

Original Article

Prevalence and risk factors of complications in adult patients with short bowel syndrome receiving long-term home parenteral nutrition

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Background and Objectives: Short bowel syndrome (SBS) is a complicated and challenging disease where home parenteral nutrition (HPN) is widely used. The complications of long-term HPN-dependent in adult patients with SBS are poorly documented. This study was mainly aimed to assess the prevalence and risk factors of HPN-associated complications in adult patients with SBS, especially the catheter-related sepsis and HPN-associated liver/biliary disorders. **Methods and Study Design:** 47 non-malignant adult patients with SBS who received HPN for more than 2 years in our clinical nutrition center were included. Patients were divided into two groups according to whether HPN-associated complications were present or not. Student's t-test and χ^2 test were applied to compare the differences between the two groups. **Results:** The mean frequency of catheter-related sepsis was 0.31 ± 0.05 per catheter year of HPN. An higher incidence of catheter-related infections ($p < 0.001$) and shorter delay between HPN onset and first infection ($p < 0.001$) were identified as risk factors for catheter-related sepsis. A total of 25 patients (53.2%) developed HPN-associated liver/biliary diseases. The identified risk factors for HPN-associated liver/biliary disorders were higher rate of catheter-related infections ($p = 0.009$), shorter delay between HPN onset and first infection ($p = 0.017$), higher energy content of HPN ($p = 0.014$), higher glucose rate of HPN ($p = 0.009$), and lower lipid rate of HPN ($p = 0.022$). **Conclusion:** Our study revealed that adult patients with SBS receiving long-term HPN treatment developed a low prevalence of catheter-related sepsis but a rather high prevalence of HPN-associated liver/biliary disorders. We also identified several risk factors for HPN-associated complications which should be taken notice of in clinical practice.

Key Words: long-term home parenteral nutrition, short bowel syndrome, adult patients, complications, risk factors

INTRODUCTION

Short bowel syndrome (SBS) is a condition characterized by compromised bowel absorptive capacity that cause patients to be unable to maintain protein-energy, fluid, electrolyte, or micronutrient balances under a normal unrestricted diet. SBS results mostly from congenital defect, disease-associated loss of absorption and extensive intestinal resection.¹ The remaining length of intestinal tract is important for clinical diagnosis. SBS is associated with high rate of morbidity and mortality, a reduced quality of life and large health care expenses.² Management of patients with SBS is complicated and challenging. A multidisciplinary approach is required including dietary, fluid and pharmacological management, co-morbid complications treatment and even surgery occasionally.^{3,4}

Parenteral nutrition support, especially home parenteral nutrition (HPN), has been widely used to treat patients with SBS since 1960s.^{5,6} For patients with SBS, HPN dependence might be either permanent or transient, which mainly depends on the resection extent and postsurgical intestinal adaptation.⁷ It has been reported that 47% of patients with SBS required long-term HPN.⁸ Generally, it is accepted that the time to discontinue HPN may be at first 2 years in adult patients with a colon in continuity.^{9,10}

Children can achieve HPN independence after much longer periods (5-10 years) after full bowel adaptation.^{11,12} In addition, late HPN (more than 2 years) discontinuation in adult patients with SBS has also been reported.^{8,13} Therefore, the timing of HPN discontinuation may vary depending on the characteristics of the individual intestinal rehabilitation capacity of the remnant gastrointestinal tract and other factors. However, HPN is still considered as the primary treatment for patients with irreversible HPN unless intestinal transplantation is performed.^{14,15}

Long-term survival of patients with SBS receiving HPN has been achieved both in children and adult patients in multiple centers worldwide.^{8,9,12,16} In our clinical nutrition center, we reported a female case (aged 32 years) who attained normal pregnancy after 5 years HPN due to

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entire small intestine and right colon resection.¹⁷ However, several HPN-associated complications such as catheter-related infections and liver/biliary disorders occurred during long-term HPN, which were consistent with reports from other clinical nutrition centers.¹⁸⁻²⁰ Prevalence and risk factors of HPN-associated liver diseases of children receiving long-term HPN have been reported.¹² However, the prevalence and risk factors of HPN-associated complications in adult patients with SBS receiving long-term HPN are poorly documented. Herein, we report a series of adult patients with SBS receiving long-term HPN for more than 2 years over a 30-year follow-up period in our center, to better define the prevalence and risk factors for HPN-associated complications, especially the catheter-related sepsis and HPN-associated liver/biliary disorders.

METHODS

Between January 1985 and June 2015, adult patients with SBS who received HPN for more than 2 years in our clinical nutrition center, Department of General Surgery, Zhongshan Hospital of Fudan University, were studied. The inclusion criteria were as follows: 1) patients diagnosed as SBS at the ages >18 years, 2) patients received HPN for more than 2 years. The exclusion criteria were as follows: 1) patients diagnosed as SBS at the ages <18 years, 2) patients with evolving primary malignancies either present at the time of short bowel occurrence or recurring during follow-up, 3) patients with liver/biliary abnormalities diagnosed before the initiation of HPN or identified as unrelated to HPN (i.e. inborn liver disease, acquired toxic or viral liver disease), and 4) patients that have discontinued HPN within 2 years. This study was approved by the ethics committee of the Zhongshan Hospital of Fudan University (No.: B2013-106R). Patients were given informed consent and patients' anonymities were preserved.

When the patients first visited our center, the following specifics of each patient were recorded: demographic characteristics, the primary diagnosis (including the aetiology of SBS), characteristics of the intestinal tract, characteristics of surgical procedures, and HPN dependence. The remnant small bowel was evaluated on the basis of operative records and expressed as a length. Surgical procedures of digestive circuit anastomosis were classified into 3 types: end-enterostomy (type 1), jejunocolic anastomosis (type 2), and jejunoileo-colic anastomosis (type 3).⁹

Follow-up included a 24 h telephone hotline number for emergencies and regular outpatient follow-up visits to adapt the composition and volume of the nutrient solution to meet the body requirements and to detect the occurrence of HPN-associated complications. At each visit, data related to the current program of HPN, venous catheter, biochemical and imaging examination, hospital stays, and cause of death, if any, were recorded. The composition of the HPN (i.e. glucose, amino acids, lipid emulsion, trace elements and vitamins) varied during the 30 years of the study. If no HPN-associated complications occurred, we calculated the average value of HPN characteristics regarding the composition, volume, frequency, and duration time of the infusions at the end of the follow-up. If HPN-associated complications occurred, we calculated

the average value of HPN characteristics before the occurrence of relevant complications to identify whether HPN characteristics were risk factors for these complications.

We paid key attention to the prevalence of long-term HPN-associated catheter-related sepsis and liver/biliary disorders. Catheter-related sepsis was defined as episodes of fever with clinical and biological parameters of infection if no symptoms or signs point to other reasons. If the same pathogen was cultured from the catheter and peripheral vein, the diagnosis would then be confirmed. We also recorded the delay between HPN onset and the first catheter infection. The occurrence of catheter occlusion, catheter displacement and catheter breakage, if any, were also recorded.

Chronic HPN-associated liver diseases are characterized by abnormalities in liver biochemistries including steatosis (elevated alanine transaminase levels >1.5 times normal upper limit) and cholestasis (elevated conjugated bilirubin or alkaline phosphatase and γ -glutamyl transpeptidase (GGT) levels >1.5 times normal upper limit) that persist for at least 6 months.²¹ In this study, biochemical abnormalities were classified as steatosis, cholestasis, and both steatosis and cholestasis. In addition, the occurrences of biliary abnormalities (eg, sludge and lithiasis) were determined by routine ultrasonography examination performed systematically upon starting of HPN. Generally, ultrasonography examination was performed once yearly when chronic cholestasis or HPN-associated liver diseases occurred, and when there was clinical suspicion of biliary complication.²¹

Statistical analysis

We firstly described the patients' characteristics and HPN characteristics of all included patients in this study. Then, the prevalence of catheter-related complications including catheter-related sepsis, catheter occlusion, catheter displacement, and catheter breakage was described. To analyze risk factors of catheter-related sepsis, patients were divided into two groups according to the frequency of catheter-related sepsis. Finally, the prevalence of HPN-associated liver/biliary disorders was described and the risk factors were analyzed by dividing patients into two groups depending on the presence or absence of liver/biliary disorders.

For quantitative data, results were expressed as mean \pm standard error (mean \pm SE). The Student's t-test was used to compare the differences of continuous variables of two groups. For qualitative data, results were expressed as effective number and percentage. Qualitative data were compared using χ^2 test. All statistical analyses were performed using the Stata version 11.0. $p < 0.05$ was considered statistically significant.

RESULTS

Patients' characteristics

A total of 47 adult patients with SBS who received long-term HPN were included in this study (Table 1). Almost half of these patients (48.9%) were diagnosed as SBS between the ages of 40-60 years. The most common reasons for SBS were mesenteric infarction (40.4%) and volvulus (29.8%). The post-duodenal remnant small bow-

Table 1. Patients' characteristics of 47 adult patients with short bowel syndrome receiving long-term home parenteral nutrition

Characteristics	Patients (%)
Total	47
Gender	
Men	21 (44.7)
Women	26 (55.3)
Ages diagnosed as short bowel syndrome	
<40	17 (36.2)
40-60	23 (48.9)
>60	7 (14.9)
Causes of bowel resection	
Mesenteric infarction	19 (40.4)
Volvulus	14 (29.8)
Chronic intestinal pseudo-obstruction	5 (10.6)
Cohn's disease	4 (8.5)
Surgical complications	2 (4.3)
Traumatism	2 (4.3)
Radiation enteritis	1 (2.1)
Remnant small bowel length (cm)	
<50	33 (70.2)
50-100	10 (21.3)
>100	4 (8.5)
Digestive circuit anastomosis	
End-enterostomy (type 1)	11 (23.4)
Jejunocolic anastomosis (type 2)	32 (68.1)
Jejunioileocolic anastomosis (type 3)	4 (8.5)

Table 2. Home parenteral nutrition (HPN) characteristics of 47 adult patients with short bowel syndrome receiving long-term HPN

Characteristics	Mean±SE
Duration of HPN (years)	8.13±4.81
Age at HPN onset (years)	45.1±14.8
Times of HPN infusions (d/w)	5.42±0.74
Duration of infusion (h/d)	12.6±2.10
Oral/Enteral nutrition (n/total)	47/47
Delay between HPN onset and the first infection (years)	1.02±0.46
Parenteral volume (ml/kg/d)	33.6±4.26
Parenteral energy intake (kcal/kg/d)	20.1±2.21
Parenteral glucose intake (g/kg/d)	3.01±0.49
Parenteral glucose intake (% energy intake)	59.1±4.71
Parenteral lipid intake (g/kg/d)	0.91±0.10
Parenteral lipid intake (% energy intake)	38.8±3.67
Types of catheters	
CVC	32 (68.1%)
PICC	15 (31.9%)
Outcome, n (%)	
Weaning off HPN	3 (6.4%)
Continuing HPN	38 (80.8%)
Death	6 (12.8%)

CVC: central venous catheter; PICC: peripherally inserted central venous catheters; n: number.

el length of the majority of patients (70.2%) was <50 cm. Meanwhile, the common digestive circuit anastomosis was jejunocolic anastomosis (type 2). The longest follow-up female patient described, before undergoing an emergency operation resecting the entire small intestine and right colon due to volvulus 30 years ago.

HPN characteristics

HPN characteristics of included patients are described in

Table 2. Most of the patients (32/47) applied traditional central venous catheter (CVC) to receive HPN while only 15 patients (15/47) applied peripherally inserted central venous catheter (PICC). The overall duration mean HPN was 8.13±4.81 years with HPN onset at ages of 45.1±14.8 years. In particular, 16 patients (34.0%) had HPN duration longer than 10 years, and the longest HPN duration was 30 years. The mean daily infusion time was 12.6 hours, and the mean HPN infusion time was 5.42 days per week. All patients received oral/enteral nutrition in our study. The delay between HPN onset and the first catheter infection was 1.02±0.46 years. The mean parenteral energy intake was 20.1 kcal/kg/d and the mean volume was 33.6 mL/kg/d. The composition of the parenteral nutrition varied with a mean glucose 3.01 g/kg/d (accounting for 59.1% non-protein calories) and 0.91 g/kg/d lipid (accounting for 38.8% non-protein calories), respectively. At the end of the follow up, 38 patients (80.8%) were still depending on HPN, while 6 patients (12.8%) died from long-term HPN associated severe liver diseases. Interestingly, 3 patients (6.4%) weaned off HPN after a mean HPN duration of 4.5 years.

Catheter associated complications and risk factors

Catheter-related sepsis was the most common catheter associated complication and the most common reason for hospital readmission. The mean frequency of catheter-related sepsis was 0.31±0.05 per catheter year of HPN with a median frequency of 0.30 per catheter year of HPN (Table 3). Only 2 patients never experienced catheter-related sepsis episodes during the follow-up. It needs to be emphasized that the mean frequency of catheter-related sepsis of the longest follow-up patient was only 0.19 per catheter year of HPN. In addition, we observed that the frequency of catheter sepsis was much higher during the first 2 years of HPN than afterwards. Catheter occlusion was the second most common catheter associated complication in this study with a mean frequency of 0.06±0.01 per catheter year of HPN. Fibrin sheaths and blood clots were frequent reasons for catheter occlusion. Catheter displacement and breakage were rare (<0.01 per catheter year of HPN) complications associated with improper operation.

We divided the entire study population into two groups according to the catheter-related sepsis incidence, as below or above the median value (0.30 per catheter year of HPN). Risk factors for catheter-related sepsis are summarized in Table 4 and were higher incidence of catheter-related infections ($p<0.001$) and shorter delay between HPN onset and the first infection ($p<0.001$). Interestingly, although not statistically significant ($p>0.05$), we found that patients with more help of an experienced nurse at home and patients applying PICC to receive HPN tended to have a low the catheter-related sepsis incidence rate.

HPN-associated liver/biliary disorders

A total of 25 patients (53.2%) developed HPN-associated liver/biliary disorders during the follow-up (Table 3). Out of 47 patients, 5 (10.6%) and 7 (14.9%) patients developed steatosis and cholestasis, respectively. Thirteen patients (27.7%) developed both steatosis and cholestasis. It needs to be emphasized that the liver function of the

longest follow-up patient was normal except for the period of pregnancy. In addition, 11 patients (23.4%) developed cholelithiasis, and 7 of them underwent a cholecystectomy for acute cholecystitis.

The entire study population was divided into two groups according to whether the HPN-associated liver/biliary disorders were present or not. Risk factors for biochemical liver/biliary disorders are summarized in Table 5 and included a higher rate of catheter-related infections ($p=0.009$), shorter delay between HPN onset and the first infection ($p=0.017$), higher energy content of HPN ($p=0.014$), higher glucose rate of HPN ($p=0.009$), and lower lipid rate of HPN ($p=0.022$).

DISCUSSION

This study included 47 adult patients with SBS receiving long-term HPN for more than 2 years, over a period of 30 years. As far as we know, this is the first study to focus on the prevalence and risk factors of long-term HPN-associated complications in adult patients with SBS. The mean frequency of catheter-related sepsis was 0.31 per catheter year of HPN, and the identified risk factors for catheter-related sepsis were higher incidences of catheter-related infections and shorter delays between HPN onset and the first infection. The prevalence of HPN-associated liver/biliary disorders was 53.2%, and the identified risk factors were higher rates of catheter-related infections, shorter delays between HPN onset and the first infection, higher energy content of HPN, higher glucose rate of HPN, and lower lipid rate of HPN.

It was reported that HPN-dependency in patients with SBS was 74%, 64% and 48% at 1, 2, and 5 years, respectively.⁸ In this study, the reason why we only included patients who received more than 2 years of HPN was that 2 years is the theoretical duration of intestinal adaptation.⁹

Table 3. Prevalence of home parenteral nutrition (HPN) associated complications in adult patients with short bowel syndrome receiving long-term HPN

Complications	Frequency
Catheter sepsis (per catheter year)	0.31±0.05
Catheter occlusion (per catheter year)	0.06±0.01
Catheter displacement (per catheter year)	<0.01
Catheter breakage (per catheter year)	<0.01
Liver/biliary associated problems (%)	
None	22/47 (46.8)
Steatosis	5/47 (10.6)
Cholestasis	7/47 (14.9)
Steatosis and cholestasis	13/47 (27.7)
Cholelithiasis	11/47 (23.4)

Interestingly, 3 patients weaned off HPN after a mean duration of 4.5 years in this study. In detail, we found that the remnant small bowel lengths of these 3 patients were >100 cm with part of the colon, which was consistent with previous reports that HPN dependency was reduced with a remaining colon >57% and a small bowel remnant length >75 cm.²² Enteral nutrients have been reported to be of particular importance in promoting the intestinal adaptive response, presumably by stimulating pancreaticobiliary, gastrointestinal and gut hormone secretions.²³ In order to promote the structural and functional adaptive changes of remnant small bowel, all of the included patients in our study received oral/enteral nutrition.²⁴ Our findings suggested that postsurgical intestinal adaptation in adult patients with SBS might be achieved after 2 years of HPN dependency if there was enough remnant length of small bowel and colon together with oral/enteral nutrition stimulation.

It has been reported that survival rates of patients with SBS were over 80% and 70% at 2 and 5-years, respec-

Table 4. Comparison of two groups according to the catheter-related sepsis incidence as below and above the median value (0.30 per catheter year of HPN)

	<0.30	≥0.30	<i>p</i>
Number of patients	23	24	
Incidence of catheter-related infections (per catheter year)	0.25±0.03	0.38±0.07	<0.001
Help of an experienced nurse at home (n/total)	14/23	9/24	0.109
Remnant small bowel length <50 cm (n/total)	14/23	19/24	NS
Digestive circuit anastomosis (n/total)			NS
Type 1	6/23	5/24	
Type 2	14/23	18/24	
Type 3	3/23	1/24	
Types of catheters			0.096
CVC	13/23	19/24	
PICC	10/23	5/24	
Age at HPN onset (years)	45.6±14.3	43.2±15.5	NS
HPN duration (years)	9.81±6.69	7.33±4.29	NS
Delay between HPN onset and the first infection (years)	1.27±0.48	0.79±0.28	<0.001
Oral/Enteral nutrition (n/total)	23/23	24/24	NS
Parenteral volume (mL/kg/d)	32.7±4.07	34.6±4.34	NS
Parenteral energy intake (kcal/kg/d)	19.7±1.91	20.4±2.47	NS
Parenteral glucose intake (g/kg/d)	2.92±0.51	3.09±0.47	NS
Parenteral glucose intake, (% energy intake)	58.5±5.08	59.6±4.38	NS
Parenteral lipid intake (g/kg/d)	0.90±0.09	0.92±0.10	NS
Parenteral lipid intake (% energy intake)	38.3±3.99	39.2±3.35	NS
Parenteral infusions (d/w)	5.33±0.79	5.53±0.70	NS
Parenteral infusion time (h/d)	12.3±2.20	12.9±2.01	NS

CVC: central venous catheter; PICC: peripherally inserted central venous catheters; n: number.

Table 5. Comparison of two groups according to whether the HPN-associated liver/biliary diseases were present or not

	Present	Absent	<i>p</i>
Number of patients	25	22	
Incidence of catheter-related infections (per catheter year)	0.36±0.09	0.29±0.07	0.019
Help of an experienced nurse at home (n/total)	12/25	9/22	NS
Remnant small bowel length <50 cm (n/total)	21/25	12/22	0.028
Digestive circuit anastomosis (n/total)			NS
Type 1	6/47	5/47	
Type 2	17/47	15/47	
Type 3	2/47	2/47	
Types of catheters			NS
CVC	15/23	17/24	
PICC	8/23	7/24	
Age at HPN onset (years)	42.3±14.4	48.2±14.9	NS
HPN duration (years)	9.86±5.19	7.48±6.05	NS
Delay between HPN onset and the first infection (years)	0.88±0.37	1.19±0.50	0.017
Oral/Enteral nutrition(n/total)	25/25	22/22	NS
Parenteral volume (mL/kg/d)	34.6±3.99	32.7±4.38	NS
Parenteral energy intake (kcal/kg/d)	20.9±2.41	19.3±1.77	0.014
Parenteral glucose intake (g/kg/d)	3.21±0.08	2.76±0.10	0.001
Parenteral glucose intake (% energy intake)	60.7±4.26	57.2±4.58	0.009
Parenteral lipid intake (g/kg/d)	0.89±0.09	0.95±0.10	0.032
Parenteral lipid intake (% energy intake)	37.6±3.12	40.1±3.88	0.022
Parenteral infusions (d/w)	5.40±0.78	5.47±0.71	NS
Parenteral infusion time (h/d)	12.9±1.86	12.2±2.32	NS

CVC: central venous catheter; PICC: peripherally inserted central venous catheters; n: number.

tively.^{9,25} In our study, 6 patients died from long-term HPN associated severe liver diseases during the follow-up. We analyzed the characteristics of these 6 patients and found that digestive circuit anastomosis of 4 patients was end-jejunostomy (type 1). Meanwhile, the remnant small bowel length of 5 patients was <50 cm, which was consistent with the previous report that survival rates were lowest in patients with end-jejunostomy and ultra-short small bowel.²⁶

Catheter-related infections were the most frequent catheter-related complications while catheter-related sepsis accounted for 80% of catheter-related infections.²⁷ The mean frequency of catheter-related sepsis in our study was 0.31 per catheter year, which was slightly lower than the previously reported results (0.34 per catheter year).²⁷ However, when we only calculated the incidence of catheter-related sepsis during the first 2 years of HPN, the mean frequency of catheter-related sepsis was 0.38 per catheter year. These findings were in accordance with the results of other published studies that catheter-related sepsis was more likely to occur during the first 2 years of HPN.^{28,29} Thus, the overall low frequency of in our study might be explained by the very long term HPN duration.

We tried to detect new risk factors involving the catheter-related sepsis in this study. Unfortunately, we failed to show any new risk factors except for previously reported risk factors: higher incidence of catheter-related infections and shorter delay between HPN onset and the first infection.¹² Interestingly, although not statistically significant, we found that patients with more help of an experienced nurse at home and patients applying PICC to receive HPN tended to have a lower catheter-related sepsis incidence rate. This finding indicated the importance of HPN training by an experienced nurse not only in hospital but also at home.²⁷ In addition, the finding was also con-

sistent with previously reports that the catheter-related sepsis incidence rate between PICC and CVC was not significantly different.²⁸ The longer HPN duration was reported to be associated with a lower incidence of catheter-related infection in previous studies.²⁹ However, we failed to identify the HPN duration as a risk factor for catheter-related sepsis. It might be explained by the exclusion criteria that we excluded patients with HPN duration of less than 2 years. As mentioned above, catheter-related sepsis was more likely to occur during the first 2 years of HPN. However, the mean HPN duration was much longer than 2 years in this study. Therefore, HPN duration might slightly contribute to the incidence of catheter-related sepsis. We observed that short delays between HPN onset and the first infection was a risk factor for catheter-related sepsis, which was consistent with the results in children.³⁰ The results indicated that early episodes of catheter-related infections might suggest the higher incidence of catheter-related sepsis during a long term of HPN. However, a prospective study including more patients should be performed to confirm these findings.

The mean frequency of catheter occlusion was 0.06 per catheter year of HPN in this study, which was similar to the previous results.²⁷ Although the catheter displacement and catheter breakage rarely occurred during the long-term duration of HPN, strict catheter care procedures should be taken to reduce the incidence of these complications.³¹

Disorders of the liver/biliary system were the most common complications in patients receiving HPN.³² The prevalence of HPN-associated liver/biliary diseases were variously reported by different studies.^{18,19,21} For example, the reported incidences of abnormal enzyme elevations varied from 25% to 100% in adult patients receiving HPN.

There are several potential reasons for the great difference among studies. Firstly, the definition of hepatic dysfunction in most of studies primarily relied on the elevated concentration of liver enzymes and bilirubin, rather than validated by biopsy. Secondly, the composition of the HPN formulation has greatly changed over the past 30 years. Therefore, the different composition of the HPN might affect the incidence of HPN-associated liver/biliary disorders. In this study, the overall incidence of HPN-associated liver/biliary disorders was 53.2%, which was in consistent with the previous results of adult patients receiving long-term HPN.^{18,21}

Various factors have been reported to contribute to the incidence of HPN-associated liver/biliary disorders.³² Lack of enteral nutrition stimulation has been reported to increase the incidence of HPN-associated liver/biliary disorders by reducing the release of gastrointestinal hormones, such as CCK, stimulated by food intake.³³ Thus, various methods should be taken to optimize the enteral route for feeding. All patients in this study received oral/enteral nutrition even in a small amount where necessary. Catheter-related sepsis has been reported to be significantly associated with cholestasis and various measures should be taken to treat catheter sepsis and minimize the recurrence.³⁴ Short residual small bowel has also been identified as a risk factor of HPN-associated liver/biliary diseases in various studies.^{36,37} In this study, 70.2% of patients had a short remnant small bowel length (<50 cm), which might contribute to the incidence of HPN-associated liver/biliary disorders.

HPN formulation and nutrient intakes have also been reported to contribute to the incidence of HPN-associated liver/biliary disorders.³² Excessive calorie intake is primarily responsible for the development of steatosis by stimulating insulin release to promote hepatic fat deposition.³⁸ Therefore, over-feeding should be avoided in patients receiving HPN. A balanced dextrose-fat PN formulation with less overall calories was reported to decrease the incidence of steatosis.³⁷ Intravenous fat emulsion (IVFE) was reported to play an important role in the development of liver/biliary disorders, which depended on the different fat sources, the phytosterol contents, and the dosage. Long-chain triglycerides (LCT) might be more likely to introduce hepatic complications than MCT-LCT mixture.³⁹ The phytosterol content of IVFE might also contribute to the development of cholestasis by impairing bile flow and causing biliary sludge and stones.⁴⁰ In addition, high dose of IVFE was associated with HPN-associated liver/biliary disorders, especially when used long-term.²¹ It is recommended that the IVFE content should not exceed 2.5 g/kg/d in adult patients.⁴¹ In this study, the mean parenteral energy intake was 20.1 kcal/kg/d, and provided a relatively balanced energy source by adjusting the dextrose-fat ratio.

Infusion time is another concern that might contribute to the development of HPN-associated liver/biliary disorders. Cyclic infusion of HPN, referring to the infusion of a daily supply of HPN components over a <24 h period, has been reported to result in a reduction of serum liver enzyme concentrations and conjugated bilirubin concentrations in patients receiving HPN when compared with continuous infusion.⁴² In our study, the mean daily infu-

sion time was 12.6 hours, and the mean time of HPN infusions was 5.42 days per week.

In conclusion, our study described a series of adult patients with SBS receiving long-term HPN for more than 2 years over a period of 30 years and focused on the prevalence and risk factors of catheter-related sepsis and HPN-associated liver/biliary disorders. However, due to the limited number of patients, the results of this study should be interpreted with caution. Further research is recommended in other clinical nutrition centers to further elucidate the prevalence and risk factors of HPN-associated complications in adult patients with the SBS receiving long-term HPN. Furthermore, the best treatment methods of these complications should be assessed in further studies.

AUTHOR DISCLOSURES

The authors declare no conflicts of interest.

REFERENCES

- O'Keefe SJ, Buchman AL, Fishbein TM, Jeejeebhoy KN, Jeppesen PB, Shaffer J. Short bowel syndrome and intestinal failure: consensus definitions and overview. *Clin Gastroenterol Hepatol.* 2006;4:6-10. doi: 10.1016/j.cgh.2005.10.002.
- Lloyd A, Kerr C, Breheny K, Brazier J, Ortiz A, Borg E. Economic evaluation in short bowel syndrome (SBS): an algorithm to estimate utility scores for a patient-reported SBS-specific quality of life scale (SBS-QoL). *Qual Life Res.* 2014;23:449-58. doi: 10.1007/s11136-013-0516-4.
- Matarese LE, Jeppesen PB, O'Keefe SJ. Short bowel syndrome in adults: the need for an interdisciplinary approach and coordinated care. *JPEN J Parenter Enteral Nutr.* 2014;38:60S-4S. doi: 10.1177/0148607113518946.
- Iyer KR. Surgical management of short bowel syndrome. *JPEN J Parenter Enteral Nutr.* 2014;38:53S-9S. doi: 10.1177/0148607114529446.
- Dudrick SJ, Wilmore DW, Vars HM, Rhoads JE. Long-term total parenteral nutrition with growth, development, and positive nitrogen balance. *Surgery.* 1968;64:134-42.
- Hortencio TD, Arendt BM, Teterina A, Jeejeebhoy KN, Gramlich LM, Whittaker JS, Armstrong D, Raman M, Nogueira RJ, Allard JP. Changes in Home Parenteral Nutrition Practice Based on the Canadian Home Parenteral Nutrition Patient Registry. *JPEN J Parenter Enteral Nutr.* 2015. [Epub ahead of print] doi: 10.1177/0148607115609289.
- Ziegler TR, Leader LM. Parenteral nutrition: transient or permanent therapy in intestinal failure? *Gastroenterology.* 2006;130:S37-42. doi: 10.1053/j.gastro.2005.09.063.
- Amiot A, Messing B, Corcos O, Panis Y, Joly F. Determinants of home parenteral nutrition dependence and survival of 268 patients with non-malignant short bowel syndrome. *Clin Nutr.* 2013;32:368-74. doi: 10.1016/j.clnu.2012.08.007.
- Messing B, Crenn P, Beau P, Boutron-Ruault MC, Rambaud JC, Matuchansky C. Long-term survival and parenteral nutrition dependence in adult patients with the short bowel syndrome. *Gastroenterology.* 1999;117:1043-50.
- Bakker H, Bozzetti F, Staun M, Leon-Sanz M, Hebuterne X, Pertkiewicz M, Shaffer J, Thul P. Home parenteral nutrition in adults: a european multicentre survey in 1997. ESPEN-Home Artificial Nutrition Working Group. *Clin Nutr.* 1999;18:135-40. doi: 10.1054/clnu.1999.0021.

11. Vargas JH, Ament ME, Berquist WE. Long-term home parenteral nutrition in pediatrics: ten years of experience in 102 patients. *J Pediatr Gastroenterol Nutr.* 1987;6:24-32.
12. Peyret B, Collardeau S, Touzet S, Loras-Duclaux I, Yantren H, Michalski MC, Chaix J, Restier-Miron L, Bouvier R, Lachaux A, Peretti N. Prevalence of liver complications in children receiving long-term parenteral nutrition. *Eur J Clin Nutr.* 2011;65:743-9. doi: 10.1038/ejcn.2011.26.
13. Pironi L, Forbes A, Joly F, Colomb V, Lyszkowska M, Van Gossum. Survival of patients identified as candidates for intestinal transplantation: a 3-year prospective follow-up. *Gastroenterology.* 2008;135:61-71. doi: 10.1053/j.gastro.2008.03.043.
14. American Gastroenterological Association. American Gastroenterological Association medical position statement: short bowel syndrome and intestinal transplantation. *Gastroenterology.* 2003;124:1105-10. doi: 10.1053/gast.2003.50139.
15. Goulet O, Ruemmele F, Lacaille F, Colomb V. Irreversible intestinal failure. *J Pediatr Gastroenterol Nutr.* 2004;38:250-69.
16. Lloyd DA, Vega R, Bassett P, Forbes A, Gabe SM. Survival and dependence on home parenteral nutrition: experience over a 25-year period in a UK referral centre. *Aliment Pharmacol Ther.* 2006;24:1231-40. doi: 10.1111/j.1365-2036.2006.03106.x.
17. Wu ZH, Huang DX, Zhang YW, Wu ZG. Normal gestation after 5 years on home parenteral nutrition. *Clin Nutr.* 1993;12:43-6.
18. Chan S, McCowen KC, Bistrrian BR, Thibault A, Keane-Ellison M, Forse RA, Babineau T, Burke P. Incidence, prognosis, and etiology of end-stage liver disease in patients receiving home total parenteral nutrition. *Surgery.* 1999;126:28-34. doi: 10.1067/msy.1999.98925.
19. Allan P, Stevens P, Chadwick P, Teubner A, Abraham A, Carlson G, Lal S. Osteomyelitis in adult patients on long-term parenteral nutrition: 2745 patient-years of experience in a national referral centre. *Clin Nutr.* 2015;35:1135-9. doi: 10.1016/j.clnu.2015.09.002.
20. Dray X, Joly F, Reijasse D, Attar A, Alves A, Panis Y, Valleur P, Messing B. Incidence, risk factors, and complications of cholelithiasis in patients with home parenteral nutrition. *J Am Coll Surg.* 2007;204:13-21. doi: 10.1016/j.jamcollsurg.2006.09.008.
21. Cavicchi M, Beau P, Crenn P, Degott C, Messing B. Prevalence of liver disease and contributing factors in patients receiving home parenteral nutrition for permanent intestinal failure. *Ann Intern Med.* 2000;132:525-32.
22. Carbonnel F, Cosnes J, Chevret S, Beaugerie L, Ngo Y, Malafosse M, Parc R, Le Quintrec Y, Gendre JP. The role of anatomic factors in nutritional autonomy after extensive small bowel resection. *JPEN J Parenter Enteral Nutr.* 1996;20:275-80.
23. DiBaise JK, Young RJ, Vanderhoof JA. Intestinal rehabilitation and the short bowel syndrome: part 1. *Am J Gastroenterol.* 2004;99:1386-95. doi: 10.1111/j.1572-0241.2004.30345.x.
24. Chaer Borges V, Teixeira da Silva Mde L, Goncalves Dias MC, Gonzalez MC, Linetzky Waitzberg D. Long-term nutritional assessment of patients with severe short bowel syndrome managed with home enteral nutrition and oral intake. *Nutr Hosp.* 2011;26:834-42. doi: 10.1590/S0212-16112011000400025.
25. Scolapio JS, Fleming CR, Kelly DG, Wick DM, Zinsmeister AR. Survival of home parenteral nutrition-treated patients: 20 years of experience at the Mayo Clinic. *Mayo Clin Proc.* 1999;74:217-22. doi: 10.4065/74.3.217.
26. Jeppesen PB. Spectrum of short bowel syndrome in adults: intestinal insufficiency to intestinal failure. *JPEN J Parenter Enteral Nutr.* 2014;38:8S-13S. doi: 10.1177/0148607114520994.
27. Howard L, Ashley C. Management of complications in patients receiving home parenteral nutrition. *Gastroenterology.* 2003;124:1651-61.
28. Safdar N, Maki DG. Risk of catheter-related bloodstream infection with peripherally inserted central venous catheters used in hospitalized patients. *Chest.* 2005;128:489-95.
29. Colomb V, Fabeiro M, Dabbas M, Goulet O, Merckx J, Ricour C. Central venous catheter-related infections in children on long-term home parenteral nutrition: incidence and risk factors. *Clin Nutr.* 2000;19:355-9. doi: 10.1054/clnu.2000.0132.
30. Moukarzel AA, Haddad I, Ament ME, Buchman AL, Reyen L, Maggioni A, Baron HI, Vargas J. 230 patient years of experience with home long-term parenteral nutrition in childhood: natural history and life of central venous catheters. *J Pediatr Surg.* 1994;29:1323-7.
31. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 2002;51:1-29.
32. Kumpf VJ. Parenteral nutrition-associated liver disease in adult and pediatric patients. *Nutr Clin Pract.* 2006;21:279-90.
33. Kelly DA. Liver complications of pediatric parenteral nutrition--epidemiology. *Nutrition.* 1998;14:153-7.
34. Chung C, Buchman AL. Postoperative jaundice and total parenteral nutrition-associated hepatic dysfunction. *Clin Liver Dis.* 2002;6:1067-84.
35. Kaufman SS. Prevention of parenteral nutrition-associated liver disease in children. *Pediatr Transplant.* 2002;6:37-42.
36. Stanko RT, Nathan G, Mendelow H, Adibi SA. Development of hepatic cholestasis and fibrosis in patients with massive loss of intestine supported by prolonged parenteral nutrition. *Gastroenterology.* 1987;92:197-202.
37. Ito Y, Shils ME. Liver dysfunction associated with long-term total parenteral nutrition in patients with massive bowel resection. *JPEN J Parenter Enteral Nutr.* 1991;15:271-6.
38. Quigley EM, Marsh MN, Shaffer JL, Markin RS. Hepatobiliary complications of total parenteral nutrition. *Gastroenterology.* 1993;104:286-301.
39. Baldermann H, Wicklmayr M, Rett K, Banholzer P, Dietze G, Mehnert H. Changes of hepatic morphology during parenteral nutrition with lipid emulsions containing LCT or MCT/LCT quantified by ultrasound. *JPEN J Parenter Enteral Nutr.* 1991;15:601-3.
40. Ellegard L, Sunesson A, Bosaeus I. High serum phytosterol levels in short bowel patients on parenteral nutrition support. *Clin Nutr.* 2005;24:415-20. doi: 10.1016/j.clnu.2005.01.001.
41. Mirtallo J, Canada T, Johnson D, Kumpf V, Petersen C, Sacks G, Seres D, Guenter P, Task Force for the Revision of Safe Practices for Parenteral N. Safe practices for parenteral nutrition. *JPEN J Parenter Enteral Nutr.* 2004;28:S39-70.
42. Hwang TL, Lue MC, Chen LL. Early use of cyclic TPN prevents further deterioration of liver functions for the TPN patients with impaired liver function. *Hepatogastroenterology.* 2000;47:1347-50.