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Original article

Home parenteral nutrition provision modalities for chronic intestinal failure in adult patients: An international survey

Loris Pironi [a, *], Ezra Steiger [b], Chrisoffer Brandt [c], Francisca Joly [d], Geert Wanten [e], Cecile Chambrier [f], Umberto Aimasso [g], Anna Simona Sasdelli [a], Sarah Zeraschi [h], Darlene Kelly [i], Kinga Szczepanek [j], Amelia Jukes [k], Simona Di Caro [l], Miriam Theilla [m], Marek Kunecki [n], Joanne Daniels [o], Mireille Serlie [p], Florian Poullenot [q], Jian Wu [r], Sheldon C. Cooper [s], Henrik H. Rasmussen [t], Charlene Compher [u], David Seguy [v], Adriana Crivelli [w], Maria C. Pagano [x], Sarah-Jane Hughes [y], Francesco W. Guglielmi [z], Nada Rotovnik Kozjek [aa], Stéphane M. Schneider [ab], Lyn Gillanders [ac], Lars Ellegard [ad], Ronan Thibault [ae], Przemysław Matras [af], Anna Zmarzly [ag], Konrad Matysiak [ah], Andrè Van Gossum [ai], Alastair Forbes [aj], Nicola Wyer [ak], Marina Taus [al], Nuria M. Virgili [am], Margie O'Callaghan [an], Brooke Chapman [ao], Emma Osland [ap], Cristina Cuerda [aq], Peter Sahin [ar], Lynn Jones [as], Andre Dong Won Lee [at], Luisa Masconale [au], Paolo Orlandoni [av], Ferenc Izbéki [aw], Corrado Spaggiari [ax], Marta Bueno [ay], Maryana Doitchinova-Simeonova [az], Carmen Garde [ba], Aurora E. Serralde-Zúñiga [bb], Gabriel Olveira [bc], Zeljko Krznaric [bd], Laszlo Czako [be], Gintautas Kekstas [bf], Alejandro Sanz-Paris [bg], Estrella Petrina Jáuregui [bh], Ana Zugasti Murillo [bi], Eszter Schafer [bj], Jann Arends [bk], José P. Suárez-Llanos [bl], Simon Lal [bm], The Home Artificial Nutrition and Chronic Intestinal Failure Special Interest Group of ESPEN, The European Society for Clinical Nutrition and Metabolism

[a] St. Orsola University Hospital, Bologna, Italy
[b] Cleveland Clinic Foundation, Cleveland, OH, USA
[c] Rigshospitalet, Copenhagen, Denmark
[d] Beaujon Hospital, Clichy, France
[e] Radboud University Medical Center, Nijmegen, the Netherlands
[f] Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Lyon, France
[g] Città della Salute e della Scienza, Torino, Italy
[h] Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom
[i] Mayo Clinic College of Medicine, Rochester, MN, USA
[j] Stanley Dudrick's Memorial Hospital, Skawina, Poland
[k] University Hospital of Wales, Cardiff, United Kingdom
[l] University College Hospital, London, United Kingdom
[m] Rabin Medical Center, Petach Tikva, Israel
[n] M. Pirogow Hospital, Lodz, Poland
[o] Nottingham University Hospital NHS Trust, Nottingham, United Kingdom
[p] Academic Medical Center, Amsterdam, the Netherlands
[q] CHU de Bordeaux, Hôpital Haut-Lévêque, Pessac, France
[r] University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom
[s] University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom
[t] Center for Nutrition and Bowel Disease, Aalborg University Hospital, Aalborg, Denmark
[u] Hospital of the University of Pennsylvania, Philadelphia, PA, USA
[v] CHRU de Lille, Lille, France
[w] Hospital Universitario Fundacion Favaloro, Buenos Aires, Argentina
[x] Federico II University, Napoli, Italy

* Corresponding author. Center for Chronic Intestinal Failure Department of Digestive System St. Orsola-Malpighi Hospital, University of Bologna, Via Massarenti, 9, 40138, Bologna, Italy. Fax: +39 051 6364193.
E-mail address: loris.pironi@unibo.it (L. Pironi).

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[y] Regional Intestinal Failure Service, Belfast Health and Social Care Trust, Northern Ireland, United Kingdom
[z] San Nicola Pellegrino Hospital, Trani, Italy
[aa] Institute of Oncology, Ljubljana, Slovenia
[ab] CHU Archet, Nice, France
[ac] Auckland City Hospital, Auckland, New Zealand
[ad] Sahlgrenska University Hospital, Gothenburg, Sweden
[ae] Nutrition unit, CHU Rennes, Nutrition Metabolisms and Cancer Institute, NuMeCan, INRA, INSERM, Université Rennes, Rennes, France
[af] Medical University of Lublin, Lublin, Poland
[ag] J. Gromkowski City Hospital, Wroclaw, Poland
[ah] H.Święcicki University Hospital, Poznań, Poland
[ai] Hôpital Erasme, Brussels, Belgium
[aj] Norfolk and Norwich University Hospital, Norwich, United Kingdom
[ak] University Hospital, Coventry, United Kingdom
[al] Ospedali Riuniti, Ancona, Italy
[am] Hospital Universitari de Bellvitge, Barcelona, Spain
[an] Flinders Medical Centre, Adelaide, Australia
[ao] Austin Health, Melbourne, Argentina
[ap] Royal Brisbane and Women's Hospital, Herston, Australia
[aq] Hospital General Universitario Gregorio Marañon, Madrid, Spain
[ar] St. Imre Hospital, Budapest, Hungary
[as] Royal Prince Alfred Hospital, Sydney, Australia
[at] Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil
[au] ULSS 22 Ospedale Orlandi, Bussolengo, Italy
[av] INRCA – IRCCS, Ancona, Italy
[aw] Szent György Teaching Hospital of County Fejér, Székesfehérvár, Hungary
[ax] AUSL di Parma, Parma, Italy
[ay] Hospital Universitario Arnau de Vilanova, Lleida, Spain
[az] Bulgarian Executive Agency of Transplantation, Sofia, Bulgaria
[ba] Hospital Universitario Donostia, San Sebastian, Spain
[bb] Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City, Mexico
[bc] IBIMA, Hospital Regional Universitario de Málaga, Universidad de Málaga, Málaga, Spain
[bd] University Hospital Centre Zagreb, Zagreb, Croatia
[be] University of Szeged, Szeged, Hungary
[bf] Vilnius University Hospital Santariskiu Clinics, Vilnius, Lithuania
[bg] Miguel Servet Hospital, Zaragoza, Spain
[bh] Complejo Hospitalario de Navarra, Pamplona, Spain
[bi] Hospital Virgen del Camino, Pamplona, Spain
[bj] Magyar Honvedseg Egészségügyi Központ (MHEK), Budapest, Hungary
[bk] Tumor Biology Center, Freiburg, Germany
[bl] Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain
[bm] Salford Royal NHS Foundation Trust, Salford, United Kingdom

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SUMMARY

Background & aims: The safety and effectiveness of a home parenteral nutrition (HPN) program depends both on the expertise and the management approach of the HPN center. We aimed to evaluate both the approaches of different international HPN-centers in their provision of HPN and the types of intravenous supplementation (IVS)-admixtures prescribed to patients with chronic intestinal failure (CIF).

Methods: In March 2015, 65 centers from 22 countries enrolled 3239 patients (benign disease 90.1%, malignant disease 9.9%), recording the patient, CIF and HPN characteristics in a structured database. The HPN-provider was categorized as health care system local pharmacy (LP) or independent home care company (HCC). The IVS-admixture was categorized as fluids and electrolytes alone (FE) or parenteral nutrition, either commercially premixed (PA) or customized to the individual patient (CA), alone or plus extra FE (PAFE or CAFE). Doctors of HPN centers were responsible for the IVS prescriptions.

Results: HCC (66%) was the most common HPN provider, with no difference noted between benign-CIF and malignant-CIF. LP was the main modality in 11 countries; HCC prevailed in 4 European countries: Israel, USA, South America and Oceania ($p < 0.001$). IVS-admixture comprised: FE 10%, PA 17%, PAFE 17%, CA 38%, CAFE 18%. PA and PAFE prevailed in malignant-CIF while CA and CAFE use was greater in benign-CIF ($p < 0.001$). PA + PAFE prevailed in those countries where LP was the main HPN-provider and CA + CAFE prevailed where the main HPN-provider was HCC ($p < 0.001$).

Conclusions: This is the first study to demonstrate that HPN provision and the IVS-admixture differ greatly among countries, among HPN centers and between benign-CIF and cancer-CIF. As both HPN provider and IVS-admixture types may play a role in the safety and effectiveness of HPN therapy, criteria to homogenize HPN programs are needed so that patients can have equal access to optimal CIF care.

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1. Introduction

Home parenteral nutrition (HPN) is the primary and life-saving treatment for patients with chronic intestinal failure (CIF) [1]. 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 (IVS) is required to maintain health and/or growth" [2]. Chronic IF can be due to five pathophysiological mechanisms (short bowel, intestinal fistulas, intestinal dysmotility, intestinal mechanical occlusion or extensive small bowel mucosa disease) which can originate from either non-malignant (benign-CIF) or malignant (malignant-CIF) diseases [2]. Patients with CIF require IVS for months, years or sometimes lifelong [1,2]. They are discharged onto HPN programs which aim at providing evidence-based therapy, minimizing HPN-related complications (such as central venous catheter (CVC)-related infections and metabolic complications) and maximizing the patient's quality of life (QoL) [3,4]. The European Society for Clinical Nutrition and metabolism (ESPEN) guidelines on benign-CIF recommend that at discharge: patients are metabolically stable, able physically and emotionally to cope with the HPN therapy, and have an adequate home environment; patients should be cared for by a multidisciplinary team with skills and experience in IF and HPN management; patient/caregiver training for HPN management should be patient-centered with a multidisciplinary approach, together with written guidelines; HPN patients should have access to infusion pumps or devices with specified safety features together with ancillary products, safe compounding and delivery systems. Thus, the safety and effectiveness of a HPN program depends on the expertise and the management modalities available at the HPN center.

It has been suggested that the management and the provision of HPN programs differ greatly among countries and among HPN centers. However, only one study, performed in 2010, objectively described this feature [5]. There are no recent data on the approaches of international CIF centers in the methods routinely adopted for HPN provision. Using the ESPEN database for CIF, we carried out an international cross-sectional survey to evaluate the approaches of different international HPN centers in their provision of HPN and the types of intravenous supplementation (IVS)-admixtures supplied to patients with CIF.

2. Materials and methods

This international cross-sectional observational study was part of a large survey developed by the Home Artificial Nutrition and Chronic Intestinal Failure (HAN & CIF) special interest group of ESPEN, aimed at investigating the applicability of the clinical classification of CIF [6]. The recruitment of HPN centers, patient inclusion criteria, modalities of data collection and recorded items have already been extensively described [6] and are summarized below.

2.1. Participating centers and patient inclusion criteria

Sixty-five HPN centers from 22 countries enrolled all adult patients (≥18 year old) who were dependent on HPN for either benign-CIF or malignant-CIF on March 1st 2015. The term malignant-CIF indicates the presence of an active malignant disease at time of enrollment on the study (and thus excludes patients in whom the malignancy has been cured; these patients were surveyed within the benign-CIF group).

2.2. Data collection and schedule

Data were collected into a structured questionnaire embedded in an Excel (Microsoft Co., 2013) database, termed "the CIF Action day", available at the web page of the HAN&CIF group on the ESPEN website [7].

Demographic, clinical, CIF, underlying disease, IVS and HPN program characteristics were gathered and the clinical classification of CIF was calculated for each patient [6]. The HPN-provider was categorized as health care system local pharmacy (LP) or home care company (HCC). The term HPN-provider referred to the supplier of the IVS-admixture, infusion pump or other regulatory device, the ancillaries required for infusion and CVC medication. The IVS-admixture was categorized as: fluids and electrolytes (FE); commercially premixed ready-to-use parenteral nutrition admixture (PA); commercially premixed parenteral nutrition admixture plus extra FE (PAFE); parenteral nutrition admixture customized (tailored) to the individual patient requirements (CA); parenteral nutrition admixture customized to the individual patient requirements alone or plus extra FE (CAFE).

2.3. Ethical statement

The research was based on anonymized information taken from patient records at the time of data collection. The study was conducted with full regard to confidentiality of the individual patient. Ethical committee approval was obtained by the individual HPN centers according to local regulations. Collected data were used only for the study purpose. The identity of the contributing centers has also been anonymized for data analysis and presentation.

2.4. Statistical analysis

The daily mean volume and energy of IVS were calculated as follows: daily total volume (mL/day) or energy (kcal/day) = amount per day of infusion x number of infusions per week/7; daily volume or energy per kg of patient body weight (mL/kgBW/day or kcal/kgBW/day) = amount per day of infusion x number of infusions per week)/7/kg patient body weight. The patients' body mass index (BMI) was calculated by Quetelet's formula (weight (kg)/height (m^2).

Data are reported as mean ± standard deviation (SD) and as absolute and relative frequencies. The non-parametric Kruskal Wallis test, the Fisher's exact test and the Chi-square test were applied where appropriate.

The IBM SSPS Statistics package for Windows, version 23.0 (BM Co., Armonk, NY, USA) was used for the analyses. Two-tailed P values less than 0.05 were considered as statistically significant.

3. Results

3.1. Participating centers and patient cohorts

A total of 3239 patients were included, 2919 with benign-CIF (90.1%) and 320 with malignant-CIF (9.9%) (Table 1). All the HPN centers enrolled benign-CIF patients, while only 45 centers enrolled malignant-CIF patients. The malignant-CIF cohort had statistically significant older age, lower BMI, shorter duration of HPN, IVS of greater daily volume and energy, and a 10-times greater occurrence of patients with IF due to mechanical obstruction (Table 2). In both benign-CIF and malignant-CIF, two-thirds of patients were females.

In the benign-CIF cohort, the underlying diseases were Crohn's disease (22.4%), mesenteric ischemia (17.7%), surgical complications (15.8%), primary chronic intestinal pseudo-obstruction (9.7%),

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Table 1
Patients on home parenteral nutrition for chronic intestinal failure (CIF) due to non-malignant (benign) or malignant disease, enrolled by countries contributing in the survey.

	Total n.	Benign-CIF n. (%)	Malignant-CIF n. (%)
UK	781	738 (94.5)	43 (5.5)
France	478	441 (92.3)	37 (7.7)
Italy	362	326 (90.1)	36 (9.9)
Poland	283	224 (79.2)	59 (20.8)
Denmark	262	233 (88.9)	29 (11.1)
The Netherlands	257	229 (89.1)	28 (10.9)
Spain	43	40 (93.0)	3 (7.0)
Slovenia	39	31 (79.5)	8 (20.5)
Sweden	25	24 (96.0)	1 (4.0)
Hungary	22	20 (90.9)	2 (9.2)
Belgium	21	21 (100)	0
Germany	10	1 (10)	9 (90)
Bulgaria	5	4 (80)	1 (20)
Croatia	3	3 (100)	0
Lithuania	3	2 (66.7)	1 (33.3)
USA	429	389 (90.7)	40 (9.3)
Israel	90	71 (78.9)	19 (21.1)
Mexico	4	3 (75)	1 (25)
Argentina	44	44 (100)	0
Brazil	7	7 (100)	0
Australia	44	41 (93.2)	3 (6.8)
New Zealand	27	27 (100)	0
Total	**3239**	**2919 (90.1)**	**320 (9.9)**

post-radiation enteritis (7.3%), others (21.3%, with <3% each-one) and not reported (5.9%). In the malignant-CIF cohort, the type of active cancer was not specified in 62% cases, gastrointestinal (28%) and extra-abdominal (10%). Concurrent enteritis due to radio- or chemo-therapy was described in 5% of cases and peritoneal carcinomatosis was reported in 12%.

Table 2
Characteristics of the cohorts of patients with chronic intestinal failure (CIF) enrolled in the study: patients without malignant disease (Benign-CIF), n. 2919; patients with a malignant disease (Malignant-CIF), n.320.

	Benign-CIF	Malignant-CIF	P
Gender			0.202
Males	36.8%	39.45	
Females	63.2%	60.6%	
Age, years	54.9 ± 16.0	60.6 ± 13.5	<0.001
BMI, kg/m^2	22.2 ± 4.4	21.5 ± 4.4	0.002
HPN duration, months	58.1 ± 71.5	17.1 ± 30.9	<0.001
Pathophysiological mechanism of IF			<0.001
SBS-J	38.6%	28.8%	
SBS-JC	19.9%	9.7%	
SBS-JIC	5.9%	2.8%	
Fistulas	7.0%	3.4%	
Dysmotility	17.5%	3.4%	
Mechanical Obstruction	4.4%	45.9%	
Mucosal Disease	6.8%	5.9%	
IVS volume, mL/day	1877.0 ± 1016.6	1967.6 ± 817.8	0.004
IVS energy, kcal/day	1088.0 ± 649.4	1315.9 ± 560.9	<0.001
Clinical classification of CIF (IVS, mL/day)			<0.001
FE1, ≤1000	5.8%	3.1%	
FE2, 1001-2000	2.2%	1.3%	
FE2, 2001-3000	0.5%	0	
FE4, >3000	0.3%	0	
PN1, ≤1000	15.9%	10.3%	
PN2, 1001-2000	40.9%	47.2%	
PN3, 2001-3000	23.1%	29.4%	
PN4, >3000	11.3%	8.8%	

BMI, body mass index; HPN, home parenteral nutrition; SBS-J, short bowel syndrome with end jejunostomy; SBS-JC, short bowel syndrome with jejuno-colon anastomosis; SBS-JIC, short bowel syndrome with jejuno-ileo anastomosis and total colon: IVS, intravenous supplementation; FE, fluid and electrolytes; PN, parenteral nutrition.

3.2. HPN-providers and IVS-admixture types in the total group

The HPN-provider was LP in 1111 (34.4%) and HCC in 2117 (65.6%) patients (not reported in 11). The IVS-admixture type was FE in 312 (9.7%), PA in 556 (17.2%), PAFE in 541 (16.8%), CA in 1227 (37.9%) and CAFE in 595 (18.4%) cases. The IVS-admixture types significantly differed between the two modalities of HPN provision; when the HPN was provided by a HCC, the IVS-admixtures were CA or CAFE in two-thirds of cases, while PA or PAFE accounted for more than 50% of the IVS-admixtures provided by the LP (Table 3).

3.3. HPN-providers and IVS-admixture types by countries

HCCs provided all HPN in the UK and Israel, were almost exclusive providers (≥80% of patients) in the USA, Mexico and South America, and were the main providers (56–63% of cases) in France, Italy, Poland and Oceania. LPs provided all the HPN programs in Denmark, two thirds of programs in the Netherlands and more than 90% of cases in the other 9 European countries which contributed to the survey (Fig. 1).

In those countries, except Poland, where most or all the HPN programs were provided by a HCC, CA and CAFE represented more than 50% of the IVS-admixtures. Where the LP was the main HPN-provider, PA and PAFE prescription prevailed (Fig. 2).

3.4. HPN-providers and IVS-admixture types by the nature of the underlying disease

The percentage split of the two HPN-providers did not differ between benign-CIF and malignant-CIF, while CA and CAFE were the IVS-admixture types in almost two-thirds of benign-CIF and PA and PAFE were the IVS-admixture types in more than 50% of malignant-CIF (Fig. 3).

4. Discussion

This large international survey demonstrates that the modality of HPN provision and the type of IVS-admixture supplied differ greatly among countries, among HPN centers and between benign-CIF and malignant-CIF. Although it has been long suggested that HPN management is not homogeneous between countries, as well as among HPN centers within an individual country, this is the first study to provide objective data to confirm the significant variation in practice that exists in HPN provision. The strengths of the study are the large numbers of participating countries and the worldwide distribution of contributing HPN-centers and enrolled patients. A

Table 3
Intravenous supplementation (IVS)-admixture type by home parenteral nutrition (HPN)-provider in patients with chronic intestinal failure (P < 0.001).

	Total n.	FE n. (%)	PA n. (%)	PAFE n. (%)	CA n. (%)	CAFE n. (%)	P
HCC	2117	224 (10.5)	149 (7.0)	304 (14.3)	906 (42.8)	534 (25.2)	<0.001
LP	1111	88 (7.9)	407 (36.6)	237 (21.3)	318 (28.6)	61 (5.4)	

HCC, home care company.
LP, health care system local pharmacy.
FE, fluids and electrolytes.
PA, commercially premixed ready-to-use parenteral nutrition admixture.
PAFE, commercially premixed ready-to-use parenteral nutrition admixture plus extra fluids and electrolytes.
CA, parenteral nutrition admixture customized (tailored) to the individual patient requirements.
CAFE, parenteral nutrition admixture customized (tailored) to the individual patient requirements plus extra fluids and electrolytes.

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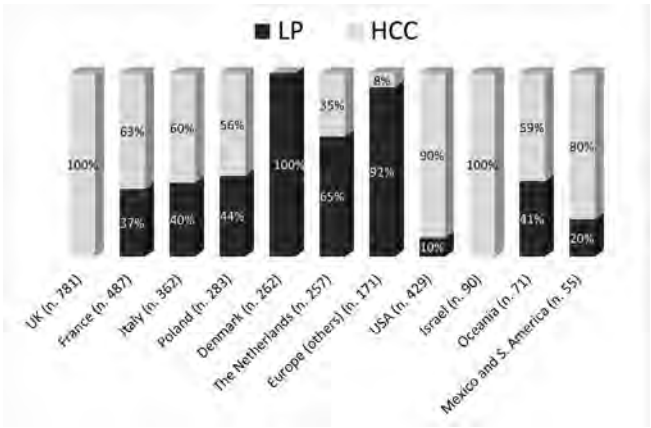

Fig. 1. Home parenteral nutrition (HPN)-providers by countries in patients with chronic intestinal failure. **LP,** health care system local pharmacy**. HCC,** home care company. ($P < 0.001$). **Europe others:** Belgium, Bulgaria, Croatia, Germany, Hungary, Lithuania, Slovenia, Spain, Sweden. **Oceania:** Australia, New Zealand. **S. America**: Argentina, Brazil.

potential limitation of the study is the relatively small number of malignant-CIF patients recruited, in comparison with those with benign-CIF (Table 1). Notably, the percentage of patients with malignant-CIF in this study was lower than that expected compared to previous published data [8–13]; this could be due to the voluntary basis of HPN center participation possibly attracting primarily those centers mainly caring for patients with benign-CIF. Indeed, it is possible that patients with malignant-CIF are primarily managed by oncologists or internists, outside established HPN or CIF centers. Another explanation could be that, in previous surveys on HPN prevalence, a significant percentage of patients with a diagnosis of cancer were not actually felt to have CIF, but had been placed on HPN because of refusal of an otherwise functioning enteral tract or simply because they already had a CVC positioned for chemotherapy. However, as expected, the benign-CIF and the malignant-CIF cohorts of the present study consistently differed in all their clinical and IVS characteristics, thus supporting that the malignant-CIF cohort is representative of those patients typically

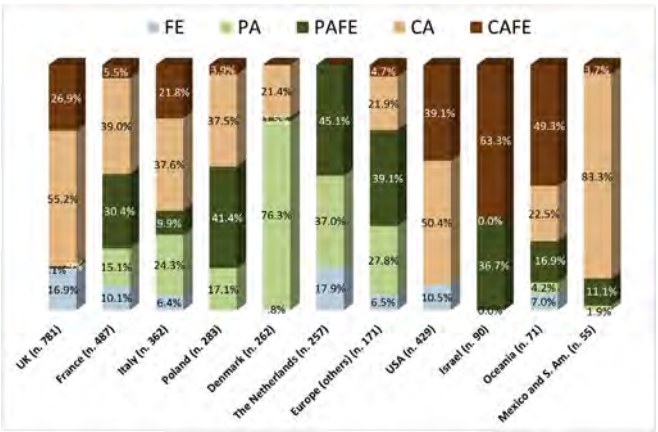

Fig. 2. Intravenous supplementation (IVS)-admixture type by countries in patients with chronic intestinal failure. **FE**, fluids and electrolytes; **PA**, commercially premixed ready-to-use parenteral nutrition admixture; **PAFE**, commercially premixed ready-to-use parenteral nutrition admixture plus extra fluids and electrolytes; **CA**, parenteral nutrition admixture customized (tailored) to the individual patient requirements; **CAFE**, parenteral nutrition admixture customized (tailored) to the individual patient requirements plus extra fluids and electrolytes ($P < 0.001$). **Europe others:** Belgium, Bulgaria, Croatia, Germany, Hungary, Lithuania, Slovenia, Spain, Sweden. **Oceania:** Australia, New Zealand. **S. Am.**: Argentina, Brazil.

with an obstructed intestinal tract needing high volume IVS-supplementation (Table 2).

Importantly, our data demonstrated an association between the prescribed IVS-admixture type and the modality of HPN-provision. Commercially PA or PAFE were more frequently used when the LP was the HPN-provider, while CA or CAFE were more frequently used when the HPN-provider was a HCC (Table 3). This would indicate that, when required, a HCC is readily able to provide an IVS-admixture tailored to the individual patient's needs. Indeed, as CIF is a rare condition, not all the LP may have developed the expertise and/or implemented the facilities to produce CA in a sufficient quantity to overcome the production costs.

The data confirm that the modality of HPN provision differ greatly among countries, with a range of 0–100% of cases for both HCC and LP (Fig. 1). The non-homogeneous provision modality within individual countries indicates that differences may exist also among individual HPN centers. The association between the modality of HPN provision and the IVS-admixture types reported in the total cohort was also observed within the individual countries (Fig. 2). The primary aims of an HPN program are prevention of HPN-related complications and maximization of the patient/family QoL [3]. The protocol for patient/caregiver training and the facilities and ancillaries for IVS management may be very relevant to the CVC-related complications and the availability of a portable infusion pump may significantly change the QoL of patients [3]. Differences between means of HPN provision may therefore have implications for the safety and efficacy of an HPN program. This suggests that criteria for the implementation of HPN provision should be formally devised in order to homogenize this feature of the HPN program and to give patients the same opportunity to receive appropriate HPN therapy regardless of where they live.

The results further demonstrated that the IVS-admixture type but not the HPN-provider differed between benign-CIF and malignant-CIF. The IVS-admixtures tailored to the patient requirements (CA and CAFE) were mainly used in benign-CIF, while premixed (ready-to-use) IVS-admixture (PA and PAFE) were mainly used in malignant-CIF (Fig. 3). This difference may be due to the characteristics of the two patient populations, in terms of pathophysiological mechanisms of IF as well as in the aims of the HPN program and the expected patient outcome. The clinical scenarios of benign-CIF and malignant-CIF are quite different. In malignant-CIF, the cause of IF was more homogeneous, being represented by mechanical obstruction in almost 50% of cases, often due to peritoneal carcinomatosis. In benign-CIF, the mechanisms of IF were represented by SBS and fistula in almost 70% of patients and the oral food and beverage intake and the intestinal fluid and electrolytes losses may greatly differ among patients, particularly those with benign disease, highlighting their need for tailored PN prescriptions [6]. Furthermore, patients with benign-CIF have a high survival probability and may have a high chance of intestinal rehabilitation, with most being independent of a caregiver or any home healthcare assistance [3]. Thus, patients with benign disease often require fine tuning of the HPN program and a tailored IVS-admixture in order to maximize the prevention of long-term metabolic complications as well as the daily time free of IVS infusion. In patients with malignant-CIF, HPN may be required while receiving cancer-directed treatment and/or receiving palliative care [4]. The expected duration of HPN is much shorter, either because of a transient need related to cancer treatment plans or to the short life expectancy of advanced cancer. These patients are often home-bound, dependent on a caregiver and require home healthcare assistance; hence rapid discharge from hospital with a pre-mixed formula is often clinically appropriate and in the patients' best interest. The lack of differences in HPN-provider between benign-CIF and malignant-CIF was probably due to the bias in the

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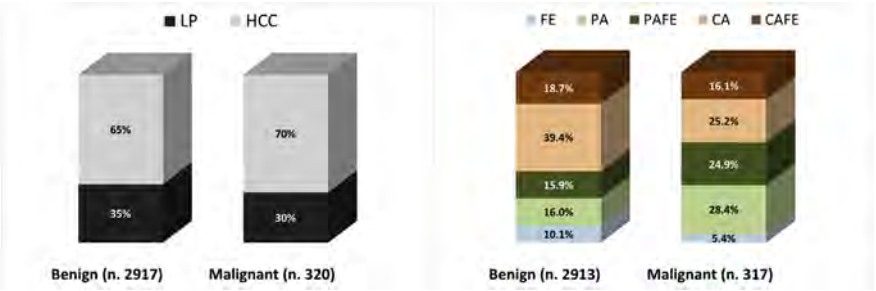

Fig. 3. Home parenteral nutrition (HPN)-provider (P = 0.083) and intravenous supplementation (IVS)-admixture type (P < 0.001) by nature of the underlying disease in patients with chronic intestinal failure. **HPN-provider**: **LP**, health care system local pharmacy. **HCC**, home care company. **IVS-admixture**: **FE**, fluids and electrolytes; **PA**, commercially premixed ready-to-use parenteral nutrition admixture; **PAFE**, commercially premixed ready-to-use parenteral nutrition admixture plus extra fluids and electrolytes; **CA**, parenteral nutrition admixture customized (tailored) to the individual patient requirements; **CAFE**, parenteral nutrition admixture customized (tailored) to the individual patient requirements plus extra fluids and electrolytes.

enrollment of the HPN centers that were mostly devoted to benign-CIF, such that the same HPN provider would be used for all patients under the center's care.

In conclusion, the modality of HPN provision and the IVS-admixture types differ greatly among countries, among HPN centers and between benign-CIF and malignant-CIF. As both HPN provider and IVS-admixture types may play a role in the safety and effectiveness of HPN therapy, criteria to homogenize HPN programs are needed, both within and between countries so that patients can have equal access to optimal CIF care.

Contributing coordinators and centers by country

Argentina

Adriana N. Crivelli, Hector Solar Muñiz; Hospital Universitario Fundacion Favaloro, Buenos Aires

Australia

Brooke R. Chapman; Austin Health, Melbourne

Lynn Jones; Royal Prince Alfred Hospital, Sydney

Margie O'Callaghan; Flinders Medical Centre, Adelaide

Emma Osland, Ruth Hodgson, Siobhan Wallin, Kay Lasenby; Royal Brisbane and Women's Hospital, Herston

Belgium

Andre Van Gossum: Hôpital Erasme, Brussels

Brazil

Andre Dong Won Lee; Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo

Bulgaria

Maryana Doitchinova-Simeonova; Bulgarian Executive Agency of Transplantation, Sofia

Croatia

Zeljko Krznaric; University Hospital Centre Zagreb, Zagreb

Denmark

Henrik Højgaard Rasmussen; Center for Nutrition and Bowel Disease, Aalborg University Hospital, Aalborg

Chrisoffer Brandt, Michael Staun; Rigshospitalet, Copenhagen

France

Cecile Chambrier; Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Lyon

Francisca Joly, Vanessa Boehm, Julie Bataille, Lore Billiauws; Beaujon Hospital, Clichy

Florian Poullenot; CHU de Bordeaux, Hôpital Haut-Lévêque, Pessac

Stéphane M. Schneider; CHU Archet, Nice

David Seguy; CHRU de Lille, Lille

Ronan Thibault; Nutrition unit, CHU Rennes, Nutrition Metabolisms and Cancer institute, NuMeCan, INRA, INSERM, Université Rennes, Rennes

Germany

Jann Arends; Tumor Biology Center, Freiburg

Hungary

Laszlo Czako, Tomas Molnar, Mihaly Zsilak-Urban; University of Szeged, Szeged

Ferenc Izbéki; Szent György Teaching Hospital of County Fejér, Székesfehérvár

Peter Sahin, Gábor Udvarhelyi; St. Imre Hospital, Budapest

Eszter Schafer; Magyar Honvedseg Egészségügyi Központ (MHEK), Budapest

Israel

Miriam Theilla; Rabin Medical Center, Petach Tikva

Italy

Anna Simona Sasdelli, Loris Pironi; St. Orsola University Hospital, Bologna

Umberto Aimasso, Merlo F. Dario; Città della Salute e della Scienza, Torino

Valentino Bertasi, Luisa Masconale; ULSS 22 Ospedale Orlandi, Bussolengo

Francesco W. Guglielmi, Nunzia Regano; San Nicola Pellegrino Hospital, Trani

Paolo Orlandoni; INRCA — IRCCS, Ancona

Maria C. Pagano, Santarpia Lidia, Lucia Alfonsi; Federico II University, Napoli, Italy

Corrado Spaggiari; AUSL di Parma, Parma

Marina Taus, Debora Busni; Ospedali Riuniti, Ancona

Lithuania

Gintautas Kekstas; Vilnius University Hospital Santariskiu Clinics, Vilnius

México

Aurora E. Serralde-Zúñiga; Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City

New Zealand

Lyn Gillanders; Auckland City Hospital, Auckland

Poland

Marek Kunecki; M. Pirogow Hospital, Lodz

Przemysław Matras; Medical University of Lublin, Lublin

Konrad Matysiak; H.Święcicki University Hospital, Poznań

Kinga Szczepanek; Stanley Dudrick's Memorial Hospital, Skawina

Anna Zmarzly; J. Gromkowski City Hospital, Wroclaw

Slovenia

Nada Rotovnik Kozjek; Institute of Oncology, Ljubljana

Spain

Marta Bueno; Hospital Universitario Arnau de Vilanova, Lleida

Cristina Cuerda; Hospital General Universitario Gregorio Marañon, Madrid

Carmen Garde; Hospital Universitario Donostia, San Sebastian

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Nuria M. Virgili; Hospital Universitari de Bellvitge, Barcelona

Gabriel Olveira; IBIMA, Hospital Regional Universitario de Málaga, Universidad de Málaga, Málaga

Mª Estrella Petrina Jáuregui; Complejo Hospitalario de Navarra, Pamplona

Alejandro Sanz-Paris; Miguel Servet Hospital, Zaragoza

José P. Suárez-Llanos; Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife

Ana Zugasti Murillo; Hospital Virgen del Camino, Pamplona

Sweden

Lars Ellegard; Sahlgrenska University Hospital, Gothenburg

The Netherlands

Mireille Serlie, Cora Jonker; Academic Medical Center, Amsterdam

Geert Wanten; Radboud University Medical Center, Nijmegen

United Kingdom

Sheldon C. Cooper; University Hospitals Birmingham NHS Foundation Trust, Birmingham

Joanne Daniels; Nottingham University Hospital NHS Trust, Nottingham

Simona Di Caro, Niamh Keane, Pinal Patel; University College Hospital, London

Alastair Forbes; Norfolk and Norwich University Hospital, Norwich

Sarah-Jane Hughes; Regional Intestinal Failure Service, Belfast Health and Social Care Trust, Northern IrelandAmelia Jukes, Rachel Lloyd; University Hospital of Wales, Cardiff

Simon Lal, Arun Abraham, Gerda Garside, Michael Taylor; Salford Royal NHS Foundation Trust, Salford

Jian Wu, Trevor Smith, Charlotte Pither, Michael Stroud; University Hospital Southampton NHS Foundation Trust, Southampton

Nicola Wyer, Reena Parmar, Nicola Burch; University Hospital, Coventry

Sarah Zeraschi; Leeds Teaching Hospitals NHS Trust, Leeds

United States of America

Charlene Compher; Hospital of the University of Pennsylvania, Philadelphia, PA

Darlene Kelly; Mayo Clinic College of Medicine, Rochester, MN

Denise Jezerski, Ezra Steiger; Cleveland Clinic Foundation, Cleveland, OH

Statistical analysis performed by: Dr. Marianna Mastroroberto, MD, PhD; Department of Medical and Surgical Sciences, University of Bologna, Italy.

Statement of authorship

LP devised the study protocol, collected the data, analyzed the results and drafted the manuscript. The Home Artificial Nutrition & Chronic Intestinal Failure Special Interest Group of ESPEN discussed and approved the protocol study, discussed the results and reviewed the manuscript before submission. According to the authorship rules described in the protocol study, all the co-ordinators of the participating centers were considered coauthors of the study and received the manuscript upon submission. All authors approved the final version of the manuscript before submission.

Conflicts of interest

None declared.

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