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Assessment of parenteral nutrition prescription in Canadian acute care settings

Daniela Adjemian M.D. [a,b], Bianca M. Arendt Ph.D. [a], Johane P. Allard M.D., F.R.C.P.C. [a,c,*]

[a] Toronto General Hospital, University Health Network, Toronto, Ontario, Canada
[b] Hospital Clínico de la Universidad de Chile, Santiago, Chile
[c] Department of Medicine, University of Toronto, Toronto, Ontario, Canada

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ABSTRACT

Background: Parenteral nutrition (PN) prescription can be challenging in patients with complex conditions and has potential complications.
Objective: To assess PN prescription, monitoring, and PN-related complications in a Canadian acute care setting.
Methods: This was a prospective cohort study in which patients receiving PN were assessed by an auditor for nutritional status, PN-related prescription, monitoring, and complications. In addition, length of stay and mortality were recorded.
Results: 147 patients (mean ± SD 56.1 ± 16.4 y) with complex diseases (Charlson comorbidity index, median [p25–p75] 2 [1–4]) were enrolled. Before starting PN, 18.6%, 63.9%, and 17.5% of patients were classified as subjective global assessment A, B, and C, respectively. Body mass index remained unchanged during the period on PN. On average, 89% and 73% of patients received <90% of their energy and protein requirements, respectively, but 65% received oral or enteral nutrition at some point during PN. The average daily energy provided by PN increased and stabilized on day 10, reaching 87.2 ± 20.1% of the requirements. Line sepsis (6.8% of patients) and hyperglycemia (6.9%) were the most common complications. The overall mortality was 15.6%. For those alive, length of stay was 30 (range: 4–268) d. PN was discontinued because of transitioning to an oral diet (56.6%), enteral nutrition (17.6%), home PN (14.7%), palliative care (5.1%), death (4.4%), or other (1.5%).
Conclusion: Most patients were malnourished at the start of PN. Energy and protein provided from PN were less than requirements, and the goals were reached with delay. Mortality was high, possibly as a result of complex diseases.

Introduction

Parenteral nutrition (PN) is an expensive treatment and should be used only when the gastrointestinal tract is not functional or cannot be accessed or the patient's nutrient needs cannot be met by oral or enteral nutrition (EN) [1,2]. Indications include intestinal obstruction, ileus or severe dysmotility, severe pancreatitis, high-output fistula, short bowel syndrome, and complications of severe intestinal inflammatory disease [3,4]. The European Society for Parenteral and Enteral Nutrition guidelines recommend the use of PN in this patient population with various types of intestinal failure (IF) [5]. To improve outcome of acute IF, treatment should be provided by a multidisciplinary team in a specialized facility or rehabilitation center rather than in acute care hospitals. PN alone or in combination with EN is often the preferred option in IF as a result of altered absorption of the gastrointestinal tract.

Complications associated with PN are not negligible and include catheter infections, hyperglycemia, hepatic dysfunction, hyperlipidemia, and refeeding syndrome [4,6–8]. Furthermore, PN used without oral or enteral intake is associated with gut atrophy, loss of intestinal barrier function, altered gut microflora, increased bacterial adherence, increased microbe translocation, and B- and T-cell dysfunction [3,9]. In addition, in the intensive care unit (ICU) setting, PN may be associated with higher infection rate, longer length of stay (LOS), and higher mortality compared with EN [10,11].

* Corresponding author: Tel.: +1 416 340 4800 × 5159; fax: +1 416 348 0065.
E-mail address: Johane.allard@uhn.on.ca (J. P. Allard).

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Bloodstream infection rates vary widely among PN patients from 1.3% to 39% [12,13]. Even though there is evidence on how to reduce catheter-related infections, studies have still found high rates in patients on PN [14]. One cohort study in patients with central venous catheters (CVC) found that PN was an independent risk factor for bloodstream infections [15]. Another study in 19 Canadian hospitals found an overall rate of bloodstream infections of 4.9%. PN increased the risk of bloodstream infection fourfold [16].

The aim of this study was to assess PN care in acute care settings by determining whether PN was provided in the appropriate patient population, PN prescription and monitoring were adequate, and PN-related complications were within or less than rates reported in the literature.

Methods

Patients and procedures

This was a prospective cohort study in adults admitted to Toronto General Hospital or Princess Margaret Hospital, Toronto, Ontario, Canada, both part of the University Health Network, Toronto.

Patients at nutritional risk admitted on medical, surgical, or ICU wards were initially identified by attending physicians and nurses and assessed by the ward dietitian. When indicated, patients were referred to the nutrition support team (NST) for PN. Consecutive patients receiving PN were recruited between July 2012 and September 2013 and followed from the first day until their last day on PN. As per standard of care, patients were initially assessed simultaneously by the NST dietitian and NST pharmacist for formal nutritional evaluation and medication history, respectively, followed by PN prescription. Residents or fellows were also involved in the consultations. When necessary, the NST nurse would also assess the patients. Consults were then reviewed by the NST gastroenterologist once or twice a week or on the same day if required.

Data collection

Data were collected by chart review, by direct communication with the NST, and by nurses on each floor. Information collected included demographic characteristics; primary diagnosis; indications for PN; nutritional assessment, including body mass index (BMI) (weight [kg]/height [m]^2) and subjective global assessment (SGA) [17]; updated Charlson Comorbidity Index [18]; energy and protein requirements calculated by the dietitian; PN prescribed by NST; PN received; other sources of energy intake; vascular access information, and PN-relevant laboratory measures. In addition, complications possibly associated with PN were recorded: hyper-/hypoglycemia, catheter-related sepsis as defined by Sihler et al. [19] and Tomlinson et al. [20], hypertriglyceridemia, fatty liver, refeeding syndrome, and elevated liver enzymes. LOS and mortality were also recorded.

Indications for PN

Indications for PN were classified as prolonged ileus; intolerance to EN from any gastrointestinal symptoms; malabsorption syndrome from any causes; gastrointestinal disorders (obstruction, bleeding, ischemic bowel, motility disorder); increased losses (fistula, esophageal leak, anastomotic leak, chylothorax, high-output stoma/ileostomy not active); bridge or top-up to oral diet or EN (supplemental PN); and other reasons.

Prescription of PN

Estimated energy requirements were calculated mostly using the Harris-Benedict formula with adjusted body weight when appropriate and an activity factor (AF) [21–23]:

1. For men: $Resting\ energy\ expenditure\ (kcal/d) = 66 + 13.7 \times (weight\ in\ kg) + 5 \times (height\ in\ cm) - 6.8 \times (age\ in\ years) \times AF$
2. For women: $Resting\ energy\ expenditure\ (kcal/d) = 655 + 9.6 \times (weight\ in\ kg) + 1.8 \times (height\ in\ cm) - 4.7 \times (age\ in\ years) \times AF$
   AF used: 1.1–1.5.
   Energy requirements were also calculated using the following formulas:
3. For ventilated patients, Penn State or Penn State Modified [22,24]:
   1. $Penn\ State\ (kcal/d) = (Mifflin \times 0.96) + (Tmax \times 167) + (Ve \times 31) - 6212$
   2. $Penn\ State\ Modified\ (kcal/d) = (Mifflin \times 0.71) + (Tmax \times 85) + (Ve \times 64) - 3085$, for patients ≥ 60 y with BMI ≥ 30 kg/m^2
      Mifflin was calculated:
      a. For men: $Weight\ in\ kg \times (10) + height\ in\ cm \times (6.25) - age\ in\ years \times (5) + 5$
      b. For women: $Weight\ in\ kg \times (10) + height\ in\ cm \times (6.25) - age \times (5) - 161$
      Tmax is maximum body temperature in the previous 24 h in degrees centigrade, and *Ve* is minute ventilation in L/min.
4. For non-ventilated patients, a weight-based formula (kcal/kg) between 20 to 40 kcal/kg was used, depending on disease and weight [23,25–27].
   Actual body weight was used, except for patients with obesity, ascites, or edema, for whom Hamwi's equation was applied for weight calculation:
   c. For men: $Weight\ in\ lb = 106 + [(height\ in\ inches - 60) \times 6]$
   d. For women: $Weight\ in\ lb = 100 + [(height\ in\ inches - 60) \times 5]$
   Weight in kilograms was multiplied by 2.2 to obtain weight in pounds.

Calculations of energy requirements were compared using a Bland-Altman analysis to assess agreement between the two methods [28].

Protein requirements (g/kg) were estimated by the dietitian based on American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines [27] and clinical judgment. The patients received individually compounded PN. Fluid and electrolytes were prescribed according to individual needs, and all received multivitamin and trace elements.

Infused PN was recorded over 24 h. The daily energy and proteins from PN were averaged and expressed as a percentage of requirements calculated by the dietitian.

PN supply was considered adequate if the energy received was ≥90% of the estimated requirements and low if it was <90%. Other sources of energy, such as propofol, EN, and glucose-based solutions were also considered. As a result of limited resources, calorie counts for oral intake were not possible; thus oral intake was recorded as yes/no. The protein intake by PN was considered adequate if it reached ≥90% of the requirements estimated by the dietitian [1,29].

Catheter information

Number of PN days with peripheral or CVC, type of CVC, number of lumens, date of insertion/removal, and incidence or suspicion of line sepsis were recorded. Catheter-related bloodstream infection was defined following the Centers for Disease Control and Prevention definition: "Bloodstream infection with either a positive tip culture or a positive blood culture drawn from the CVC with the same organism isolated simultaneously from a peripheral site and clinical manifestations with no other apparent source of infection" [19,20].

Ethical statement

The study was approved by the University Health Network Research Ethics Board. Patients were included in the study after informed consent was signed by either patients or their substitute decision maker.

Statistical analysis

Results were expressed as mean ± SD, median (percentiles: 25–75), median (range), or percentage (%) depending on the variable type and distribution. To compare patient groups, Student's *t* test and one-way analysis of variance with Tukey post hoc test were used for normally distributed continuous variables and Kruskal-Wallis and Mann-Whitney *U* test for non–normally distributed variables. Bland-Altman plot was used to evaluate the agreement between energy requirement formulas. SPSS Version 20 was used for the analyses. Statistical significance was set at $P < 0.05$.

Results

General characteristics

The study included 147 patients described in Table 1. The most common diagnosis at admission was cancer (36.7%), followed by digestive diseases (25.9%). Most patients were hospitalized in surgical units (59%). Even though there was a high prevalence of normal or higher BMI, most patients were at least moderately malnourished (SGA rating B or C). There was no difference in BMI and SGA when comparing patients by wards (data not shown). Nevertheless, patients hospitalized in medical units had a significantly higher Updated Charlson Comorbidity Index scores

Table 1
General characteristics

Characteristics	Value
Age, y	56.1 ± 16.4
Male sex, *n* (%)	76 (51.7)
Body mass index, kg/m^2	23.5 ± 6.4
Body mass index, *n* (%)	
<18.5 kg/m^2	28 (22.2)
≥18.5–24.99 kg/m^2	54 (42.9)
≥25.0 kg/m^2	44 (34.9)
SGA, *n* (%)	
A	18 (18.6)
B	62 (63.9)
C	17 (17.5)
Type of ward, *n* (%)	
Medical	25 (17.2)
Surgical	86 (59.3)
ICU	34 (23.4)
Updated Charlson Comorbidity Index, median (p25–p75)	2 (1–4)
Primary diagnosis on admission, *n* (%)	
Digestive disease	38 (25.9)
Infections	7 (4.8)
Hepatobiliary disease	7 (4.8)
Cardiovascular disease	5 (3.4)
Pulmonary disease	12 (8.2)
Hematological disease	6 (4.1)
Cancer	54 (36.7)
Others	18 (12.2)

ICU, intensive care unit; SGA, subjective global assessment.
Values given are mean ± SD, median (p25–p75), or *n* (%) of patients.

compared with surgical units (4.0 [2.5–6.0] versus 2.0 [1.0–3.5], $P < 0.001$).

Indication for PN

The most common indications for PN were gastrointestinal disorders caused by obstruction, bleeding, ischemic bowel, or motility disorder (29.9% of patients) (Table 2). Prolonged ileus was the second most recorded reason (16.7%). Prolonged ileus and intolerance to EN from any gastrointestinal symptoms were associated with fewer days on PN (11 and 10 d, respectively). However, the differences among all indications were not significant (Kruskal-Wallis test, $P = 0.23$).

The median duration of PN was 14.5 (8–26) d for all patients with no difference in PN days among medical, surgical, and ICU wards (14 [6–24], 14 [8–26], and 16 [11–28] d, respectively). PN duration was 20 (11–30) d for malabsorption and 19 (11–27) d for other gastrointestinal disorders. PN duration was not different between cancer patients (15.5 [7–25.75] d) and non-cancer patients (13 [8–23] d) ($P = 0.59$).

Table 2
Initial indication and duration of parenteral nutrition

Initial indication for PN ($n = 144$)	*n* (% of patients)	Days on PN Median (p25–p75)
Prolonged ileus	24 (16.7)	11 (5–20)
Intolerance to EN from any GI symptoms	18 (12.5)	10 (7–17)
Malabsorption syndrome from any cause	13 (9.0)	20 (11–30)
GI disorders	43 (29.9)	19 (11–27)
Increased losses	19 (13.2)	16 (7–24)
Bridge or top up to PO/EN	18 (12.5)	14 (9–34)
Other reasons	9 (6.3)	18 (6–23)

EN, enteral nutrition; GI, gastrointestinal; PN, parenteral nutrition; PO: oral diet.

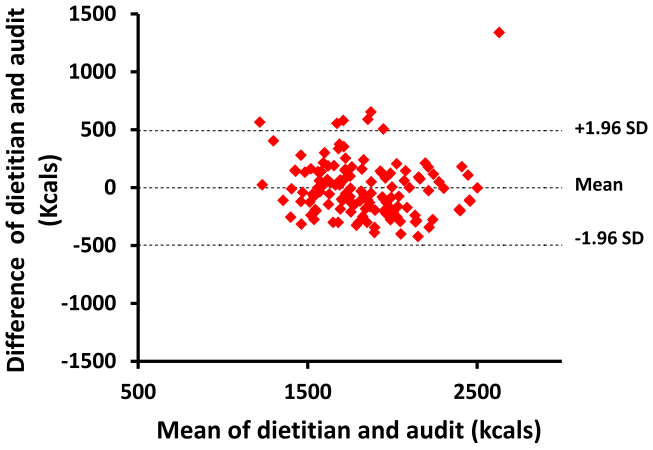

Fig. 1. Calculated energy requirements by dietitian versus audit (kcals).

Comparison of energy requirements

The comparison between energy requirement equations (Fig. 1) revealed a high level of agreement with a mean difference of –2.7 kcal. The limits of agreement were –496.1 and 490.7 kcal. One patient with cystic fibrosis was very different from the others, because a cystic fibrosis equation plus 500 kcal was used by the dietitian to increase the energy.

Parenteral nutrition supply

The patients received 72.0 ± 16.5% of their energy requirements by PN alone. There was no difference in energy provided to the patients when comparing PN alone versus PN and other sources (EN, peripheral intravenous glucose-based solutions, and propofol) ($P = 0.36$). Therefore, the remaining analyses were conducted using only the energy/protein provided by PN.

Only 10.2% and 0.8% of the patients received 90% to 110% and >110% of their energy requirements by PN, respectively (Fig. 2). Of the patients with <90% of their energy requirements from PN, 64.9% received oral or EN at some point along with PN, with higher oral or enteral intake in those receiving PN for >13 d (76% of patients) versus those with shorter duration (53% of patients) ($P = 0.007$). Furthermore, the energy from PN per day (Fig. 3) had a gradual increase in the delivery of energy and stabilization on

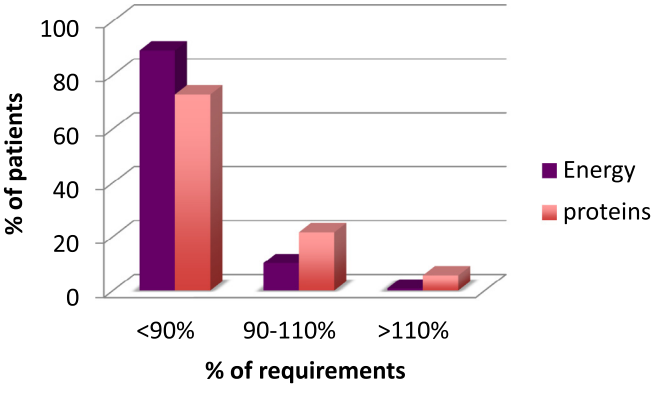

Fig. 2. Average energy and proteins provided by parenteral nutrition as a percentage of goal requirements.

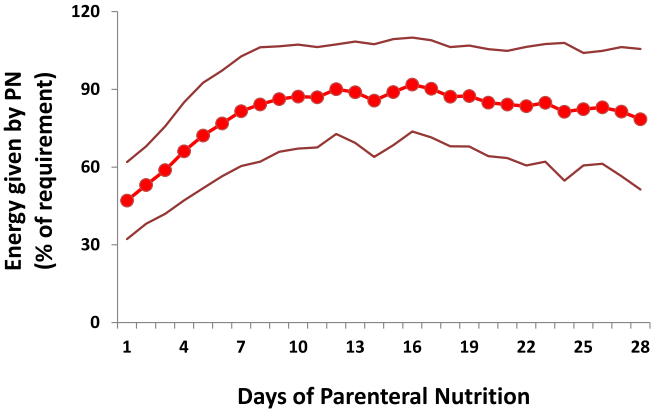

Fig. 3. Energy given by parenteral nutrition (PN) as a percentage of goal requirements during the first 28 d.

day 10, reaching 87.2 ± 20.1% of the requirements. This was maintained until day 27, when energy from PN started to decrease. On the day with maximum energy delivered by PN, 66.4% of patients received ≥90% of their energy requirements.

Proteins provided by PN reached 80.6 ± 20.5% of the patients' requirements; 27.2% of patients reached ≥90% of their protein requirements (Fig. 2). Similar to the findings for energy, most patients (65.9%) reaching <90% of their protein requirements through PN received oral or EN at some point together with PN. On the day with maximum protein delivered by PN, 71.2% of patients received ≥90% of their requirements.

Patients with prolonged ileus and intolerance to EN from any gastrointestinal symptom received less energy and/or protein by PN (as a percentage of requirements) compared with other indications for PN (data not shown). They tend to receive peripheral PN for ≤8 d and were SGA A or B admitted on medical or surgical wards. Most transitioned from peripheral PN to oral diet. To investigate which patients could have had an inadequate indication for PN, we analyzed the 13 patients (9.3%) receiving PN for <5 d. The main indication in this population was ileus (38.5% of these patients). In general, patients were nil by mouth for 2 (0–6) d before PN, and this was not different among wards. Patients in surgical and medical units received more protein per day than ICU patients: surgical 81.8 ± 20.6%; medical 92 ± 23.8%; ICU 71.1 ± 14.7% of the requirements ($P < 0.05$ surgical versus ICU, $P < 0.01$ medical versus ICU). Finally, PN was on hold at some point in 30.5%, 31.8%, and 33.3% of the patients in surgical, medical, and ICU wards, respectively.

Complications

Most patients (70.5%) did not experience PN-related complications. The most prevalent complications were catheter sepsis and hyperglycemia (6.8% and 6.9% of all patients, respectively). Hypoglycemia and suspicion of refeeding syndrome were identified less often (2.7% and 2.1% of patients, respectively). It was difficult to determine whether other complications like hypertriglyceridemia, fatty liver, or elevated liver enzymes were secondary to PN.

Catheters for PN administration and line sepsis

Only 4.8% of patients received PN exclusively through a peripheral catheter, 71.4% had a CVC, and 22.4% had both. Peripherally inserted central catheters were most common (76.2%). Most patients (81.3%) had one catheter for the duration of PN, 13.7% had one catheter change, and 5.1% more than one catheter change. Peripherally inserted central catheters with ≥2 lumens were most commonly associated with line sepsis.

Patients with line sepsis compared with those without had higher BMI (25.8 [18.3–39.6] versus 21.9 [11.1–46] kg/m^2, $P = 0.018$) and longer time on PN (28 [4–73] versus 14 [2–165] d, $P = 0.013$). Seventy-three percent of patients with a confirmed line sepsis had at least two episodes of elevated blood glucose greater than 6.1 mmol/L compared with 38% of those without line sepsis ($P < 0.001$).

Laboratory

PN-relevant laboratory measures were recorded from baseline until week 4. There was no significant change in glycemia, liver function tests, and blood lipid profile over time (data not shown).

Reason for discontinuing PN and outcomes

PN was discontinued in 56.6% of the patients because they transitioned to oral diet; 17.6% started with EN; 14.7% went home with PN (HPN); 5.1% were palliative; and 4.4% died. Other reasons accounted for 1.5%. Most of the patients requiring HPN (45%) had cancer as main diagnosis, with 55% having ovarian cancer. In addition, bowel obstruction accounted for 35% of HPN and 85% of those patients had cancer. The two other most common reasons for HPN were short bowel syndrome (15%) and transplant (including intestinal) (15%). A third of the patients (34%) were admitted to ICU for 15 (range: 1–139) d during their hospitalization. The overall mortality was 15.6%. Time to death was 49 (range: 12–129) d, and time to discharge alive was 30 (range: 4–268) d.

Discussion

Our data indicate that most patients received PN during their hospitalization because of gastrointestinal disorders and prolonged ileus. The energy requirements calculated by different equations had agreement; however, a high percentage of patients received on average less than 90% of their calculated energy and protein requirements with a slow progression toward goals. The most common complications were catheter sepsis and hyperglycemia. Patients' conditions were complex, with prolonged LOS and high mortality.

The provision of PN energy and protein was not optimal. Part of this may be due to concerns over refeeding syndrome and fluid overloading, as well as concomitant partial oral/enteral intake. However, the increase in PN and stabilization should have been reached more rapidly. According to ASPEN guidelines [27], in patients with PN and suspicion of refeeding syndrome it should take 3 to 4 d to reach the goal. In the present study it took 10 d to stabilize and reach 87% of the requirements.

Similar results have been reported by Kraft et al. [1]. They studied a slightly older population with similar BMI and found that 77.6% of patients received <90% of caloric needs. However, 69% received peripheral PN restricting the amount of calories as a result of limitations in solution osmolarity. Nardo et al. [29] examined PN prescription and administration in 200 adults hospitalized in different wards. Patients required PN for a median of 8 d, which was less than in our study, and PN was prescribed by different staff on each ward. Although the proportion of

patients who received <90% of the energy (16.5%) and protein requirements (13.5%) was small, overfeeding was present in >50% of the patients. This indicates that PN prescription could be accurate but administration could be inadequate, especially if not prescribed by an NST.

We did not assess the reasons for the slow progression of PN delivery, which could be related to fluid intolerance, illness severity, or risk of refeeding syndrome (73% of patients). This slow PN progression seems beneficial because only 2.1% of patients had refeeding syndrome. More than 50% of the PN patients in medical and surgical wards received concomitant oral or enteral nutrition, and the proportion was higher in those on PN for >13 d. This may reflect progressive improvement or a more chronic condition than those with PN of shorter duration. Because oral nutrition was not measured as a result of restricted personnel, it was difficult to determine how big the total nutritional deficit was, particularly in those with PN of >13 d who received oral or enteral nutrition more often.

Among the 20% of patients receiving PN for <7 d, most had an ileus. ASPEN guidelines suggest that patients with low nutritional risk can wait 7 d after ICU admission before starting PN. If patients receive EN, supplemental PN should be considered after 7 to 10 d independent of the nutritional risk and only if patients are tolerating <60% of energy and protein requirements from EN [27]. This suggests that in patients with low nutritional risk and ileus, the need for PN should be assessed after 7 d of admission to ICU to prevent unnecessary PN prescriptions. Some authors have stated that postoperative ileus is not a contraindication for EN [30], and it is not necessary to have bowel sounds to start EN [31]. Another study reported that PN prescriptions were inappropriate because of premature initiation for postoperative ileus [32].

The results indicated agreement between requirements calculated by different equations. This suggests that Harris-Benedict or a weight-based formula can be used if the weight of the patient and the stress of his or her diseases are considered. For ICU patients, the Penn State formula is preferable because it includes other factors such as maximum temperature and minute volume ventilation, which could influence the requirements [24]. Our data did not detect any difference between formulas. Ideally, indirect calorimetry should be used because it is the gold standard to estimate basal metabolic rate.

Most patients did not have any PN-related complications. In our study the rate of line sepsis was 6.8%, which is similar to that found in the literature (1.3%–39%) [12,13]. The rate of hyperglycemia in our study (6.9%) was less than reported (17%–79%) [33,34]. The relatively large number of patients discharged on HPN, most with cancer, bowel obstruction, or short bowel syndrome, is explained by the fact that the participating centers provide quaternary and advanced oncology care. Therefore, the study population may not be generalizable to community hospitals.

The LOS and mortality were greater than previously reported in a large cohort of patients in Canadian hospitals, where the subgroup of patients receiving PN or EN had longer LOS compared with patients with oral supplementation [35]. In our study, increased LOS and mortality reflect the complexity of the patients as supported by the Charlson Comorbidity Index.

The strength of this study is the prospective cohort design including 147 consecutive patients receiving PN. However, there were some limitations regarding accessibility of information on PN infusion hours and line sepsis. Particularly for oncology patients, PN hours were poorly documented in the chart. Also, it would have been ideal to have calorie and protein counts for the patients who had concomitant oral nutrition to see if overall requirements were met.

Conclusion

In this prospective study conducted in an acute care setting, most patients starting PN were malnourished. Although PN was prescribed appropriately, the increase in the provision of energy and protein was slow and did not meet the requirements. Complications from PN were within reported ranges but mortality was high, possibly because of complex diseases.

Disclosures

Daniela Adjemian received a partial postdoctoral research fellowship from Baxter Corporation Canada. Johane Allard received unrestricted grants from Baxter Corporation Canada. Bianca Arendt had no conflict of interest.

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Bianca Arendt and Johane Allard equally contributed to the conception and design of the research. All authors drafted and revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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