

Clinical Practice Guidelines for Nutrition Support
in Mechanically Ventilated, Critically Ill Adult Patients¹

Address for correspondence:

Dr. Daren Heyland
Kingston General Hospital
Kingston, Ont. Canada K7L 2V7
Phone: 613 549 6666 ext 3339
Fax: 613 548-2577
Email: dkh2@post.queensu.ca

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Structured Abstract

Objective: To develop evidence-based clinical practice guidelines for nutrition support (i.e. enteral and parenteral nutrition) in mechanically ventilated critically ill adults.

Options:

The following interventions were systematically reviewed for inclusion in the guidelines: enteral nutrition (EN) vs. parenteral nutrition (PN); early vs. late EN; dose of EN; composition of EN (immune-enhancing additives, carbohydrate, lipids, protein/peptides, pH & fibre); strategies to optimize delivery of EN and minimize risks (i.e. feeding protocols, rate of advancement, checking residuals, use of bedside algorithms, motility agents, small bowel vs. gastric feedings, elevation of head of the bed, closed delivery systems, pre/pro/synbiotics, bolus administration, gastrostomy vs. nasogastric feedings); enteral nutrition in combination with supplemental PN; use of PN vs. standard care in patients with an intact GI tract; dose of PN and composition of PN (protein, carbohydrates, intravenous lipids, additives, vitamins, trace elements, immune enhancing substances) and the use of intensive insulin therapy.

Outcomes: The outcomes considered were mortality (ICU, hospital, and long term), length of stay (ICU and hospital), quality of life, and specific complications.

Evidence: We systematically searched Medline and Cinahl (cumulative index to nursing

and allied health), Embase, and the Cochrane Library for randomized controlled trials and meta-analyses of randomized controlled trials that evaluated any form of nutrition support in critically ill adults. We also searched reference lists and personal files, considering all articles published or unpublished available by August 2002. Each included study was critically appraised in duplicate using a standard scoring system.

Values: For each intervention, we considered the validity of the randomized trials and/or meta-analyses, the effect size and its associated confidence intervals, the homogeneity of trial results, safety, feasibility, and the economic consequences. The context for discussion was mechanically ventilated patients in Canadian ICUs.

Benefits, Harms, and Costs: The major potential benefit from implementing these guidelines is improved clinical outcomes of critically ill patients (reduced mortality and ICU stay). Potential harms of implementing these guidelines include increased complications and costs related to the suggested interventions.

Summaries of Evidence and Recommendations:

When considering nutrition support in critically ill patients, we strongly recommend that EN be used in preference to PN. We recommend the use of a standard, polymeric enteral formula that is initiated within 24-48 hours following resuscitation, that patients be cared for in the semi-recumbent position, and that arginine-containing enteral products not be used. Strategies to optimize delivery of EN (starting at the target rate,

use of a feeding protocol using a higher threshold of gastric residuals volumes, use of motility agents, and use of small bowel feeding) and minimize the risks of EN (elevation of the head of the bed) should be considered. Use of products with fish oils, borage oils and antioxidants should be considered for patients with Acute Respiratory Distress Syndrome and EN supplemented with glutamine should be considered for trauma patients. A low fat, glutamine enriched formula should be considered for patients with severe burns. When initiating EN, we strongly recommend that PN not be used in combination with EN. When PN is utilized, we recommend that it be supplemented with glutamine, where available. Strategies that maximize the benefit and minimize the risks of PN (hypocaloric dose, withholding lipids, and the use of intensive insulin therapy to achieve tight glycemic control) should be considered. There are insufficient data to generate recommendations in the following areas: use of indirect calorimetry; optimal pH of EN; supplementation with trace elements, antioxidants, or fiber; optimal mix of fats and carbohydrates; use of closed feeding systems; continuous vs. bolus feedings; use of probiotics; type of lipids and mode of lipid delivery.

Validation: This guideline was peer-reviewed and endorsed by official representatives of the Canadian Critical Care Society, Canadian Critical Care Trials Group, Dietitians of Canada, Canadian Association of Critical Care Nurses, the Canadian Society for Clinical Nutrition, and the American Society of Parenteral and Enteral Nutrition.

Sponsors: This guideline is a joint venture of the Canadian Critical Care Society, the

Canadian Critical Trials Group, the Canadian Society for Clinical Nutrition and the Dietitians of Canada. The Canadian Critical Care Society and the Institute of Nutrition, Metabolism, and Diabetes of the Canadian Institutes of Health Research provided funding for development of this guideline.

Introduction

In critically ill patients malnutrition is associated with impaired immune function, impaired ventilatory drive and weakened respiratory muscles leading to prolonged ventilatory dependence and increased infectious morbidity and mortality (1). Malnutrition is prevalent in ICU patients, has been reported as being as high as 40 %, and is associated with poor patient outcomes (2).

The benefits of nutrition support in the critically ill include improved wound healing, a decreased catabolic response to injury, improved gastrointestinal structure and function, and improved clinical outcomes including a reduction in complication rates and length of stay with accompanying cost savings (3). However, nutrition support is not without adverse effects or risks. Early enteral nutrition can be associated with high gastric residual volumes, bacterial colonization of the stomach, and an increased risk of aspiration pneumonia (4,5). Parenteral nutrition has been associated with gut mucosal atrophy, overfeeding, hyperglycemia, an increased risk of infectious complications and increased mortality in critically ill patients (6). Both forms of nutrition support can increase health care costs and workloads of care providers.

Despite the widespread use of nutrition support, many areas in clinical practice remain controversial. Variation in nutrition support practices in ICUs throughout the world are widely reported. The use of nutrition support in ICUs has been shown to vary from 14 to 67 % of all patients in the ICU (7,8,9,10,11). Recent surveys report the use of PN ranging from 12% to 71 % and the use of enteral nutrition ranging between 33 to 92 % of patients receiving nutrition support in the ICU (7-11).

Recent review papers have documented that nutrition support *does* influence morbidity and mortality in critically ill patients (3,6,12). Therefore, strategies to improve the delivery of nutrition support are relevant and may result in decreased morbidity and mortality. Systematically developed practice guidelines that focus on these strategies will allow practitioners to make decisions about appropriate nutrition support care and will aim at improving the quality of patient care and maximizing the efficiency with which resources are used.

Published data on clinical practice guidelines for nutrition support in the critically ill are limited. Two existing documents (13,14) were appraised using a validated instrument for evaluation of clinical practice guidelines (15). Neither was acceptable according to the criteria in this instrument. The American Society of Parenteral and Enteral Nutrition (ASPEN) document (13) was not intended to establish practice guidelines for nutrition support, but rather to review published literature and to make recommendations for future research directions. It lacks representation from key disciplines, it only addresses specific disease states in critically ill patients and does not address the more basic issues related to optimizing delivery of nutrition support in the ICU setting. The American College of Chest Physicians consensus statement (14) fails to describe a valid method to identify and interpret the evidence, is based mostly on expert opinion and does not mention a source of external funding. It also lacks broad representation and external validation from other disciplines. Recently, ASPEN guidelines were updated to reflect a more current, evidence-based approach to the practice of nutrition support (16). Pertaining to critical illness, the panel simply

concluded that “specialized nutrition support should be initiated when it is anticipated that critically ill patients will be unable to meet their nutrients orally for a period of 5-10 days” and “enteral nutrition is the preferred route of feeding.” There were no guidelines put forward to assist practitioners in how to best optimize the benefits and minimize the risks of specialized nutrition support in critical illness.

The development of detailed, original, evidence-based guidelines is needed to facilitate more effective, efficient and consistent delivery of nutrition support that can lead to improved patient outcomes in the adult critical care setting. This paper describes the systematic approach that was used to develop these guidelines and the recommendations that emerged.

Method:

In October 2001, a workshop was held that brought together various stakeholders interested in nutrition support in the critical care setting. In attendance were representatives of the Canadian Critical Care Society, Canadian Critical Care Trials Group, Dietitians of Canada, Canadian Association of Critical Care Nurses, Canadian Society for Clinical Nutrition, the Institute of Nutrition, Metabolism, and Diabetes of the Canadian Institute of Health Research, Nestle Canada and Abbott Labs. The attendees were ICU physicians, surgeons, gastroenterologists, dietitians, nurses, pharmacists, nutrition scientists, invited international experts and representatives from the nutrition industry.

In small group sessions a process to develop evidence based nutrition support

guidelines for the ICU setting was developed. Several areas of nutrition practice were identified as important components that needed to be systematically reviewed.

A panel to develop clinical practice guidelines was appointed and consisted of representatives from key disciplines i.e. epidemiologists, intensivists, surgeons, gastroenterologists, dietitians, nurses, and pharmacists from across Canada. External reviewers included international experts and industry representatives (Appendix 1).

Search strategy:

To locate relevant articles to be included in these practice guidelines, four bibliographic databases (Medline, Embase, CINAHL and the Cochrane Library) were searched. Search terms included: nutritional support or dietary supplementation or enteral nutrition or parenteral nutrition or peripheral parenteral nutrition or total parenteral nutrition or nutritional support team or nutritional requirements or nutritional assessment or parenteral nutrition solutions and critical care or critical illness or intensive care units. These searches spanned from 1980 to August 2002. In addition, personal files and relevant review articles were searched for additional studies. There were no language restrictions on included papers. Unpublished manuscripts were included in the review process. Data reported in abstract only were excluded.

Study Selection Criteria:

Studies were selected for inclusion in the review process if they met the following criteria:

Study design: randomized clinical trials or meta-analysis of randomized controlled trials (pseudo-randomized trials were excluded).

Population: mechanically ventilated, critically ill adult patients (elective surgery patients were excluded)

Intervention: any form of enteral nutrition (EN) or parenteral nutrition (PN)

Outcome: mortality (ICU, hospital, long term), length of stay, quality of life, complications and cost. Studies with only surrogate outcomes were excluded.

For the purpose of this review process, we defined a critically ill patient as a patient cared for in an ICU environment who had an urgent or life threatening complications (high baseline mortality rate) to distinguish them from patients with elective surgery who also are cared for in some ICU's but have a low baseline mortality rate (< 5 %).

Based on the above search and study selection criteria, the included articles covered the range of topics listed in Appendix 2. Additional topics including checking gastric residuals, methods of detecting aspiration, timing of initiation of PN, protein sparing therapy, use of nutrition support teams, peripheral PN vs central line PN were considered of interest but no randomized controlled trials on these topics evaluating clinically important outcomes were available for inclusion in the review process. In addition, practical aspects of tube placement and management for enteral nutrition and catheter placement for parenteral nutrition are beyond the scope of this paper.

The panel agreed to review all randomized controlled trials and the most recent

meta-analyses for all topics. Each randomized trial was critically appraised independently by each member of a pair of reviewers according to an explicit procedure. Appraisers were given instructions on how to appraise studies and for each trial the following descriptors were abstracted: intervention, study population, nature of allocation, co-interventions, exclusions after randomization, double-blinding, event rates, relative risk, and other outcomes. Authors of primary studies were contacted for supplementary information or clarification if necessary. Clinical trials were assigned “level 1” if randomization was concealed, outcome adjudication was blinded, and an intention to treat analysis was performed. Trials were assigned “level 2” if any one of the above characteristics was unfulfilled. For each intervention that had more than 2 similar studies, where possible, we combined data from all studies to estimate the common risk ratio and associated 95% confidence intervals for death and infectious complications. The common risk ratios and their confidence intervals were estimated using the random effects model of DerSimonian and Laird (17) as implemented in RevMan 4.1 (18). We considered $P < 0.25$ to be supportive of a trend and $P < 0.05$ to be statistically significant.

For each meta-analysis included in the review process, the following descriptors were abstracted: intervention, number of trials, population selection criteria, search strategy, independent validity assessment, method of pooling results, assessment of homogeneity, pooled event rates, and other outcomes. Patients’ perspectives could not be elicited due to the inability of most critically ill patients to engage in discussions about their nutrition.

In advance of the panel meeting, each pair of reviewers achieved consensus on the data abstracted from the included studies and written summaries were prepared and precirculated to all panel members. The panel then met to translate the summaries of evidence into clinical recommendations. The context for discussion was mechanically ventilated, adult patients in Canadian ICUs. At the meeting, we considered the validity of the randomized trials, the effect size of each intervention and its associated confidence intervals, the homogeneity of trial results, safety, feasibility of implementing the new intervention including impact on workload, and the cost related to each intervention. We did not conduct a formal economic evaluation of any of the interventions. For every intervention, each of these items was scored using a semi-quantitative scale (0 to 3+) by the guideline panel. These scores made transparent the weights used to derive the summary recommendations. The language of the recommendations was linked to the semi-quantitative scores and the strength of the evidence as shown in Table 1. Where possible, recommendations were generated for specific sub-populations of critically ill patients (trauma, burns, malnourished, etc). Otherwise, the guidelines were developed to apply to the average mechanically ventilated patient or the general situation. We recognize that these recommendations may not apply in all situations and individual patient or site characteristics will need to be considered.

After the panel meeting, the draft guidelines were written and circulated to panel members for approval. Revisions were made prior to submitting the

guidelines for structured external review (see Appendix for list of reviewers). The external reviewers were asked to provide feedback on whether there were additional studies pertinent to the topic, whether the guideline was logical, clear, and practical, and to critique the guideline development process. Members of the panel considered the comments of all reviewers and revised the guidelines based on this feedback. The final guideline was returned to panel members for final approval and then to official sponsors for their respective endorsements.

Results: [see Table of Contents on website for relevant sections]

Table 1. Language of Summary Recommendations

Conditions	Language of recommendation
If there were no reservations about endorsing an intervention.	"strongly recommended"
If evidence was supportive but there were minor uncertainties about the safety, feasibility, or costs of the intervention	"recommended"
If the supportive evidence was weak and/or there were major uncertainties about the safety, feasibility, or costs of an intervention.	"should be considered"
If there was either inadequate or conflicting evidence	No recommendation i.e. "insufficient data"

APPENDIX 1

Panel Members:

Chair: Daren Heyland, MD

Executive Assistant: Rupinder Dhaliwal, RD.

Members: Cathy Alberda, RD; Carmen Christman, RD (Dietitians of Canada); John Drover ,M.D.; Dominique Garrel, MD; Leah Grahmlich, MD; Jan Greenwood, RD; Khursheed Jeejeebhoy, MD; Brian Jureswitsch, Pharmacist; Jim Kutsogiannis, MD; Gwynne MacDonald, RN; Michelle McCall, RD; John Muscedere, MD; Guiseppe Pagliarello, MD; Courtney Somers-Balota, RD

External Advisors: Steve McClave, MD; Todd Rice MD; Rene Stapleton, MD; Paul Wischmeyer, MD

References

1. Dark DS, Pingleton SK. Nutrition and nutritional support in critically ill patients. *J Intensive Care Med* 1993;8;16-33.
2. Giner M, Laviano A, Meguid MM, et al. In 1995 a Correlation between malnutrition and poor outcomes in critically ill patients still exists. *Nutrition* 1996 12;23-29.
3. Heyland DK. Nutritional support in the critically ill patient, a critical review of the evidence. *Crit Care Clin.* 1998 Jul;14(3):423-40.
4. Heyland DK, Cook DJ, Schoenfeld PS, et al. The effect of acidified enteral feeds on gastric colonization in the critically ill patient: Results of a multicenter randomized trial. *Crit Care Med.* 2001 Oct;29(10):1955-61.
5. Mentec H, Dupont H, Bocchetti M, et al. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med.* 2001 Oct;29(10):1955-61..
6. Heyland DK, MacDonald S, Keefe L, et al. Total parenteral nutrition in the critically ill patient; A meta-analysis. *JAMA.* 1998 Dec 16;280(23):2013-9.
7. Payne-James J, De Gara CJ, Grimble GK, et al. Artificial Nutrition support in hospitals in the United Kingdom-1991:second national survey. *Clinical Nutrition* 1992;11:187-192
8. Hill SA, Nielsen MS, Lennard-Jones JE. Nutrition Support in intensive care units in England and Wales: a survey. *European Journal of Clinical Nutrition* 1995;49;371-378
9. De Jonghe B, Appere-De-Vechi C, Fournier M, et al. A prospective survey of nutritional support practices in intensive care units patients: what is prescribed ? what is delivered ? *Crit Care Med* 2001;29;1:8-12
10. Preiser JC, Berre J, Carpentier Y, et al. Management of nutrition in European intensive care units: results of a questionnaire. *Int Care Med* 1999;25;95-101
11. Heyland DK, Schroter-Noppe D, Drover J, et al. Nutrition support practice in Canada: Results of a national survey. *JPEN* 2003 (in press).
12. Heyland DK, Novak F, Drover J, et al. Should immunonutrition become routine in critically ill patients; A systematic review of the evidence. *JAMA.* 2001 Aug 22-29;286(8):944-53. Review
13. Klein S, Kinney J, Jeejeebhoy K, et al. Nutrition support in clinical practice: review of published data and recommendations for future research directions. National Institutes of Health, American Society for Parenteral and Enteral Nutrition, and American Society for Clinical Nutrition. *JPEN J Parenter Enteral Nutr.* 1997 May-Jun;21(3):133-56.
14. Cerra FB, Benitez MR, Blackburn GL, et al. Applied Nutrition in ICU patients, A Consensus Statement of the American College of Chest Physicians. *Chest* 1997;111-769-778
15. Cluzeau FA, Littlejohns P, Grimshaw JM, Feder G, Moran SE. Development and application of a generic methodology to assess the quality of clinical guidelines. *International Journal for Quality in Health Care* 1999;11:21-28.
16. Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients. *JPEN*

2002;26:1-138.

17. DerSimonian R, Laird N. Meta-Analysis in Clinical Trials. *Controlled Clinical Trials* 7:177-188, 1986.
18. RevMan 4.1 User's Guide. The Cochrane Collaboration, 2000.