Study Protocol:

International Nutrition Survey 2014

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Background

Malnutrition is common among critically-ill patients, and has negative effects on clinical outcomes[1,2]. Artificial nutrition therapy in the form of enteral or parenteral nutrition is therefore considered an integral part of the standard care received by the critically-ill. While it has long been widely accepted that it is unethical to withhold nutrition therapy from those at risk of malnutrition, it is only recently that evidence has been generated to demonstrate that various nutrition practices influence clinically important outcomes such as length of stay, morbidity and mortality[3-7]. Current data suggest that providing at least 80% of prescribed amounts of protein and energy is associated with improved clinical outcomes[8]. Despite these benefits, enteral or parenteral feeding should always be adopted with caution, as nutrition practices themselves are not without adverse effects or risks[9-10]. Making decisions regarding the most effective and safe means of feeding patients in the ICU can be challenging, and consequently considerable variation exists in nutrition practices in this setting[11].

Clinical Practice Guidelines (CPGs) are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances"[12], and therefore aid in the implementation of evidence based medicine[13,14]. The Canadian Clinical Practice Guidelines for Nutrition Therapy in Mechanically Ventilated, Critically Ill Adult patients published in 2003 and most recently updated in 2013[15], sought to improve nutrition practices in ICUs across Canada and worldwide by providing guidance to assist health practitioners to select and deliver the most appropriate form of nutrition therapy at the appropriate time via the most appropriate route[16]. A validation study prior to the widespread dissemination of the Canadian Critical Care Nutrition CPGs concluded that adoption of the recommendations should lead to improved nutrition practices and potentially to better patient

outcomes[17]. A rigorous development process, as adopted in the production of the Canadian Critical Care Nutrition CPGs, is not sufficient to ensure that guidelines are effective. To change clinical practice, attention must extend beyond initial development to guideline implementation, dissemination and evaluation[18]. Optimal implementation strategies will vary by ICU, health care system and regiom and should be guided by local factors including the ICU's barriers and facilitators to following best practice. Evaluating and monitoring nutrition performance should be part of an ongoing improvement strategy as implementation of best practice strategies may lead to improved nutrition care and clinical outcomes[15]. The few studies regarding the process of knowledge translation conducted in the ICU setting have demonstrated that guidelines and guideline implementation strategies improve the processes[19-21], outcomes[22,23], and the costs[20,22] of caring for critically-ill patients. Consequently, we conducted a cluster randomized control trial (RCT) comparing the effectiveness of multi-faceted educational activities to passive dissemination of the Canadian Critical Care Nutrition CPGs. A total of 58 ICUs across Canada participated in the cluster RCT with surveys completed in May 2003 and at 12 month follow-up in May 2004. Although there were no significant differences in the change in adequacy of enteral nutrition (EN) (i.e. amount of enteral nutrition received as a percent of prescribed) between the active and passive intervention arms from baseline to follow-up, significant improvement in several important aspects of nutrition support practices were detected overall, with an increase in the adequacy of EN from 42.9% to 51.3%. No changes in clinical outcomes were observed. A limitation of this study was the inadequate timeframe for meaningful changes in nutrition practices to occur.

In 2007, 2008, 2009, 2011 and 2013 as part of our ongoing international quality improvement initiative we conducted surveys of current nutrition practices in the critical care

setting. By repeating the International Nutrition Survey in 2014, we aim to describe current practices in nutrition therapy and to monitor changes over time both within Canada and worldwide. As part of the 2008 survey we developed, validated, and implemented a system to reward top performers in critical care nutrition, and recognized these ICUs through presentation of a best of the best plaque. We have continued to reward top performing sites in all subsequent surveys.

In previous surveys we observed large variation in performance across ICUs, with significant gaps between guideline recommendations and current nutrition practices. Overall, low nutritional adequacy has been observed across sites internationally, with ICUs delivering only approximately 60% of prescribed calories and protein. Although enteral nutrition (EN) is the preferred route of delivering nutrition, feeding is often inappropriately reduced or interrupted, limiting the delivery of optimal nutrition therapyIn a subset of nutritionally "high risk" patients from the International Nutrition Survey 2013 (patients mechanically ventilated for >7 days, BMI of <25 and $\geq$35 and with a Nutrition Risk in the Critically Ill score (NUTRIC) of $\geq$5) we showed that 74% failed to receive 80% of energy targets[25]. These findings all suggest that vast improvements in nutrition therapy in the critically ill are possible.

However, the International Nutrition Surveys showed that some ICUs are able to consistently adhere to many of the CPG recommendations. Eligible sites were ranked based on their performance on the following 5 criteria: adequacy of provision of energy, use of EN, early initiation of EN, use of promotility drugs and small bowel feeding tubes, and adequate glycemic control. By acknowledging top performers and their achievements, we hope to inspire a culture of excellence as it pertains to international nutrition practice in the ICU setting[26]. Determining best-achievable practice relative to the CPGs and gaining information about these top-

performing institutions compared to ICUs that do not perform as well can be useful in development of strategies for the improvement of nutrition practices. For example, in past surveys we illuminated that ICUs with a dietitian tend to perform better, while being located in Asia or the USA is associated with poor performance[25,26]; poorly performing sites can use such information to make changes to their practices.

In addition to the quality improvement focus of this initiative we have been able to use the large dataset to answer important clinical questions concerning the relationship between nutrition practices and clinical outcomes. The variable and suboptimal nutrition performance of some of these participating sites needs to be considered in light of emerging data that suggest that inadequate delivery of energy and protein is associated with increased mortality. Using our dataset of 2772 ICU patients from 167 ICUs derived from the international survey in 2007[27], we showed a significant inverse linear relationship between the odds of mortality and total daily calories received. An increase of 1000 calories per day was associated with an overall reduction in mortality (Odds Ratio for 60 day mortality 0.79 (95% Confidence Intervals [CI] 0.65-0.97, p=0.02)) and an increase in ventilator-free days (2.47, 95% CI, 0.54-4.41, p=0.01). This beneficial treatment effect of increased energy on clinical outcomes was observed in patients with a BMI <25 and >35 with no benefit for patients in the BMI 25-<35 group.

It is projected that by administering the international nutrition survey again in 2014 we will continue to highlight opportunities to improve nutrition practices both in Canada and worldwide.

Study Objectives

1. To describe current nutrition practices in ICUs in Canada and worldwide.

2. To compare nutrition practices in ICUs between specific hospital and ICU site (e.g. geographic location, ICU structure, ICU size, hospital type) and patient characteristics (e.g. medical vs. surgical).
3. To compare nutrition practices in ICUs to recommendations of the Canadian CPGs.
4. To monitor nutrition practices in ICUs in Canada and worldwide over time.
5. To identify strengths and weaknesses in nutrition practices and areas to target for improvement.

Methods

Study Design and Participants

The proposed project is a period prevalence survey of critical care nutrition practices in Canada and across the World. Participating ICU sites will be recruited by disseminating study information through our existing network of critical care practitioners who were involved in previous surveys, the communication channels of national enteral and parenteral nutrition societies and critical care societies and e-mailing individual healthcare providers or societies with an interest in critical care or nutrition therapy. To be eligible, ICUs must have a minimum of 8 beds and be affiliated with a registered dietitian. In certain circumstances, sites without a registered dietitian will be accepted if they demonstrate that an individual with knowledge of clinical nutrition is available to complete data collection. Also, smaller units (i.e. fewer than 8 beds) that express a keen interest in participating and have the resources to do so may be granted permission to participate on a case by case basis.

Interested participants will contact the Primary Investigator, Project Leader or Project Assistant for further information about the project and receive instructions on data collection procedures (See Instruction Manual).

Data Collection

On September 17th, 2014, registered dietitians (or other practitioners) at participating ICUs will complete the survey. A secure web-based data collection tool will be employed (see www.criticalcarenutrition.com). Dietitians will be asked to enter the characteristics of their hospital and ICU plus general aspects of nutrition practice (e.g. use of feeding protocol or algorithms). In addition, they will be asked to extract data on the personal characteristics and clinical condition of patients from the patient charts. Eligible patients will be defined as those meeting all the inclusion criteria, i.e.:

1) individuals ≥18 years of age
2) mechanically ventilated within 48 hours of ICU admission
3) who have been in the ICU for ≥72 hours

Data collection will be completed for each consecutive eligible patient until data on 20 patients has been accrued. Some data will be collected daily from the date of admission to a maximum of 12 days.

Questions on hospital and ICU site characteristics will include: Location, Hospital type (teaching vs. non-teaching), ICU type (open vs. closed), hospital size (number of beds), ICU size (number of beds), registered dietitian full time equivalent (FTE) per bed, presence of an ICU Medical Director, use of feeding protocol, use of nutrition assessment, use of insulin infusion protocol. The patient data required will include: admission category (surgical vs. medical), diagnosis, sex, age, height, weight, baseline APACHE II score, SOFA score, type of nutrition received, amount of nutrition received, blood sugar levels, insulin dose, use of pro-kinetics, use of supplementation, and head of the bed elevation. Patients will be followed for up to 60 days (in

hospital) to record length of mechanical ventilation, length of ICU and hospital stay, and mortality.

Data collection and online entry is estimated to take approximately 2-3 hours per patient. A 'help' link on the website will provide additional instructions if required. Participants will be able to download case report forms for manual data collection if computer access is restricted on their unit or if this mode of data collection is preferred.

Data Management and Statistical Analysis

All case report forms will be checked for errors, inconsistencies, and omissions by a study investigator and verified by a second research associate. Front and backend data checks will also be incorporated into the web-based data collection procedure. Queries regarding accuracy of the data will be directed to the primary contact at the specific site. Data will be stored on a high performance computing virtual library (HPCVL) located in Kingston, Ontario. The server and database are in a physically secure location, and reside on a private network only accessible through specifically created portals. Access, based on a unique username and password, will be granted to users to enter, edit and view data on a specific ICU basis. The address of all attempts to access the server, successful or otherwise, will be logged. An SSL secure connection will be used for the website. This prevents network traffic between a user and the server from being read by malicious third parties.

Site and patient characteristics will be described using means with ranges for continuous variables (or medians and interquartile range for skewed data) and counts with percentages for categorical variables. Differences in these characteristics between sites will be calculated using

the t-test or Wilcoxon-Mann-Whitney test for continuous variables, and Chi-squared test for categorical variables.

Adequacy of nutrition (an indicator of overall performance) will be calculated as the amount of calories or protein received (from either enteral (EN) or appropriate parenteral nutrition (PN) but not oral) plus propofol, divided by the amount prescribed as per the baseline assessment and expressed as a percentage. Days without EN or PN will be included and counted as 0% adequacy. Days after permanent progression to exclusive oral intake will be excluded from the calculation of nutritional adequacy. We arbitrarily selected $\geq$80% nutritional adequacy as an indicator of high performance.

Through creation of a "best of the best" award, we seek to determine which sites are achieving the top level of performance and, using a multivariable regression model, illuminate which hospital and ICU characteristics are associated with top performance. To be eligible, ICUs must have at least 8 beds, already have a feeding protocol in place, and have a willing individual with knowledge of clinical nutrition to complete data collection. Sites must submit data on a minimum of 20 patients, and be willing to subject their data to source verification. Since a site can excel at providing calories and protein, at the expense of glycemic control, we considered it important that top performing sites both provide optimal amounts of calories and protein and have adequate glycemic control. Furthermore, we acknowledge that it is not possible to provide goal calories to all patients, so we awarded points for adoption of strategies to improve nutritional adequacy (use of early EN, promotility drugs, and small bowel tubes) in addition to the resultant nutritional outcome (adequacy of caloric intake). The relative weightings of each of the criteria reflect the importance of the overall efforts (adequacy) and the strength of clinical recommendations: "strongly recommend"=5, "recommend"=3, "should consider"=1.

Dissemination of Results

Each participating ICU will receive a 30-page individualized performance report that compares their nutrition practice to the recommendations of the Canadian Critical Care Nutrition CPGs and highlight their strengths and weaknesses in comparison to other ICUs in the database. This report will be of significant value to participating ICUs and the results will illuminate opportunities for improvement. This could potentially translate into improved clinical outcomes for critically ill patients.

Results will be disseminated through the Critical Care Nutrition website. CERU will also provide tools on the Critical Care Nutrition website for local dissemination of results on websites of participating sites. A manuscript for publication in a scientific journal may also be prepared.

Ethics

No major ethical issues are foreseen as potential obstacles to the execution of this International survey. The proposed research is within the range of minimal risk as defined by the Tri-Council Policy Statement Article C1. The study is an observational quality improvement initiative and does not include any intervention. Patient data includes information collected as part of routine care and will be extracted from charts retrospectively. Consequently, in previous surveys the need for informed patient consent was waived at individual sites, with few exceptions. Ethics approval has been obtained from Queen's University Research Ethics Board and all participating sites will be asked to contact their ethics board to ascertain if they require approval.

Participating sites will be provided with an information sheet that clearly explains all pertinent information regarding the study. Although no financial compensation or other form of remuneration will be offered to participants, participating sites will be provided with benchmarked performance reports.

Confidentiality will be maintained at all times. No personal identifiers will be placed on any study documentation. Only authorized personnel will be granted access to survey data. All information stored in a computer database will be password protected. At the end of the study, all paper documents pertaining to the study will be shredded using a paper shredder at CERU.

Feasibility Issues

The CERU is a leader in critical care nutrition support research and through previous and ongoing studies have excellent links with ICUs across Canada and throughout the World. The divergent range of experience and expertise among personnel at CERU will be utilized to support the conduct of this international project. Health practitioners have explicitly expressed an interest in participating in this study and recruitment of ICU sites is not foreseen to be a problem.

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