problems: Poor faith in nutrition literature Poor understanding of guidelines process

Conversation on the ASPEN List-Serve (Dec 1, 2015 2:40 pm)

2016 ASPEN SCCM Guidelines Committee

Historical Timeline

• 2001-2003 Canadian CPGs – External consultants
• 2004-2009 ASPEN SCCM Guidelines
• Current 2016 Guidelines Effort
  Committee convened Jan 2012
  Harmonization process with Canadians over 2 yrs
  Lit searches, >750 RCTs entered, DAFs completed
  Manuscript compiled over one year: Jan-Dec 2014
  Sections written, GRADE tables constructed, editing
  Manuscript submission Jan 19, 2015
  Review process – 3 Boards 2 Journals
  Final acceptance June 2015 ASPEN, Sept 2015 SCCM
  Available online Jan 15, 2016 and in print Feb 15, 2016

Evaluating Quality of Evidence

GRADE = Grading of Recommendations Assessment, Development, Evaluation

GH Guyatt (J Clin Epidemiol 2011;64:380-415)

• Evaluate literature using initial rank
  RCT (++++) vs Observational study (+)

• Change score based on methodologic quality issues
  RCT – ↓Score (consistency, directness, precision, bias)
  Observational study – ↑Score (strong association, unmeasured factors, dose-response gradient)

• Determine strength of recommendation based on QOE
  Strong (we recommend)
  Weak (we suggest)
  No recommendation now
Evaluating Quality of Evidence

Build GRADE Tables, Forrest Plots from Data Abstraction Forms (DAFs)

Over 750 RCTs
Two DAFs on all RCTs
None on observational trials

Construction of GRADE Tables

Risk of Bias:
- blinding, ITT

Inconsistency:
- other RCTs

Imprecision:
- small numbers

Indirectness:
- applicability

Total number of recommendations (n=94)

Ungraded 56
Very Low 20
Low 9
Mod-High 9
None 56
Weak 30
Strong 8

QOE Strength

Potential of Meta-Analysis

Early EN vs No Early EN (p=0.01)

Infection

Heterogeneity
- p=0.08 apples vs oranges

Relative Risk
- risk 74% of controls (26% reduction)

Expert Consensus and Scientific Rigor

• Criticism of 2009 Guidelines
  - Methodology questionable, less objective, use of expert opinion
  - Absence of RCTs in many areas
  - Scientific rigor is no different than other guidelines

• Committee philosophy
  - Take advantage of experts involved, still provide guidelines
  - Anonymous vote committee members each recommendation (>70%)

Assessing Quality of Evidence

Don’t Mistake Scientific Rigor

Committee philosophy
- Avoid GRADE methodologic “doublespeak”
- “Based on small unblinded imprecise potentially biased RCTs, we suggest…” [Quality of Evidence: Very Low]
- Goal to provide clinical value to practitioners

Deadline for Study Inclusion

Ron Koretz, MD

• Deadline for study inclusion of December 31, 2013
• Rationale – Inclusion of any one trial post-date would require literature search of every section in the entire manuscript
• Don’t misinterpret: “Guidelines will be obsolete by time of publication”
- Not operating in a vacuum
- Cognizant of trials, peer review occurring after deadline
- Making changes to manuscript up through September 2015
- Evidence post-date does not contradict recommendations

SCCM ASPEN 2016 Guidelines (JPEN Feb 2016) (CCM Feb 2016)
Potential Flaws in Observational Trials

Hosp Mortality (OR) 1st 2nd 3rd Signif
All patients Arabi 1.00 1.23 1.99 p=0.02
All patients Heyland 1.00 1.22 1.28 p=0.0005
All pts (no oral days) 1.00 0.77 0.73 p=0.0001

Potential Flaws in Meta-Analysis

Good MA of poor studies is still poor
GRADE standardizes QOE but not selection criteria
MA fails to predict large subsequent RCT 35% of time

Potential Flaws in Large RCTs

• Generalizability: Internal validity - Methodologic design
External validity - Generalizability
Example: EPaNIC Trial (Infuse IV glucose, tight glucose control)
• Assessment of Harms: RCTs short in duration, less likely to identify uncommon harms of Rx than observational trials
Example: Rice ARDSNet Trophic Feeds (Did F/U 12 mos later!)
• Multiplicity: Repeated tests of statistical significance (looking for subsets, study endpoints) likely to produce ≥1 significant results
Example: Doig PN Trial (EN not feasible) - 520 endpoints x 4 groups
• Rigidity toward P value: “p=0.05 – You are either pregnant or not”
Appropriate initial trial to reject Null hypothesis (two Rxs are equal)
Less relevant – Previous pos trials, equivalence, non-inferiority
Don’t dismiss trend

Potential Flaws in RCTs

• Type 1 Alpha Error
Early signif difference would disappear with more subjects
Example:
<table>
<thead>
<tr>
<th>Mortality</th>
<th>Under feed</th>
<th>Full feed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1Arabi 1st Single Center (n=240)</td>
<td>30.0%</td>
<td>42.5%</td>
</tr>
<tr>
<td>2Arabi 2nd Multi-Center (n=885)</td>
<td>27.2%</td>
<td>28.9%</td>
</tr>
</tbody>
</table>

• Type 2 Beta Error
No diff seen early, but diff would emerge with more subjects
Example: Charles UVA trial permissive underfeeding in trauma
Half vs Full feeds (prot 1.5 gm/kg/d) SICU setting (n=84)
No difference ICU or Hosp LOS, infection, mortality

DM Bier (AJCN); M Egger (Systemat Rev Health Care (BMJ Books 2001, pg 218)

LeLorier (NEJM 1997:337:536)
Important Balance Between Clinicians and GRADE Experts on Guidelines Committee

Clinicians:
- Typically do RCTs
- Have expertise in field
- May minimize methodologic flaws

Example: Our committee on EN vs PN in Traumatic Brain Injury

GRADE Experts:
- Many are epidemiologists
- Do meta-analyses
- Often not experts in field
- May miss clinical issues
- Led by methodologic quality

PN vs EN

Meta-Analyses

- Simpson, Doig (Int Care Med 2005;31:12-23) Harvey
- CALORIES (NEJM 2014;371:1673)

PN EN

(p=0.04)

Simpson, Doig

University of Kentucky Neurosurgery Experience

Byron Young, MD - Clinician

- Rapp 1983 Head Injury Study (n=38) PN EN Mortality 0% 44% *
  (EN = Standard do nothing late EN)
- Young 1987 Head Injury Study (n=51) PN EN Mortality (n=60) 43.5% 35.7%
  (EN = early gastric feeds)
- Charash 1994 Trauma Study (n=63) PN EN Pneumonia 50% 18% *
  Mortality 23% 0% *
  (EN = early small bowel feeds) * (p<0.05)


Impact of Clinical Issues

Nutritional Risk
- Disease severity
- Nutritional status
- Timing of nutritional intervention

First week
- Argument to AVOID feeding
  - Height of dz process, inflammt, insulin resit, 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

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 mgmnt, 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
- Danger: Large but underpowered negative studies on PN Rx
Conclusions

• Remain flexible
• Carefully interpret and appropriately respond to large RCTs
• Management, Rx decisions based on totality of information¹
  Notion that evidence can be placed in hierarchies is "illusionary"
• ASPEN SCCM Guidelines
  Rigorous evidence-based
  Expert consensus involved (voting, recs with very low QOE)
• Guidelines never take priority over clinical judgment
  Should be interpreted in context of institutional setting
  Importance – Organizes info, provides references, good start

Evaluating the Guidelines and the Quality of Evidence

Stephen A. McClave, MD
Professor of Medicine, University of Louisville

“I have a commercial relationship with the following companies and will provide practice recommendations that are based on formal structured review of the literature”.
- Nestle Speakers Bureau
- Abbott Speakers Bureau
- Metagenics Speakers Bureau
- Nutricia Speakers Bureau
- Covidien Consultant

Presentation Overview/Summary

The development of the 2016 ASPEN/SCCM Guidelines was a rigorous scientific endeavor that required four years to complete and publish a final manuscript. The Guidelines Committee was multidisciplinary and represented leaders in ASPEN, former board members, and officers from our society. The GRADE process for evaluating the literature was adopted between the time of the publication of the last 2009 Guidelines and the current Guidelines. Through a harmonization process with the Canadians, each of nearly 750 randomized controlled trials were evaluated by two committee members, graded, and entered into an electronic database. Having GRADE experts on the committee allowed for the derivation of Forest plots for the various topics under review. The committee made a conscious effort to provide clinical recommendations that would be valuable to practicing clinicians. Understanding the strength and weaknesses of observational trials, randomized controlled trials, and meta-analyses is important in understanding how the recommendations are graded and the strength of the recommendations determined. No single study should drive practice, but the larger well-conducted RCT’s should have the greatest influence. Experts in study design need to work closely with clinicians on the committee to result in a balanced interpretation of the literature. Any recommendations for critical care management in the ICU should keep in mind that decisions made in the first week could have lasting impact even after the patient is discharged from the ICU.

Learning Objectives:

At the conclusion of the presentation, the learner will be able to:
1. Interpret Forest plots from a meta-analysis.
2. Understand the differences in strength and weaknesses between observational studies and randomized controlled trials.
3. Have an appreciation of the scientific rigor required for the development of societal guidelines.

Learning Assessment Questions:

1. When grading an RCT for quality of evidence, which of the following is true?
   A. Concealed randomization is worse because it indicates secrecy.
   B. Double-blinded is worse because the investigators cannot see confounding factors.
   C. Comparison of groups at baseline is important to identify a homogenous population and to avoid errors of randomization.
D. Lengthy descriptions of co-interventions are bad as they detract from the key message of the manuscript.

2. When evaluating a Forest plot, which of the following is TRUE?
   A. Odds-ratio or risk-ratio tend to underestimate the treatment effect.
   B. Heterogeneity refers to differences between the individual patients.
   C. Confidence intervals indicate the degree to which the reader will understand the study results.
   D. Absolute risk reduction can be calculated directly from the table.

3. Which of the following is TRUE regarding the differences between observational studies and randomized controlled trials?
   A. Larger numbers of patients in RCTs make meta-analyses of multiple studies difficult.
   B. Larger numbers in observational trials offset the likelihood of a confounding factor.
   C. Observational trials tend to overestimate the treatment effect.
   D. Good design of an RCT guarantees it will have good practicality for clinical practice.

Learning Assessment Answers:

1. Answer = C. Rationale: Comparison of the groups at baseline it is very important to know that the population is homogenous, that there are no errors in randomization, and that the outcome effects at the end of the trial were not due to differences between groups at the beginning of the trial. Randomization is better if it is concealed. It is important to adequately describe co-interventions and blinding both the patient and the investigators from knowledge about which group gets the experimental treatment is important for scientific integrity.

2. Answer = D. Rationale: By looking at the events divided by the total number of patients in both the treatment and the control columns of the Forest plot, the absolute risk reduction can be calculated. The treatment effect described by the absolute risk reduction is always smaller than the effect size described by relative risk which tends to overestimate the treatment effect. Confidence intervals give an indication of the likelihood that if the tests were repeated, the new results would fall within that range. Heterogeneity refers to differences between the studies, not the individual patients.

3. Answer = C. Rationale: Observational trials tend to overestimate the treatment effect, whereas RCTs tend to show a lower treatment effect. Good methodologic design refers to internal validity, but that does not necessarily guarantee that the study results will be widely generalizable (which is a factor of external validity). Larger numbers of patients in observational studies can amplify a confounding factor decreasing the accuracy of the results. The larger the number in the randomized controlled trial the better, and presumably, the more accurate the results. Larger and better quality RCTs make meta-analyses better not worse.

References

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