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Non-interventional, retrospective data of long-term home parenteral nutrition in patients with benign diseases: Analysis of a nurse register (SERECARE)

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ABSTRACT

Objectives: The aim of this study was to evaluate the safety and efficacy of home parenteral nutrition (HPN) service in patients with benign chronic intestinal failure (CIF).
Methods: This was a 10-y retrospective, non-interventional, multicenter study conducted with adult and pediatric patients with CIF who received HPN service. We analyzed data prospectively collected from a dedicated register by HPN nurses.
Results: From January 2002 to December 2011 a total of 794 patients (49.7% male, median age 1 y for children and 57 y for adults) were included in the analysis. Over the 10-y period, 723 central venous catheter (CVC) complications occurred, of which 394 were infectious (54.5%), 297 were mechanical (41.1%), and 32 (3.3%) were defined as CVC-related thrombosis. The complication rate was higher in children (1.11 per patient) than in adults (0.70 per patient). During the observation period, the rates of both infectious and mechanical complications showed a global declining trend and ~75% of patients had neither infectious nor mechanical CVC complications. HPN efficacy was evaluated in 301 patients with a minimum follow-up of 36 mo. Body mass index and Karnofsky score showed that the median growth significantly increased ($P < 0.001$) over baseline for adults and pediatric patients in the 0 to 2 age range.
Conclusions: The use of a structured register has proved to be a key strategy for monitoring the outcomes of long-term treatment, improving time efficiency, and preventing potential malpractice. To our knowledge, this is the largest survey ever documented; the results were consistent despite the heterogeneity of the centers because of duly applied standard rules and protocols.

Introduction

Intestinal failure (IF) is defined as "the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth" by recent European Society for Clinical Nutrition and Metabolism (ESPEN) recommendations [1]. This guideline recognizes a functional classification for IF: Chronic intestinal failure (CIF) is defined as type III, which may evolve after type II acute IF. In adults, IF

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(and consequently CIF) can be classified into five major pathophysiologic conditions: short bowel, intestinal fistula, intestinal dysmotility, mechanical obstruction, and extensive small bowel mucosal disease. In children, IF may be correctly defined according to IF functional classifications established by ESPEN guidelines on CIF in adults [1] even if they can also be divided into three categories (short bowel syndrome [SBS], neuromuscular disorders of the gastrointestinal tract, and congenital enterocyte disorders) according to pathogenesis [2–5].

Home parenteral nutrition (HPN) represents the primary treatment for CIF [1,6]. In Europe, the annual incidence of HPN is between 4 and 6 per million inhabitants and the prevalence is between 2 and 40 per 10^6 inhabitants [7,8]. In the United States, the prevalence is 79 per million inhabitants [9]. HPN is a lifesaving and possibly long-lasting (months, years, or life) treatment for patients with CIF owing to benign disease [10]. Since its introduction in the 1970s, the prevalence of HPN use has increased, fostering the demand for HPN services and generating the need for national healthcare agencies to address the uneven distribution of national HPN resources [11].

The safety and efficacy of HPN services need to be evaluated according to objective and measurable indicators agreed on by both expert professionals and patients. Furthermore, a set of predictable clinical outcomes of the patients on HPN must be designed to evaluate the efficacy of HPN therapy. In 2013, Dreesen et al. used a two-round Delphi approach to identify the top 10 outcome indicators that should be used to measure the quality of care for HPN patients with benign CIF [12,13]. Since then, a set of clinical and quality outcome indicators has been developed that allows the goals of treatment to be defined. The quality indicators were developed by an expert panel of health care clinicians in Europe and were subdivided into patient and therapy outcomes. The top-scoring quality outcome for clinicians was the rate of central venous catheter (CVC)-related infections. Patient priorities and concerns were investigated by a survey of HPN patients with underlying benign disease in nine centers in eight countries. This cohort identified the incidence of CVC-related infections, survival, and quality of life (QoL) as the most important quality and clinical indicators of their care [13].

Monitoring is the mainstay for collecting indicators. Appropriate monitoring requires dedicated and expert professionals who record objective data in a structured database according to scheduled times. In Italy, HPN programs for benign CIF are prescribed by CIF and HPN teams and are provided by the local health care units (LHCUs) of the city in which the patient lives [8]. The LHCU can directly deliver the HPN program or can buy an HPN service provided by a commercial company. The Baxter HPN service started its activity in 1984, delivering parenteral nutrition (PN) admixture bags to patients in the home setting.

The aim of the present study was to evaluate the safety and efficacy of long-term HPN service using the data from the SERECARE register, owned and maintained by Baxter S.p.A. Data from this register built were recorded by Baxter nurses during their clinical practice on patients with benign CIF in Italy. To our knowledge no other similar nationwide public register exists. The SERECARE register could be considered representative for the whole HPN experience in Italy because the enrolled patients came from 91 of 107 provinces and 54 centers.

Methods

Study design

This was a retrospective, non-interventional, multicenter study with adult (>18 years) and pediatric (0–18 y) patients treated with HPN for benign CIF, provided by the Baxter HPN service in Italy.

Patient inclusion and exclusion criteria

Although SERECARE is an active register, we decided to analyze data only from patients on HPN for benign CIF in the participating study centers between January 1, 2002 and December 31, 2011 to keep uniform data in terms of nurse protocol and program governance. Patients having a diagnosis of cancer were excluded from the study.

Outcome indicators

Outcome indicators were as follow:

[1] HPN service performance: nurse follow-up visits, patient and/or caregiver training for HPN management;
[2] HPN safety measures: CVC-related complications, rehospitalization rate; and
[3] HPN efficacy variables: body mass index (BMI) and Karnofsky score.

Data collection and recording

For each patient, the HPN program provided by the Baxter HPN service was prescribed and followed by the physician leading the HPN or CIF referral center. Patients were included in the SERECARE register by a trained nurse (employed by Baxter S.p.A), according to predefined standard operating procedures (SOPs). Patients were prospectively assessed over follow-up according to nursing visits as scheduled by clinical practice.

Data were prospectively recorded from January 1, 2002 to June 30, 2012 at each visit scheduled by clinical practice. The cutoff date of the follow-up was June 30, 2012 to ensure that patients enrolled on December 31, 2011 had a minimum follow-up period of 6 mo.

Table 1 shows the collection of data register. Patient first inclusion in the SERECARE register occurred at the first HPN nurse visit (baseline). Afterward, data were collected at each subsequent visit, according to the clinical practice. Information about safety, effectiveness, and other quality indicators outcomes was collected.

HPN service

This service was created in 2002 by Baxter S.p.A. as a comprehensive bundle including home delivery of drugs, customer service assistance available 24/7, and

Table 1
Information collected in the SERECARE register at different visits

Data collected	Baseline visit (inclusion in the SeraCare register)	Additional visits (according to clinical practice)	End-of-study visit (end of data collection in the SeraCare register)
Informed consent	X		
Inclusion/exclusion criteria	X		
Demographic data and disease characteristics (sex, age, underlying disease, geographical origin, duration of treatment before beginning of observation)	X		
Safety variables (CVC-related complications, hospitalizations)		X	
Efficacy variables (BMI, Karnofsky score*)		X	
HPN service performance (follow-up visits, training, retraining)	X	X	
Reason for withdrawal from the SeraCare register			X

BMI, body mass index; CVC, central venous catheter; HPN, home parenteral nutrition
*Functional status assessment of adults.

a specialized team of nurses dedicated to training the caregivers until full autonomy is reached, recognize promptly any possible inconvenience and record data (139 items) into the SERECARE register. The Baxter HPN service provides all the ancillaries required for PN infusion and CVC care, as well as an experienced nurse network that provides patient care and training of caregivers for HPN management. During the home visits, the nurses collect the data concerning the indicators of safety and efficacy of the HPN program. Nurse activities are described in the appendix.

SERECARE register

The SERECARE register is nested within the larger JANUA database run by Baxter S.p.A. The JANUA web platform consists of nine registries. One of these is the SERECARE register, the long-term HPN register, developed for recording information related to the nursing service provided by Baxter S.p.A with the support of parenteral nutrition experts and opinion leaders. Nurses were trained to access and use the register via SOPs and entered data through precoded fields that defined limits and error or accuracy warnings.

All the information collected was automatically recorded in the database and accessible through the JANUA web platform.

Patient information and consent

Informed consent was obtained from all patients before imputing any data into the SERECARE register. All patients received written and verbal information regarding the register at a prior interview. This information clarified that participation in the register was voluntary and that the patient could withdraw at any time and for any reason. Withdrawal from the study did not affect the patient's medical care. All patients were given the opportunity to ask questions about the nature of the register.

There is no approval by any Institutional Review Board because the HPN service was executed by Baxter on behalf of the local health authorities according to a written contract, which included nursing data collection to monitor the quality of the service. The patient, or legal proxy, was provided with a patient information sheet and was asked to sign an informed consent form before any information being entered the register. A copy of the patient information sheet and the signed informed consent form were given to the patient by the nurse.

Patient confidentiality

Patients' data were protected by the Italian Personal Data Protection Code (Law 196, June 30, 2003). A unique patient number was assigned to each patient at register inclusion immediately after informed consent was obtained. The investigator ensured that the patient's confidentiality was maintained. In the register, patients were identifiable only by their patient study number.

Protection of human subjects

The study was conducted in accordance with the Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Patients [14].

Statistical analysis

The study Population included all patients included in the SERECARE register between January 1, 2002 and December 31, 2011. To compare effectiveness data collected during follow-up visits and to analyze the trend over time, patients were included if they had a minimum of follow-up visits 36 mo after starting HPN. Consistent with study objectives, the data analysis was predominantly descriptive in nature.

Owing to the nature of the source data, there were no requirements for laboratory processing, data transport, or data archiving. Data quality control was conducted by the CRO trial form support" during the data cleaning process. When the data was present and out of range, the nurse involved in data entry was contacted for hard-copy value confirmation.

The default summary statistics for quantitative variables are the number of observations (n), number of missing values, mean, SD, median, minimum (min) and maximum (max). The default summary statistics for qualitative variables was the number (n) and percentage (%) of patients with no missing data per category. The number of missing values were presented as a "not available" category. Where applicable, the results were presented by visit and change from baseline. Some analyses were stratified by age use the following strata: <0 to ≤ 6 y; <7 to ≤ 18 y; <18 to ≤ 40 y; <40 to ≤ 64 y; and >64 y. Where appropriate, the analyses were stratified by pediatric population (0–18 y), adult population (>18 y), and on the basis of the underlying disease. No imputation of missing data or dropouts was performed. A non-paired Wilcoxon rank-sum test was used to assess differences in the HPN safety and efficacy variables collected from pediatric and adult populations. Student's t test was used to evaluate BMI and Karnofsky variation during the follow-up period. Spearman's correlation was used to examine the relationship between the number of follow-up visits and the number of CVC-related complications. SAS version 9.4 (SAS Institute, Cary, NC, USA) was used for the statistical analysis.

Results

Patient population and rate of patient inclusion in the SERECARE register

Patient characteristics are reported in Table 2. The median age was 1 y (range, 0–18 y) and 57 y (range, 19–90 y) for the pediatric and adult patients, respectively. The youngest enrolled patient was 3 mo of age, whereas the oldest was 90 y of age. Most patients belonged to the <40 to ≤ 64 y age range (33.1%). Most centers had either 1 to 5 patients (68% of the centers) or >20 patients (18.2% of the centers). Only five (9.1%) centers had 6 to 10 patients and only five (9.1%) centers had 11 to 20 patients. Most centers were in the Northwest regions (49.2%) followed by the southern region (27.8%).

From 2002 to 2012 there was a progressive increase in the number of patients under observation each year. A growing trend in the number of the new observed patients was also seen; from 2011 to 2012 the number of new cases in the pediatric population more than doubled (Fig. 1).

The median duration of the observation was 1.7 y (range, 0–26 y), from a minimum of a few days to a maximum of 26 y. The total duration of the observation was of 873 571 d (273 842 d for the pediatric population and 599 729 d for the adult population). Eighty patients were not analyzed because they lacked information about the inserted catheter.

HPN service activity

Nurse follow-up visits

The number of follow-up visits was 9381 (pediatric population = 31.3%; adult population = 68.7%). The annual mean ($\pm$ SD) number of visits per patient was 5.2 ($\pm$ 3.2), with a median of 4.5/y. A similar pattern was observed in both populations, from a minimum of 1 visit (baseline) to a maximum of $\sim$37 visits. Routine visits were 81.7% of the total and the mean duration of each visit was 2 h.

Patient or caregiver training for HPN management

Patients received a mean $\pm$ SD of 1.3 $\pm$ 0.8 training episodes, 68.9% of which were at HPN initiation with a mean $\pm$ SD duration of 10 $\pm$ 3.9 d. Of total training episodes, 30.4% were for retraining, with a mean $\pm$ SD duration of 2 $\pm$ 2.2 d. The reasons for the retraining included the type of infusion pump substitution (30.4%), change of the Baxter caregiver (14.5%), change of the CVC type (13.1%), change of therapy (3.5%), and other causes (38.2%). The most common "other" reasons were new product or protocol (12.7%), retraining after suspension (8.8%), patient retraining (7.8%), and retraining local territory nurse (4.6%). Information was not available for one (0.4%) patient.

HPN safety

CVC-related complications

In all, 723 CVC-related complications were reported, of which 394 were infectious (54.5%), 297 were of mechanical origin (41.1%), and 32 were deep vein thrombosis (3.3%; Table 3). To ensure that all complications were reported by nurses, the four centers with higher recruiting performed a data source verification, finding an average accuracy of 96% on mechanical complication and 95% on infectious complications.

Table 2
Patient population

Characteristic	Pediatric population	Adult population	Total
	n (%)	n (%)	N (%)
Total patients observed	267 (30.55)	607 (69.45)	874 (100)
Total patients analyzed	238 (30)	556 (70)	794 (100)
Sex			
Female, n (%)	107 (45)	292 (52.5)	399 (50.3)
Male, n (%)	131 (55)	264 (47.5)	395 (49.7)
Age (y)			
<0 to ≤6	185 (77.7)	–	185 (23.3)
<7 to ≤18	53 (22.3)	–	53 (6.7)
<18 to ≤40	–	108 (19.4)	108 (13.6)
<40 to ≤64	–	263 (47.3)	263 (33.1)
>64	–	185 (33.3)	185 (23.3)
Macro areas of residence*			
Northwest	82 (34.5)	309 (55.6)	391 (49.2)
Northeast	33 (13.9)	42 (7.6)	75 (9.4)
Center	37 (15.5)	32 (5.8)	69 (8.7)
South	64 (26.9)	157 (28.2)	221 (27.8)
Islands	22 (9.2)	15 (2.7)	37 (4.7)
Republic of San Marino	–	1 (0.2)	1 (0.1)
Underlying pathology in adults			
Extensive small bowel mucosal disease	–	10 (1.8)	–
Intestinal fistula	–	17 (3.1)	–
Intestinal dysmotility	–	31 (5.6)	–
Short bowel	–	207 (37.2)	–
Others (including mechanical obstruction)	–	221 (39.7)	–
N/A	–	70 (12.6)	–
Underlying pathology in pediatrics			
Extensive small bowel mucosal disease	32 (13.4)	–	–
Intestinal fistula	1 (0.4)	–	–
Intestinal dysmotility	17 (7.1)		
Short bowel	109 (45.8)		
Others (including mechanical obstruction)	43 (18.1)		
N/A	36 (15.1)	–	–
Duration of follow-up in pediatrics (y)			
≤4	163 (68.5)	–	–
>4	75 (31.5)	–	–
Duration of follow-up in adults (y)			
≤1	–	184 (33.1)	–
<1 to ≤3	–	167 (30)	–
<3 to ≤10	–	147 (26.4)	–
>10	–	58 (10.4)	–

*Single regions were distributed within the macro areas of residence.

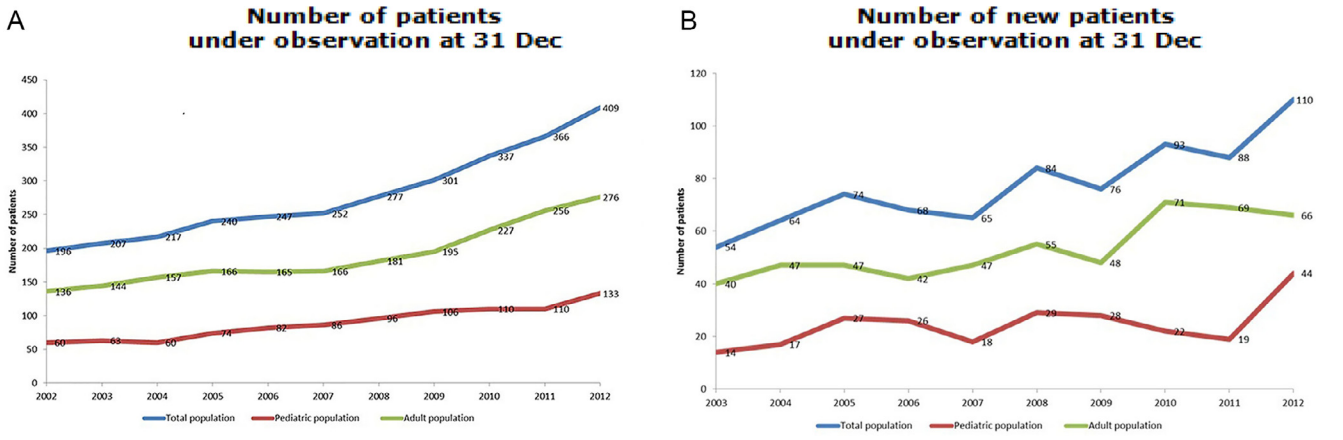

Fig. 1. Trend of patient enrollment in the survey during period of 2002 to 2012. Annual numbers of patients (left graph) and annual numbers of new patients (right graph) (total patients: blue line; pediatric patients: red line; adult patients: green line) suffering from benign chronic intestinal failure enrolled in the survey and included in the SERECARE register between January 1, 2002 and December 31, 2011. The cutoff date of the follow-up period was June 30, 2012 to ensure that patients enrolled on December 31, 2011 had a minimum follow-up period of 6 months. Values near the lines indicate number of patients under observation.

Table 3
Categorization of the CVC-related complications observed in the 794 patients enrolled in the study between 2002 and 2011

Type of CVC-related complications			
Infectious, n (%)			
	Suspected infection CVC	170	23.5
	Catheter infection	130	18
	Recurrent infections	36	5
	Skin infection	33	4.6
	Suspected tunnel infection	25	3.5
	Total	394	54.5
Mechanical, n (%)			
	CVC external break	165	22.8
	Migration CVC	49	6.8
	Occlusion CVC	46	6.4
	Internal break CVC	14	1.9
	Subcutaneous infusion	11	1.5
	Catheter decubitus	9	1.2
	Information not available	3	0.4
	Total	297	41.1
CVC-related thrombosis, n (%)		32	3.3
Number of observed complications, n (%)		723	100

CVC, central venous catheter.

The complication rate per patient in the observed population was higher in children: 297 events (41%) occurred in the 238 children (rate 1.24/patient; range: 0–11) versus 426 events (59%) in the 556 adults (rate 0.76/patient; range: 0–10). The rate of infectious complications per 1000 catheter-days was 0.45 (0.51 in the pediatric population and 0.41 in the adult population), whereas the rate of mechanical complications per 1000 catheter-days was 0.34 (0.53 in the pediatric population and 0.25 in the adult population).

By analyzing CVC-related complications rates per 1000 catheter-days over time in the study population, an alternating change in the rate of infectious complications until 2008 was recorded (Fig. 2). The rate of infectious complications decreased until 2011 (with the exception of a slight increase in 2010). On the other hand, the the overall mechanical complications rate increased from 2002 to 2005, subsequently decreasing until 2009, then increasing again in 2011 (Fig. 2).

In the pediatric population, the rate of infectious complications showed an increase up to 2005, remaining high until 2007, then decreasing from 2008 to a minimum level in 2011. In the adult population, an alternating fluctuating profile with a trend of continuous decline until 2011 was observed (Fig. 3).

The rate of mechanical complications in the pediatric and adult populations showed a similar trend. The highest levels were observed in the period 2004 to 2005, followed by a decrease until 2010. Finally, an increasing tendency was recorded in the final year of follow up (Fig. 4).

CVC-related complications per patient in both adult and pediatric population over the 2001 to 2011 study period were examined (Table 4). The mean number of infective episodes per patient was higher in the pediatric population than in adult patients, even if only a trend toward statistical significance was observed ($P = 0.0589$; Table 4). Otherwise, the mean number of mechanical complications per patient was significantly higher in the pediatric population than in adult patients ($P < 0.0001$; Table 4).

Stratifying the patients in different groups according to the number of CVC complications during the study period, ~75% of patients had neither infective nor mechanical episodes. In all, 16% and 13.% of the patients experienced one infectious and mechanical complications, respectively. Only 3.3% and 1.6% of the patients had more than three infectious and mechanical complications, respectively (Table 5).

Moreover, the overall rate of complications per 1000 catheter-days per patient was statistically significantly higher in the pediatric patients than in adults ($P = 0.0264$ and <0.0001, for infectious and mechanical episodes, respectively; Table 6)

CVC complications and treatment outcome

The analysis of treatments that successfully resolved infectious complications showed that antibiotic therapy was commonly prescribed in both groups (Table 7) as standard catheter salvage protocol. When possible, antibiotic was chosen based on antibiogram. Unfortunately, we have no data regarding this. In addition, in the collected data, no information was available for cases in which the CVC replacement was preceded by an unsuccessful antibiotic therapy.

Most of the mechanical complications were resolved by repairing the CVC (44.8%). In 34% of cases, replacing the CVC was required (Table 7).

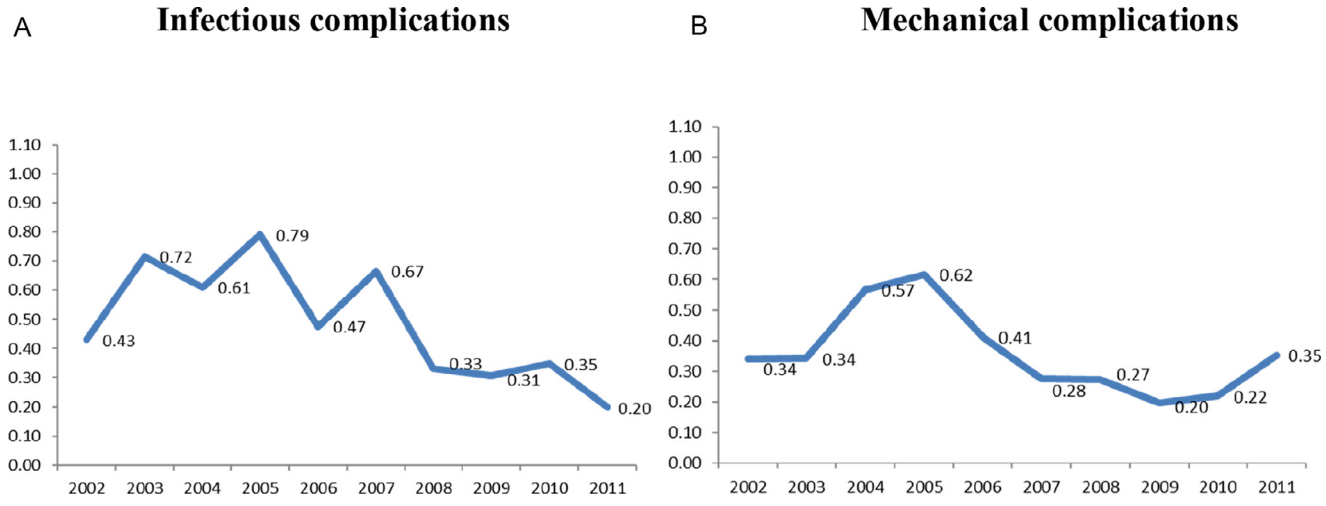

Fig. 2. The overall rate of central venous catheter (CVC)-related complications per 1,00 catheter-days (trend from 2002 to 2011 in the study population). Annual rate of infectious (left graph) and mechanical complications (right graph) per 1000 catheter-days recorded in the study population between January 1, 2002, and December 31, 2011. Values near the lines indicate CVC-related complications rate per 1000 catheter-days.

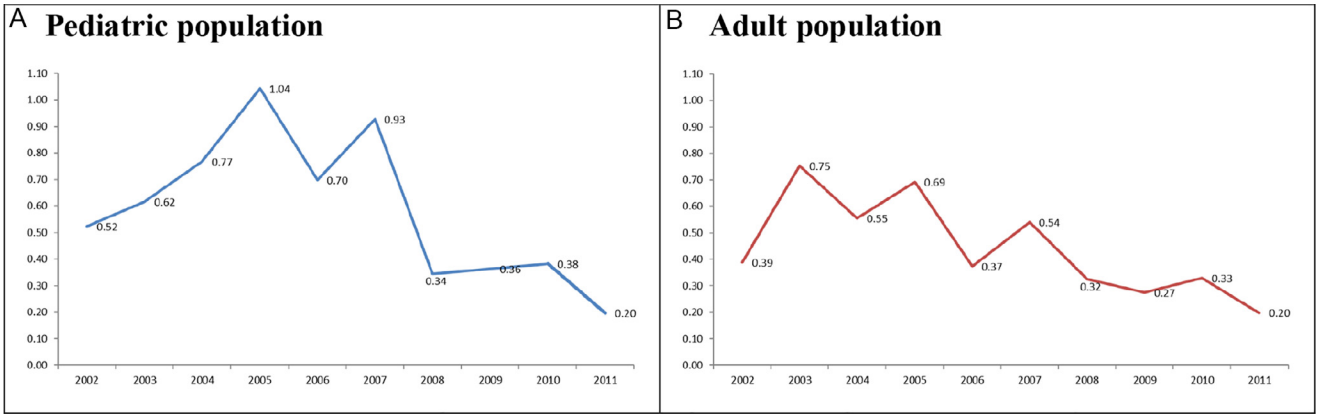

Fig. 3. The overall rate of infectious complications per 1000 catheter-days (trend from 2002 to 2011 in the age categories). Annual rate of infectious complications per 1000 catheter-days recorded in the pediatric (left graph) and adult (right graph) populations between January 1, 2002, and December 31, 2011. Values near the lines indicate central venous catheter-related infectious complications rate per 1000 catheter-days.

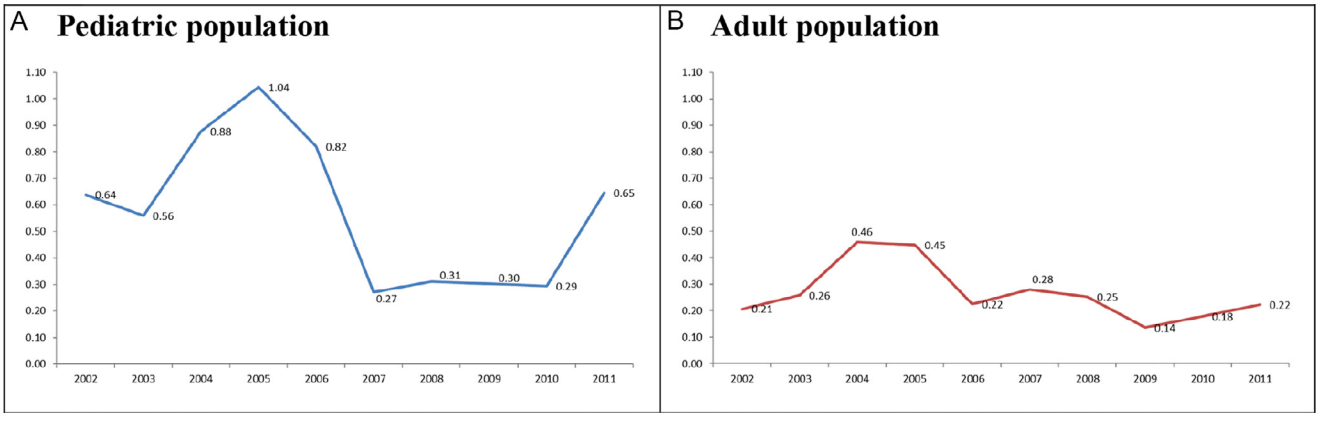

Fig. 4. The overall rate of mechanical complications per 1000 catheter-days (trend from 2002 to 2011 in the age categories. Annual rate of mechanical complications per 1000 catheter-days recorded in the pediatric (left graph) and adult (right graph) populations between January 1, 2002, and December 31, 2011. Values near the lines indicate central venous catheter-related mechanical complications rate per 1000 catheter-days.

Table 4
Rate of CVC-related infectious and mechanical complications per patient in the two analyzed populations

	Infectious			Mechanical		
	Pediatric population (n =238)	Adult population (n = 556)	Total (N = 794)	Pediatric population (n =238)	Adult population (n = 556)	Total (N = 794)
Mean rate (±SD)	0.60 (1.29)	0.45 (1.06)	0.50 (1.14)	0.61 (1.16)	0.27 (0.75)	0.37 (0.91)
Median rate	0	0	0	0	0	0
Min	0	0	0	0	0	0
Max	11	10	11	9	7	9
P-value, Wilcoxon rank-sum test	0.0589			<0.0001		

Table 5
Number of infectious and mechanical complications per patient (classes)

Number of complications	Patients with infectious complications, n (%)		Patients with mechanical complications, n (%)	
0	584	(73.6)	(621)	(78.2)
1	127	(16)	(103)	(13)
2	36	(4.5)	(44)	(5.5)
3	21	(2.6)	(13)	(1.6)
>3	26	(3.3)	(13)	(1.6)
Overall	794	(100)	(794)	(100)

Table 6
Rate of infectious and mechanical complications per 1000 catheter-days per patient by population

	Infectious			Mechanical		
	Pediatric population (n =238)	Adult population (n = 556)	Total (N = 794)	Pediatric population (n =238)	Adult population (n = 556)	Total (N = 794)
Mean (±SD)	0.75 (1.70)	0.43 (1.15)	0.53 (1.35)	0.85 (2.48)	0.25 (0.83)	0.43 (1.55)
Median	0	0	0	0	0	0
Min	0	0	0	0	0	0
Max	9.4	10.9	10.9	27.8	11.1	27.8
P-value, Wilcoxon rank-sum test	0.0264			<0.0001		

Table 7
Treatment of CVC infectious complications by age categories*

	Antibiotic therapy, n (%)		CVC replacement, n (%)		Not known, n (%)		Total events, n
Adult	112	(44.4)	121	(48)	19	(7.5)	252
Pediatric	88	(62)	38	(26.8)	16	(11.3)	142
Total	200	(50.8)	159	(40.4)	35	(8.9)	394

CVC, central venous catheter.
*Patients who recorded more than one complication were reported as two different events.

A correlation analysis between the number of follow-up visits and the number of CVC complications showed a positive correlation between the two variables (Fig. 5), that is, the patients with more complications had more visits.

Rehospitalization rate

During the observational period, 1222 rehospitalizations were observed with an absolute rate of 1.53 events per patient. Twenty-two (1.3%) hospitalizations were in a day-hospital regimen (i.e., no overnight stay) and 1200 (98.7%) were in the ward. The decision of the type was done according to clinical judgment by the physician on duty. The cause of rehospitalization was CVC complication in 68.1% of day-hospital patients and in 29.5% of those on a hospital ward. In the other cases, hospitalization was due to the underlying disease or to causes unrelated to either CVC or disease complications.

The median (interquartile range) duration of the hospitalization in the hospital ward was 11 (5–21) days. Mean length of stay

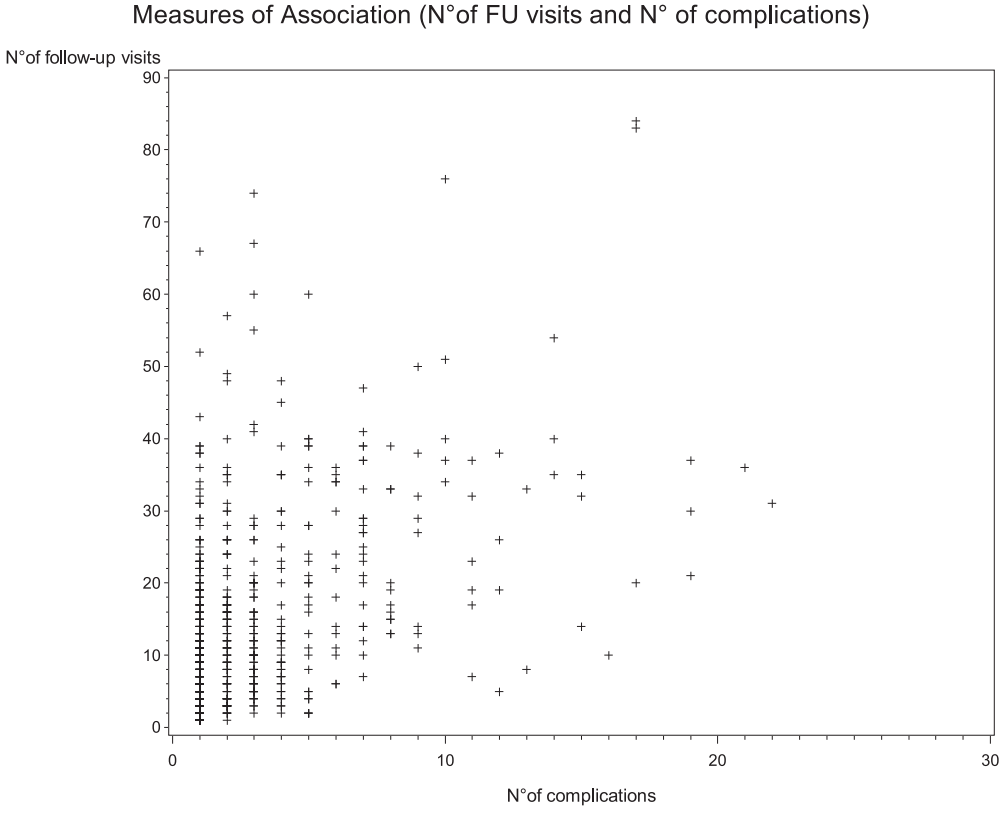

Fig. 5. Measures of Association (number of FU visits and number of complications).
Number of follow up (FU) visits and number of CVC related complications recorded during the study period. Pearson Correlation Coefficient was used to assess the correlation between these two variables, r = 0.49176, $P < 0.0001$.

Table 8
Patient status on June 30, 2012

Patient included in the study group, N (%)	794 (100)
On HPN treatment and in the register, n (%)	253 (31.4)
Withdrawn from the register before June 30, 2012, n (%)	541 (68.1)
Reasons for withdrawal, n (%)	
Oral nutrition	234 (29.5)
Death	182 (22.9)
Hospitalization	16 (2)
Transferred to another program	14 (1.8)
Enteral diet	12 (1.5)
Refusal of LHCU to continue Baxter service	11 (1.4)
Other	72 (11.6)

HPN, home parenteral nutrition; LHCU, local health care units.

(days) in hospital did not differ between complications related or not to catheter ($P = 0.2933$).

HPN efficacy

Patient outcome

The patient outcome at the end of the study period is reported in Table 8.

HPV efficacy outcome variables

Three-hundred and one patients had at least one follow-up visit at 36 mo during the study period. For these patients, the trend of the treatment efficacy outcome indicators (BMI, Karnofsky score) over time was analyzed.

Body mass index variations. In the study population, when comparing BMI values (for the pediatric population the BMI *z*-score was only used) at each follow-up visits with the value recorded at baseline, a statistically significant increase was observed at each time points for both the adult population and pediatric patients (0–2 y). By contrast, there was no significant BMI *z*-score in children 2–18 y of age (Table 9).

Karnofsky score variations. A significant increase of the Karnofsky score over the baseline value was observed in adult patients along the study observation time (Table 10).

Discussion

The results of this retrospective survey demonstrated the utility of a structured register in monitoring the safety and the efficacy of long-term HPN provided by a specialized service. Monitoring represents the key strategy to follow up the outcomes of HPN long-term treatments. The ESPEN guidelines on CIF recommend a regular audit of therapy and outcomes against standards to ensure safety and efficacy of an HPN program [8,11]. The guidelines highlight that accreditation programs for HPN providers must ensure regular audits measured against quality measures. Among the factors that promote appropriate HPN monitoring are the adequacy of dedicated professional resources and the availability of structured protocols and dedicated tools to collect data [8]. The ESPEN guidelines recommend that a recognized instrument for measuring quality of life should be used regularly to monitor HPN patients. Moreover, patients need to be contacted by the HPN team on a regular basis according to their clinical characteristics and requirements [8,11]. The SERECARE register is a dedicated database that is completed by trained and specialized nurses who visit the patient at home. Nurses follow structured and regularly updated protocols provided for by the Baxter service that administers HPN therapy according to the prescriptions of the hospital HPN or CIF center. To evaluate the HPN service activity, the number of follow-up home visits and the number of training

Table 9
Variations of BMI over time

	BMI and BMI *z*-score*									
Population	Months from baseline	n	Missing	Mean difference	SD	Median	Min	Max	*P*-value (Student's *t* test)	*P*-value (Wilcoxon rank-sum test)
Pediatric population (0–2 y)	12	55	2	2.33	1.88	1.85	−2.07	5.64	<0.001	<0.001
	24	51	6	4.43	2.30	4.22	0.00	9.54	<0.001	<0.001
	36	54	3	5.81	2.67	6.29	0.78	10.55	<0.001	<0.001
	>36	36	21	11.03	4.31	10.60	2.55	20.77	<0.001	<0.001
Pediatric population (2–18 y)	12	26	4	0.08	1.00	−0.04	−2.16	2.44	0.687	0.690
	24	25	5	−0.07	1.13	−0.20	−1.87	2.98	0.756	0.307
	36	27	3	−0.02	1.47	0.04	−2.66	3.91	0.931	0.442
	>36	23	7	0.75	1.52	1.08	−2.67	3.67	0.028	0.210
Adult population (≥18 y)	12	195	19	0.64	1.96	0.33	−6.64	8.08	<0.001	<0.001
	24	194	20	0.81	2.06	0.71	−5.78	8.82	<0.001	<0.001
	36	195	19	0.68	2.25	0.69	−6.83	7.03	<0.001	0.001
	>36	139	75	0.42	2.47	0.39	−5.55	8.65	0.048	0.028

BMI, body mass index
*BMI was calculated for the adult population while for the pediatric calculation the *z*-score was calculated by physician based on the World Health Organization's Child Growth Standards.

Table 10
Variations of Karnofsky score over time

Months from baseline	n	Missing	Mean change	SD	Median	Min	Max	*P*-value (Student's *t* test)	*P*-value (Wilcoxon rank-sum test)
12	202	12	1.83	7.47	0.00	−40	40	<0.001	<0.001
24	199	15	1.99	9.65	0.00	−54	40	0.004	<0.001
35	202	15	1.78	11.19	0.00	−50	40	0.025	<0.001
>36	142	72	2.32	14.13	0.00	−60	40	0.052	<0.001

episodes for the HPN management, carried out by the nurses of the HPN service to each patient, was collected through the SERECARE register. This survey represented the largest ever documented, with a follow-up in adults of >10 y. Noteworthy, 10.4% of the patients had a follow-up of >10 y demonstrating the lifesaving benefit of the HPN treatment. Overall, the present results agree with data previously reported by individual HPN/CIF center surveys [15–28]. Moreover, the present results regarding the nursing activity of the HPN service demonstrated that each patient was visited on a mean ± SD of 5.2 ± 3.2 times and received 1.3 ± 0.8 training episodes. Approximately 70% of the training episodes were initial training, whereas the remaining were retraining.

According to the ESPEN guidelines, the outcome indicators of HPN safety collected by SERECARE were CVC-related infectious complications, mechanical complications, and the related hospital readmission rates. In the present survey, the rate of total CVC-related infections ranged from 0.20 to 0.79 per 1000 catheter-days, with a mean of 0.45 in the study period. A progressive decrease of CVC-related infectious complications was observed over time with the lowest rate reported in the last year of follow-up. This trend showed no differences among the age categories. These results match those of other related studies in the same period [20,24], albeit with a much higher clinical evidence. In the last decade, several improvements were introduced in the Baxter service CVC management protocol, which may have contributed to the decrease in the rate of CVC-related infections such as chlorhexidine patches for exit-site disinfection. Moreover, the action that might have had the greatest effect was the use of a rigorous asepsis protocol at home managed by a specialized nurse during the years. The results also confirm a previously reported susceptibility of some patients to have a higher frequency of CVC-related infection [25]. O'Keefe et al. identified the characteristics of patients who had a higher rate of CVC-related infections: younger age, Crohn's disease, short bowel syndrome with jejunostomy, the presence of a central vein thrombosis, poor catheter care technique, and smoking habit [29]. More studies on this issue are required. In ~50% of the cases, the CVC-related infections were successfully treated with antibiotic therapy. Dreesen et al. reviewed 39 studies [18], finding that the overall catheter-related bloodstream infection (CRBSI) rate ranged between 0.38 and 4.58 episodes per 1000 catheter-days (median 1.31). Individual center surveys showed a high degree of variability, with the incidence of CVC-related infections being reported to occur from 0.08 to 10.8 times per 1000 catheter-days [10,15–18,20–23,27,30]. This variability may be influenced by the use of agents such as taurolidine as part of the prevention protocol [22] for CVC-related infections.

In the present study, data on the CVC-related mechanical complications showed results similar to those of the infectious complications. However, there was an increase in the mechanical complication rate in the last year of observation with a mean incidence over the study period of 0.43 per 1000 catheter-days. Few data on this issue are available in the literature; however, the incidence observed in our study was ~50% of that recently reported by the largest Danish CIF center (0.80) [25]. We also observed a rehospitalization incidence of 1.53 events per patient over the entire observational period. The previously reported incidence of rehospitalization ranged from 0.89 to 11.5 times per 1000 catheter-days [20,24]. Our safety evaluation was based on the rehospitalization rate owing to CVC-related complications accounting for ~33% of total rehospitalizations, with a mean duration of 18 d. A catheter-salvage protocol (see the appendix) was in place during the observational period.

On the other hand, patient BMI and Karnofsky score were recorded as objective indicators of the HPN efficacy. In terms of efficacy, by comparing BMI, BMI *z*-scores, and Karnofsky scores at each follow-up visit with the value recorded at baseline, a significant increase was observed at each time point with no substantial difference among pathologies. Also, these data are in agreement with the reported improvement of nutritional and functional status after starting HPN [28,31–33].

Unfortunately, the inclusion of patients receiving different HPN programs, because of different characteristics of their ICF and the lack of a control group, does not allow us to draw reliable conclusions regarding the effectiveness of each HPN treatment. Owing to the variety of geographic locations from which the patients were enrolled and given the variability of program management, we retain that these results might be extended to the Italian setting even if the limited availability of nationwide HPN services might hamper generalization in countries with reduced access to public health care systems. Although there are no professional society guidelines for monitoring patients receiving HPN [34] and a valid definition of mutually agreed and clinically applicable CRBSI definition is lacking [35], we observed a reduced CRBSI rate compared with other studies [18]. A possible explanation of this result was the standardized protocol performed by a group of specialized nurses who have given continuity to the service over time, promptly monitoring deviations and near-misses and suggesting improvements to procedures.

A limitation of this retrospective study was the possible selection bias, which exists when procedures for patient selection or factors influencing patient's participation affect the study outcome. However, the risk for this bias was minimized by the inclusion in the SERECARE register of all the patients who were referred by Baxter services independently of the HPN/CIF prescribing center.

Conclusion

The results of this 10-y multicenter survey of patients on long-term HPN for CIF owing to benign disease show that the SERECARE register as part of an HPN service and completed by experienced nurses allows prospective and timely collection of safety and efficacy indicators of the treatment. Moreover, collected data on safety and efficacy indicators allowed an increase in the performance of the HPN service. The uniformity of these results is maintained despite the heterogeneity of the clinical centers involved in the study. Guidelines for CIF recommend monitoring as a key activity to provide the appropriate management of patients on long-term HPN. The presented study sets a standard for rules and protocols to be applied in the long-term HPN in CIF patients, in a similar way to those used in the dialysis protocol, which are known for being of great benefit. Monitoring is a time-consuming activity for the health care professional. A register to perform regular and objective monitoring by the home care nurse is a valuable tool that may lead to time efficiency and prevent potential malpractice. It should be an integrated part of a certified HPN service.

Acknowledgments

Data analysis and initial medical writer was performed by the CRO TFS.

Appendix

1. During the initial visit (“loading”) personal and administrative data are collected in the register. The nurse performs the initial training, made up of two parts: theoretical and practical; the latter lasts on average 10 to 14 d when the nurse records training data and information about the catheter.

The procedure can be outlined as follows:

a. Work area arrangement
b. Hand washing
c. Material control
d. Checking of the parenteral nutrition (PN) bag
e. Preparation of the PN bag according to procedures
f. Addition into the PN bag of the prescribed supplement (i.e., lipids, vitamins, trace elements)
g. Drug administration
h. Insertion of venous lines
i. Pump functions
j. Secondary infringements
k. Infusion start procedure
l. Infusion speed control
m. Heparinization of the catheter
n. Catheter washing
o. End of the infusion procedure
p. Venous access medication
q. Changing the cap in the partially implanted system
r. Needle insertion into the fully implanted system
s. Maneuvers to be carried out in case of a complication of the venous line (obstruction, breakage or displacement of the venous catheter)
t. Storage of bags and medication material
u. Acknowledgment of mechanical and infectious complications of the venous line; identification of these complications and consequent remedial actions. The complications were assessed and recorded based on agreed standard nurse protocol: e.g., a catheter-related infection was defined in presence of clinical sign (fever, local pain, positivity of hemoculture); a suspected infection was defined when no data from hemoculture was available in presence of clinical signs (fever, local pain); a recurrent infection was defined as three events in a 3-mo period; a thrombosis was suspected based on clinical signs (pain, paresthesia, visible venous collaterals, swelling and local pain irradiating to arm and neck).

2. Checking of the catheter is reprocessed at each change of the central venous catheter (e.g., removal, etc.)
3. After training, the patient is placed in a monitoring program that generally involves the collection of the follow-up card during the subsequent home visits scheduled as follow:
   a. During the first 2 wk following training;
   b. During the fourth week of therapy after the end of training;
   c. During the sixth week of therapy after the end of training;
   d. Every 8 wk of therapy after completion of training;
   e. After 1 y, the survey shall be carried out every 12 wk;
   f. If the infusions are suspended and the patient must remain in the catheter maintenance service, the examination is carried out every 12 wk.
4. The complications card is collected when the patient notifies us (during visits or by phone) of any change in the program due to hospitalization or unwanted event.

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