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Choice of access route for artificial nutrition in cancer patients: 30 y of activity in a home palliative care setting

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ABSTRACT

Objectives: Malnutrition negatively affects the quality of life, survival, and clinical outcome of patients with cancer. Home artificial nutrition (HAN) is an appropriate nutritional therapy to prevent death from cachexia and to improve quality of life, and it can be integrated into a home palliative care program. The choice to start home enteral nutrition (HEN) or home parenteral nutrition (HPN) is based on patient-specific indications and contraindications. The aim of this observational study was to analyze the changes that occurred in the criteria for choosing the access route to artificial nutrition during 30 y of activity of a nutritional service team (NST) in a palliative home care setting, as well as to compare indications, clinical nutritional outcomes, and complications between HEN and HPN.

Methods: The following parameters were analyzed and compared for HEN and HPN: tumor site and metastases; nutritional status (body mass index, weight loss in the past 6 mo); basal energy expenditure and oral food intake; Karnofsky performance status; access routes to HEN (feeding tubes) and HPN (central venous catheters); water and protein-calorie support; and survival and complications of HAN.

Results: From 1990 to 2020, HAN was started in 1014 patients with cancer (592 men, 422 women; 65.6 ± 12.7 y of age); HPN was started in 666 patients (66%); and HEN was started in 348 patients (34%). At the end of the study, 921 patients had died, 77 had suspended HAN for oral refeeding and 16 were in the progress of HAN. The oral caloric intake was <50% basal energy expenditure in all patients: 721 (71.1%) were unable to eat at all (HEN 270, HPN 451), whereas in 293 patients (28.9%), artificial nutrition was supplementary to oral intake. From 2010 to 2020, the number of central venous catheters for HPN, especially peripherally inserted central catheters, doubled compared with that in the previous 20 y, with a decrease of 71.6% in feeding tubes for HEN. At the beginning, patients on HEN and HPN had comparable nutrition and performance status, and there was no difference in nutritional outcome after 1 mo of HAN. In 215 patients who started supplemental parenteral nutrition to oral feeding, total protein-calorie intake allowed a significant increase in body mass index and Karnofsky performance status. The duration of HEN was longer than that of HPN but was similar to that of supplemental parenteral nutrition.

Conclusions: Over 30 y of nutritional service team activity, the choice of central venous catheters as an access route to HAN increased progressively and significantly due to personalized patient decision-making choices. Nutritional efficacy was comparable between HEN and HPN. In patients who maintained food oral intake, supplemental parenteral nutrition improved weight, performance status, and survival better than other types of HAN.

Introduction

Choosing to start home artificial nutrition (HAN) in patients with cancer in a palliative care setting involves nutritional and ethical problems, which concern not only clinical conditions but also, and primarily, the patient's quality of life (QoL) [1]. Since malnutrition is present in ≤80% of patients with cancer [2] and negatively

ER, RO, and LP contributed to the conception and design of the study. ER and RO contributed to data analyses and data interpretation. ER drafted the manuscript and coordinated the NST of the ANT Foundation and data collection. ER, MG, FA, SS, and LV substantially contributed to the data collection. RP was responsible for project administration and supervision. All authors contributed to the interpretation of data, critically revised, and approved the final version of this manuscript. The authors have no conflicts of interest to declare.

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affects the clinical outcome, HAN represents an appropriate nutritional treatment for improving survival and performance status, even in patients with advanced cancer [3,4]. Choosing a patient candidate for HAN is one of the most critical decisions for dietitians who must use appropriate selection criteria to ensure the benefits of HAN are greater than its potential damage [5].

Artificial nutrition can be provided through feeding tubes for home enteral nutrition (HEN) or central venous catheters (CVCs) for home parenteral nutrition (HPN). The choice of the access route is still a controversial topic, and HEN and HPN are often seen as competitors [6,7]. Therapeutic efficacy, minor complications, and low costs are the parameters that facilitate the choice of HEN when the gastrointestinal (GI) tract is functioning, whereas HPN becomes the choice when the digestive system cannot be used or HEN is not sufficient [8]. Clinical nutrition has markedly changed in the past 3 decades, and new techniques and technologies have reduced the incidence of complications and lowered the costs of HPN [7]. Additionally, the choice of access route for HAN must take into consideration the patient's will and preference [9].

This study describes the changes in the choice of access route to HAN during the past 3 decades and compares the efficacy and cost−benefit of HEN and HPN in a home palliative care setting using the observational retrospective analysis of the 30-y activity managed by the nutrition service team (NST) of the Italian non-profit organization, the National Tumor Assistance (ANT) Foundation [10].

Materials and methods

Nutritional counseling

The home care model managed by the ANT Foundation employs a hospital-at-home approach in which a multidisciplinary team of physicians, nurses, and psychologists, all trained in palliative care, works around the clock 24 h/7 d a week to assist patients with cancer [10].

The NST has been working in ANT since 1990 and consists of a gastroenterologist-nutritionist and a nutrition-dedicated nurse. The nutritionist assessed the nutritional status of the at-home patient and verified the presence of the eligibility criteria for HAN [5]:

- Malnutrition and/or negative energy balance. Nutritional status was assessed using body mass index (BMI), calculated with the Quetelet formula (kg/m^2; normal value: ≥18.5), and the percentage of weight loss in the previous 6 mo [(initial weight − actual weight/initial weight) × 100; normal value: <10%]. Protein-calorie malnutrition is present when both parameters were altered. The oral intake of food was estimated using a nutritional investigation of the composition and frequency of meals. The energy balance was considered negative when the patient could not eat for more than 1 wk or the energy intake was <50% of basal energy expenditure (BEE, calculated using the Harris−Benedict formula [11]) for >1 to 2 wk, with consequent loss of body weight (BW).
- Life expectancy. Life expectancy was estimated using the Karnofsky performance status (KPS) [12] and clinical and laboratory parameters reported in the Palliative Prognostic Score [13] and was based on the site, type, and staging of cancer and the presence and localization of metastases. The patient was eligible for HAN if the supposed life expectancy ≥6 wk.
- Physical, psychological, and environmental conditions. The patient was considered eligible if there was no severe organ failure, the pain was well controlled, the patient and/or the caregiver were able to independently understand and manage HAN, and environmental and hygiene conditions were adequate.
- Informed consent. The nutritionist explained the methods, benefits, and possible complications related to HAN and required written informed consent for the treatment and data collection from the patient and caregiver. The data analyzed in this study were retrieved from a prospectively collected database.

When artificial nutrition was set up in the hospital, the ANT nutritionist performed counseling when the patient arrived at home and decided if and how to continue nutritional therapy at home.

Pathogenesis of malnutrition

The choice of artificial nutritional treatment derives from a careful analysis of the pathogenesis of malnutrition and/or inadequate nutrient intake [5,14].

The main indication to start HAN was malnutrition due to the organic consequences of cancer or treatment. When the pathogenesis of malnutrition was hypermetabolism or anorexia, pharmacologic therapy was attempted (anticytokine agents, anabolic agents, metabolism inhibitors, appetite-stimulating drugs) [15]. If drug therapy was ineffective, there was an indication to start HAN.

Access route for artificial nutrition

The choice of access route for artificial nutrition occurred according to the International Guidelines of the European Society of Clinical Nutrition and Metabolism [4,16,17]. A CVC for parenteral nutrition was the indication when access to the GI tract for enteral nutrition was contraindicated (perforation, intestinal occlusion, or chylothorax); not possible (paralytic ileus, digestive hemorrhage, multiple intestinal surgery); or ineffective (high-flow fistulas, short-bowel syndrome, radiation enteritis) [18]. Supplemental parenteral nutrition (SPN) was used when food intake, including oral nutritional supplements, was inadequate and insufficient to maintain protein-calorie intake [4,16,19]. Patient will and preference were taken into consideration in the choice of the access route for HAN.

When artificial nutrition was set up in the hospital, the already predisposed access route was used.

Nasogastric (NG) and nasojejunal (NJ) tubes, percutaneous endoscopic gastrostomy/jejunostomy (PEG/PEJ), and surgical gastrostomy/jejunostomy tubes for feeding administration were used for HEN.

For HPN, the CVC type was mainly the central percutaneous catheter and the peripherally inserted central catheter (PICC), the latter performed at the patient's home by the PICC Service of the ANT Foundation. Patients who had previously placed a partially tunneled or a totally implanted Port-a-cath used these CVCs for HPN.

Handling the HAN

The HAN was performed using commercial solutions, and all the material (blends and infusion sets for the HEN, bags containing standard formulas and material for attaching/detaching the HPN, material for dressing the access routes) was provided by the National Health System. All material for HAN was delivered once a week to the patient's home by the ANT Foundation's Family Service.

The nutrition-dedicated nurse trained a caregiver (generally a family member) at home for the independent management of the HAN infusion line. In a few cases, the patient was self-sufficient for HAN management for both HEN (11.5%) and HPN (2.8%). For HEN, the training lasted ~1 to 3 d. The infusion mode required the use of a nutritional pump for most of the patients with HEN (82.3%). For HPN, the training lasted ~4 to 5 d. The nurse trained the caregiver to respect the correct rules of asepsis to manage the HPN (preparation of a sterile work area, antiseptic handwashing, preparation of the bag and the infusion line, attacchment and detachment of the infusion line from the CVC). At the end of the training, a video tutorial performed by NST was available on the website of the Italian Society of Parenteral and Enteral Nutrition (SINPE) for the patient and caregiver as a practical manual [20]. HPN infusion was performed by gravity with dial flow in all of the of cases. The dial flow allowed for adequate control of the regularity of the infusion time, even when the HPN was administered during the night (73.8%), whereas the nutritional pump was perceived as more constraining and not strictly necessary. Dressing the access routes to HAN was performed once or twice a week by the nurse.

The monitoring of HAN at the patient's home was carried out regularly: once or twice a week by the nutritionist and several times a week (as required) by the nurse. During the follow-up visits, clinical, nutritional, and biochemical parameters were collected in a nutrition folder. For any emergency related to HAN, the patient and/or the caregiver could contact the nutritionist or nurse by phone.

Statistical analysis

The annual trend in the choice of the access route for HAN was analyzed using linear regressions. The dependent variables were the number of patients starting HEN or HPN each year and the number of patients for each access route (surgical gastrostomy, surgical jejunostomy, PEG/PEJ and NG/NJ tube for HEN; partially tunneled CVC; totally tunneled CVC; PICC; and central percutaneous catheter for HPN) per year, whereas the independent variable was time (year).

The comparison of daily intake of fluid, total energy, energy/BW, total protein, and protein/BW between HEN and HPN was analyzed using the Mann−Whitney U test.

ΔKPS was calculated as KPS (after 1 mo) − KPS (at the start of HAN), and ΔBMI was calculated as BMI (after 1 mo) − BMI (at the start of HAN). The comparison of ΔKPS and ΔBMI among the types of HAN was performed using the Kruskal−Wallis test followed by pairwise comparisons (HEN vs HPN-no feed; HEN vs SPN; HPN-no feed vs SPN).

Kaplan−Meier survival curves display the survival of patients from the start of HAN. The association between the type of HAN (HEN, HPN-no feed, and SPN) and

Table 1
Characteristics of the patients starting HAN

	HEN (n = 348)	HPN (n = 666)
Age, mean ± SD	68.4 ± 12.4	64.6 ± 12.4
Sex, n (%)		
Men	249 (71.6)	229 (50.8)
Women	99 (28.4)	222 (49.2)
Primary tumor site, n (%)		
Head and neck	149 (42.8)	116 (17.4)
Esophagus	56 (16.1)	47 (7)
Stomach	69 (19.8)	153 (23)
Pancreas	7 (2)	65 (9.8)
Colon	14 (4)	128 (19.2)
Lung	23 (6.6)	21 (3.1)
Breast	4 (1.2)	16 (2.4)
Uterus	1 (0.3)	14 (2.1)
Ovary	0 (0)	59 (8.9)
Other organs*	25 (7.2)	47 (7.1)
KPS, mean ± SD	52.2 ± 9.9	51.9 ± 9.8

HEN, home enteral nutrition; HPN, home parenteral nutrition; KPS, Karnofsky performance status

survival was analyzed using a Cox regression model adjusted for age and sex. HEN patients were considered the reference group for the regression analysis.

All analyses were executed using SPSS version 25 (IBM, Armonk, NY, USA).

Results

Patients and clinical features

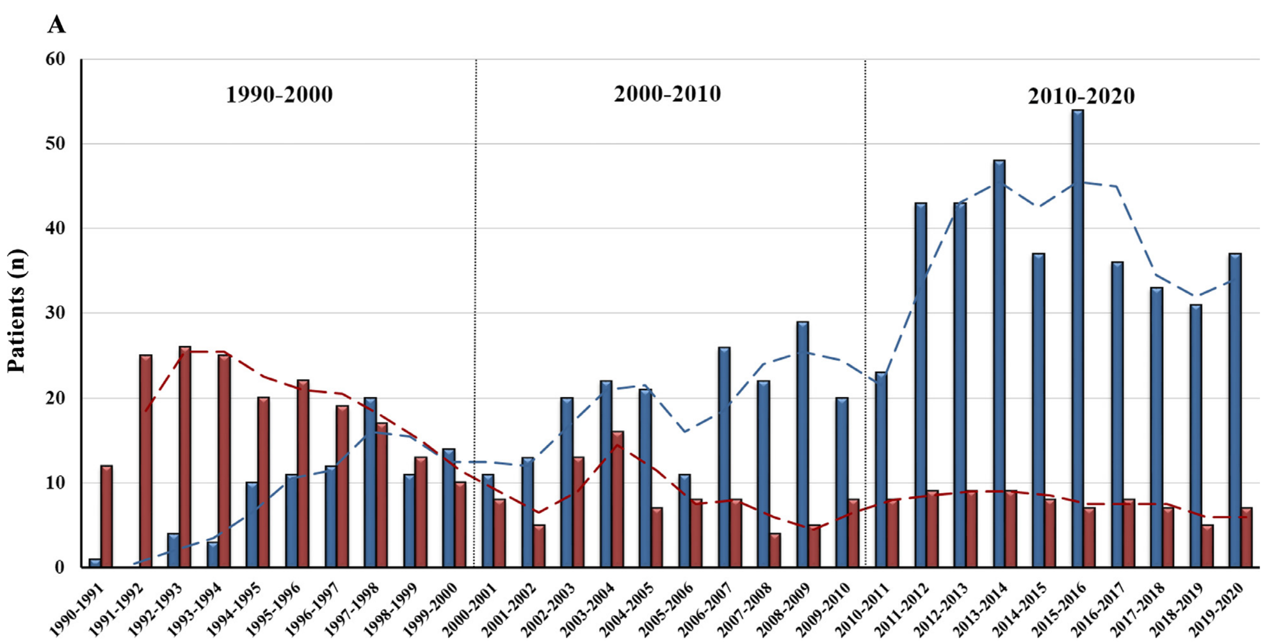
Data were collected from July 1, 1990 to June 30, 2020, by the NST of the ANT Foundation operating in Bologna and its province in Italy. During this period, HAN was started in 1014 patients (Table 1): 592 men and 422 women (age: 65.6 ± 12.7 y). HEN was started in 348 patients (34.3%), and HPN was started in 666 patients (65.7%). The most common primary tumor sites were the head and neck region (25.9%) and the GI tract (55.1%). At the start of HAN, 405 patients (39.9%) had widespread metastasis to other organs; 550 patients (54.2%) had locoregional metastases, of which 253 (24.8%) were intraperitoneal (peritoneal carcinomatosis); 59 patients (5.8%), almost all with head and neck localization in radiotherapy, had no metastasis. The KPS score at the start of HAN was similar in patients starting HEN and HPN ($P = 0.653$).

During the observation period, 77 patients suspended artificial nutrition for oral refeeding. Of these patients, 52 (67.5%) were had head and neck cancer and had undergone radiotherapy. They resumed oral feeding when post-actinic dysphagia improved. At the end of the study, 16 patients had HAN in progress, and 921 patients had died. HAN continued until death in almost all cases (94.8%).

Choice of access route for HAN

Over the 30 y of NST activity, a progressive shift occurred in the choice of the access route (Fig. 1): From 1990 to 2020, the number of patients starting HEN significantly decreased ($P < 0.001$), whereas the number of patients starting HPN significantly increased ($P < 0.001$).

HEN was the primary indication (63.9%) for patients with dysphagia (n = 366; Fig. 2). In these patients, NG tubes were the first choice in the 1990–2000 decade, but since 2010, there has been a complete reversal between HEN and HPN (Fig. 3).



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Access route for HAN	β coefficient (95% CI)	*P*-value
HEN	–.756 (–.749 /–.373)	<.001
HPN	.880 (1.137 / 1.737)	<.001

Fig. 1. Annual changes in the choice of access route for the HAN. (**A**) Data are shown as the number of patients starting HEN and HPN for each year. (**B**) Linear regression showing the association between the annual number of patients starting HEN or HPN and time (year). Data are shown as β coefficient (95% CI). HAN, home artificial nutrition; HEN, home enteral nutrition; HPN, home parenteral nutrition.

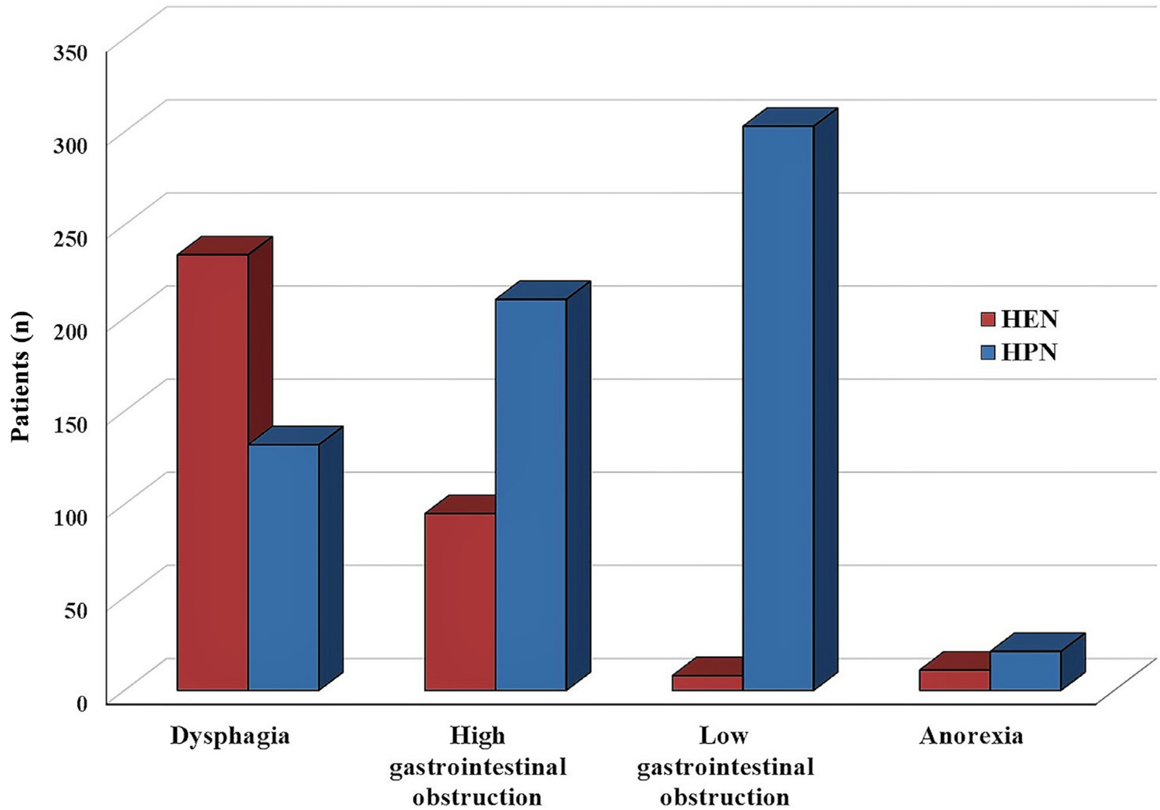


Fig. 2. HAN indication for patients with dysphagia, high and low gastrointestinal obstruction, and anorexia. Data are shown as the number of patients starting HEN or HPN for each condition from 1990 to 2020. HAN, home artificial nutrition; HEN, home enteral nutrition; HPN, home parenteral nutrition.

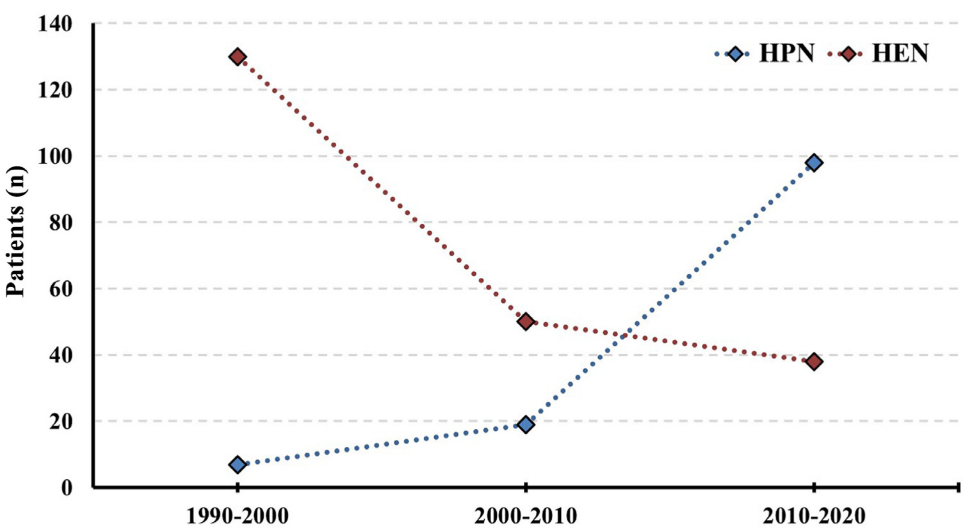
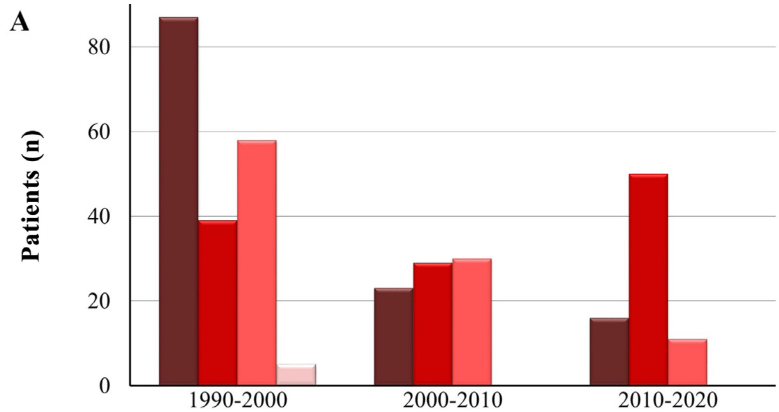


Fig. 3. Changes in the HAN access route for patients with dysphagia. Data are shown as the number of patients with dysphagia starting HEN or HPN for each decade. HAN, home artificial nutrition; HEN, home enteral nutrition; HPN, home parenteral nutrition.

HPN was the main indication (83.3%) for patients with high or low GI obstruction (616 patients; Fig. 2).

The access routes for HEN were the NG/NJ tube (36.2%), PEG/PEJ (33.9%), surgical jejunostomy (28.4%), and surgical gastrostomy (1.4%). The trend in the choice of feeding tube for HEN is shown in Figure 4. The number of patients fed by NG/NJ tubes, surgical gastrostomy, and jejunostomy significantly decreased from 1990 to 2020 ($P < 0.001$, $P < 0.001$, and $P = 0.003$, respectively). In the last decade, PEG was the main choice of access route to the GI tract.

The access routes for HPN were the central percutaneous catheter (32.7%), PICC (47.7%), totally tunneled catheter (14.9%) and partially tunneled catheter (4.6%). The changes in the choice of the CVC for the HPN are shown in Figure 5. The number of patients who had placed PICCs or totally tunneled catheters significantly

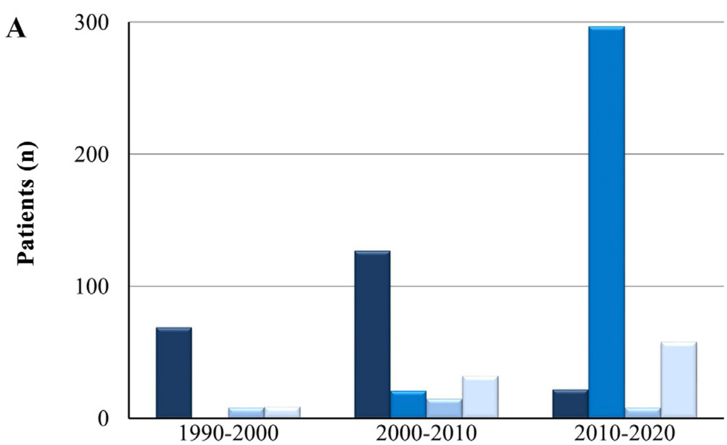


	1990-2000	2000-2010	2010-2020
Nasogastric/jejunal tube	87	23	16
PEG/PEJ	39	29	50
Surgical jejunostomy	58	30	11
Surgical gastrostomy	5	0	0

B

Access route for HEN	β coefficient (95% CI)	*P*-value
Nasogastric/jejunal tube	−.743 (−.502 /−.242)	<.001
PEG/PEJ	.214 (−.043 / .157)	.254
Surgical jejunostomy	−.785 (−.285 /−.152)	<.001
Surgical gastrostomy	−.522 (−.045 /−.010)	.003

Fig. 4. Changes in the choice of feeding tube for the HEN from 1990 to 2020. (**A**) Data are shown as the number of patients for each decade according to the access route for HEN. (**B**) Linear regression showing the association between the annual number of patients for each feeding tube for HEN and time (year). Data are shown as β coefficient (95% CI). HEN, home enteral nutrition.



	1990-2000	2000-2010	2010-2020
Central percutaneous catheter	69	127	22
PICC	0	21	297
Partially tunneled	8	15	8
Totally tunneled	9	32	58

B

Access route for HPN	β coefficient (95% CI)	*P*-value
Central percutaneous catheter	−.257 (−.420 / .078)	.170
PICC	.828 (1.032 / 1.764)	<.001
Partially tunneled	−.035 (−.067 / .056)	.855
Totally tunneled	.653 (.119 / .313)	<.001

Fig. 5. Changes in the choice of the CVC for the HPN from 1990 to 2020. (**A**) Data are shown as the number of patients for each decade according to the type of CVC for HPN. (**B**) Linear regression showing the association between the annual number of patients for each type of CVC and time (year). Data are shown as β coefficient (95% CI). CVC, central venous catheter; HPN, home parenteral nutrition; PEG/PEJ, percutaneous endoscopic gastrostomy/jejunostomy.

Table 2
Daily intake supplied by HEN and HPN

	HEN	HPN	*P*-value
Fluid (mL)	1286 ± 321	1698 ± 318	<0.001
Total energy (kcal)	1578 ± 448	1625 ± 318	<0.010
Energy/BW (kcal/kg)	30 ± 9	31 ± 8	<0.001
Total protein (g)	62 ± 17	69 ± 16	<0.001
Protein/BW (g/kg)	1.2 ± 0.4	1.3 ± 0.4	<0.001

BW, body weight; HEN, home enteral nutrition; HPN, home parenteral nutrition
Data expressed as mean ± SD
Statistical analysis performed by Mann–Whitney U test
*Duodenum, liver, biliary tract, bladder, kidney, prostate, bone, brain, skin, lymphoma.

increased from 1990 to 2020 (P <0.001). In particular, 297 PICCs (44.6% of the total) were positioned from 2010 to 2020, wherever the central percutaneous catheter was the main choice in the previous 20 y.

Oral and artificial nutrition

At the start of HAN, the BEE of patients was the same for both HEN (1185 ± 184 kcal/d) and HPN (1191 ± 186 kcal/d). All patients had a negative energy balance, and 432 (42.6%) were malnourished. Most of the patients (71.1%) did not feed at all: 270 HEN and 451 HPN (HPN-no feed). In the remaining 293 patients (28.9%), the mean oral caloric intake was 160 kcal/d for HEN and 320 kcal/d for HPN. Total energy intake for SPN was 1885 ± 312 kcal/d. Daily intake of fluids, calories, and proteins was significantly higher for HPN than HEN (Table 2).

Table 3 shows the variation of KPS (ΔKPS) and BMI (ΔBMI) after 1 mo of HAN: SPN patients showed a significantly higher increase of KPS and BMI compared with HEN and HPN-no feed patients ($P < 0.001$).

Survival

Survival analysis was performed on the 921 patients who died at the end of the study (Fig. 6). The mean survival time was 22.5 ± 32.5 wk for HEN patients, 13.4 ± 15.1 wk for HPN-no feed patients. and 23.8 ± 23 wk for SPN patients. The association between the type of artificial nutrition therapy (HEN, HPN-no feed, or SPN) and survival was evaluated using a Cox regression model adjusted for age and sex, considering HEN patients as the reference group. The results showed that HPN-no feed was associated with an increased mortality hazard (odds ratio [OR], 1.7; $P < 0.001$) and poorer survival than HEN (Fig. 6B), although no significant difference in survival was observed between SPN and HEN (OR, 0.9; $P = 0.415$; Fig. 6B).

Table 3
Variation in KPS and BMI after 1 mo of HEN, HPN-no feed, and SPN

	HEN	HPN-no feed	SPN	*P*-value
ΔKPS (1 mo)	1.4 ± 5.8	0.6 ± 5.5	4.0± 5.9	0.248*; <0.001†,‡
ΔBMI (1 mo)	0.06 ± 0.25	0.04 ± 0.25	0.21 ± 0.23	0.857*; <0.001†,‡

BMI, body mass index; HEN, home enteral nutrition; HPN, home parenteral nutrition; KPS, Karnofsky performance status; SPN, supplemental parenteral nutrition
Data expressed as the mean ± SD
Statistical analysis was performed by the Kruskal–Wallis independent sample test
*Pairwise comparison between HEN and HPN-no feed.
†Pairwise comparison between HEN and SPN.
‡Pairwise comparison between HPN-no feed and SPN.

Complications of HAN

The main complications of HAN concerned the access site and involved 56 of 348 HEN patients (16.1%) and 78 of 666 HPN patients (11.7%; Table 4).

The most frequent complications for NG tubes and PEG were occlusion and spontaneous removal, both resolved by replacement at the patient's home.

Catheter-related bloodstream infection (CRBSI) was the major complication of HPN, with an incidence of 33 cases for 76 372 d of nutritional use of CVC (0.43/1000 catheter-days). In the 2010–2020 decade, 11 CRBSIs out of 385 CVCs (2.8%; 0.24/1000 catheter-days), significantly less than 22 cases out of 281 CVCs (7.8%; 0.68/1000 catheter-days), occurred in the previous 20 y. CVC-related thromboses increased from 3 cases (1.1%; 0.09/1000 catheter-days) observed before 2010 to 8 cases (2.1%; 0.18/1000 catheter-days) in the last decade.

Complications of CVC required transfer to a hospital in 22 patients, resolved in a day hospital for 6 patients, whereas hospitalization (average 12 d) was required for 16 patients.

Costs of HAN

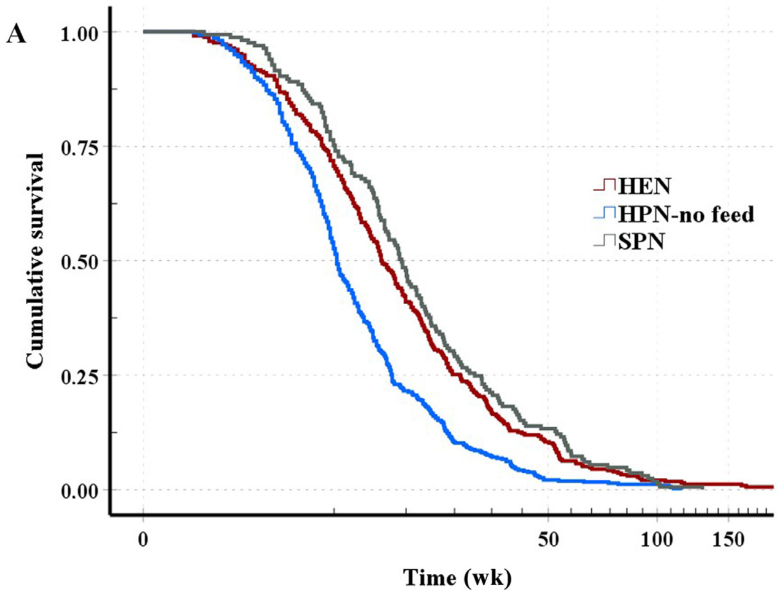
The 2019 data were considered to estimate the costs. The daily cost of NST was ~$25.29, paid for by the ANT Foundation through grants and private donations. The daily cost of the solution, infusion line, and dressing kits was $45.50 for HPN and $9.90 for HEN, paid for by the National Health System.

Discussion

The ANT Foundation's care model provides a palliative care program that, taking into consideration the physical effects of the disease and the subjective experience of the patient, offers the opportunity to live the last period of life in one's home environment by acting on pain, suffering, and physical and psychological difficulties and ensuring respect for privacy, dignity, and autonomy of patients and their families [10]. To prevent death from malnutrition and improve the QoL of cancer patients with hypophagia, a nutrition counseling service was started in 1990 in Bologna (Italy) in the framework of the home palliative care program provided by the ANT Foundation [5].

The decision to start artificial nutrition in patients with advanced cancer not only depends on the presence of malnutrition but also on bioethical considerations regarding the need to feed patients expected to survive weeks or days [21–23]. The European guidelines stated that stopping anticancer treatments is not a contraindication for HAN [24]. Artificial nutrition may be integrated into palliative care programs when a benefit on QoL is expected, and the risk for dying from malnutrition is higher than that due to cancer progression [1,4]. The Position Paper from the Italian Society of Medical Oncology and the SINPE reiterates and codes that "HAN may be integrated into palliative care programmes, according to individual-based evaluations, quality of life implications, life expectancy and patients' awareness" [24]. The use of valid selection criteria for HAN eligibility assumes a central role in identifying patients who can benefit from HAN and decreasing the risk for excessive and indiscriminate use of nutritional therapy, which could lead to therapeutic obstinacy [5].

The choice of the access route to HAN has always been a controversial topic [7], debated among HEN supporters when the GI tract is adequate, and who argue that HPN is more effective despite the greater risk for complications and expense.



B

		Estimated survival time (wk)		Hazard ratio		
	n	Mean (SD)	Median (95% CI)	B coefficient	Odds ratio (95% CI)	*P*-value
HEN	334	22.5 (32.5)	13.3 (11.7-14.9)	–	–	
HPN-no feed	422	13.4 (15.1)	8.6 (7.9-9.2)	0.528	1.7 (1.5-2)	<0.001
SPN	165	23.8 (23)	16(13.9-18.1)	−0.079	0.9 (0.8-1.1)	0.415

Fig. 6. Survival according to the nutritional therapy. (**A**) Kaplan−Meier survival curves for patients in HEN, HPN-no feed, and SPN groups. (**B**) Estimated survival time for patients in HEN, HPN-no feed, and SPN groups. Data are expressed as the mean (SD) and median (95% CI). The association between artificial nutrition therapy (HEN, HPN-no feed, and SPN) and survival was analyzed using a Cox regression adjusted for age and sex. HEN patients were considered the reference group. HEN, home enteral nutrition; HPN, home parenteral nutrition; SPN, supplemental parenteral nutrition.

Table 4
Complications of HEN and HPN

	n	%
HEN (n = 348)		
Occlusion	21	6.0
Spontaneous removal	13	3.7
External breakage	4	1.2
PEG-related infection	3	0.9
Gastrointestinal (diarrhea or severe constipation)	15	4.3
HPN (n = 666)		
Catheter-related bloodstream infection	33	4.9
Occlusion	13	1.9
External breakage	4	0.6
Catheter-related thrombosis	11	1.7
Phlebitis/Thrombophlebitis	4	0.6
Significant electrolyte abnormalities	9	1.4
Severe hyperglycemia	4	0.6

HEN, home enteral nutrition; HPN, home parenteral nutrition.
Data are expressed as the number and percentage of patients.

In the published literature on artificial nutrition, there are no evidence-based data to definitively establish what is the optimal access site to provide HAN in cancer patients, and the discussion seems to stagnate on the fact that HEN and HPN are competitive. Conversely, the choice should be dictated only by specific indications and contraindications and tailored to each patient [6,17].

Over 30 y of activity of the NST on patients with advanced cancer assisted at home by the ANT Foundation, the criteria for choosing the access route to the HAN changed substantially, often in contrast to the international guidelines.

An experienced nurse dedicated to training the caregiver for the safe management of the infusion line for HPN was employed in NST only from the mid-1990s, which influenced the choice of access route to HAN in the first period of our activity. The NG tube, which is easy to position and manage at home, was the first choice for patients with dysphagia in the first decade, but since 2000, there has been a gradual reversal in favor of CVC. A hospital nutritional screening protocol, started in 2014, allowed for the early recognition of the onset of dysphagia in patients with head and neck cancer in radiotherapy. The easy and quick positioning of a PICC in these patients, instead of a PEG, allowed for an immediate start of HPN, which was suspended on average 10 wk later, due to oral refeeding.

Since 2000, the choice of CVC as an access route for HAN has progressively increased, due to the following factors:

- The presence of an effective and safe NST for at-home management and monitoring of the central venous line allowed for the "protected" discharge from hospital wards of patients in HPN.
- Patients in palliative care often already had a CVC in place due to the lack of a peripheral venous system and the need for other infusion therapies, such as chemotherapy. In these patients, we considered it ethical and more acceptable to use the CVC to infuse nutritional support instead of placing an additional access to the GI tract by tube, if the indication was for HEN.
- Being able to choose between HEN and HPN and therefore between the feeding tube and CVC, most of the patients decided on an intravenous device, considering it a more comfortable intervention.

- The positioning of a PICC quickly at home allowed for the early start of the HPN, and this was important considering the short life expectancy in palliative care settings. In many cases, where there was an indication for HEN, the need for hospitalization for the positioning of a PEG or a jejunostomy would have required longer times for the start of nutritional support and a further physical and psychological burden with an inevitable negative affect on the patient's already compromised QoL.

In most patients, the device for HPN was the non-tunneled CVC. Port-a-cath was useful and better accepted by the patients who used this device cyclically, such as in chemotherapy and/or non-continuous HPN. In the present study, the infusion was conducted daily for all HPN patients, so the type of device did not protect the CVC from the risk for infection. The presence of a nurse dedicated to the correct management and monitoring of the infusion line allowed for containing the number of infectious complications [25], without significant differences between non-tunneled and tunneled CVCs. Furthermore, the resolution of the PICC's infectious and obstructive complications was easier than that of port-a-cath, as these complications could be quickly treated at home with the removal of the PICC, resolution of the infection, reimplantation of a new PICC, and restart of the HPN.

Since 2010, there has been a 39% increase in CVC-related thrombosis compared with the previous 20 y, due to the greater risk associated with the insertion of the PICC, especially in cancer patients [26].

In the past 10 y, there has been a significant reduction in the incidence of CRBSIs, due to the following factors:

- Low risk for PICC infection in outpatients [27];
- New materials for handling the infusion line, such as sutureless devices, needleless caps and disinfectant small caps, and pre-filled syringes for washing the PICC [28];
- Introduction of multichambered bags (so-called "all-in-one bags") [29];
- A rigid policy of hand-washing and antisepsis rules for training the caregiver to manage the infusion line more safely [30].

Survival was longer for HEN than for HPN-no feed, although the nutritional conditions and performance status were similar at the start of HAN. These data probably derive from the different types and staging of cancer. In fact, the tumor site in HEN patients was mainly located in the head and neck region, with no or local metastasis, whereas in HPN patients, the localization of the disease was primarily in the abdominal region (stomach, pancreas, and colon), with peritoneal carcinomatosis and widespread metastasis to other organs. In patients who maintained partial oral nutrition, SPN allowed for a significant improvement in survival, compared with patients with HEN. This result may be due to the less serious stage of cachexia in these patients compared with those who did not eat at all.

Conclusions

The observational study of 30 y of activity has shown a progressive change in choice parameters of the access route to HAN. In the past 10 y, CVCs doubled, due to the patient-tailored decision-making process. The advent of PICC at home and the new techniques and technologies allowed for safe management and reduced infectious complications of HPN.

There were no differences between HEN and HPN in nutritional outcome. Patients who partially ate and infused SPN improved their nutrition and performance status after 1 mo of HPN, significantly more than other types of HAN.

Limitations

The present study had some limitations. The first evaluation of nutritional status was performed by the ANT home palliative physician without the regular use of validated nutritional screening.

Proper and reliable monitoring of body composition requires bioelectric impedance analysis, which was not conducted in all patients but has become part of our investigative background in the past 2 y.

The BEE calculation was estimated using a predictive equation, and its accuracy may not be appropriate for calculating energy expenditure in patients with advanced cancer because it does not take into adequate consideration the metabolic requirements induced by cancer. The use of indirect calorimetry, although expensive and time-consuming, could allow for an accurate measurement of energy expenditure, improving the efficacy and safety of artificial nutrition. This will be the focus of our next study.

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References

[1] Marín Caro MM, Laviano A, Pichard C. Nutritional intervention and quality of life in adult oncology patients. Clin Nutr 2007;26:289–301.
[2] Hopkinson JB, Wright DNM, McDonald JW, Corner JL. The prevalence of concern about weight loss and change in eating habits in people with advanced cancer. J Pain Symptom Manage 2006;32:322–31.
[3] Caccialanza R, De Lorenzo F, Gianotti L, Zagonel V, Gavazzi C, Farina G, et al. Nutritional support for cancer patients: still a neglected right? Support Care Cancer 2017;25:3001–4.
[4] Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr 2017;36:11–48.
[5] Ruggeri E, Giannantonio M, Agostini F, Ostan R, Pironi L, Pannuti R. Home artificial nutrition in palliative care cancer patients: Impact on survival and performance status. Clin Nutr 2020;39:3346–53.
[6] Cotogni P. Enteral versus parenteral nutrition in cancer patients: evidences and controversies. Ann Palliat Med 2016;5:42–9.
[7] Chow R, Bruera E, Chiu L, Chow S, Chiu N, Lam H, et al. Enteral and parenteral nutrition in cancer patients: a systematic review and meta-analysis. Ann Palliat Med 2016;5:30–41.
[8] August DA, Huhmann MB. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. J Parenter Enter Nutr 2009;33:472–500.
[9] Scolapio J, Picco M, Tarrosa V. Enteral versus parenteral nutrition: the patient's preference. JPEN J Parenter Enter Nutr 2002;26:248–50.
[10] Casadio M, Biasco G, Abernethy A, Bonazzi V, Pannuti R, Pannuti F. The National Tumor Association Foundation (ANT): a 30 year old model of home palliative care. BMC Palliat Care 2010;9:12.
[11] Harris J, Benedict F. A biometric study of human basal metabolism. Proc Natl Acad Sci U S A 1918;4:370–3.
[12] Karnofsky DA, Burchenal JH. The clinical evaluation of chemotherapeutic agents in cancer. New York, NY: Columbia University Press; 1949.
[13] Pirovano M, Maltoni M, Nanni O, Marinari M, Indelli M, Zaninetta G, et al. A new palliative prognostic score: a first step for the staging of terminally ill cancer patients. J Pain Symptom Manage 1999;17:231–9.
[14] Mattox TW. Treatment of unintentional weight loss in patients with cancer. Nutr Clin Pract 2005;20:400–10.
[15] Mattox TW. Cancer cachexia: cause, diagnosis, and treatment. Nutr Clin Pract 2017;32:599–606.
[16] Arends J, Baracos V, Bertz H, Bozzetti F, Calder PCC, Deutz NEPEP, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. Clin Nutr 2017;36:1187–96.
[17] Pironi L, Boeykens K, Bozzetti F, Joly F, Klek S, Lal S, et al. ESPEN guideline on home parenteral nutrition. Clin Nutr 2020;39:1645–66.
[18] Virizuela JA, Camblor-Álvarez M, Luengo-Pérez LM, Grande E, Álvarez-Hernández J, Sendrós-Madroño MJ, et al. Nutritional support and parenteral nutrition

in cancer patients: an expert consensus report. Clin Transl Oncol 2018;20:619–29.
[19] Russell MK, Wischmeyer PE. Supplemental parenteral nutrition: review of the literature and current nutrition guidelines. Nutr Clin Pract 2018;33:359–69.
[20] The management of Home Parenteral Nutrition. Italian Society of Parenteral and Enteral Nutrition (SINPE). Updated January 2016. http://www.sinpe.org/video/la-gestione-della-nutrizione-parenterale-domiciliare/. Accessed September, 2020.
[21] Bozzetti F. Nutritional support of the oncology patient. Crit Rev Oncol Hematol 2013;87:172–200.
[22] Druml C, Ballmer PE, Druml W, Oehmichen F, Shenkin A, Singer P, et al. ESPEN guideline on ethical aspects of artificial nutrition and hydration. Clin Nutr 2016;35:545–56.
[23] Ellershaw J, Ward C. Care of the dying patient: the last hours or days of life. BMJ 2003;326:30–4.
[24] Caccialanza R, Pedrazzoli P, Cereda E, Gavazzi C, Pinto C, Paccagnella A, et al. Nutritional support in cancer patients: a position paper from the Italian Society of Medical Oncology (AIOM) and the Italian Society of Artificial Nutrition and Metabolism (SINPE). J Cancer 2016;7:131–5.
[25] Loveday HP, Wilson JA, Prieto J, Wilcox MH. epic3: revised recommendation for intravenous catheter and catheter site care. J Hosp Infect 2016;92:346–8.
[26] Jones D, Wismayer K, Bozas G, Palmer J, Elliott M, Maraveyas A. The risk of venous thromboembolism associated with peripherally inserted central catheters in ambulant cancer patients. Thromb J 2017;15:25.
[27] Chopra V, O'Horo JC, Rogers MAM, Maki DG, Safdar N. The risk of bloodstream infection associated with peripherally inserted central catheters compared with central venous catheters in adults: a systematic review and meta-analysis. Infect Control Hosp Epidemiol 2013;34:908–18.
[28] Bell T, O'Grady NP. Prevention of central line–associated bloodstream infections. Infect Dis Clin North Am 2017;31:551–9.
[29] Boullata JI, Gilbert K, Sacks G, Labossiere RJ, Crill C, Goday P, et al. A.S.P.E.N. Clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. J Parenter Enter Nutr 2014;38:334–77.
[30] Cotogni P, Barbero C, Garrino C, Degiorgis C, Mussa B, De Francesco A, et al. Peripherally inserted central catheters in non-hospitalized cancer patients: 5-year results of a prospective study. Support Care Cancer 2015;23:403–9.