

# Survey of Nutrition Practice in Patients with Severe Sepsis among Canadian Registered Dietitians

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## ABSTRACT

**Purpose:** The purpose of this study was to determine the opinions and reported nutrition practices of Canadian Registered Dietitians (RDs) with regard to feeding patients with severe sepsis.

**Methods:** In 2017, surveys were sent to 112 eligible Canadian RDs in 10 provinces who were practicing in an intensive care environment. The survey included embedded branching logic questions developed to address major facets of sepsis, critical illness, and nutrition. The survey instrument assimilated all data in an anonymous manner, so respondents could not be linked to their answers.

**Results:** Of the 64 RDs who responded (57% response rate), the majority practiced in adult intensive care (81%), within an academic center (59%), and in a mixed unit (73%). A wide variability of Canadian RDs' opinions and practice was reported in determining energy requirements, enteral nutrition (EN) practice, EN with vasoactive agents, parenteral nutrition (PN), and supplemental micronutrients.

**Conclusions:** Practice variability of Canadian RDs likely reflects gaps in both evidence and guidelines for severe sepsis. Further research efforts are needed to customize nutritional requirements in the patient with evolving sepsis, EN with patients at high risk for gastrointestinal dysfunction, optimizing PN, and the role of micronutrients.

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## RÉSUMÉ

**Objectif.** L'objectif de cette étude était de déterminer les opinions et les pratiques de la nutrition déclarées des diététistes canadiens en ce qui concerne l'alimentation des patients atteints d'une septicémie grave.

**Méthodes.** En 2017, des sondages ont été envoyés à 112 diététistes canadiens admissibles des 10 provinces qui pratiquaient dans une unité de soins intensifs. Le sondage comprenait des questions intégrées à enchaînement logique conçues pour aborder les facettes importantes de la septicémie, des maladies graves et de la nutrition. L'instrument de sondage récoltait anonymement toutes les données, d'une manière telle que les répondants ne pouvaient être identifiés à partir de leurs réponses.

**Résultats.** Parmi les 64 diététistes qui ont répondu (taux de réponse de 57 %), la majorité pratiquait dans une unité de soins intensifs pour adultes (81 %), dans un centre universitaire (59 %), et dans une unité mixte (73 %). Une grande variabilité quant aux opinions et pratiques des diététistes a été rapportée relativement à la détermination des besoins énergétiques, aux pratiques d'alimentation entérale (AE), à l'AE avec des agents vasoactifs, à l'alimentation parentérale (AP) et à la supplémentation en oligo-éléments.

**Conclusions.** La variabilité dans la pratique des diététistes canadiens reflète probablement le manque de données probantes et de directives sur la septicémie grave. D'autres efforts de recherche sont nécessaires pour personnaliser les besoins nutritionnels des patients atteints d'une septicémie en évolution et l'AE chez les patients à haut risque de dysfonctionnement gastro-intestinal, pour optimiser l'AP et pour déterminer le rôle des oligo-éléments.

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## INTRODUCTION

Severe sepsis has been defined as “life threatening organ dysfunction caused by a dysregulated host response to infection” [1]. It affects a third of patients in intensive care units (ICU) [2], and accounts for 1 in 18 deaths in Canada [3]. In efforts to improve outcomes, optimizing nutrition has recently received much attention [4]. At baseline, malnutrition with acute hospitalizations occurs in over 30% of patients, with potentially a higher prevalence in critically ill patients [5–7]. Severe sepsis presents further nutrition challenges given the dynamic realities of the clinical course, vasoactive medications, inflammation, stress, preexisting comorbidities, and organ dysfunction with supportive technologies.

To provide evidence-based nutrition care for patients with severe sepsis, Canadian Registered Dietitians (RDs) must

navigate through several different North American guidelines and research studies. These may include the Dietitians of Canada Practice-Based Evidence in Nutrition [8], Academy of Nutrition and Dietetics Evidence Analysis Library [9], and guidelines from the American Society for Parenteral and Enteral Nutrition/Society of Critical Care Medicine (ASPEN/SCCM) [10, 11], Surviving Sepsis Campaign (SSC) [12], and Canadian Critical Care Nutrition (CCCN) [13]. Understandably, discrepancies exist among these guidelines because of data interpretation and timing of publication. Furthermore, the applicability of adult and critical illness recommendations to pediatric and septic patients may be problematic due to key pathophysiologic, clinical, and therapeutic differences [14, 15], and the quality of evidence is low [16]. Finally, the guidelines are not entirely inclusive, and do not

address such areas as titrating nutrition based on clinical evolution and vasoactive agents. To address these shortcomings, RDs can review additional published research, but these studies report conflicting results [4].

The purpose of this study was to identify the opinions and practices of Canadian RDs on nutrition care of the severely septic patient to delineate what additional information is required to optimize management.

## METHODS

### Survey development

PubMed, EMBASE, and Google Scholar were searched using the keywords “sepsis”, “critical illness”, and “nutrition” and limited to the most recent 3 years. After the literature was retrieved and their references reviewed, the search was broadened by removing the 3-year time limitation. Two researchers (GH, TB) reviewed the relevant articles ( $n = 75$ ) and determined 5 pertinent domains for the survey: determining nutritional requirements, enteral nutrition (EN), EN with vasoactive agents, total parenteral nutrition (PN), and supplemental micronutrients. Relevant items addressing these 5 domains were created and reviewed by 2 RDs with at least 5 years of ICU experience to ensure face validity, completion ease, and clarity. To mitigate leading questions and redundancy and to ensure that crucial content and study objectives were adequately addressed this review was followed by a 20-minute interview guided by a clinical sensibility-testing tool [17]. The survey was modified based on the results of the interview and converted to REDCap [18], a web-based application: (i) designed to support data capture for research studies; (ii) ensures secure web authentication, secure layer encryption, and anonymous participant responses; and (iii) maintained by the University of Saskatchewan. Feedback for ease of completion and final revisions were guided by the aforementioned RDs. The University of Saskatchewan Ethics Board approved the final version (Bio #16-295).

### Survey format and definitions

The survey (Supplementary File<sup>1</sup>) consisted of 39 possible questions divided into the 5 domains, preceded by 6 questions on personal and ICU demographics. Each domain had required responses that, in some instances, were followed by an embedded branching logic algorithm. Sepsis was clearly defined at the beginning of the survey as “life threatening organ dysfunction caused by a dysregulated host response to infection” [1] and related to either the primary diagnosis responsible for an admission, or a subsequent complication of an ICU admitted patient. Immunonutrition was defined as “utilizing enteral or parenteral nutrition to modulate immune and inflammatory responses.”

### Survey characteristics

Email contact information for RDs practicing in Canadian ICUs was obtained from provincial, university, hospital, and local sources. In early 2017, a letter of initial contact briefly outlining the rationale and content of the survey was emailed, stating “we want to sample the practice and opinions of pediatric and adult RDs across Canada about nutrition in critically ill septic patients.” This was followed by another email containing a link to the REDCap survey. Second and third reminder emails were sent to nonresponders at approximately 3-week intervals. No incentives were provided for survey participants.

### Data management and statistics

Data were collected and managed using REDCap [18]. Anonymous data were analyzed using STATA 14 software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, Texas). Proportions were calculated for each question.

## RESULTS

### Respondents' demographics

Of the 145 RDs identified through 42 different Canadian institutions throughout all 10 provinces, 18 no longer practiced in the ICU and declined the invitation while 15 were on leave and not able to participate in the survey. Hence, the response rate of eligible and available RDs was 64 of 112 (57%). One survey was incomplete but included in the analyses. To preserve respondent anonymity, institutional representation could not be determined. Demographics are shown in Table 1.

### Determining nutritional requirement

Sixty-three (98%) RDs utilized the following nutrition guideline(s) for their septic patients: ASPEN/SCCM ( $n = 56$ ; 88%), CCCN Clinical Practice ( $n = 47$ ; 73%), SSC ( $n = 10$ , 16%), and others ( $n = 9$ ; 14%). Predictive equations to determine estimated nutritional requirements included: Penn State ( $n = 26$ ; 41%), 25–30 kcal/kg/day ( $n = 22$ ; 34%), WHO ( $n = 6$ ; 9%), Harris Benedict ( $n = 4$ ; 6%), and others ( $n = 6$ ; 9%). Twenty-five percent ( $n = 16$ ) of RDs used stress factors in conjunction with predictive equations, ranging from  $\leq 1.2$  times ( $n = 3$ ; 5%) to 1.6 times of calculated caloric requirements ( $n = 2$ ; 3%). Nutritional therapy goals were based on clinical course ( $n = 56$ ; 88%), immunonutrition ( $n = 36$ ; 56%), anthropometrics ( $n = 32$ ; 50%), serum biomarkers ( $n = 25$ ; 39%), indirect calorimetry (IC) ( $n = 14$ ; 22%), and other factors ( $n = 16$ ; 25%; i.e., ventilation status and vasoactive agent requirements). Only 31% ( $n = 20$ ) of RDs had access to IC. Initiation timing of IC included  $< 24$  h ( $n = 3$ ; 5%), 24 to  $< 72$  h ( $n = 3$ ; 5%), 72 h to 1 week ( $n = 6$ ; 29%),

<sup>1</sup>Supplementary data are available with the article through the journal Web site at <http://dcjournal.ca/www.nrcresearchpress.com/doi/suppl/10.3148/cjdp-2018-029>.

**Table 1.** Respondents' demographics (n = 64).

Demographics	No. (%)
<b>Clinical practice</b>	
Pediatric intensive care	10 (16)
Adult intensive care	52 (81)
Both pediatric and adult intensive care	2 (3)
<b>Primary practice setting</b>	
Academic or tertiary care center	38 (59)
Community hospital	26 (41)
<b>Type of intensive care unit</b>	
Medical intensive care unit	11 (17)
Neurointensive care unit	1 (2)
Surgical intensive care unit	2 (3)
Cardiac intensive care unit	3 (5)
Mixed unit	47 (73)
<b>Experience in intensive care (y)</b>	
≤4	17 (27)
Between 5 and 12	18 (28)
>12	29 (45)
<b>Number of septic patients/y</b>	
≤40	18 (28)
Between 40 and 80	28 (44)
>80	18 (28)
<b>Participation in multidisciplinary daily rounds with all ICU patients</b>	
Yes	46 (72)
No	18 (28)
<b>Access to indirect calorimetry</b>	
Yes	20 (31)
No	44 (69)

and >1 week (n = 4; 6%). Key serum biomarkers included C-reactive protein (n = 21; 33%), prealbumin (n = 23; 60%), albumin (n = 10; 16%), and others (n = 12; 19%; i.e., white cell count, serum electrolytes, lactate, nitrogen balance).

### Enteral nutrition

Whenever possible, early EN was initiated by 100% of RDs, either within the first 24 h (n = 23; 36%) or between 24 and 48 h (n = 41; 64%) after admission. Seventeen RDs (27%) intentionally underfed patients with trophic feeds for <24 h (n = 2; 12%), 24–48 h (n = 10; 59%), 48–72 h (n = 4; 24%), and >72 h (n = 1; 6%), largely due to hemodynamic concerns (n = 14; 83%). Twelve RDs (19%) started EN at goal volume as opposed to initiating feeds at lower rates and progressing to goal volume as tolerated (n = 52; 81%). Prescribed EN and major immunonutrition strategies are summarized in Table 2. Seventy-two percent of RDs (n = 46) used gastric residual volumes (GRV) to determine EN tolerance; 17% of these RDs used GRV as the sole indicator, whereas the majority (83%) also observed for other signs of intolerance such as

**Table 2.** Prescribed enteral nutrition and utilization of immunonutrition strategies (n = 64).

Response	No. (%)
<b>Question: With enteral nutrition in your severely septic patients, do you:</b>	
Avoid omega-3 fatty acids	55 (86)
Target protein intake as per preferred guidelines	61 (95)
Prefer whole protein over peptide formula	49 (77)
Avoid hypertonic formula	40 (63)
Avoid high fibre formula	43 (67)
<b>Question: If immunonutrition has a role in prescribing nutrition to severely septic patients, in what manner do you implement your plan?</b>	
Early enteral nutrition	8 (13)
If TPN required, utilization of SMOFlipids®	9 (14)
Omega-3 fatty acids in enteral feeds	8 (13)
Other immunonutrition strategies	7 (11)

Note: RD, registered dietitian; TPN, total parenteral nutrition.

nausea (72%), emesis (100%), abdominal distention (100%), abdominal pain (92%), and diarrhea (42%).

### Enteral nutrition with vasoactive agents

The majority of RDs did not practice in ICUs that had specific guidelines for EN and hypotension in sepsis (n = 60; 94%), vasoactive agents (n = 57; 81%), and early detection of nonocclusive mesenteric ischemia (NOMI) (n = 59; 92%). Table 3 summarizes hemodynamic situations where concerns about inadequate mesenteric perfusion outweighed potential benefits of providing EN. Reasons for holding EN in the context of vasoactive agents are summarized in Table 3. Norepinephrine (n = 42; 69%), epinephrine (n = 40; 66%), vasopressin (n = 40; 66%), dopamine (n = 21; 34%), and dobutamine (n = 16; 26%) were the most concerning vasoactive agents to consider with EN. Eighty-six percent of RDs thought vasoactive agents were the cause or contributor of NOMI while the remaining 14% believed they have no role. Sixty-two percent of respondents thought EN was a contributor of NOMI, while the remaining 38% believed EN had no role. In the RDs' opinion, the early clinical indicators of NOMI were abdominal distention (n = 12; 19%), lactemia (n = 12; 19%), and ileus (n = 9; 14%), with 48% (n = 31) indicating no clinical indicator was stronger than another when considered alone. Events from medical history that were thought to raise the risk of developing NOMI included: abdominal surgery (n = 45; 70%), trauma (n = 41; 64%), burn (n = 24; 38%), and postoperative cardiac surgery (n = 35; 55%).

### Parenteral nutrition

Sixty-nine percent (n = 44) of RDs used total PN if motility agents and small bowel feeding was not successful or possible.

**Table 3.** Mesenteric perfusion, vasoactive medications, and enteral nutrition (n = 64).

Response	No. (%)
<b>Question: In severe sepsis are there hemodynamic situations where concerns about inadequate mesenteric perfusion outweighs the potential benefits of providing enteral nutrition?</b>	
A patient with previous hypotension and concern with reperfusion injury	18 (28)
A patient with current hypotension	14 (22)
A patient at significant risk for developing imminent hypotension	8 (13)
Hemodynamic instability with very high or increasing requirements of vasoactive support	60 (94)
Hemodynamics do not influence enteral nutrition	2 (3)
<b>Question: Should enteral nutrition be held in the following circumstances?</b>	
Patients on any vasoactive agents	2 (3)
Only patients on particular vasoactive agents	1 (2)
Only patients on vasoactive agents at certain doses	15 (23)
Any patient with hemodynamic instability requiring very high or increasing vasoactive support	57 (89)
Vasoactive support does not influence enteral nutrition	3 (5)

Fifty-eight percent (n = 37) used supplemental PN to provide adequate intake if goal EN was not achieved before 72 h (n = 4; 6%), within 72–96 days (n = 10; 16%), 5–7 days (n = 19; 30%), and >7 days (n = 5; 8%) postadmission. If PN was prescribed, fish oil containing lipid emulsions (n = 45; 70%) were utilized more often than soybean (n = 17; 27%) and olive oil based (n = 16; 25%) solutions. Thirty-three percent (n = 21) of RDs considered initiating lipid-free PN largely because of concomitant propofol sedation infusions (n = 8; 13%) and elevated triglycerides (n = 6; 19%).

### Supplemental micronutrients

Most RDs (n = 55; 87%) did not routinely supplement septic patients with micronutrients. If supplementation was prescribed, the most common nutrients were zinc (n = 5; 8%) and selenium (n = 4; 6%) for the duration of mechanical ventilation to ICU discharge, but only 4 RDs routinely monitored serum levels of these supplemental nutrients.

### DISCUSSION

In our survey of Canadian ICU RDs, we found a wide variability in opinions and practice in nutrition care for the patient with evolving sepsis including determining energy requirements, EN practice, EN with vasoactive agents, PN, and supplemental micronutrients.

Determining energy requirements in severe sepsis is challenging. Both ASPEN/SCCM [10, 11] and European Society for Clinical Nutrition and Metabolism (ESPEN) [19] guidelines suggest IC to measure energy expenditure when available and predictive equations when not. In reality, 70% of respondents did not have access to routine IC, and predictive equations typically cannot be customized to address the progressing sepsis pathophysiology requiring escalation of supportive technologies and vasoactive medications. Instead, alternative strategies during the acute

phase were considered by RDs that included compensatory stress factors (25%) in conjunction with predictive equations and consideration of serum biomarkers (39%), immunonutrition (56%), and clinical trajectory (88%). These practices, however, differ from ASPEN/SCCM guidelines [10, 11] that discourage the use of stress factors and recognize serum biomarkers as inaccurate or investigational. The need for further research in this area has already been identified [20], together with the advocacy for increasing access to IC.

Although most guidelines support early EN in critically ill patients, hemodynamic instability in severe sepsis is often seen early in the ICU admission. In our study, all RDs practiced early EN (within 48 hours), but a third intentionally used trophic or hypocaloric strategies. The rationale behind hypocaloric management was not explored in our questionnaire, but is best supported by SSC suggestions [12] to avoid full caloric feeding in the first week of ICU stay. Perhaps hypocaloric choices were made in anticipation of hemodynamic instability, as the majority of RDs (95%) reported holding EN with hypotension because of mesenteric perfusion concerns. Another quarter of RDs also considered thresholds for patients with previous hypotension and vasoactive medications at high doses. This is consistent with ASPEN/SCCM guidelines [10] that recommend withholding EN in patients that require initiation or escalation of vasoactive medication. Although there was little consensus on early clinical signs of NOMI, the majority of RDs felt that both EN and vasoactive medications were related to its development. Considering the difficulties to diagnose NOMI in the ICU, its significant consequences, and the risk factors that include shock, hypotension, and alpha-adrenergics [21], further research in determining intestinal ischemia may be beneficial for prescribing nutrition care in sepsis. At present, only computed tomography angiography has the necessary noninvasive diagnostic accuracy in

adults, suggesting a growth area for real-time diagnostic modalities [22].

The majority of RDs used GRV in their assessment for EN tolerance in their patients with severe sepsis. In contrast, the CCCN [13] and SSC [12] guidelines state that GRVs should not be routinely monitored except in patients with feeding intolerance. This discrepancy may be attributable to the dogmatic practice of measuring GRVs as a standardized assessment of EN tolerance. More likely, it mirrors conclusions from a thorough review that agreed with measuring GRVs—given the absence of high-grade evidence—for patients at high risk of gastrointestinal dysfunction [23]. Mesenteric ischemia in severe sepsis can lead to significant gastrointestinal dysfunction, and future research may identify a role for GRV in sepsis.

The majority of respondents would initiate exclusive and/or supplemental PN within the first week of sepsis if goal EN could not be achieved. This is consistent with ESPEN [19] guidelines that recommend PN for all patients receiving less than targeted EN after 2 days to decrease negative energy balances. However, ASPEN/SCCM [10] and SSC [12] guidelines do not suggest this practice, regardless of perceived nutrition risk. These incongruities require further investigation. Related, nearly half of the RDs considered modulating their patient's immune response (immunonutrition) in their nutrition plan. The most common strategy included prescribing SMOFlipid® or fish oils if PN was required. Alternative lipid emulsions may provide outcome benefits over conventional soybean oil emulsions that have been implicated as pro-inflammatory and heightening oxidative stress [24]. Fish oils [24] and SMOFlipid® [25] for example, may decrease the severity of sepsis through anti-inflammatory, immunologic, and antioxidant properties. Nearly a third of RDs took it a step further to utilize only lipid-free PN in the acute phase. Patient selection may be key, as modulating immune responses with nutrition could either be a powerful therapeutic adjuvant or cause harm when incorrectly timed. These current knowledge gaps may represent the most significant future contributions of nutrition management in severe sepsis.

Finally, although Canadian RDs did not commonly prescribe micronutrient supplementation, a small minority used zinc and selenium. While CCCN [13], ASPEN/SCCM [10], and SSC [12] guidelines recommend against their routine use, current clinical trials have been registered on ClinicalTrials.gov to study zinc, genistein, L-citrulline, vitamin D, and thiamine in sepsis. Caution in prescribing micronutrients should be exercised, as their utilization is not supported by robust evidence.

Our study has several limitations. First, because our response rate was 57%, the risk of sampling bias must be considered. Guideline-directed RDs may have been more inclined to participate in the questionnaire, but this potential bias source was not evaluated. To ensure anonymity, we did not link responses with respective institutions. However, over 40% and 15% of respondents did practice in community

hospitals and pediatric ICUs, respectively, suggesting a breadth of Canadian centres involved. Second, whether the responses reflect actual practice is unknown; at the very least they represent Canadian RDs' opinions on optimal nutrition in septic patients. Ideally, more concise sepsis nutrition guidelines are necessary before more research is conducted to measure practice against a unified standard of care. Third, we utilized a novel survey that was not evaluated for reliability or piloted. Some of the questions may have been difficult to interpret or were not entirely clear to the respondents, suggesting another area for potential biases. Finally, how these findings generalize to other countries is uncertain. However, given the variation within the cited North American and European ICU nutrition guidelines, wide discrepancies likely exist in other international jurisdictions.

Our study's major strength is the recognition that the variability of Canadian RDs practice for severe septic patients reflects current evidence gaps. These gaps provide exciting opportunities to potentially enhance outcomes, but will likely require coordinated multicentre efforts guided by protocolized sepsis care plans. Given the high incidence and mortality of severe sepsis, the benefits of optimal nutrition supported by high-grade evidence cannot be overstated.

## RELEVANCE TO PRACTICE

Despite several guidelines addressing nutrition in critical illness, many recommendations are supported by poor quality of evidence or provide contradictory guidance. These gaps are largely reflected by Canadian RDs' variable opinions and practice with the severely septic patient. Their responses in regards to determining nutritional requirements, EN with vasoactive agents, role of PN in the acute phase, and supplemental micronutrients provides valuable insight for relevant research questions to optimize nutrition management for these difficult patients.

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