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ESPEN Guideline

ESPEN guideline on home parenteral nutrition

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SUMMARY

This guideline will inform physicians, nurses, dieticians, pharmacists, caregivers and other home parenteral nutrition (HPN) providers, as well as healthcare administrators and policy makers, about appropriate and safe HPN provision. This guideline will also inform patients requiring HPN. The guideline is based on previous published guidelines and provides an update of current evidence and expert opinion; it consists of 71 recommendations that address the indications for HPN, central venous access device (CVAD) and infusion pump, infusion line and CVAD site care, nutritional admixtures, program monitoring and management. Meta-analyses, systematic reviews and single clinical trials based on clinical questions were searched according to the PICO format. The evidence was evaluated and used to develop clinical recommendations implementing Scottish Intercollegiate Guidelines Network methodology. The guideline was commissioned and financially supported by ESPEN and members of the guideline group were selected by ESPEN.

1. Introduction

Parenteral nutrition (PN) is a type of medical nutrition therapy provided through the intravenous administration of nutrients such as amino acids, glucose, lipids, electrolytes, vitamins and trace elements [1]. It is categorized as total (or exclusive) PN, where it meets the patient's nutritional needs in entirety, and as supplemental (partial or complementary) PN, where nutrition is also provided via the oral or enteral route [1]. PN can be administered either in, or outside, the hospital setting; the latter defined as home parenteral nutrition (HPN) [1].

HPN is the primary life-saving therapy for patients with chronic intestinal failure (CIF) due to either benign (absence of malignant disease) or malignant diseases [2–4]. HPN may also be provided as palliative nutrition to patients in late phases of end-stage diseases [1]. As HPN is sometimes used to prevent or treat malnutrition in patients with a functioning intestine, who decline medical nutrition via the oral/enteral route, HPN and CIF cannot be considered synonymous [2]. Thus, on the basis of underlying gastrointestinal function and disease, in tandem with patient characteristics, four clinical scenarios for the use of HPN can be

Abbreviations: AIO, all-in-one parenteral nutrition admixture; CDC, Centers for Disease Control and Prevention; CIF, chronic intestinal failure; CRBSI, catheter-related bloodstream infection; CVAD, central venous access device; CVC, central venous catheter; EN, enteral nutrition; HPN, home parenteral nutrition; IF, intestinal failure; NST, nutrition support team; PICC, peripherally inserted central venous catheter; PN, parenteral nutrition; QoL, quality of life; RCT, randomized controlled trial.

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identified [2–4]: HPN as primary life-saving therapy for a patient with CIF due to benign disease; HPN for CIF due to malignant diseases, often transiently occurring during curative treatments; HPN included in a program of palliative care for incurable malignant disease, to avoid death from malnutrition; HPN used to prevent or treat malnutrition in patients with a functioning intestine, who decline other types of medical nutrition ('no-CIF scenario'). The goal and characteristics of the HPN program, as well as the specific needs of the patient, may differ among the four clinical scenarios (Table 1).

The first European Society for Clinical Nutrition and Metabolism (ESPEN) guideline on HPN was published in 2009 [3]. It consisted of 26 recommendations, 10 were based on some evidence (grade B recommendations) but 16 were mostly based on expert opinion ('grade C recommendations') [3]. In 2016, ESPEN guidelines for CIF due to benign disease was published, including 11 recommendations on HPN management, 17 on PN formulation and 22 on the prevention and treatment of central venous catheter (CVC)-related complications [4]. The grade of evidence was very low for 31 recommendations, low for 14, moderate for 3 and high for 2, whereas the strength of the recommendations was weak for 18 and strong for 32 [4]. Most of the recommendations from both guidelines are still valid, particularly those covering nutritional requirements, metabolic complications and central venous access device (CVAD) management. Other guidelines and standards for HPN have also been provided by scientific societies and government bodies [5–15]; however, a systematic review revealed substantial differences among the recommendations published [10]. Furthermore, the management and provision of HPN differs among countries and among HPN centers within countries [16,17], although HPN provision by different programs should be homogeneous in order to ensure equity of patient access to an appropriate and safe HPN service.

Thus, an updated version of ESPEN guidelines on HPN care was commissioned in order to incorporate new evidence since the publication of the previous ESPEN guidelines, as well as to highlight recommendations on safe HPN administration and also to include the patient's perspective.

1.1. Aim

The aim of the present guideline is to provide recommendations for the appropriate and safe provision of HPN. This guideline does not include recommendations for the patient's nutrient requirements in specific conditions, for which the reader can refer to previous ESPEN guidelines [3,4,15].

2. Methods

The present guideline was developed according to the standard operating procedure for ESPEN guidelines [18]. It is an update of previous guidelines [3–15]. The guideline was developed by an expert group from seven European countries, representing different professions including eight physicians (LP, FB, FJ, SK, SL, AVG, GW, SCB), a pharmacist (SM), a nurse (KB) and two patient representatives (ML, CW).

2.1. Methodology of guideline development

Based on the standard operating procedures for ESPEN guidelines and consensus papers, the first step of the guideline development was the formulation of so-called PICO questions, which address specific **p**atient groups or **p**roblems, **i**nterventions, **c**ompares different therapies and are **o**utcome-related [18]. In total, 17 PICO questions were created and were split into six main chapters, "indications for HPN", "CVAD and infusion pump", "infusion line and CVAD site care", "nutritional admixtures", "program monitoring" and "management".

The PICO questions for the different topics were allocated to subgroups/experts who reviewed the previous guidelines and standards [3–15] and performed a literature search to identify suitable meta-analyses, systematic reviews and primary studies (for details see "search strategy" below). A total of 71 recommendations were formulated to answer the PICO questions. The grading system of the Scottish Intercollegiate Guidelines Network (SIGN) was used to grade the literature [19]. Allocation of studies to the different levels of evidence is shown in Table 2. The working group

Table 1
Aims of the HPN program, intravenous supplementation and patient care requirements, categorized according to the clinical scenarios based on the underlying clinical condition.

HPN program and patient care requirement	Benign CIF scenario	Malignant scenarios	No CIF scenario
Aim (additional to avoiding death from malnutrition)	Social, employment & familial rehabilitation; improved quality of life; intestinal rehabilitation	• Treatment of CIF due to ongoing oncological therapy or to gastrointestinal obstruction • Palliative care	Alternative to other potentially effective modalities of nutritional support (e.g. enteral) refused by the patient.
Expected duration	Temporary or permanent (life-long)	Mostly temporary: • Short <6 months • Long: >6 months	Temporary or permanent
Intravenous supplementation requirements	Supplemental or total; high fluid volume and electrolyte contents often required	CIF: mostly supplemental, but can be total; mostly normal volume (high volume may be required in GI obstruction) Palliative: mostly total; normal/low volume	Mostly supplemental with normal volume
Type of PN admixture more frequently required	"Tailored" or "customized" (compounded), requiring refrigeration	"Premade" or "premixed" (ready-to-use)	"Premade" or "premixed" (ready-to-use)
Patient mobility and dependency on caregiver	Mostly ambulatory and independent (depending on age and co-morbidity). Travelling for work and holidays often required	CIF: ambulatory or housebound, mostly dependent Palliative: housebound, from bed to chair, dependent	Ambulatory, or housebound (neurological disorders), sometimes dependent
Patient homecare nurse assistance requirement	Rare; depending on age and co-morbidity	Frequent	Sometimes

CIF, chronic intestinal failure; HPN, home parenteral nutrition; PN, parenteral nutrition.

Table 2
Levels of evidence.

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

According to the Scottish Intercollegiate Guidelines Network (SIGN) grading system. Source: SIGN 50: A guideline developer's handbook. Quick reference guide October 2014 [19].

added commentaries to the recommendations detailing the basis of the recommendations made.

Recommendations were graded according to the levels of evidence available [20] (see Table 3). In some cases, a downgrading was necessary, for example, due to the lack of quality of primary studies included in a meta-analysis. The wording of the recommendations reflects the grades of recommendations; level A is indicated by "shall", level B by "should" and level 0 by "can/may". A good practice point (GPP) is based on experts' opinions due to the lack of studies; in this situation, the choice of wording was not restricted.

Between February 21st and March 25th 2019, online voting on the recommendations was undertaken using the "guideline-services.com" platform. All ESPEN members were invited to agree or disagree with, and to comment upon, each of the original 72 recommendations and 7 statements generated by the guideline committee. A first draft of the guidelines was also made available to participants at the same time. 61 recommendations and 5 statements reached an agreement of >90%, 10 recommendations reached an agreement of >75–90% and 2 statements reached an agreement of ≤75%. Those recommendations/statements with an agreement >90% (i.e. those with a strong consensus) were directly passed, while all others were revised according to the comments made and then voted on again during a consensus conference which took place in Frankfurt on April 29th 2019. Apart from one, all recommendations received an agreement of >90%. Two former statements were transformed into recommendations, both with >90% agreement. Three of the original recommendations were deleted. Thus, the final guidelines comprise of 71 recommendations and 5 statements (Table 4). To support the recommendations, the ESPEN guideline office created evidence tables of relevant meta-analyses, systematic reviews and (R)CTs, all of which are available online as supplemental material to these guidelines.

2.2. Search strategy

The literature search was performed separately for each PICO question in March 2018. Pubmed, Embase and Cochrane databases were searched using the filters "human", "adult" and "English". Table 5 shows the search terms used for the PICO questions. The results were pre-screened based on the abstracts of articles. In addition to the above databases, websites from nutritional (nursing) societies in English speaking or bilingual countries including the English language were searched for practice guidelines.

1. Indications for HPN

1. What are the indications for HPN?

Recommendation 1

HPN should be administered to those patients unable to meet their nutritional requirements via the oral and/or enteral route and who can be safely managed outside of the hospital.

Grade of Recommendation: GPP – Strong consensus (95.8% agreement)

Commentary

Several guidelines and standards on HPN have been published [3–15]. PN is a life-saving therapy to those unable to meet their nutritional requirements by oral/enteral intake. Clearly, no randomized controlled trial (RCT) can be conducted to compare HPN with placebo to confirm the life-saving efficacy of HPN therapy in this condition [3]. Furthermore, no absolute contraindications exist to the use of PN. However, the presence of organ failures and metabolic diseases, such as heart failure, renal failure, type 1 diabetes, may be associated with reduced tolerance to PN and may require careful and specific adaptations of the HPN program to meet the patient's specific clinical needs.

Six guidelines and one expert opinion-based standard on HPN in this setting were compared in a systematic review [10]. Although the guidelines generally covered the same topics, substantial differences were observed among the recommendations. Most did not provide information on intravenous medication, metabolic bone disease and indications in patients with malignant disease. Moreover, grading discrepancies among various guidelines were found, as identical recommendations were often labeled with different grades. Thus, the present guideline updates the recommendations from previous guidelines and standards relating to the appropriateness and safety of HPN. Nutritional requirements in specific clinical conditions, as well as the diagnosis and treatment of CVAD and metabolic complications are not addressed in the present guideline. Recommendations in previous ESPEN guidelines about the latter topics are still valid [3,4].

Table 3
Grades of recommendation [18].

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population; or A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
0	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2++ or 2+
GPP	Good practice points/expert consensus: Recommended best practice based on the clinical experience of the guideline development group

Table 4
Classification of the strength of consensus, according to the AWMF [20] methodology and results of the online and consensus conference voting.

		Online Voting	Consensus Conference
Strong consensus	Agreement of >90% of participants	61 R + 5 S	10 R
Consensus	Agreement of >75–90% of participants	10 R	1 R
Majority agreement	Agreement of >50–75% of participants	2 S[a]	–
No consensus	Agreement of <50% of participants	–	–
Deleted		–	3 R[b]

R = Recommendation; S = Statement.
[a] These two statements were converted into recommendations.
[b] Two recommendations were deleted during the revision after the online voting, one recommendation was deleted during the consensus conference.

Table 5
Search strategy.

PICO question	Search terms used in combination with “home parenteral nutrition”, “human” and “adult”
1. What are the indications for HPN?	“guidelines"
2. What are the criteria for an effective HPN program?	“registries"
3. What are the criteria for a safe HPN program?	“indications"
	“malignant” OR “cancer",
	“ program"
	“organization and administration OR management"
	“multidisciplinary” AND “team"
4. Which venous access device should be chosen	“central venous catheter” OR “central venous access device"
5. Which infusion control devices should be used for HPN?	“peripherally AND inserted AND central AND catheters"
	“infusion pumps"
6. Which should be the appropriate infusion line management?	“central venous catheter related infection"
	“catheter-associated infection OR contamination OR sepsis OR complications OR occlusion"
	“catheter dressing OR ointment OR lock"
	“catheter hub"
	“skin antisepsis"
	“aseptic technique"
	“catheter exit site”
	“hand decontamination"
	“swimming OR bathing OR showering"
	“sutureless device"
	“catheter securement"
	“administration set OR intravenous tubing"
	“gloves"
	“needleless connector OR device"
	“antiseptic barrier cap"
	“port needle"
	“pre-filled syringes"
	“taurolidine"
7. Which nutritional admixture bag should be chosen	“admixture"
8. What are the critical steps during the preparation of PN admixtures?	“premade OR premixed OR multichambered OR ready to use OR “all in one"
9. How should PN admixture be delivered?	“compounded OR customized"
10. What should be the HPN admixture time and rate of infusion?	“stability"
	“delivery"
	“infusion”
	“rate"
	“blood glucose"
	“glycaemia"
11. How should patients on HPN be monitored?	“monitoring"
	“follow-up"
	“tolerance"
	“complications"
	“quality of care"
12. Which are the local and personnel preconditions for HPN ?	“intestinal failure"
13. Which are the requirements for the hospital centers that care for HPN patients?	“central venous catheter complications"
14. Which are the requirements for the nutritional support team?	“program"
15. How should emergencies be managed?	“organization and administration OR management"
16. How should travelling with HPN be organized?	“multidisciplinary AND team"
17. Which criteria should be used to monitor the safety of HPN program provision?	“emergency"
	“admission"
	“central venous catheters complications"
	“travel OR travelling"
	“quality of health care"
	“quality of care"

2. What are the criteria for effective HPN program ?

Recommendation 2

HPN should be prescribed as the primary and life-saving therapy for patients with transient-reversible or permanent-irreversible CIF due to non-malignant disease

Grade of Recommendation B – Strong consensus (94.7% agreement)

Commentary

CIF has been defined as a chronic "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", in metabolically stable patients [2]. CIF can be due to either benign or malignant disease and may be reversible or irreversible [2].

The underlying diseases and the mechanisms of CIF due to benign disease in adults have been described in a recent international ESPEN survey [21]. Crohn's disease, mesenteric ischemia, surgical complications, chronic intestinal pseudo-obstruction and radiation enteritis were the main underlying diseases, accounting for around 75% of cases. Short bowel syndrome was the main mechanism (around two-thirds of cases), while the remaining 33% of cases were due to intestinal dysmotility, enterocutaneous fistulas, intestinal mechanical obstruction and extensive mucosal diseases [21].

HPN is the primary and life-saving therapy for CIF [4]. The outcome of patients on HPN for CIF due to benign disease has been reported in many single and multicenter retrospective studies [22–28] and by an ESPEN prospective five year follow up [29–31]. These studies demonstrated that: weaning from HPN after one to two years of starting may occur in 20%–50% of patients; the five year survival probability on HPN ranges from 70 to 80% depending on the underlying disease; CIF may be associated with life-threatening complications of either the underlying disease or HPN, the latter accounting for around 14% of total deaths (such as CVAD-related complications and intestinal failure associated liver disease); the outcome of patients in terms of reversibility, treatment-related morbidity and mortality, and survival probability is strongly dependent on care and support from an expert multidisciplinary nutrition support team (NST).

In Europe, the prevalence of HPN for CIF due to benign disease has been estimated to range from five to 20 cases per million population [22], with the exception of Denmark, where 80 cases per million have been recently reported [26].

Recommendation 3

HPN can be considered for patients with CIF due to malignant disease

Grade of Recommendation 0 – Strong consensus (95.8% agreement)

Recommendation 4

HPN should be prescribed to prevent an earlier death from malnutrition in advanced cancer patients with CIF, if their life expectancy related to the cancer is expected to be longer than one to three months, even in those not undergoing active oncological treatment.

Grade of Recommendation B - Consensus (90% agreement)

Commentary

A mean survival of around 48 days has been reported in patients with malignant obstruction receiving palliative care without artificial nutritional support [32]. International guidelines [15,33–35] generally advocate the use of PN in patients with malignancy who have failed oral and enteral nutrition (EN) and who have an expected survival longer than one to three months, which is the longest predictable survival in an individual unable to maintain adequate oral nutrition without artificial nutritional support.

A meta-analysis by Naghibi et al. [36] reported that 45% of incurable cancer patients receiving HPN for malignant intestinal obstruction can survive more than three months. The median and mean survival length was found to be 83 days and 116 days, respectively (55% mortality at three months and 76% mortality at six months, respectively) [36]. These data are in keeping with those of a large prospective multinational case series of 414 patients on HPN, 67% of whom had intestinal obstruction, (median survival 91 days, 50% mortality three months and 77% mortality at six months) [37].

The clinical challenge is to accurately identify those patients who are likely to survive long enough to benefit from HPN treatment. Recently, a nomogram has been developed from variables recognized as independent prognostic factors (Glasgow prognostic score, presence and site of metastases and Karnofsky performance status), aimed at estimating the 3-, 6-months and overall survival of incurable aphagic cachectic cancer patients considered for HPN [38].

It is noteworthy that the authors of a recent Cochrane review [39] concluded that they were very uncertain whether total HPN improves length of life in people with malignant bowel obstruction, largely as a result of the lack of published evidence. However, the authors reached these conclusions after applying strict Cochrane methodology (allocation concealment, comparability of treatment groups, blinding of participant and personnel) when reviewing the literature; this approach may be appropriate for evaluating medication efficacy, but may be less applicable to assessing the role of essential nutrition [40].

Six prospective studies [41–46] on HPN-dependent patients for $\geq$ 1 month showed a benefit on health related quality of life (QoL) measured by validated tools (EORTC QLQ-C30 or FACT-G, or TIQ). There are three RCT evaluating the impact of HPN in patients outcome [47–49], with the largest [48,49] reporting an improvement in energy balance and, as-treated analysis, prolonged survival, increased body fat and a greater maximum exercise capacity. The most recent RCT [50] comparing the effects of 6-month HPN to 'best nutritional care' in cachectic gastrointestinal cancer patients reported that HPN maintained or increased fat-free mass and improved QoL. It is noteworthy that a group of experts has identified QoL as one of the most important outcome indicators of HPN in cancer patients [51].

Specific contraindications for HPN support in cancer patients include [33]:

a) patients who are not adequately informed about the aims of HPN, of its limited benefits and potential complications
b) patients who are not informed of their predicted prognosis, or of the possibility of changing/withdrawing the treatment when it becomes futile
c) patients who are not sufficiently metabolically stable to be discharged home on PN

Recommendation 5

HPN can be considered for patients without intestinal failure who are not able or do not want to meet their nutritional requirements via the oral/enteral route. The patient should be clearly informed about HPN benefits and risks.

Grade of Recommendation GPP – Consensus (89.5% agreement)

Commentary

HPN surveys and registries report a percentage of cases who were not categorized as having either benign or malignant intestinal failure (Table 6) [52–57]. These may include patients needing artificial nutritional support who refused - or were not able to cope with - otherwise effective and clinically-recommended EN [58].

Table 6
Indications for HPN in adult patients in different countries according to data from national registries and surveys.

National report, year (ref #)	Total Patients (n.)	Benign GI disease (%)	Cancer on treatment (%)	Cancer-palliative (%)	Others (%)
SPAIN (SENPE Registry), 2016 [52]	256	44	10	25	Not specified, 21
US (ASPEN Registry), 2011–2014 [53]	1064	89	3	0.5	Malnutrition, 4.5 Neurological swallowing disorder, 0.1 Not specified, 2.9
UK (BANS report) 2015 [54]	1144	81.5	18.5		Indications for HPN in the total cohort: - Short bowel, 47 - Fistula, 8 - Malabsorption, 20 - GI obstruction, 10 - DR-Malnutrition, 6% - Swallowing Disorder. or Anorexia, 1 - Others, 8
ITALY (SINPE survey), 2012 [55,56]	46.1 (/10^6 inhabitants)	20	61		Neurological disease, 12% Not specified, 7
CANADA (CNS Registry), 2011–2014 [57]	187	66	34		

GI, gastrointestinal; DR, disease-related.

Such patients may have cancer and an indwelling CVAD for chemotherapy; alternatively, they may have dysphagia and elect not to have EN [59–61]. Since it is difficult to deny nutritional support in clinical practice, HPN can sometimes be prescribed in these settings. Patients without CIF who are not able or do not want to meet their nutritional requirements via the oral/enteral route should be fully informed about the risks of PN therapy, which will likely be higher (including life-threatening risks related to HPN) than EN in this setting [3,4,58].

3. What are the criteria for a safe HPN program?

Statement 1

For a safe HPN program, the patient and/or the patient's legal representative have to give fully informed consent to the treatment proposed.

Strong consensus (95.7% agreement)

Statement 2

For a safe HPN program, the patient has to be sufficiently metabolically stable outside the acute hospital setting.

Strong consensus (91.3% agreement)

Statement 3

For a safe HPN program, the patients home environment has to be adequate to safely deliver the therapy proposed.

Strong consensus (95.7% agreement)

Statement 4

For a safe HPN program, the patient and/or the caregiver has to be able to understand and perform the required procedures for the safe administration of therapy.

Strong consensus (95.7% agreement)

Recommendation 6

The patient and/or the caregiver should be trained by a NST to safely infuse the PN with appropriate monitoring and prompt recognition of any complications.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 7

The prescribed nutritional admixture and ancillaries required for safe and effective therapy should be delivered by an experienced/certified health care provider.

Grade of Recommendation GPP – Strong consensus (95.7% agreement)

Recommendation 8

The NST should provide appropriate monitoring and treatment for routine and/or emergency care, with appropriate contact details provided to the patient 24 h per day, seven days per week.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

HPN is a complex, life-saving therapy that may result in serious harm if not properly prescribed, prepared and administered. The aims of an HPN program include provision of evidence-based therapy, prevention of HPN-related complications such as catheter-related bloodstream infection (CRBSI) and metabolic complications, as well as ensuring QoL is maximized [3,4]. The HPN program shall provide an individualized, safe, effective and appropriate nutrition support plan at discharge from hospital which should then be supervised and evaluated on a regular basis in the community [62,63].

Previous guidelines and standards recommend that prescription, implementation and monitoring of an individualized HPN program shall be managed by a NST in centers with HPN management expertise [3,10,51,64–74]. Patients managed by such a dedicated patient-centered NST have better outcomes and possible lower overall costs of care [22,64].

The overall care plan includes a variety of pre-discharge and post-hospital care assessments that require coordination between several heath-professionals and care providers within and outside the hospital (Table 7). In addition, besides involvement of the key-members of a NST (physician, dietician, nurse, pharmacist), specific patients will require input from physiotherapy, psychology and occupational therapy colleagues [3,67–70]. Communication with the caregivers at home (especially the home care nurse) and in the hospital seems to be a key-factor for patients [62,70]. An experienced and certified health care provider is also required for the appropriate delivery of nutritional admixture and ancillaries to patient's home. The 'adequate' metabolic and clinical stability of a patient can be assessed by vital parameters, energy, protein, fluid and electrolyte balances and glycemic control; here, the term adequate means no immediate risk of acute imbalance after hospital discharge.

If the patient can achieve a stable HPN regimen and his/her overall clinical condition is acceptable, an education program for patients and/or caregivers should be initiated to teach correct and proper HPN care.

The home care environment should be assessed before the education program starts.

Table 7
Items to be included in the assessment at patient discharged on HPN [63,74].

- Medical, physical, psychological and emotional suitability/stability of the patient
- Stability of the PN regimen (dosage and admixture)
- Level of home care and support required
- Lifestyle/activities of daily living
- Rehabilitative potential
- Potential for QoL improvement
- Potential for learning self-management of HPN (patient/caregivers)
- Knowledge and experience of the home nursing team (if no self-management)
- Basic home safety, facilities and general cleanliness instruction
- Need for extra equipment (e. g. backpack, infusion pump, hospital bed, extra drip stand)
- Home care provider of nutritional admixture, equipment and ancillaries
- Reimbursement for bags, services and supplies
- Around the clock (on-call) availability of an experienced home care provider
- Post-discharge monitoring necessities/possibilities (including scheduled laboratory tests)
- Medication prescription with administration details

2. CVAD and infusion pump

4. Which CVAD should be chosen?

Recommendation 9

The choice of CVAD and the location of the exit site shall be made by an experienced HPN NST, as well as by the patient.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 10

The exit site of the CVAD should be easily visualized and accessible for self-caring patients.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 11

Tunneled CVAD or totally implanted CVADs shall be used for long-term HPN.

Grade of Recommendation GPP – Strong consensus (90.9% agreement)

Recommendation 12

Access to the upper vena cava should be the first choice for CVAD placement, via the internal jugular vein or subclavian vein.

Grade of Recommendation B – Strong consensus (100% agreement)

Recommendation 13

Right-sided access should be preferred to the left-sided approach to reduce the risk of thrombosis.

Grade of Recommendation B – Strong consensus (95.2% agreement)

Recommendation 14

The tip of the CVAD should be placed at the level of the right atrial-superior vena cava junction.

Grade of Recommendation B – Strong consensus (100% agreement)

Commentary

The literature search did not add any new information relating to this question when compared to the previous ESPEN guideline for CIF in adults [4]. The process of choosing a CVAD for HPN must involve the patient and the NST, including the specific professional (e.g. anaesthetist, radiologist or surgeon) responsible for placing the CVAD [76,77]. The patient should be involved in choosing the location of the cutaneous exit site which should, or course, also facilitate optimal self-care [78]. Proximity to wounds, prior exit sites, tracheotomies, stomas or fistulae should be avoided. Tunneled CVAD (such as Hickman, Broviac or Groshong) or totally implantable devices (port) are usually chosen for long-term HPN (>6 months) [3]. A single lumen CVAD is preferred, as infections have been reported to occur more frequently with multiple lumen CVAD [73,79,80].

The risk of venous thrombosis is reduced with right vs. left-sided CVAD insertion [81] and, regardless of the type of catheter used and the insertion side, when the CVAD tip is located at the superior vena cava-right atrium junction [81–83].

Recommendation 15

Peripherally inserted central venous catheters (PICCs) can be used if the duration of HPN is estimated to be less than six months.

Grade of Recommendation 0 – Strong consensus (100% agreement)

Commentary

ESPEN and ASPEN guidelines [4,84] for CIF do not recommend PICCs for long-term HPN. However many series have reported successful use of PICCS for up to four years [53,57,85–92].

The concern of long term PICC use relates to the putative risk of catheter-related vein thrombosis and CRBSI compared to tunneled CVADs. A study comparing PICCs with other CVADs in long-term HPN found no difference in the CRBSI rate, a higher frequency of catheter removal because of venous-thrombosis and a shorter time between catheter insertion and the first complication in the PICC cohort [89]. A meta-analysis of comparative studies showed a lower rate of CRBSI in HPN patients using PICCs; however, no difference between PICC and tunneled CVADs was observed when the single-arm studies were analyzed [93].

In summary:

a) better description of the reasons for placement and outcomes of long-term PICC use in routine clinical practice is required
b) PICCs seem to be associated with a lower risk of CRBSI and a possible higher risk of catheter-related venous thrombosis;
c) the time to the occurrence of the first catheter-related complication seems to be shorter with PICCs.

5. Which infusion control devices should be used for HPN?

Recommendation 16

HPN should be administered using an infusion pump for safety and efficacy reasons.

Grade of Recommendation GPP – Strong consensus (91.3% agreement)

Recommendation 17

In exceptional circumstances a flow regulator can be temporarily used for HPN; administration sets with only a roller clamp should not be used.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

The introduction of infusion pumps has been one of the major technologic advances for the safe administration of PN [94]. An

infusion pump is a medical device that delivers fluids, such as nutrients and medications, into a patient's body in controlled amounts [95]. The use of an electronic (ambulatory) infusion pump with compatible delivery sets is considered as good practice [6,96,97]. Because of the (large) fluid volume, the hypertonicity of the PN admixture and the amount of glucose and potassium delivered, rapid administration or 'free flow' can potentially cause serious harm [97].

It is therefore strongly recommended to use this device whenever possible to manage and monitor the delivery of HPN [3,4,6,13,51,98]. The characteristics of a safe and effective infusion pump for HPN are described in Table 8.

Recommendation 18

A portable pump can improve the patient's QoL when compared to stationary pumps.

Grade of Recommendation 0 − Strong consensus (95.7% agreement)

Commentary

Two studies on the use of portable infusion pumps found that the ambulatory pump enabled HPN patients to gain independence [99,100]. Benefits included maintaining desired flow, low noise, long battery life as well as increased probability of social and working rehabilitation and of good QoL. If an ambulatory pump is not available (or appropriate because of the patient's condition), a standard volumetric pump with an intravenous stand is an alternative [4].

3. Infusion line and catheter site care

6. Which should be the appropriate infusion line management?

Recommendation 19

Either a sterile gauze or sterile, transparent, semipermeable dressing should be used to cover the CVAD exit site.

Grade of Recommendation B − Strong consensus (90.9% agreement)

Recommendation 20

When transparent dressings are used on tunneled or implanted CVAD exit sites, they can be replaced no more than once per week (unless the dressing is soiled or loose).

Grade of Recommendation 0 − Strong consensus (95.5% agreement)

Recommendation 21

A tunneled and cuffed CVAD with a well healed exit site might not require dressing to prevent dislodgement. Grade of Recommendation GPP confirmed − Strong consensus (100% agreement)

Commentary

The purpose of a dressing is to secure the CVAD, as well as providing barrier protection from microbial colonization and infection. Different kinds of dressings can be used for protecting the CVAD site, including (semi-permeable) transparent polyurethane dressings and gauze and tape. Transparent dressings permit continuous visual inspection of the CVAD site and require less frequent changes unless the dressing becomes damp, loose, or visibly soiled. If there is visible pus exuding from the exit or the site is bleeding, it is better to use a gauze dressing (may be replaced every two days or sooner) until the problem is resolved [73].

A recent systematic review included eight studies with patients in adult bone marrow transplantation (n = 101), hemodialysis (n = 138), gastroenterological (n = 72), adult ICU (n = 21), pediatric and adult oncology units (n = 98) and general wards (n = 76) and reported that there was no clear difference between gauze and tape and polyurethane dressings on the incidence of CRBSI. All included studies had a high risk of performance bias and were of low quality evidence [101]. A previous systematic review came to the same conclusion but the quality of the included studies was also low with small sample sizes and underpowered studies comparing different types of dressings [102]. Finally, in an older systematic review, the use of transparent dressings on CVAD was significantly associated with an elevated relative risk of catheter tip infection (RR = 1.78; 95% CI, 1.38 to 2.30) compared with gauze dressings [103].

The frequency of dressing change also remains a question of some debate. In a multicenter study, 399 bone marrow transplant patients with a tunneled CVAD (n = 230) were randomly allocated to receive CVAD polyurethane dressing changes at different time intervals (Group 1: every two or five days, Group 2: every five or ten days). There was no difference in the rate of local infection but more skin toxicity was reported in the group with shorter interval dressing changes [104]. Nevertheless, a recent systematic review concluded that there is currently inconclusive evidence as to whether longer intervals between CVAD dressing changes are associated with more or less CVAD-related infections [105].

After the healing period (+/− 3 weeks), it remains unclear if a dressing is necessary [73]. The recent ESPGHAN/ESPEN/ESPR/CSPEN guideline for pediatric parenteral nutrition access states that a tunneled CVAD with a well-healed exit site does not require dressing to prevent dislodgement (GPP); however, in children it is useful to have CVADs looped and covered [106].

Table 8
Necessary features for an HPN infusion pump [4,6,95,97].

- Easy to clean (splash-proof)
- Operating silently
- User friendly interface (display/keyboard)
- Portability: it should maximize patient's mobility (e.g. possibility to carry it in a backpack together with the PN-bag)
- Availability of a variety of pump-compatible sets with different line lengths
- Rechargeable battery pack(s) with several hours operating time
- Safety features:
  - audible and visual alarms
  - self-test at power-up
  - upstream and downstream occlusion alarms
  - anti-free flow control
- Easy to use instructions
  - Safe operation
  - Alarm silencing, modification, disabling
  - Programmable mode options that include ramp-up/ramp-down and continuous infusion modes
  - Option to "lock out" those infusion modes not required and control the panel lock to prevent accidental or child tampering
- Wireless interface (optional):
  - Infusion parameters remotely controlled
  - Pre-warnings or warnings on mobile phones
- Service and maintenance contract provided, with regular testing of proper functioning

A dressing could also potentially act as a reservoir for pathogens. One study tested this hypothesis by removing the CVAD exit site (gauze) dressing. Seventy-eight individuals with cancer and newly inserted CVADs, stratified for gender (37 men and 41 women) and transplant status, were recruited and randomly assigned to receive either a gauze dressing or no dressing, once their CVAD insertion site had healed (three weeks). There was no significant difference in CRBSI episodes ($p = 0.28$) or rehospitalization rates ($p = 0.41$) between the dressing and no-dressing group, but individuals in the dressing group developed CRBSI sooner ($p = 0.02$) than did individuals in the no-dressing group [107].

Recommendation 22

Tubing to administer HPN should be replaced within 24 h of initiating the infusion.

Grade of Recommendation B – Strong consensus (100% agreement)

Commentary

PN is considered as a medium where several factors may influence microbial growth leading to CRBSI risk [108]. In a prospective, randomized study, an intention-to-treat analysis demonstrated a higher level of intravenous tubing (administration set) colonization in tubes changed every 4- to 7-days vs. those only changed every 3-days; however, the two groups had a comparable rate of colonization when patients receiving PN ($n = 84$) were excluded from this study [109]. Another randomized trial specifically involving PN infusion, found that changing tubing every 4 days vs. every 2 days did not impact on hub contamination and CRBSI rates [110]. A Cochrane systematic review found: a) no evidence to demonstrate that CRBSI rate was affected by frequent changes of non-lipid containing tubing; b) some evidence suggesting that mortality increased within the neonatal population with infrequent giving set replacement. However, much of the evidence evaluated in this Cochrane review was derived from studies of low to moderate quality [111,112].

Currently there is no evidence that it is safe to extend the period of administration sets that contain lipids beyond an interval of 24 h and this is generally accepted as best practice [111,112]. Furthermore, the Center for Disease Control and Prevention (CDC) consider PN as an independent risk factor for CRBSI and recommend infusion set replacement after 24 h [73]. Given that HPN patients are very often on cyclic PN, infusion sets normally will be replaced every 24 h.

Recommendation 23

Strict aseptic technique for the care of home CVAD shall be maintained.

Grade of Recommendation A – Strong consensus (100% agreement)

Commentary

A recent systematic review revealed that there is not enough evidence to confirm whether patients receiving PN are more at risk of developing CRBSI that those who did not receive PN therapy [113]. Nevertheless, CRBSI is a common complication in patients receiving HPN. In a study of 172 adult HPN patients, 94 CRBSIs were diagnosed on 238 CVADs. Previous catheterizations and the presence of an enterocutaneous stoma were significantly related with a higher infection risk [114]. In another study with HPN patients, 465 CRBSIs developed in 187 patients (18%) during the three years study period [115].

Cotogni et al. [116] reported that the incidence of CRBSIs is low (0.35/1000 catheter-days), particularly for PICCs (0/1000; $P < 0.01$ vs Hohn and tunneled catheters) and for ports (0.19/1000; $P < 0.01$ vs Hohn and $P < 0.05$ vs tunneled catheters)

A systematic review in adult patients receiving HPN showed an overall CRBSI ranged between 0.38 and 4.58 episodes/1000 catheter days (median 1.31). Gram-positive bacteria of human skin flora caused more than half of infections [117].

Recommendation 24

Hand antisepsis and aseptic non-touch technique should be used when changing the dressing on CVADs.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

Hand antisepsis is the most important measure to prevent contamination. Using gloves does not obviate the need for hand antisepsis. Gloves can be used when contact with blood, body fluids, secretions and excretions can be anticipated. The CDC leaves the choice of using gloves to local or federal regulations, rules, or standards [73]. There is only indirect evidence demonstrating the use of non-sterile gloves is not inferior to sterile ones even in more invasive procedures such as minor skin excisions and outpatient cutaneous surgical procedures, [118,119].

Recommendation 25

A 0.5–2% alcoholic chlorhexidine solution shall be used during dressing changes and skin antisepsis; if there is a contraindication to chlorhexidine, tincture of iodine, an iodophor, or 70% alcohol shall be used as an alternative.

Grade of Recommendation A – Strong consensus (95.2% agreement)

Commentary

There is a body of evidence that demonstrates that the incidence of CRBSI is significantly reduced in patients with CVAD who receive chlorhexidine gluconate versus povidone-iodine for insertion-site skin disinfection [73,120–124]. This is also the reason why chlorhexidine is mentioned in most checklists for CVAD insertion [125].

Recommendation 26

Hand decontamination, either by washing hands with soap and water but preferably with alcohol-based hand rubs, should be performed immediately before and after accessing or dressing a CVAD.

Grade of Recommendation B – Strong consensus (95.2% agreement)

Commentary

Hand decontamination is a key factor in the prevention of health-care related infections which includes CVAD-related infections [73]. Several products are available: alcohol-based decontamination, non-alcohol-based decontamination, antimicrobial/antiseptic hand-washes or agents or liquid soap and water. Before using a hand-rub solution, hands should be free from dirt and organic material. The solution must come into contact with all surfaces of the hand. The hands must be rubbed together vigorously, paying particular attention to the tips of the fingers, the thumbs and the areas between the fingers, until the solution has evaporated and the hands are dry. This should be done immediately before and after direct patient care or contact and after removal of any gloves [126].

Results from a systematic review supported the use of alcohol-based hand rubbing: it removed microorganisms effectively, required less time and irritated hands less often than did hand-washing with soap or other antiseptic agents and water [127]. Furthermore, the availability of bedside alcohol-based solutions increased compliance with hand hygiene among health care workers [127]. Other randomized trials also favored the use of alcohol-based solutions [128,129].

Recommendation 27

A needle-free connector should be used to access intravenous tubing.

Grade of Recommendation B – Strong consensus (100% agreement)

Recommendation 28

Needle-free systems with a split septum valve may be preferred over some mechanical valves due to increased risk of infection with mechanical valves.

Grade of Recommendation 0 – Strong consensus (100% agreement)

Commentary

Needleless connectors are an easy access point for infusion connection. They were introduced and mandated to prevent needlestick injuries, reducing the risk of transmission of blood-borne infections to healthcare personnel [73]. In several studies, the use of needleless connectors appears to be effective. Compared to the use of standard caps or 3-way stopcocks, they can reduce internal microbial contamination and so the incidence of CRBSI, but they have to be properly disinfected [130–132].

The majority of needleless connectors fall into one of two categories; namely those with no moving internal parts (e.g. an external split septum) and connectors which moving internal components. Based on available data, split septum connectors should be preferentially used instead of mechanical valves [73,133]. The issue becomes more complicated when the risk of (tip) occlusion due to negative displacement or blood reflux is also taken into account, depending on the type of connector used [134]. Needleless connectors have to be changed no more frequently than every 72 h or according to manufacturers' recommendations [73].

Recommendation 29

Contamination risk shall be minimized by scrubbing the hub connectors (needleless connectors) with an appropriate antiseptic (alcoholic chlorhexidine preparation or alcohol 70%) and access it only with sterile devices.

Grade of Recommendation A – Strong consensus (100% agreement)

Recommendation 30

For passive disinfection of hub connectors (needleless devices) antiseptic barrier caps should be used.

Grade of Recommendation B – Strong consensus (90.9% agreement)

Commentary

Needleless connectors are used on virtually all CVAD, providing an easy access point for infusion connection. Infection guidelines strongly recommend proper disinfection of access ports [135]. A systematic review revealed that the greatest risk for contamination of the CVAD after insertion was the needleless connector, with 33–45% contaminated, and compliance with disinfection was as low as 10%, but the optimal technique or disinfection time were not identified [136]. Another systematic review recommended scrubbing with chlorhexidine-alcohol for 15 s [137]. However, if the membranous septum of a needleless luer-activated connector is heavily contaminated, conventional disinfection with 70% alcohol does not reliably prevent entry of microorganisms [138]. Since compliance with a time-consuming manual disinfection process is low, the use of an antiseptic barrier cap (placed on a luer needleless connector), which cleans the connection surface by continuous passive disinfection, was associated with a decrease in CRBSI [138,139].

Recommendation 31

If HPN is delivered via an intravenous port, needles to access ports should be replaced at least once per week.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

An implanted intravenous port is a small device with direct access to a central vein, used to draw blood and give treatments, including intravenous fluids, drugs, blood transfusions and PN. The port is placed just underneath the skin, usually in the chest. A catheter is attached to a subcutaneous pocket (made of titanium) with the tip ending at the right atrial-superior vena cava junction. To gain access, a needle is inserted through the skin and the rubbery self-healing membrane of the port. The CDC guideline considers the timeframe to replace needles as an 'unresolved' issue [73]. There is also a possible higher risk of colonization of administration sets with PN. On the other hand, one retrospective study demonstrated that weekly changing of exit-site needles and transparent dressings on intravenous ports seems to be safe and cost-effective but, in this study, patients on PN had a significantly greater risk of developing an infection from Candida Species [140]. In a study with patients on continuous chemotherapy, needles were in place for an average of 28 days without adverse effect [141]. Because there is no clear evidence, we suggest replacing port needles at least once-a-week with the use of PN. This also gives the opportunity for some patients to safely take a bath or shower when the needle has been removed and replaced afterwards.

Recommendation 32

The CVAD or CVAD site should not be submerged unprotected in water.

Grade of Recommendation B – Strong consensus (95.2% agreement)

Commentary

A study in children suggested that swimming did not increase the risk of tunneled CVAD-related infections [142]. No firm recommendation could be made in a review of 45 articles and 16 pediatric HPN programs regarding swimming and CVADs but the authors also reported a fatal event immediately after swimming [143]. Using a closed-hub system and waterproof catheter hub connections significantly reduced the incidence of CRBSIs (particularly infections caused by gram-negative pathogens) in another group of pediatric patients [144].

The CDC guidelines (recommendation B) allow showering if precautions can be taken to reduce the likelihood of introducing organisms into the catheter (e.g. if the catheter and connecting device are protected with an impermeable cover during the shower) [73]. The ESPGHAN/ESPEN/ESPR/CSPEN guideline for pediatric PN access allows swimming (GPP) when a water-resistant dressing is used to cover the whole catheter and, after swimming, the exit site should be cleaned and disinfected [106].

Recommendation 33

Sodium chloride 0.9% instead of heparin should be used to lock long-term CVAD.

Grade of Recommendation B – Strong consensus (95.5% agreement)

Commentary

Historically, heparin was the most commonly used catheter lock solution. However, a retrospective study [145], a randomized prospective study [146] and two systematic reviews [147,148] demonstrated that normal saline flushing is not inferior to heparin flushing regarding CVAD occlusion, reflux dysfunction and flow dysfunction. ASPEN guidelines state that "no recommendations can be made as to which flush solution should be used to maintain patency for HPN CVAD due to the lack of studies" [84].

For the primary prevention of CVAD-related venous thrombosis, ESPEN guidelines for CIF recommend insertion of the catheter using ultrasound guidance and placement of the tip at the superior vena cava-right atrium junction, suggest flushing CVAD with saline and do not recommend routine thromboprophylaxis with drugs (heparin, warfarin) [4]. ESPEN guidelines for CIF do not recommend heparin for the prevention of CRBSIs [4], because it promotes intraluminal biofilm formation and therefore potentially increases the risk of CRBSIs [149,150]. German guidelines give a GPP grade for their recommendation of using saline and a grade B for their recommendation of not using heparin [11]. A grade B

recommendation for the use of saline instead of heparin to flush and lock the CVAD is appropriate, given that this approach does not increase the risk of CVAD occlusion and has a lower risk of biofilm formation in the CVAD lumen.

Recommendation 34

As an additional strategy to prevent CRBSIs, taurolidine locking should be used because of its favorable safety and cost profile.

Grade of Recommendation B – Strong consensus (100% agreement)

Commentary

For the primary prevention of CRBSI, ESPEN guidelines for CIF [4]:

a) recommend education of staff and patients/caregivers; implementation of an adequate policy of hand washing and disinfection by patients and staff; handwashing and disinfection by patients and caregivers before touching CVAD as well as after CVAD care; disinfection of the hub connector every time it is accessed; use of tunneled single-lumen catheters whenever possible; use of chlorhexidine 2% for antisepsis of hands, CVAD exit site, stopcocks, catheter hubs and other sampling ports and regular change of IV administration sets.
b) suggest performing site care, including catheter hub cleaning on at least a weekly basis; changing CVAD dressings at least once weekly; avoiding CVAD care immediately after changing or emptying ostomy appliances and disinfecting hands after ostomy care.
c) do not recommend the use of in-line filters; routine replacement of CVADs; antibiotic prophylaxis and heparin lock.

ESPEN guidelines for CIF were published in 2016. Since then, no additional relevant literature was found concerning the above recommendations, but two high quality double blinded RCTs [151,152] and one extensive retrospective analysis [153] have been published on antimicrobial CVAD locking with various taurolidine formulations, that have considerably changed the available body of evidence and the strength of recommendation about the use of taurolidine for the prevention of CRBSI. All studies were performed in the setting of HPN support for adult benign CIF. Tribler et al. investigated CVAD locking with taurolidine 1.4%-citrate-heparin in comparison to control (low-dose heparin 100 IE/mL) in a single center study in 41 high-risk Danish HPN patients who had been stratified according to their prior CRBSI incidence [151]. In 20 patients who received the taurolidine-containing formulation, no CRBSIs occurred in contrast to CRBSIs in 7 out of 21 controls (incidence 1.0/1000 CVC days; $p < 0.05$). Costs in the taurolidine arm were lower because of fewer admission days related to CRBSI treatment.

Since locking with heparin solutions has been suspected of promoting CRBSI, Wouters et al. compared a pure taurolidine 2% lock to another control (saline 0.9%) in a multicenter trial [152]. Patients were stratified in a new catheter group and a pre-existing catheter group. Overall 102 patients were analyzed. In the new catheter group, CRBSIs/1000 catheter days were significantly lower (0.29 vs 1.49) in the taurolidine arm while in patients who entered the trial with a pre-existing catheter CRBSI rates were also lower in the taurolidine arm (0.39 vs 1.32; $p > 0.05$ due to under-powering). Mean costs per patient were significantly lower for taurolidine. Drug-related adverse events were rare and generally mild.

Wouters et al. also retrospectively analyzed long-term complications and adverse events in adult HPN patients from a national referral center who all used taurolidine locks between 2006 and 2017 [153]. In total, 270 HPN patients used taurolidine during 338.521 catheter days. CRBSIs, catheter related venous thrombosis and occlusions occurred at rates of 0.60, 0.28, and 0.12 events per 1000 catheter days, respectively. In 24 (9%) patients, mild to moderate adverse events resulted in discontinuation of taurolidine. A subsequent switch to 0.9% saline resulted in an increased CRBSI rate (adjusted rate ratio 4.01, $P = 0.02$). Several risk factors were identified for CRBSIs (including lower age and increased infusion frequency), thrombosis (site of vein insertion), and occlusions (type of access device).

Recommendation 35

If a PICC is used for HPN, a sutureless device should be used to reduce the risk of infection.

Grade of Recommendation B – Strong consensus (100% agreement)

Recommendation 36

For the securement of medium– to long-term PICCs (> 1 month) a subcutaneously anchored stabilization device can be used to prevent migration and save time during dressing change.

Grade of Recommendation 0 – Strong consensus (100% agreement)

Commentary

A prospective study with 254 HPN patients revealed that use of sutureless devices for CVAD securement decreased the risk of CRBSI and dislocation ($p < 0.001$) [116]. A multiple treatment meta-analysis found that sutureless securement devices were as likely to be the most effective at reducing the incidence of CRBSI but the quality evidence was low [101]. For the securement of medium-to long-term PICCs, a subcutaneously anchored stabilization device can be used; it seems safe and cost-effective [154]. In the UK, the National Institute for Health and Care Excellence (NICE) recommends the adoption of this device (SecurAcath) for securing PICCs within the National Health Service in England [155]. Another study demonstrated that the use of SecurAcath saved time during dressing change compared with an alternative securement device (Statlock) but training on correct placement and removal was critical to minimize pain [156]. Besides sparing time during dressing change, it also can prevent migration of the PICC [157].

Recommendation 37

In multilumen catheters, a dedicated lumen should be used for PN infusion.

Grade of Recommendation GPP – Strong consensus (95.5% agreement)

Commentary

A previous ESPEN guideline recommended use of a single-lumen CVAD or of a dedicated lumen on a multilumen CVAD for PN administration [9]. The CDC guidelines gave no recommendation regarding the use of a dedicated lumen for PN [73]. Recently, Australian authors reviewed the available literature for comparative rates of CRBSIs in patients who received their PN in any health setting through a dedicated lumen compared with those who had PN administered through multilumen CVADs from 2286 records that were identified through database searching; they found only two studies that fit inclusion criteria in a qualitative synthesis [158]. These studies included 650 patients with 1349 CVADs showing an equal distribution of CRBSIs between groups [158]. This lack of evidence for the use of a dedicated lumen to reduce infections most likely resulted from the poor way study results were reported with a high risk of bias, indicating the need for well-powered high-quality research in this field. Therefore, the panel of the present guideline strongly agreed to confirm the recommendation made by the earlier ESPEN guidelines [9].

Recommendation 38

Routine drawing of blood samples from CVAD should be avoided if possible due to an increased risk of complications.

Grade of Recommendation B – Strong consensus (95.2% agreement)

Commentary

When risk factors for CRBSI occurrence were retrospectively studied in 125 adults who received HPN by reviewing medical records from a national home care pharmacy in patients who used HPN at least twice weekly for > 2 years between 2006 and 2011, it was found in adults (331 CVADs, CRBSI rate 0.35/1000 catheter days) using univariate analysis that the use of subcutaneous infusion ports instead of tunneled catheters ($p = 0.001$), multiple lumen catheters ($p = 0.001$), increased frequency of lipid emulsion infusion ($p = 0.001$), obtaining blood from the CVC ($p < 0.001$), and infusion of non-PN medications via the CVC ($p < 0.001$), were significant risk factors for CRBSI occurrence [159].

Although high quality studies in the field of (H)PN are lacking, indirect evidence from a retrospective multivariate analysis of 452 totally implantable vascular devices in French cystic fibrosis patients that were used for administration of antibiotics, showed that removal, either due to obstruction (21%), infection (9%), septicemia (7%) or vascular thrombosis (5%), could be linked, apart from the CVC material (polyurethane vs silicone), to their routine use for blood sampling (versus never) [160].

4. Nutritional admixtures

7. Which nutritional PN admixture bag should be chosen?

Statement 5

The HPN-admixture shall meet the patient's requirement.

Strong consensus (95.7% agreement)

Recommendation 39

Either commercially available ready-to-use admixtures or customized and tailored to the individual patient's requirements admixtures can be used for HPN.

Grade of Recommendation GPP – Strong consensus (95.7% agreement)

Recommendation 40

Customized and tailored HPN admixtures can be prepared either by individual compounding or by ready-to-use prepared and adapted commercial multi-chamber bags, according to the manufacturer instructions and using aseptic admixture technique preferably in a laminar flow cabinet.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

The PN admixture provided for HPN should meet the individual patient's requirements [3,4]. PN admixtures can be compounded in single bags, dual chamber bags or three in one/all-in-one (AIO) bags (these contain separate compartments for lipid emulsion/glucose/amino acids to be opened and mixed before infusion). Vitamins and trace elements can be added prior to infusion in the home setting, if appropriate compatibility and stability [3,4]. Dual and three chamber bags have advantages for HPN patients as they have a longer shelf life. Some AIO bags do not require refrigeration, which provides advantages for HPN patients while travelling. Stability is also markedly prolonged by refrigeration that requires a dedicated refrigerator for HPN storage [4].

The clinical advantages or disadvantages of individually compounded ("tailored" or "customized") PN admixture in comparison with commercially available ready-to-use ("premade" or "premixed") PN admixture adapted to the patient's requirements has been addressed by previous guidelines, but published data did not support definitive recommendations. ESPEN guidelines do not address whether commercial ready to use bags (with or without additions) have any advantages over customized bags in the home setting [3,4]. ASPEN clinical guidelines state that commercial ready to use bags are considered as an available option for patients alongside customized PN formulations to best meet patients' needs [161] However, this was based on literature comparing different types of bags in the hospital inpatient setting and not at home. The guideline also states that an evaluation of clinical outcomes, safety and cost should be considered before making the final determination. However, they highlight that most of the controlled clinical trials do not directly compare the use of commercial ready-to-use bags with customized PN systems for patient outcomes, efficacy or safety and focus instead on evaluations following conversion from one delivery approach to another system [161]. German guidelines advocate the use of "all-in-one nutrient mixtures" and advise that multi-bottle systems should not be used because of increased risks and more difficult handling [11,162].

The literature search for this guideline provided eleven articles that were considered to have some relevance to the question of comparison of commercial ready-to-use and customized PN admixture in non-critically ill patients [163–173]. Only one of the eleven articles, a conference abstract, compared different types of PN bags in the homecare setting, with all other articles evaluating the use of PN in hospital inpatients [163]. The results suggested that customized PN may be associated with a lower microbiological risk than commercial ready-to-use bags for patients with CIF; however, differences were not-statistically significant and this paper has not been published in full [163]. There were no studies found that compared commercial ready-to-use and customized PN in relation to clinical outcome or cost in HPN patients. There are no data on the use of different nutritional admixtures for people with CIF as result of benign vs. malignant disease.

The results of the studies comparing commercial ready-to-use and customized PN in hospital inpatients may have some relevance for further studies in HPN patients. A number of studies in the hospital setting demonstrated that commercial ready-to-use PN is cheaper than customized PN; this may be due to lower acquisition costs, reduced preparation time and avoidance of costs associated with the development of CRBSI [164–168]. A retrospective study of in-hospital PN found that adding supplements to multi-chamber PN bags on the hospital ward increased blood stream infection risk [169], although this has not been confirmed in other studies [170]. Studies evaluating ready-to-use and customized PN in hospital highlight that the commercial ready-to-use PN may not suitable for all patients [165,171,172]. A recent systematic review comparing pharmacy compounded PN bags and multi-bottle systems for in-patients noted that methodological factors limited evidence quality and highlighted the need for more prospective studies [173].

Given the paucity of data in the HPN setting, further studies are clearly needed to investigate the cost implications, safety and clinical outcomes of using commercial ready-to-use PN-admixtures for patients with benign and malignant CIF.

8. What are the critical steps during the preparation of PN admixtures?

Recommendation 41

Customized AIO admixture stability should be documented for the individual admixture based on checks by appropriate lab methods.

Grade of Recommendation B – Strong consensus (100% agreement)

Recommendation 42

Customized AIO admixture stability shall not be extrapolated from the literature.

Grade of Recommendation GPP – Strong consensus (95.2% agreement)

Commentary

AIO stability has to be documented for the individual admixture based on checks by appropriate lab methods. Literature extrapolation for stability is not adequate due to the complexities of the admixtures [11,174,175].

Electrolytes are prone to incompatibilities (precipitations, multi-valent cations and negative charged lipid emulsifier leading to emulsion destabilization). Their correct admixing into the appropriate macro-element component is crucial; in selected cases with a high calcium need, organic instead of inorganic components might be preferable [175]. Easy to use and validated methods may be used to check for stability like for the Oil/Water stability of AIO admixtures [176].

Recommendation 43

AIO admixture shall be completed immediately before infusion by adding trace elements and vitamins according to stability and compatibility data.

Grade of Recommendation GPP – Strong consensus (91.3% agreement)

Commentary

AIO admixture shall be completed by adding trace elements and vitamins in aseptic conditions according to stability and compatibility data. For structural/and or organizational reasons, the addition may also be performed immediately before infusion through appropriately trained persons.

In order to prevent incompatibilities, including degradation of essential elements, vitamins may be preferably added by the end of the infusion cycle or as a bolus. Appropriate risk assessment for the Good Manufacturing Practice modalities but also the extent of standardization have to be addressed [11,177,178].

Recommendation 44

Drug admixing into AIO admixture shall be avoided, unless specific pharmaceutical data are available to document compatibilities and stability of the AIO.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

AIO admixtures show a high potential of drug interactions leading to incompatibilities or stability issues. They are normally not suited for drug admixing and, when necessary, the specific pharmaceutical data have to be provided and documented as this final product represents an individual drug product; the product performance and reliability after interaction with drugs is not covered by the manufacturer [176,179].

Recommendation 45

AIO admixtures shall be labelled for the individual patient indicating the composition (dose) of the individual components according to standards, the date, the patient's name and indication for handling such as storage, admixes to be made, infusion rate.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

AIO admixtures have to be labelled for the individual patient. Labels shall indicate the patient's name, the composition (dose) of the individual components according to standards, the date of manufacturing and expiring, instructions for handling like storage, admixes to be made, infusion rate, as well as avoidance of medication errors [177,179,180]. Specific pharmaceutical support within the NST is required and efficacious [181].

9. How should PN admixture be delivered?

Recommendation 46

For customized AIO admixtures, the cold chain should be guaranteed during transport and at the patient's home.

Grade of Recommendation B – Strong consensus (100% agreement)

Commentary

Clearly, pharmaceutical safeguards must be applied for PN delivery, storage and administration at home throughout the patient's therapy. For customized AIO PN admixtures, the cold chain has to be guaranteed [175].

10. What should be the HPN admixture time and rate of infusion?

Recommendation 47

The hanging time for an HPN-admixture should be no longer than 24 h.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 48

At the end of cyclic PN administration, the infusion rate can be reduced to avoid rebound hypoglycemia (e.g. half of the infusion rate over the last half an hour).

Grade of Recommendation GPP – Strong consensus (93.8% agreement)

Commentary

The generally accepted maximum hanging time for a ready-to-use admixture are 24 h. The giving set has to be changed upon each new PN dosing [11,175,178,179].

At the end of a (cyclic) PN-infusion, the infusion rate has to be reduced to tamper insulin need and to avoid rebound hypoglycemia (e.g. half of the infusion rate over the last half an hour). Glucose administration determines the maximum rate of PN infusion rate: (max. 5–7 mg glucose/kg/min; corresponding to about a maximum of 350 g glucose over 12 h in 70 kg adult [175,179] or 3–6 g glucose/kg per day [3].

5. Program monitoring

11. How should patients on HPN be monitored?

Recommendation 49

Patients receiving HPN shall be monitored at regular intervals, to review the indications, the efficacy and the risks of the treatment.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 50

The time between reviews should be adapted to the patient, care setting and duration of nutrition support; intervals can increase as the patient is stabilized on nutrition support

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 51

HPN monitoring should be carried out by the hospital NST in collaboration with experienced home care specialists, home care agencies and/or general practitioners.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 52

Patients and/or caregivers can be trained to monitor nutritional status, fluid balance and the infusion catheter.

Grade of Recommendation 0 – Strong consensus (95.7% agreement)

Recommendation 53

Monitoring should comprise of nutritional efficacy, tolerance of PN, patient/caregiver management of infusion catheter, QoL and quality of care (e.g. CRBSI rate, readmission rate etc.).

Grade of Recommendation GPP – Strong consensus (95.7% agreement)

Recommendation 54

In clinically stable patients on long-term HPN, body weight, body composition and hydration status, energy and fluid balance and biochemistry (hemoglobin, ferritin, albumin, C-reactive protein, electrolytes, venous blood gas analysis, kidney function, liver function and glucose) should be measured at all the scheduled (e.g. every three to six months).

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 55

In patients on long-term HPN, clinical signs and symptoms as well as biochemical indexes of vitamin and trace metal deficiency or toxicity should be evaluated at least once per year.

Grade of Recommendation GPP – Strong consensus (95.7% agreement)

Recommendation 56

In patients on long-term HPN, bone metabolism and bone mineral density should be evaluated annually or in accordance with accepted standards (e.g. DXA at max. every 18 months).

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

The purpose of monitoring is to "secure and improve QoL" of persons on HPN by assessing the nutritional efficacy of the HPN program, preventing and timely diagnosing and treating HPN-related complications and measuring QoL and quality of care [3,4]. Evidence-based guidelines for monitoring are not available due to the lack of published data [3–13]. Only one study has been published reporting monitoring practices for HPN across Europe [16]. The results showed that the majority of centers performed a 3-month monitoring interval for stable patients and emphasized that responsibility for monitoring should be assigned to a designated person on the hospital HPN specialist NST [16]. Prospective studies of the impact of different monitoring regimens on outcomes (including QoL) of HPN are warranted.

Monitoring of HPN patients should be carried out by an experienced hospital NST and by home care specialists as well as by a home care agency with experience in HPN and should also involve the general practitioner. Healthcare professionals should review the indications, route, risks, benefits and goals of nutrition support at regular intervals. In long-term HPN, patients and caregivers should be trained in self-monitoring of their nutritional status, fluid balance and infusion catheter, as well as in recognizing early signs and symptoms of complications and responding to adverse changes in both their well-being and management of their nutritional delivery system.

Parameters to be monitored, frequency and setting of monitoring are indicated in Table 9. The time between reviews depends on the patient, care setting, duration of nutrition support as well as the expected speed with which the impairment of a parameter is likely to occur. Monitoring should be more frequent during the early months of HPN, or if there is a change in the patient's clinical condition. Intervals may increase as the patient is stabilized on nutrition support. Fluid balance requires the most frequent monitoring, especially in the first period after discharge and in patients with short bowel syndrome with a high output stoma or with intestinal dysmotility with recurrent episodes of vomiting. Frequent acute dehydration episodes are responsible for kidney failure and re-hospitalization [182,183]. On the other hand, vitamin and trace metal deficiency may take more time to develop and to present clinical signs and symptoms, so that a six to twelve month interval of assessment is appropriate. However, monitoring of micronutrients is as important as monitoring other parameters, especially in patients on long-term HPN and in those who are undergoing intestinal rehabilitation and weaning from HPN. In the latter case, while intestinal rehabilitation is associated with maintenance of energy, protein, fluid and electrolyte balance without PN support, this is not necessarily the case for micronutrient balance [4]. Decreasing or totally stopping PN infusion decreases micronutrient supplementation, thus creating a risk for deficiency [4].

After hospital discharge, it is critical that the HPN NST has contact with patients and caregivers on a regular basis, initially every few days, then weekly and eventually monthly as the patient gains confidence. The clinician who is in contact should be prepared to clarify confusing issues and also to follow weight, urine output, diarrhea or stoma output, temperatures before and within an hour of starting the HPN infusion, and general health.

Healthcare professionals have identified incidence of CRBSI, incidence of rehospitalization and QoL as the three major indicators of quality of care HPN patients with either a benign [71] or malignant [51] underlying disease. Survival rate was also considered important when patients with benign disease were considered [184].

6. Management (nutrition support team, training, emergency, travelling)

12. Which are the local and personnel preconditions for HPN?

Recommendation 57

The suitability of the home care environment should be assessed and approved by the HPN nursing team before starting HPN, wherever possible.

Grade of Recommendation GPP – Strong consensus (91.3% agreement)

Recommendation 58

A formal individualized HPN training program for the patient and/or caregiver and/or home care nurses shall be performed, including catheter care, pump use and preventing, recognizing and managing complications; training can be done in an in-patient setting or at the patient's home.

Grade of Recommendation GPP – Strong consensus (91.3% agreement)

Commentary

The management of PN in the home care setting differs from hospitalized patients because there is a shift in primary responsibility from health care professionals to patients and caregivers. The general goals in the education process are promoting independence with the infusion, (self-) monitoring of HPN, preventing complications and improving or maintaining QoL [3,4] (Table 10). The HPN center NST plays a key role in the individualized decision-making process and guides all the necessary measures or steps which have to be taken [3,10,51,64–74].

Guidelines on core components for (catheter) infection control and prevention, considered as an important outcome indicator in HPN patients, give strong recommendations about the provision of education and training [72,73]. Besides preventing CRBSI and assessing QoL, the overall teaching program has many aspects to deal with and is very often driven by an experienced (nutrition support) nurse who takes the lead and responsibility for this program [3,69].

Training for HPN may be carried out in an in-patient setting or at patient's home and may take several days to weeks depending on patient skills, duration of HPN and underlying condition [3,4,74]. A recent retrospective 5-year evaluation of CRBSI occurrence and CVC salvage outcomes in adult patients requiring HPN managed at a national UK intestinal failure unit, demonstrated that by individual managing, patients can be educated at home which of course reduces hospital length of stay and may be preferable for some patients [75]. Multiple education interventions are possible including one-on-one counselling, teach-back method, written handouts, computer-assisted learning and interactive presentations. All these tools may not eliminate but reduce post discharge helpline contacts

Table 9
Parameters, frequency (after baseline assessment) and setting of monitoring on patients on HPN.

Parameter	Frequency	Setting
General condition	Daily if unstable, twice weekly to once a week if stable	Nurse at home
Body temperature		Patient and/or caregivers
Body weight	Daily if unstable, twice weekly to once a week if stable	In the hospital (outpatient visit)
		Nurse at home
		Patient and/or caregivers
Body mass index	Monthly	In the hospital (outpatient visit)
		Nurse at home
Fluid balance	The frequency and type of parameters will depend on	Nurse at home
- Urine output	etiology of CIF, and stability of patients	Patient and/or caregivers only in case of training program
- Stoma output	In case of high stool output (end jejunostomy), the	
- Number or consistency of stools	monitoring after the first discharge should be daily, then	
- Presence of edema	twice weekly to once a week when stable	
Catheter cutaneous exit site	Daily	Nurse at home
		Patient and/or caregivers only in case of training program
Full count blood	The frequency and type of parameters will depend on	At home
C-reactive protein	etiology of the underlying condition requiring HPN and the	Verify at each visit
Serum glucose	stability of patients	
Serum and urine electrolytes and minerals	Weekly or monthly, then every three to four months when	
(Na, Cl, K, Mg, Ca and P)	stable	
Serum Urea and Creatinine		
Serum bicarbonates		
Urine analysis		
Serum albumin and prealbumin	Monthly, then every three to four months when stable	At home
		Verify at each visit
Serum liver function tests including INR	Monthly, then every three to four months when stable	At home
		Verify at each visit
Liver ultrasound	Yearly	In hospital
Serum Folate, vitamins B12, A and E	Every six to twelve months	Dosage at home or in the hospital
Serum ferritin iron,	Every three to six months	Dosage at home or in the hospital
Serum 25-OH Vitamin D	Every six to twelve months	Dosage at home or in the hospital
Serum zinc, copper, selenium	Every six to twelve months	Dosage in the hospital
Serum Manganese	Yearly	Dosage in the hospital
Bone densitometry (DEXA)	Every twelve to eighteen months	In the hospital

Table 10
Content of a teaching program for patients/caregivers discharged on HPN [3,10,63,74]].

- Indication for HPN: short and/or long-term goals and HPN-regimen
- Issues around informed consent
- Role of the home care provider to provide parenteral formulations, equipment, supplies, and eventually nursing care
- Determine learning abilities and readiness to self-management and self-monitoring
  - If applicable: make a checklist for competencies achieved
- Reviewing evidence-based written policies and procedures complemented with oral instructions
- Home care environment
  - General cleanliness (for example: Is there a clean area for aseptic/sterile procedures?)
  - Presence of animals
  - Basic home safety (telephone access, clean storage for supplies, dedicated refrigerator, toilet-bathroom, sanitary water supply, …)
- Catheter care
  - Principles of infection control and prevention (including aseptic techniques)
  - Preventing, recognizing and managing catheter related complications
  - Site care
- Storage, handling, inspection of admixtures (e.g. leaks, labels, precipitates, color), ancillaries and (medication) supplies
- If applicable:
  - Safe addition of vitamins, trace elements or other additives
  - Safe administration of HPN
  - Connecting and disconnecting IV tubing to the vascular access device
  - Pre/post infusion flushing
  - Periodically assessment of performance/compliance with aseptic techniques
- Pump use, programming, pump care and troubleshooting
- Preventing, recognizing and managing non-infectious related complications or problems
- Most common mistakes
- Available contact resources and post discharge support from the HPN center as well as the home care provider
- Self HPN monitoring
- Concomitant drug therapy and administration mode (total regimen management)

provided by telephone, videoconference or patient portals [63,68,74].

Multiple education interventions are available including methods such as one-on-one counselling, written or printed materials, group meetings, demonstrations, videotapes, CDs/DVDs and internet education [3,4]. HPN is a complex therapy that requires coordination of many health care providers. The expertise of a NST is recommended to provide proper and patient-tailored

education or therapy. Self-management and preventing complications are important goals to improve QoL and to avoid unnecessary costs to healthcare.

13. Which are the requirements for the hospital centers that care for HPN patients?

Recommendation 59

Patients on HPN should be cared for by specialized, dedicated and a clearly identifiable hospital unit, normally termed "HPN center or IF center or intestinal rehabilitation center".

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 60

The HPN unit should have offices for outpatient visits and dedicated beds for patients who need hospitalization.

Grade of Recommendation GPP – Strong consensus (91.3% agreement)

Commentary

The human resources as well as structural facilities are key features to optimize the HPN care.

Specific organization and structural facilities for HPN management have been described by a position statement of the British Intestinal Failure Alliance [12], that described five standards: Unit, Team, Practice, Relationship with other internal and external units/stakeholders and outcome.

Key issues are the identification of the persons, structures and procedures responsible for the HPN care process [4,12,13], such as:

- Professionals who coordinate and manage the different phases of HPN management
- Place of initial care (center of intestinal failure, gastroenterology, surgery, other)
- Place and methods of training programs (on hospital beds, in day hospital, at home)
- Pathways of care in case of complications (example: emergency room, direct access to hospital beds, link with local hospitals of the patient residency)
- Place and procedures for CVAD positioning and managing of complications

Having access to dedicated hospital beds under the responsibility of the NST is essential for initial care as well as for managing of complications. These beds may be within an independent structure of nutrition/intestinal failure or within a more general structure, such as department of gastroenterology, oncology, surgery or other. Hospitalization is required to monitor patients and/or evaluate intestinal function in order to better adapt treatments as well as to timely and appropriately treat complications according to the NST procedures.

The HPN center needs to estimate the time that each professional has to dedicate to the single patient, in order to define the number of human resources required for managing their total number of HPN patients.

In conclusion, for better care and visibility for patients, healthcare providers and public authorities, we recommend that departments dedicated to the care of these patients be recognized with dedicated beds and resources.

14. What are the requirements of the NST?

Recommendation 61

All HPN patients should be cared for by a NST with experience in HPN management, independent from the underlying disease leading to intestinal failure.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 62

The NST consists of experts in HPN provision. This can include a physician, specialist nurses (including in catheter, wound and stoma care), dietitians, pharmacists, social worker, psychologist, as well as an appropriate practitioner with expertise in CVC placement. Surgeons with expertise in intestinal failure should also be available for structured consultation.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

Because of its complex nature, current guidelines, including the recent ESPEN guideline on CIF, agree that only experienced NST should provide HPN treatment [3–14]. The relevance of expertise in this field has been shown previously in France where increased experience in HPN support had a positive impact on patient survival [185]. To assure optimal outcomes, the team should develop an individualized training and treatment plans based on standardized protocols. Notably, CRBSI rates, which are considered a proxy for the quality of HPN support, even in high-risk patients such as those with cancer, are the lowest in expert referral centers [64,65].

The appropriate composition and size of a NST that provides HPN care to some extent depends on the number of patients under the team's care, which mostly also relates to the patient volume and scope of the hospital [186]. Key tasks of this team include establishing (contra)-indications for HPN support, development and implementation of individualized training and treatment programs, treatment of complications (vascular access related, metabolic derangements) and organization of home care [186].

Also, because of the associated complications of HPN treatment, including venous access-related problems such as infections and occlusions, metabolic derangements, formulation and medication compatibility issues that pertain to various specialties, the team that provides HPN support should be multidisciplinary in nature and include physician specialists with a background in surgery and gastroenterology, specialized nurses, dieticians and pharmacists [66,67]. In light of the profound impact on personal and family life, psychologists and social workers should also form part of the team. This latter issue was highlighted in studies showing that many HPN patients experience the lack of attention for their psychosocial problems as a shortcoming [187,188].

Concerning patients with active cancer, it is important to realize that selecting patients suitable for such a complex treatment as HPN support is challenging and discussion with the treating oncology specialist in this setting seems prudent before HPN initiation [15].

Often forgotten, it is of key importance for patients that caregivers more close to the home, such as the general practitioner and homecare nurses, although not direct team members, should be kept informed of patients' clinical course after discharge from hospital [62,63,68,70]. It has been shown in adult HPN patients who were managed at a national UK referral center that under the well-organized care of such an experienced team in close collaboration with home nurses, even a delicate process such as patient education can take place at home, resulting in reduced hospital length of stay and improved psychosocial wellbeing of both patients and their family [75].

15. How should emergencies be managed?

Recommendation 63

The NST for HPN/CIF shall have clear written pathways and protocols in place for the management of patients with complications relating to HPN.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 64

The NST for HPN/CIF shall provide patients and caregivers with written information relating to the recognition and subsequent management of HPN-related complications, including details (e.g. telephone number) of an appropriate NST member to contact in the case of an emergency, available 24 h per day.

Grade of Recommendation GPP – Strong consensus (91.3% agreement)

Recommendation 65

The NST for HPN/CIF shall disseminate clear protocols relating to the recognition, investigation and initial management of HPN-related complications to hospital emergency departments, where patients are likely to present; where appropriate and available, written protocols can also be carried by the patient or accessed electronically via a secure web-portal.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 66

When patients are admitted to hospital with HPN-related complications, their care shall be delivered by the NST for HPN/CIF; if patients are admitted to a hospital where such expertise does not exist, then clinical guidance should be provided by the NST for HPN/CIF, until the time when the patient can be transferred to the HPN/CIF center, as required.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 67

Written protocols for the management of HPN-related complications shall be developed and shared with the patient's local hospital, if it is likely that the patient will be admitted first to that hospital rather than to the HPN/CIF center in the event of an emergency; these should include contact details for the NST for HPN/CIF to advise on treatment and/or possible transfer to the HPN/CIF center. Where appropriate and available, written protocols can also be carried by the patient or accessed electronically via a secure web-portal.

Grade of Recommendation GPP – Strong consensus (95.5% agreement)

Recommendation 68

Patients shall carry details relevant to their condition, and/or have access to a secure web-portal containing relevant clinical information, when travelling away from home, in order to aid clinical teams at other hospitals should emergency treatment be required.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Recommendation 69

The NST for HPN/CIF shall ensure that patients, caregivers and general practitioners are aware of the roles and responsibilities of the health care professionals involved in aspects of the patient's condition that are unrelated to HPN, including any complications relating to the patient's underlying disease and other non-IF related conditions.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

Minimal guidance and published literature exist to-date relating to pathways for the emergency management of patients with complications relating to CIF. Such complications should be demarcated into those relating to HPN, those relating to the patient's underlying disease leading to CIF (including any underlying oncological condition) and those unrelated to CIF. The CIF team should ensure that patients and caregivers are aware of the roles and responsibilities of the health care professionals involved in each component of their condition.

There are no published studies that have systematically evaluated best practice for the delivery of emergency care for patients with HPN-related complications, for patients with benign CIF, malignant CIF or no-CIF scenarios. Two studies have demonstrated patient-education programs aimed at minimizing hospital admissions for complications associated with CIF. A retrospective study evaluated the implementation of a protocol to treat dehydration at home for HPN patients by ordering additional intravenous fluids to be kept on hand and to focus patient education on the symptoms of dehydration; this led to a greater than two-fold increase in the number of episodes of dehydration identified and treated at home [183]. Implementation of a CVC self-management education program using a quasi-experimental, sequential cohort design study of patients with cancer led to a reduction in CVC-related complications and improved patients' abilities to resolve problems and adequately respond to CVC-related emergency situations by fostering greater self-care ability; however, this study was not limited to patients with CIF [189]. Two further studies demonstrated that diagnosis and management of CRBSI can be enhanced using quality improvement methodology. An emergency department quality improvement initiative reduced the mean time to antibiotic administration for febrile children with IF by 50%. Interventions included increasing provider knowledge of IF, streamlining order entry, providing individualized feedback, and standardizing the triage process. However, there was no difference noted in the total length of subsequent hospital and ICU stays [190]. Another quality improvement project in a tertiary cancer center involving staff education and blood culture source label introduction improved CRBSI diagnosis from 36% to 88% in patients with a CVC; however, this study was also not limited to patients with CIF [191].

Established national and international guidelines clearly recommend that CIF patients are cared for by a NST with skills and experience in both CIF and HPN management [4]. The British Intestinal Failure Alliance provide some guidelines on the emergency management of HPN-related complications [12]. The NST should be responsible for the management of patients with complications related to HPN, including CVC-related complications and intestinal failure-associated liver disease. This should include the emergency management of any HPN-related issues 24 h per day, seven days per week. Patients and carers must be provided with clear written information relating to the recognition and management of HPN-related complications, including contact details of the NST in case of any emergency. The NST should generate written protocols for the management of HPN-related complications and, importantly, should have systems in-place such that specialist advice from the NST is available at all times. Where patients cannot attend the CIF center with emergency issues (for example, if distance and/or clinical need mandates immediate care at a local hospital), the NST should ensure that shared cared-protocols have been disseminated to local hospitals in advance and that the patient also has relevant details of their condition available.

Patients and caregivers should be aware that the NST may not be responsible for all aspects of their health, including the underlying disease leading to CIF. For example, patients with Crohn's disease may be under the care of a gastroenterologist at a local hospital for the monitoring and management of IBD-related issues. Similarly, for patients with malignancy, oncology and/or palliative care teams best manage emergencies relating to underlying disease. Thus, as soon as a patient is established on HPN, he/she and his/her general practitioner should be made aware of the relevant roles and responsibilities of the health care professionals involved in aspects of the patient's condition that are unrelated to HPN [3,11,14].

Patients can suffer from non-IF related conditions and these can be a significant cause of morbidity and mortality (for example,

cardiac disease, respiratory disease etc.). Care for these conditions, including any emergency needs, should continue as for patients without CIF [3,11,14]. It is important that the NST is informed immediately of any changes in these conditions, including any alterations in medication for non-IF related problems, as well as any admissions to hospital.

16. How should travelling with HPN be organized?

Recommendation 70

For a patient to travel safely, he/she shall receive a sufficient supply of PN and relevant ancillaries during the journey and at the destination and the NST responsible for the patient's care shall endeavor to establish contact with a skilled NST at the patient's destination, in case medical support is required.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

Patients on long-term HPN may need to learn how to adjust to lifestyle events such as bathing, showering, swimming, sports and travel [12]. Travelling with PN is an important factor for some patients' QoL [192,193] and independency [70,194]. However, none of the previous guidelines and position papers addressed this topic and a literature search did not provide any new information about this area in adults. So the recommendation and comments of the present guideline were based on statements of patients' representatives participating in the panel.

Pre-travel planning is essential to ensure that the patients can meet their usual PN/IV fluid requirements as well as to be able to perform PN-related procedures safely. The patient/caregivers should discuss their travel plans with their healthcare professionals/NST to ensure that they/their child are fit to travel. The doctor should issue a letter/medical certificate for the patient/caregivers confirming that they are aware they are travelling, along with a brief overview of their condition and need for PN. Medical cover/travel insurance should be arranged prior to travelling to ensure that any medical treatment needed while travelling will be possible. The patient/caregivers should ask about the potential and suitability of multi-chamber bags for their trip instead of compounded PN if they would like to consider using them. The patient/caregivers should investigate different power supplies/plugs prior to travelling to ensure they can charge pumps and batteries. A spare infusion pump should be taken on all trips, alternatively check the possibility of a replacement pump at the destination. Using homecare/compounding services at the end destination should be investigated very early during the planning period where reimbursement is possible and is available via different healthcare systems. The patient/caregivers need to calculate the number of fluid bags (PN/IV fluids) and ancillaries/medical supplies that they will need for their trip allowing for extra supplies. It is the responsibility of the patient/caregivers to know the stability of the PN, how long compounded PN can be safely stored in the dedicated PN boxes supplied by homecare companies/hospitals, before it needs to be placed in a fridge. The patient/parents should plan for additional fluids for the duration of travel, where high temperatures may be experienced, to ensure hydration is maintained. All fluids and ancillaries/medical supplies must be appropriately packed to ensure safe storage and stability both in terms of preventing damage and maintaining cold-chain temperatures, where applicable. The type of accommodation should be carefully considered in advance, especially where a fridge is required for the storage of compounded PN at 2° – 8 °C. In case of an emergency situation, a plan of action should be prepared beforehand and all important (doctor, family) contact numbers should be easily accessible. All modes of transport are possible for PN, travelling by plane will require more detailed planning. Attention to increased security checks must be respected. Prior to travel, if any special arrangements need to be made - such as additional space, extra baggage allowance, security approval – this must be arranged prior to departure. All PN/IV fluid boxes and ancillary/medical supplies baggage should be clearly labelled with a name, destination, date of travel and instructions not to open if cold-chain PN unless in the presence of the patient/caregivers. Usual healthcare professionals should consider establishing local medical support or a contact for the patient should medical support be required.

17. Which criteria should be used to monitor the safety of HPN program provision?

Recommendation 71

Incidence of catheter-related infection, incidence of hospital readmission and QoL should be used as criteria to assess the quality of care of HPN program.

Grade of Recommendation GPP – Strong consensus (100% agreement)

Commentary

Three multicenter international studies have identified and ranked the interventions determined to be essential for good quality of care (also called 'key interventions') [51,71,184]. Two studies were based on the opinions of healthcare professionals with expertise on HPN and included either benign or malignant CIF [51,71]. The third study evaluated the desired outcomes of patients with CIF due to benign disease [70,184]. The two-round Delphi approach was used, which is a technique that transforms opinion into group consensus, and the resulting set of most highly ranked key interventions was then transformed into quality indicators [51,71,184].

The top three outcome indicators identified by healthcare professionals were incidence of CRBSI, incidence of rehospitalizations and QoL for CIF due to either benign [71] or malignant [51] disease. The top three desired outcomes of patients with benign CIF were incidence of CRBSI, survival rate, and QoL on HPN [184].

The key interventions identified should be measured annually in current practice, along with questionnaires on patients' satisfaction, to identify and address any areas for further improvement [4].

According to the Donabedian paradigm [195], the outcome indicators should not be measured alone. The Donabedian model provides a framework to assess the quality of care by working with quality indicators related to structure, process and outcome of health care: 'structure' refers to general administrative standards of the organization and people providing care; 'process' refers to the manner in which care is actually provided and administered; 'outcome' refers to a set of expected or desirable results for patients [195]. Therefore, the outcome indicators reported should be monitored along with the linked process as well as structure indicators which will help to drive quality improvement.

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Conflicts of Interest

The expert members of the working group were accredited by the ESPEN Guidelines Group, the ESPEN Education and Clinical Practice Committee, and the ESPEN executive. All expert members have declared their individual conflicts of interest according to the rules of the International Committee of Medical Journal Editors (ICMJE). If potential conflicts were indicated, they were reviewed by the ESPEN guideline officers and, in cases of doubts, by the ESPEN executive. None of the expert panel had to be excluded from the working group or from co-authorship because of serious conflicts. The conflict of interest forms are stored at the ESPEN

guideline office and can be reviewed by ESPEN members with legitimate interest upon request to the ESPEN executive.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2020.03.005.

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