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Clinical practice guidelines for nutrition support in the mechanically-ventilated critically-ill adult

BY RUPINDER DHALIWAL, RD AND DAREN K. HEYLAND, MD, FRCPC, MSc

Nutrition support is a fundamental component of standard supportive care in the critically-ill patient; however, it is not without adverse effects or risks. Aggressive enteral nutrition in critically-ill patients can increase the risk of developing ventilator-associated pneumonia (VAP),¹ whereas parenteral nutrition (PN) has been associated with gut mucosal atrophy, overfeeding, and hyperglycemia, resulting in increased morbidity, mortality, and healthcare costs.² Therefore, when formulating clinical recommendations, strategies that maximize the benefits of nutrition support, while minimizing the associated risks, need to be considered. Accordingly, evidence-based guidelines were recently developed as a strategy to optimize the delivery of nutrition support, decrease variations in practice, and potentially result in improved patient outcomes. This issue of *Clinical Nutrition Rounds* reviews the need for clinical practice guidelines, the process undertaken to develop recent guidelines for nutrition support, the content and the validation of these guidelines, and effective dissemination strategies. This review will provide a useful framework for those interested in developing evidence-based guidelines in other areas.

The need for evidence-based clinical practice guidelines

Clinical practice guidelines (CPGs) are “systematically developed statements to assist practitioners with patient decisions about appropriate healthcare for specific clinical circumstances.”³ In a survey of attitudes of 302 physicians concerning evidence-based medicine, a vast majority believed that the most appropriate way to shift from “opinion-based” medicine (where there is much variation in practice) to “evidence-based” medicine (where there is less variation in care) was through the development of clinical practice guidelines.⁴ There is considerable variation in nutrition support practice in intensive care units (ICUs) across Canada and throughout the world.⁵⁻⁸ This variation in ICU practice can be decreased by the use of practice guidelines and, as illustrated in recent findings, the adoption of these guidelines can result in improved clinical outcomes (ie, decreased mortality), as well as significant cost-savings.^{9,10}

Developing the Canadian CPGs: creating the framework and the committee

In October 2001, various stakeholders interested in nutrition support were brought together at a workshop to create a process for developing evidence-based nutrition support guidelines for the ICU setting. Attendees included ICU physicians, surgeons, gastroenterologists, dietitians, nurses, pharmacists, nutrition scientists, invited international experts, and representatives from the nutrition industry. In addition, 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, Nestlé Canada, and Abbott Laboratories were also in attendance. At this meeting, the Canadian Critical Care Clinical Practice Guidelines Committee was appointed consisting of representatives from key disciplines, eg, epidemiologists, intensivists, surgeons, gastroenterologists, dietitians, nurses, and pharmacists from across Canada (see Table 1 for committee members). Several nutrition support practices that needed systematic review were identified at this meeting.



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Table 1: Canadian Critical Care Clinical Practice Guidelines Committee Members

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Literature search and article inclusion criteria

To locate relevant articles to be included in these practice guidelines, 4 bibliographic databases (Medline, Embase, CINAHL, and the Cochrane Library) were searched. The period spanned from 1980 to 2002, and was extended annually thereafter. In addition, personal files and relevant articles were reviewed for additional studies.

Study selection criteria

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

- randomized clinical trials or meta-analysis of randomized controlled trials;
- involved mechanically-ventilated, critically-ill adult patients (excluding elective surgery patients);
- included any form of enteral nutrition (EN) or parenteral nutrition (PN) or a combination;
- reported on any of the following clinically important outcomes eg, mortality (ICU, hospital, long-term), length of stay, quality of life, complications, or cost.

Article review process and synthesis of evidence

Each randomized trial was independently and critically appraised by each member of a pair of committee members according to an explicit procedure. Instructions on how to review the studies were provided to the committee members who then abstracted the following descriptors for each trial: intervention, study population, nature of allocation, co-interventions, exclusions after randomization, double-blinding, event rates, relative risk, and other outcomes.

- Clinical trials were assigned “level 1” (stronger evidence) if randomization was concealed, outcome adjudication was blinded, and an intention-to-treat analysis was performed.
- Trials were assigned “level 2” (weaker evidence) if any one of the above characteristics was unfulfilled.

Since systematic reviews and meta-analyses are the best tools to predict an overall treatment effect, this approach was used when a particular topic had >2 similar studies to estimate the common risk ratio and associated 95% confidence intervals (CI) for death and infectious complications. The Committee considered $P < 0.25$ to be supportive of a trend and $P < 0.05$ to be statistically significant.

Table 2: Language of summary recommendations

Conditions	Language of recommendation
• No reservations about endorsing an intervention	“Strongly recommended”
• Evidence supportive, but there were minor uncertainties about the safety, feasibility, or costs of the intervention	“Recommended”
• Supportive evidence weak and/or there were major uncertainties about the safety, feasibility, or costs of an intervention	“Should be considered”
• Either inadequate or conflicting	No recommendation ie, “Insufficient data”

Once each pair of reviewers agreed on the data abstracted from the reviewed articles, all the studies were then summarized according to each topic. These written “summaries of evidence” were then re-circulated to all of the committee members.

From evidence to clinical recommendations: integration of values

In order to develop meaningful recommendations, it has been suggested that values be integrated into the evidence and that the assignment of values be disclosed.¹¹ The committee translated the summaries of evidence into clinical recommendations by integrating values such as: the validity of the randomized trials, the effect size of each intervention and its associated CIs, the homogeneity of trial results, safety, feasibility of implementing the new intervention including impact on workload, and the cost related to each intervention. For every intervention, each of the items was scored by the guidelines committee using a semi-quantitative scale (0 to 3+). The final recommendation was made based on the weighting of these scores and the evidence. Four levels of recommendation were used (Table 2). Where possible, recommendations were generated for specific sub-populations of critically-ill patients (trauma, burns, malnourished, etc).

External review

After the committee meeting, draft guidelines were created and circulated to all committee members for approval. Further revisions were made prior to submitting the guidelines for structured external review. The external reviewers were international nutrition experts and industry representatives who provided feedback on the process, content, accuracy, and clarity of the guidelines and on additional studies pertinent to the topics. This feedback was considered and the guidelines were revised. The final guidelines were returned to committee members for final approval and then to official sponsors for their respective endorsements. The CPGs were published within 2 years of the inception of the idea.¹²

Table 3: Summary of topics and recommendations†

1. EN vs. PN	Does enteral nutrition (EN) compared to parenteral nutrition (PN) result in better outcomes in the critically-ill adult patient?	Based on 1 level 1 study and 12 level 2 studies, when considering nutrition support for critically-ill patients, we strongly recommend the use of enteral nutrition over parenteral nutrition.
2. Early vs. delayed nutrient intake	Does early enteral nutrition compared to late enteral nutrition result in better outcomes in the critically-ill adult patient?	Based on 8 level 2 studies, we recommend early enteral nutrition (within 24-48 hours following admission to ICU) in critically-ill patients.
3. Dose of EN: Achieving target dose of EN	Does achieving target dose of enteral nutrition result in better outcomes in the critically-ill adult patient?	Based on 1 level 2 study, when initiating enteral nutrition in head injured patients, strategies to optimize delivery of nutrients (starting at target rate, higher threshold of gastric residual volumes and use of small bowel feedings) should be considered .
4. Composition of EN: Immune enhancing diets: Diets supplemented with arginine and other select nutrients*	Compared to standard enteral feeds, do diets supplemented with arginine and other select nutrients result in improved clinical outcomes in the critically-ill adult patient?	Based on 2 level 1 studies and 12 level 2 studies, we recommend that diets supplemented with arginine and other selected nutrients not be used for critically-ill patients.
5. Composition of EN: Immune enhancing diets: Fish oils	Does the use of an enteral formula with fish oils, borage oils, and antioxidants result in improved clinical outcomes in the critically-ill adult patient?	Based on 1 level 1 study, the use of an enteral formula with fish oils, borage oils, and antioxidants should be considered in patients with acute respiratory distress syndrome (ARDS).
6. Composition of EN: Immune enhancing diets: Glutamine	Compared to standard care, does glutamine-supplemented EN result in improved clinical outcomes in the critically-ill adult patient?	Based on 1 level 1 and 4 level 2 studies, enteral glutamine should be considered in burn and trauma patients.
7. Composition of EN: Protein/peptides	Does the use of peptide based enteral formula, compared to a whole protein formula, result in better outcomes in the critically-ill adult patient?	Based on 4 level 2 studies, when initiating enteral feeds, we recommend the use of whole protein formulas (polymeric) in critically-ill patients.
8. Strategies to optimize delivery and minimize risks of EN: Feeding Protocols	Does the use of a feeding protocol result in better outcomes in the critically-ill adult patient?	There are insufficient data from randomized trials to recommend the use of a feeding protocol in critically-ill patients. If a feeding protocol is to be used, based on 1 level 2 study, a protocol that incorporates prokinetics (metoclopramide) at initiation and tolerates a higher gastric residual volume (250 mL) should be considered as a strategy to optimize delivery of enteral nutrition in critically-ill adult patients.
9. Strategies to optimize delivery and minimize risks of EN: Motility agents*	Compared to standard practice (placebo), does the routine use of motility agents result in better clinical outcomes in the critically-ill adult patient?	Based on a systematic review, in critically-ill patients who experience feed intolerance (high gastric residuals, emesis), the use of metoclopramide as a motility agent should be considered .
10. Strategies to optimize delivery and minimize risks of EN: Small bowel feeding	Does enteral feeding via the small bowel compared to gastric feeding result in better outcomes in the critically-ill adult patient?	Based on 11 level 2 studies, small bowel feeding compared to gastric feeding maybe associated with a reduction in pneumonia in critically-ill patients. In units where obtaining small bowel access is feasible, we recommend the routine use of small bowel feedings. In units where obtaining access involves more logistical difficulties, small bowel feedings should be considered for patients at high risk for intolerance to EN (on inotropes, continuous infusion of sedatives, or paralytic agents, or patients with high nasogastric drainage) or at high risk for regurgitation and aspiration (nursed in supine position). Finally, in units where obtaining small bowel access is not feasible (no access to fluoroscopy or endoscopy and blind techniques not reliable), small bowel feedings should be considered for those select patients who repeatedly demonstrate high gastric residual volumes and are not tolerating adequate amounts of EN delivered into the stomach.

† These guidelines were developed to apply to the average mechanically-ventilated patient or the general situation and the recommendations may not apply in all situations; individual patient or site characteristics will need to be considered. These guidelines should not be used as a substitute for a physician's, dietitian's, or other health practitioner's informed clinical judgment with respect to the appropriate manner to treat an individual, mechanically-ventilated, critically-ill patient.

Table 3: Summary of Topics and Recommendations – (continued)

11. Strategies to optimize delivery and minimize risks of EN: Body position	Do alterations in body position result in better outcomes in the critically-ill adult patient?	Based on 1 level 2 study, we recommend that critically-ill patients receiving enteral nutrition have the head of the bed elevated to 45 degrees. Where this is not possible, attempts to raise the head of the bed as much as possible should be considered .
12. EN in combination with PN	Does the use of parenteral nutrition in combination with enteral nutrition result in better outcomes in the critically-ill adult patient?	Based on 5 level 2 studies, for critically-ill patients starting on enteral nutrition, we recommend that parenteral nutrition not be started at the same time as enteral nutrition. In the patient who is not tolerating adequate enteral nutrition, there are insufficient data to put forward a recommendation about when parenteral nutrition should be initiated. Practitioners will have to weigh the safety and benefits of initiating PN in patients not tolerating EN on an individual case-by-case basis. We recommend that PN not be started in critically-ill patients until all strategies to maximize EN delivery (eg, small bowel feeding tubes, motility agents) have been attempted.
13. PN: PN vs. standard care	Compared to standard care (IV fluids, oral diet, etc.), does parenteral nutrition result in better outcomes in critically-ill adult patients who have an intact GI tract?	Based on a meta-analysis, in critically-ill patients with an intact gastrointestinal tract, we strongly recommend that parenteral nutrition not be used routinely.
14. Composition of PN: Glutamine	Does glutamine supplementation of parenteral nutrition influence outcomes in the critically-ill adult patient?	Based on 2 level 1 studies and 3 level 2 studies, when parenteral nutrition is prescribed to critically-ill patients, parenteral supplementation with glutamine, where available, is recommended .
15. Strategies to optimize benefits and minimize risks of PN: Hypocaloric PN*	Does hypocaloric parenteral nutrition influence outcomes in the critically-ill adult patient?	Based on 2 level 2 studies, in critically-ill patients who are not malnourished, are tolerating some EN, or when parenteral nutrition is indicated for short-term use (< 10 days), hypocaloric PN should be considered . There are insufficient data to make recommendations about the use of hypocaloric PN or withholding lipids in the following patients: those requiring PN for long term (> 10 days), obese critically-ill patients, and malnourished critically-ill patients. Practitioners will have to weigh the safety and benefits of hypocaloric PN/withholding lipids on an individual case-by-case basis in these latter patient populations.
16. Strategies to optimize benefits and minimize risks of PN: Use of lipids	Does the presence of lipids in parenteral nutrition influence outcomes in the critically-ill adult patient?	Based on 2 level 2 studies, in critically-ill patients who are not malnourished, are tolerating some EN, or when PN is indicated for short-term use (< 10 days), withholding lipids should be considered . There are insufficient data to make a recommendation about withholding lipids in critically-ill patients who are malnourished or those requiring PN for long term (> 10 days). Practitioners will have to weigh the safety and benefits of withholding lipids on an individual case-by-case basis in these latter patient populations.
17. Strategies to optimize benefits and minimize risks of PN: Intensive insulin therapy	Does tight blood sugar control result in better outcomes in the critically-ill adult patient?	Based on 1 level 2 study, in surgical critically-ill patients receiving nutrition support, intensive insulin therapy to tightly control blood sugars between 4.4-6.1 should be considered . There are insufficient data to make a recommendation regarding intensive insulin therapy in other critically-ill patients.

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Refer to www.criticalcarenutrition.com for more details and for most current version of the guidelines. These sections have been updated*

Guideline revisions

One of the challenges of developing evidence-based guidelines is the need to update them regularly. It is recommended that in order to keep guidelines current,

a multidisciplinary group of experts should review the recommendations, bring forward pertinent new evidence and research, and this should be supplemented by ongoing literature searches.¹³ It was decided that the

Table 4: There were insufficient data for the CPG committee to make recommendations on these topics¹²

1. Use of indirect calorimetry vs. predictive equations
2. Achieving target dose of EN in critically-ill patients other than head injured patients
3. Composition of EN: glutamine in critically-ill patients other than trauma or burn patients; CHO/FAT; pH; fibre; probiotics
4. EN: closed vs. open system; continuous vs. other methods of administration
5. Composition of PN: branched chain amino acids; type of lipids; zinc; intravenous glutamine in critically-ill patients who are receiving enteral nutrition
6. Mode of lipid delivery.
7. Antioxidant Strategies: combined; single and multimodal; selenium

CHO = carbohydrates

Clinical Practice Guidelines for Nutrition Support be updated on an annual basis, and more frequently if needed, depending upon the nature of randomized trials being published. Literature searches are ongoing and any new studies meeting the inclusion criteria are reviewed by the committee and then incorporated into the existing sections. The revisions are then discussed at the committee level via teleconference or at the annual meeting held in conjunction with the Canadian Society for Clinical Nutrition annual conference. Since the publication of the CPGs in October 2003, certain sections have already been revised and are posted on our web-site.¹⁴ The recommendations are found in Tables 3 and 4; in Table 3 the revised sections are indicated with an *.

How do the Canadian CPGs compare to other guidelines?

There are at least 2 other published clinical practice guidelines on nutrition support in the critically-ill adult patient.^{15,16} However, these have relied on expert opinion, lack the multidisciplinary representation, and fail to provide practical and specific recommendations on maximizing the benefits of nutrition support while minimizing the risks. When compared to international assessment criteria for guideline development and presentation, the Canadian CPGs meet or exceed these standards.¹⁷

How do we know if the CPGs are useful?

To further validate the CPGs, it was hypothesized that ICUs with a practice that was, on average, more consistent with the guidelines, would have greater success with enteral nutrition (EN). In May 2003, prior to the widespread dissemination of the CPGs, a survey of nutrition support practices was conducted in 59 ICUs across Canada to test this hypothesis. The survey revealed that ICUs that were more compliant with the recommendations from the CPGs were indeed more likely to be successful with EN. For example, ICUs that used more parenteral nutrition (PN) – defined as those

with a greater than median utilization of PN >17.5% patient days – had a much lower adequacy of EN (32.9% vs. 52.7%, $p < 0.0001$). ICUs that utilized a feeding protocol tended to have a higher adequacy of EN than those that did not (44.9% vs. 38.5%, $p = 0.03$). ICUs that initiated EN in >50% of their patients within the first 48 hours had a higher adequacy of EN than those that did not (48.1% vs. 34.4%, $p < 0.0001$). ICUs that had a >50% utilization of motility agents and/or any small bowel feedings in patients with high gastric residuals tended to have a higher adequacy of EN than those ICUs that did not (45.6% vs. 39.2%, $p = 0.04$ and 48.4% vs. 41.8%, $p = 0.16$, respectively). This validation of the CPGs suggests that their adoption should lead to improved nutrition support practice in ICUs.¹⁸

How do we implement the guidelines? Dissemination strategies

Practice guidelines have become widely available through internet technology, journals, and textbooks; however, the impact of guidelines on clinical practice has not been well documented. Passive approaches to disseminate guidelines such as peer-reviewed publications are ineffective at changing behaviour.¹⁹ In contrast, multifaceted strategies and interactive workshops have been shown to change physician behaviour and occasionally, healthcare outcomes,²⁰ yet, this has never been studied in the setting of nutrition support in the critically ill. Other strategies reported to be effective in changing behaviour include advanced organizers (material given to workshop attendees prior to the workshop to facilitate learning) and educational materials such as posters, pocket cards, manuals, reminders, listservs,²¹ and audit feedback.²²

An ongoing, cluster randomized trial of 59 ICUs across Canada is comparing different educational strategies for dissemination of the CPGs. The question being asked is: Is the use of a web-based, multifaceted strategy that includes an interactive workshop more effective in implementing clinical practice guidelines for nutrition support in the critically ill when compared to passive dissemination? The results of this trial are expected to be finalized by the end of 2004 and will provide some useful insights for practitioners about which educational interventions are more effective in disseminating guidelines, changing physician behaviour, and favourably altering patient outcomes. The CPGs, educational tools such as algorithms, protocols, pocket cards, other pertinent articles and presentations to assist in effective dissemination of the guidelines are available at the website www.criticalcarenutrition.com

Conclusion

The adoption of evidence-based clinical practice guidelines can lead to a decrease in practice variation, improved clinical outcomes (eg, mortality), and can result in significant cost-savings. Guidelines for nutrition support need to address practical issues on how to maximize the benefits of nutrition support, while minimizing the associated risks. The Canadian Clinical

Practice Guidelines for Nutrition Support in Mechanically Ventilated Critically-ill Adults are evidence-based guidelines that were recently developed through a systematic, multi-disciplinary approach and are updated annually. In order to achieve a meaningful change in nutrition support practices, guidelines need to be combined with an aggressive strategy to disseminate and implement them. It is expected that the adoption of the Canadian Clinical Practice Guidelines and their dissemination through multifaceted, web-based educational strategies will lead to improved nutrition practices across ICUs in Canada and throughout the world.

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