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Original article

Home artificial nutrition in palliative care cancer patients: Impact on survival and performance status

Enrico Ruggeri [a,*], Marilena Giannantonio [a], Federica Agostini [a], Rita Ostan [a], Loris Pironi [b], Raffaella Pannuti [a]

[a] National Tumor Assistance (ANT) Foundation, Via Jacopo di Paolo, 36 - 40128 Bologna, Italy
[b] Center for Chronic Intestinal Failure, St Orsola Hospital, University of Bologna, Via Massarenti, 9 - 40138 Bologna, Italy

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SUMMARY

Background and aims: The prevalence of malnutrition is over 70% in advanced cancer patients and impacts negatively on survival and quality of life. Artificial nutrition can be integrated into a home palliative care program. This observational study aims to describe the criteria for identifying the cancer patients that could benefit from home artificial nutrition (HAN) and to evaluate its impact on survival and performance status.
Methods: The selection criteria for patient's eligibility to HAN were: Karnofsky Performance Status (KPS) $\geq$40, life expectancy $\geq$6 weeks, inadequate caloric intake $\pm$ malnutrition, suitable psycho-physical conditions and informed consent. The access route for nutritional therapy (home parenteral nutrition, HPN; home enteral nutrition, HEN) was chosen according to the ESPEN Guidelines. The parameters considered were: primary site of the tumor; oral food intake; nutritional status; stage of cachexia; fluid, energy and protein supplied by HAN; survival.
Results: From 1990 to 2019, 43,474 cancer patients were assisted at home in Bologna (Italy). HAN started in 969 patients (2.2% of total patients, 571 men and 398 women, mean age 65.7 $\pm$ 12.7 years): HPN in 629 patients (64.9%), with gastrointestinal obstruction as the main indication; HEN in 340 patients (35.1%), with dysphagia as the main indication. Considering the 890 deceased patients, the mean survival after the start of HAN was 18.3 weeks and 649 patients (72.9%) survived more than 6 weeks. The mean survival was higher in HEN (22.1 weeks) compared to HPN patients (16.1 weeks) ($p < .001$). After one month, KPS was unchanged in 649 (67.0%), increased in 232 (23.9%) and decreased in 88 patients (9.1%). The mean KPS increased in patients starting HAN in pre-cachexia and cachexia ($p < .001$). Cachexia and refractory cachexia at the entry were associated with a reduced survival [odds ratio: 1.5 and 2.3 respectively, $p < .001$ for both condition] respect to pre-cachexia.
Conclusions: The selection criteria allow the identification of the patient who can take advantage of HAN. HAN can be effective in avoiding death from malnutrition in 73% of patients, and in maintaining or improving the KPS at one month in 90% of cases. The benefits provided by HAN on survival and performance status depend on the cachexia degree at the entry.

Introduction

Cachexia is one of the most important causes of morbidity and mortality [1,2] in oncology, occurs in more than 50% of patients, up to 80% when cancer affects the head-neck region or the gastrointestinal tract [3], and accounts for up to 20% of deaths due to cancer [4]. The pathophysiology is characterized by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism.

The artificial nutrition is an appropriate nutritional treatment for cancer cachexia when the reduction of oral food intake is due to organic consequences of tumor or treatment-related adverse events [5], and it can be integrated into a palliative care program [6]. However, the choice to start artificial nutrition in advanced cancer patients represents one of the most critical decisions for the

* Corresponding author.
E-mail address: enrico.ruggeri@ant.it (E. Ruggeri).

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specialist and requires considering not only the clinical parameters but also ethical questions. The use of appropriate selection criteria becomes essential to identify the patients eligible for artificial nutrition avoiding the risk of excessive and indiscriminate use of nutritional therapy.

Literature shows that the home setting for palliative care leads to better outcomes, reducing symptoms, preserving the quality of life and even improving survival [7]. Indeed, an efficient model of home care assistance for advanced cancer patients should exploit a multidisciplinary approach to carefully assess and manage the nutritional status of the patient.

This study aims to describe the selection criteria used for identifying the eligible patients for home artificial nutrition (HAN) and to evaluate the impact of HAN on performance status and survival in cancer patients assisted at home by a palliative care program.

The present paper reports the observational retrospective analysis of the twenty-nine years activity managed by the Nutrition Service Team (NST) of the non profit organization National Tumor Assistance (ANT) Foundation in Bologna and its province (Italy).

Materials and methods

A nutrition flow chart was designed to identify candidate patients for HAN (Fig. 1).

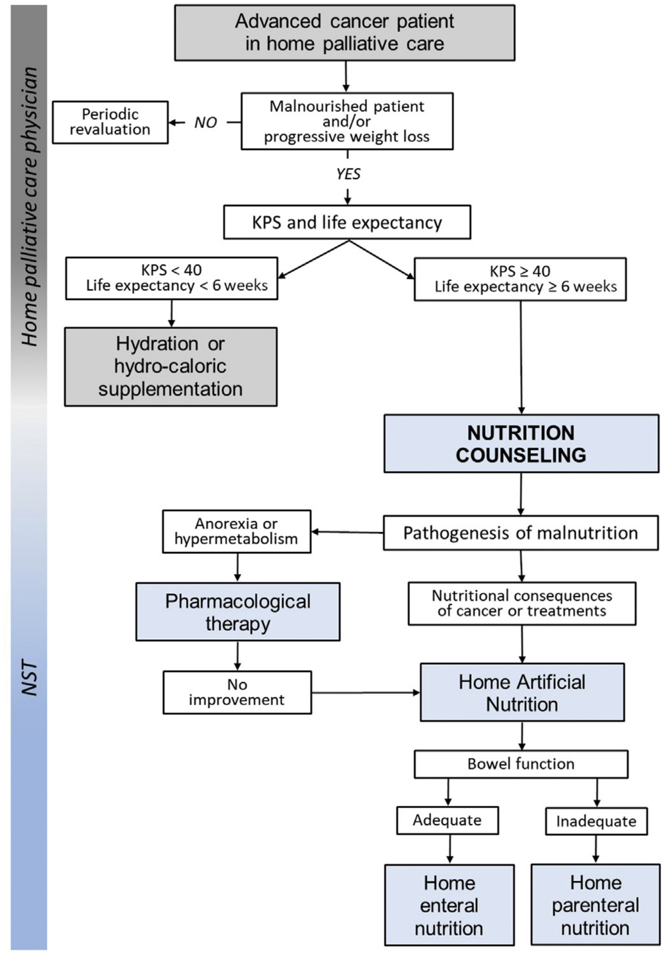


Fig. 1. Nutrition flow chart for identifying HAN candidate patients.

Home palliative care physician

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, work around-the-clock 24 h/7 days a week to assist cancer patients [8].

The home palliative care physician required the nutrition counseling for patients showing a malnutrition status or a progressive weight loss, but maintaining a KPS equal or higher than 40 and not in end of life.

Nutritional counselling

The Nutrition Service Team (NST) consists of a gastroenterologist-nutritionist and a nutrition-dedicated nurse. The nutritionist assessed the nutritional status of the patient and verified the presence of the criteria of eligibility for HAN:

1. *Malnutrition and/or negative energy balance.* The nutritional status was assessed by the Body Mass Index (BMI), calculated with the Quetelet formula (Kg/m^2; normal value: $\geq$ 18.5) and the percentage of weight loss in the last 6 months [(initial weight - actual weight/initial weight) x 100; normal value: < 10%]. The alteration of both the parameters indicated protein-calorie malnutrition. The oral intake of food was estimated by a nutritional investigation about the composition and frequency of the meals. The energy balance was considered negative when the patient could not eat for more than a week or the energy intake was lower than 50% of requirements (basal energy expenditure calculated using the Harris-Benedict formula [9]) for more than 1–2 weeks, with consequent weight loss.
2. *Life expectancy.* Life expectancy was estimated by the Karnofsky performance status (KPS) [10] and clinical and laboratory parameters reported in the Palliative Prognostic Score (PPS) [11], and was based on type and staging of cancer and presence and localization of metastases. The patient was considered eligible for HAN if the life expectancy was equal or higher than 6 weeks.
3. *Physical, psychological and environmental conditions.* The patient was considered eligible if: (a) there was no severe organ failure; (b) the pain was well controlled; (c) the patient and/or the caregiver were able to understand and manage independently the HAN; (d) the environmental and hygiene conditions were adequate.
4. *Informed consent.* The nutritionist explained methods, benefits and possible complications related to HAN and required written informed consent for the treatment and data collection from the patient and the caregiver. The data analyzed in this study were retrieved from a prospectively collected database.

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

Evaluation of the degree of cachexia

The nutritionist assessed the presence of cachexia and classified its stage (pre-cachexia, cachexia or refractory cachexia) considering the nutritional status (BMI and weight loss), the presence of anorexia and sarcopenia, the KPS and the biochemical tests for inflammatory status (albumin, C-reactive protein) according the guidelines of Fearon et al. [12].

Pathogenesis of malnutrition

The choice of artificial nutritional treatment derives from a careful analysis of the pathogenesis of malnutrition and/or inadequate nutrient intake (Table 1) [13].

The main indication to start the HAN was the malnutrition due to the organic consequences of cancer or treatment. When the pathogenesis of malnutrition was hypermetabolism or anorexia, a pharmacological therapy was attempted (anti-cytokine agents, anabolic agents, metabolism inhibitors, appetite-stimulating) [14]. If drug therapy was not effective and did not lead to obvious improvements, there was the indication to start the HAN.

Choice of access route for artificial nutrition

The choice of access route for artificial nutrition occurred according to the European Society for Clinical Nutrition and Metabolism (ESPEN) Guidelines [15–17]. For patients with adequate intestinal function, the primary choice was the home enteral nutrition (HEN), by nasogastric/nasojejunal tube (at home), percutaneous endoscopic gastrostomy/jejunostomy (PEG/PEJ, ambulatory or “day hospital”) or surgical gastrostomy/jejunostomy (hospitalization). In patients with inadequate intestinal function, the main choice was the home parenteral nutrition (HPN) by central venous catheter (CVC): for the placement of non-tunnelled, partially tunnelled, or totally implanted (Port-A-Cath) central catheter, a “day hospital” regime was required. The Peripherally Inserted Central Catheter (PICC) was placed at the patient's home by the PICC home service of ANT Foundation.

HAN was performed by 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 the dressing of the access routes) was provided by the National Health System. All the material for the HAN was delivered to the patient's home by the family service of ANT Foundation, once a week.

The nutrition-dedicated nurse trained the patient and the caregiver at home for the independent management of the HAN infusion line. For HEN, the training lasted about 1–3 days. For the HPN, the nurse trained the caregiver to respect the correct rules of asepsis for the management of the HPN [18]: preparation of a sterile work area, antiseptic hand washing, preparation of the bag and the infusion line, attack and detachment of the infusion line from the CVC. The training for HPN lasted about 4–5 days. The dressing of the access routes to HAN was always performed by the nurse, 1–2 times/week.

The monitoring of HAN was carried out regularly: 1–2 times/week by the nutritionist and several times/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

According to the Shapiro–Wilk test for normal distribution, KPS and the daily intakes of fluid, total energy, energy/BW, total protein and protein/BW are not normally distributed. The comparison between the KPS of patients with head/neck cancer and with other primary sites of the tumor and the comparison of daily intakes between HEN and HPN patients were analyzed by the Mann–Whitney *U* test. The change of body weight after a month of HAN was considered as categorical ordinal variables (decreased, unvaried, increased) and the comparison of their distribution between HEN and HPN patients were analyzed by Pearson Chi–Square test. The variation of KPS after one month of HAN was analyzed according to the degree of cachexia at the entry by Wilcoxon signed-rank test. The correlation between the change of body weight and the variation of KPS was evaluated by a Spearman Rank correlation. A two-sided $p < .05$ was considered significant.

Kaplan–Meier survival curves were used to display the survival of patients from the start of HAN. The association between the type of artificial nutrition therapy (HEN or HPN) and survival, between the KPS at the entry and survival and between the degree of cachexia and survival were analyzed by a univariate Cox regression model adjusted for age and gender. Patients in HEN and patient in pre-cachexia were considered as reference groups for the regression analysis, respectively.

The statistical analyses were executed utilizing SPSS 25.0 for windows (SPSS Inc., Chicago, IL, USA).

Results

Patients

From 1st July 1990 to 1st July 2019, the ANT Foundation assisted at home 43,474 advanced cancer patients in Bologna and its province (Italy). The HAN started in 969 patients (2.2% total assisted): 571 men and 398 women (mean age 65.7 ± 12.7 yrs, range: 12–95 yrs).

Clinical and nutritional features

Table 2 shows the clinical and nutritional characteristics of the patients starting the HAN.

Table 1
Main causes of malnutrition and/or hypophagia in cancer patients.

Pathogenesis of malnutrition and/or hypophagia	
Nutritional consequences of cancer	Dysphagia, obstruction/perforation, intestinal fistulas, malabsorption/diarrhoea, intestinal dysmotility, fluid and electrolyte abnormalities.
Nutritional consequences of treatment	Chemotherapy (anorexia, nausea/vomiting, mucositis/enteritis, paralytic ileus), surgery (malabsorption/diarrhea, adhesion-induced obstruction, odynophagia/dysphagia, hydro-electrolyte imbalances), radiotherapy (anorexia, mucositis/enteritis, xerostomia, odynophagia/dysphagia, obstruction, perforation, intestinal fistulas), opiates (constipation).
Hypermetabolism	Energy requirements for cancer, tumour-induced alterations in the host (hormones, cytokines, neuropeptides), circulating factors produced by the tumour (lipid mobilizing factor, proteolysis inducing factor).
Anorexia	Complications due to cancer and/or treatment (altered taste, aversion to food), psychological factors (anxiety, depression), impairment of the peripheral and central neurohormonal mechanisms responsible for appetite control (leptin, ghrelin).

Table 2
Characteristics of the patients starting the HAN.

Age (mean ± St. Dev)	HAN		HEN		HPN	
	65.7 ± 12.7		68.3 ± 12.4		64.2 ± 12.6	
	N	%	N	%	N	%
Total	969	100.0	340	100.0	629	100.0
Men	571	58.9	247	72.6	324	51.5
Women	398	41.1	93	27.3	305	48.5
Tumour primary site						
Gastrointestinal tract	535	55.2	144	42.4	319	62.2
Head-neck	249	25.7	145	42.6	104	16.5
Other organs	142	14.6	28	8.2	114	18.1
Lung	43	4.4	23	6.8	20	3.2
HAN indications						
Dysphagia	347	35.8	228	67.0	119	18.9
Low gastrointestinal obstruction	297	30.6	8	2.4	289	46.0
High gastrointestinal obstruction	293	30.2	93	27.4	200	31.8
Anorexia	33	3.4	11	3.2	21	3.3
KPS						
40	247	25.5	90	26.5	157	25.0
50	399	41.1	123	36.2	276	43.9
60	218	22.5	91	26.7	127	20.2
70	55	5.7	32	9.4	53	8.4
80	20	2.1	4	1.2	16	2.5
Nutritional status						
Negative energy balance	969	100.0	340	100.0	629	100.0
Protein-calorie malnutrition	417	43.0	144	42.4	273	43.4
Stage of cachexia						
Pre-cachexia	249	25.7	90	26.5	159	25.3
Cachexia	478	49.3	173	50.9	305	48.5
Refractory cachexia	242	25.0	77	22.6	165	26.2

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

The most common primary sites of the tumor were the gastrointestinal tract (55.2%) and the head-neck region (25.7%). HEN was started in 340 (35.1%) and HPN in 629 (64.9%) out of the 969 patients. The primary indication for starting the HAN was dysphagia for HEN (67.0%) and gastrointestinal obstruction for HPN (77.8%).

KPS at the start of HAN was higher than 40 in 73.5% of HEN and 75.0% of HPN. KPS was significantly higher in patients with head-neck cancer compared to other (55.9 ± 10.7 *vs* 50.8 ± 9.2 respectively, $p < .001$). Less than half of the patients (43.5%) were malnourished but all of them had a negative energy balance. At the first nutrition visit, 249 patients (25.7%) were pre-cachectic, 478 patients (49.3%) were cachectic and 242 patients (25.0%) showed a refractory cachexia status. The severity of cachexia was significantly lower in patients with cancer at the head-neck region compared to other ($p < .001$, data not shown).

Home artificial nutrition

During the observation period, 62 patients suspended artificial nutrition for refeeding by mouth; 46 of them (74.2%) were head-neck cancer patients who underwent radiotherapy and resumed feeding when post-actinic dysphagia improved. At the end of the study, 17 patients had HAN in progress and 890 patients had died. HAN continued until death in almost all the cases (94.7%).

Access routes for home artificial nutrition

The most common access routes for HEN were nasogastric/jejunal (36.5%) and PEG/PEJ (33.2%) (Fig. 2A). The most common access route for HPN was non-tunnelled CVC/PICC (80.0%) (Fig. 2B). The PICC has been the primary choice as access route for the HPN in the last 5 years of NST activity (45% of all CVC), given the possibility of positioning the catheter at the patient's home.

For each patient, the caregiver was trained for the 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%). The infusion mode required the use of a nutritional pump for most of the patients in HEN (82.3%) while HPN infusion was by gravity with a dial-flow in 100% of cases. The dial-flow allowed an adequate control of the regularity of the infusion time, even when the HPN was administered during the night (73.8%) while the nutritional pump was perceived as more constraining and not strictly necessary.

Complications of home artificial nutrition

The complications of HAN involved 49 out of 340 HEN patients (14.4%) and 72 out of 629 HPN patients (11.4%) (Table 3). The most frequent complications were the occlusion of the tube for HEN and the catheter-related bloodstream infection (CRBSI) for HPN. The incidence of CRBSI was 33 cases per 68,049 days of nutritional use of CVC (0.18 episodes/catheter years).

Daily intakes supplied by home artificial nutrition

The daily intake of fluids, total energy and energy/BW, protein and protein/BW supplied by HAN was significantly higher for HPN than HEN (Table 4). After one month from the start of HAN, body weight was unvaried in 491 patients (50.7%) and increased in 359 patients (37.0%). Body weight variation was positively correlated with KPS variations ($\rho = 0.259$, $p < .001$, data not shown).

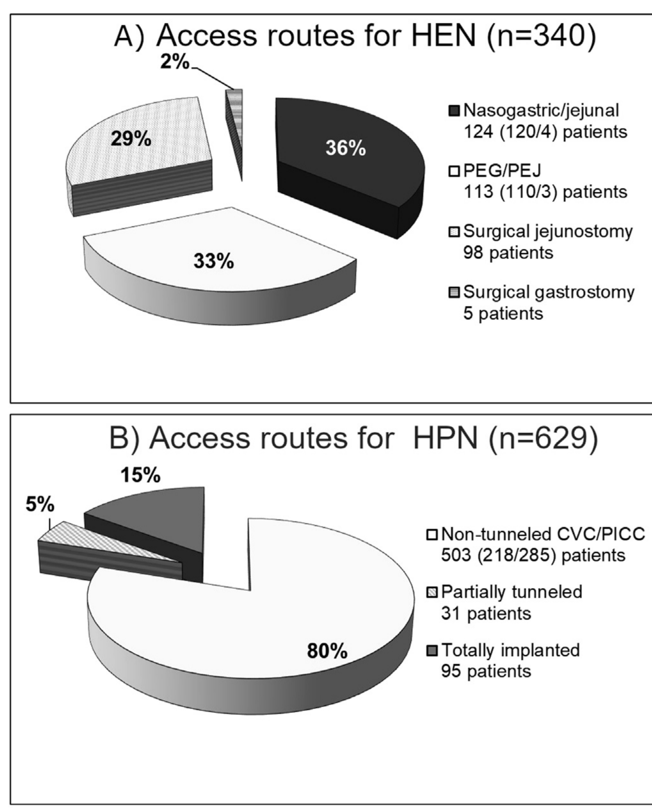


Fig. 2. Access routes for (A) HEN and (B) HPN.

Table 3
Complications of HEN and HPN.

	N	%
HEN (n = 340)		
Occlusion	21	6.2
Nasogastric tube ejection	13	3.8
Gastrointestinal (diarrhoea or severe constipation)	11	3.2
External breakage	4	1.2
HPN (n = 629)		
Catheter-related bloodstream infection	33	5.2
Occlusion	13	2.0
Deep vein thrombosis	9	1.4
Significant electrolyte abnormalities	9	1.4
Phlebitis/Thrombophlebitis	4	0.6
External breakage	4	0.6

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

Table 4
Daily intakes supplied by HEN and HPN.

	HEN	HPN	p
Fluid (ml)	1295 ± 315	1713 ± 317	<0.001
Total energy (kcal)	1590 ± 442	1684 ± 303	0.024
Energy/BW (kcal/kg)	30 ± 9	32 ± 8	<0.001
Total protein (g)	62 ± 16	70 ± 15	<0.001
Protein/BW (g/kg)	1.2 ± 0.4	1.4 ± 0.4	<0.001

HEN, home enteral nutrition; HPN, home parenteral nutrition; BW, body weight. Data are expressed as mean ± St. Dev. Statistical analysis was performed by the Mann–Whitney *U* test.

Home artificial nutrition and survival

The mean estimated survival time from the start of HAN was 18.3 ± 24.2 weeks. The survival time was higher than 6 weeks in 649 out of 890 patients (73.0%), higher than 3 months in 427 patients (48.0%) and higher than 6 months in 181 patients (20.3%) (Fig. 3A). The mean estimated survival time was 22.1 ± 31.9 weeks for the patients in HEN and 16.1 ± 18.0 weeks for patients in HPN (p < .001). The association between the type of artificial nutrition therapy (HEN or HPN) and survival was evaluated by Univariate Cox regression model adjusted for age and gender. Results showed that HPN was associated with an increased mortality hazard [odds ratio = 1.4, p < .001] and poorer survival compared to HEN (Fig. 3B).

KPS at the entry was significantly associated with estimated survival time: a higher KPS at the start of HAN predicted a longer survival [odds ratio = 0.9, p < .001, data not shown].

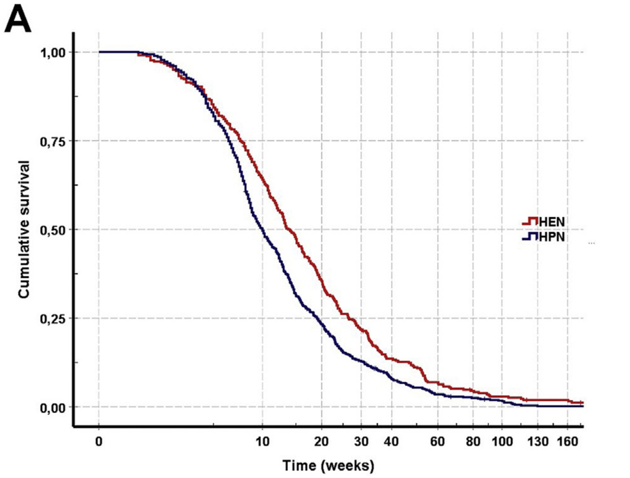
Cachexia at the entry, KPS and survival

The degree of cachexia at the entry has a significant impact on the variation of KPS evaluated at the start and after one month of HAN and on the survival of patients starting HAN.

After one month of HAN, mean KPS increased significantly in patients showing pre-cachexia and cachexia at the entry (p < .001 for both conditions) while it remained unvaried in patients with a refractory cachexia condition at the entry (p = .814) (Fig. 4A). The patients who increased their KPS showed a higher mean survival time (27.4 weeks) respect to patients with unvaried (16.6 weeks) and decreased KPS (8.4 weeks) (p < .001, data not shown).

The mean survival time was 28.7 ± 35.9 weeks for patients starting HAN in pre-cachexia, 17.1 ± 20.3 weeks for patients in cachexia and 11.9 ± 13.8 weeks for patients in refractory cachexia (Fig. 5). The association between the cachexia status at the entry and survival was evaluated by Univariate Cox regression model adjusted for age and gender. Results showed that the degree of

A



B

		Estimated survival time (weeks)		Hazard ratio		
	N	Mean (St.Dev.)	Median (95% C.I.)	B coefficient	Odds ratio (95% C.I.)	p
HEN	326	22.1 (31.9)	13.3 (11.7-14.9)	-	-	<.001
HPN	564	16.1 (18.0)	10.1 (9.0-11.3)	.308	1.4 (1.2-1.6)	

Fig. 3. Survival according to the nutritional therapy. (A) Kaplan–Meier survival curves for patients in HEN and HPN; (B) estimated survival time for patients in HEN and HPN. Data are expressed as mean (standard deviation, St. Dev.) and median (95% Confidence Interval, C.I.). The association between artificial nutritional therapy (HEN or HPN) and survival has been analyzed by a Cox regression adjusted for age and gender. Patients in HEN were considered as the reference group.

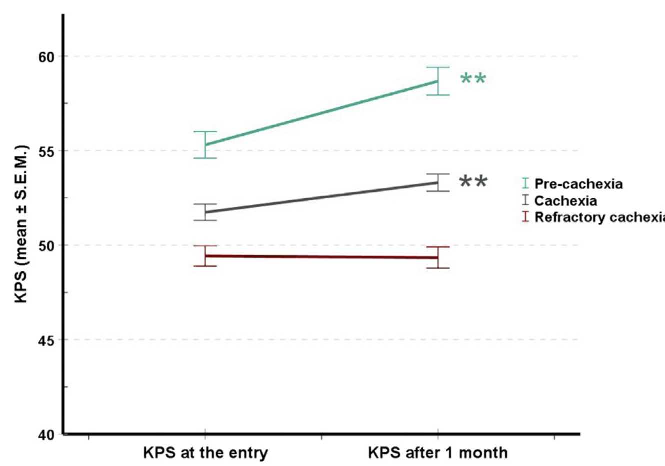


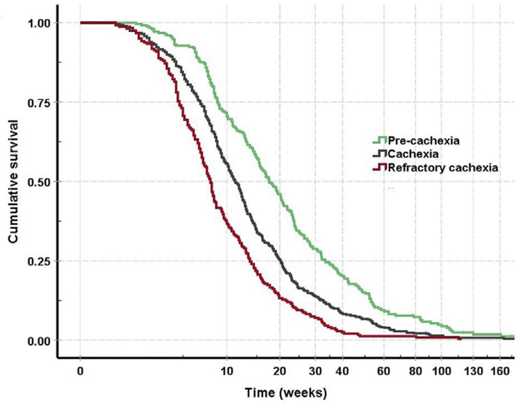
Fig. 4. KPS variation after one month of HAN according to the degree of cachexia at the entry. Data are expressed as mean ± standard error of the mean. Statistical analysis has been performed by Wilcoxon signed-rank test. **p < .001.

cachexia at the entry was negatively associated with survival: cachexia and refractory cachexia were associated with an increased mortality hazard (odds ratio = 1.6 for cachexia and odds ratio) = 2.4 for refractory cachexia, p < .001 for both condition] respect to pre-cachexia (Fig. 5B).

Costs

To estimate the costs, the data of 2018 were considered. The total number of days of HAN supplied by ANT was 4695 (3464 days of HPN and 1231 of HEN). The daily cost of NST was about 19.17€, paid by the ANT Foundation through grants and private donations; the daily cost of the solution, infusion line and dressing kits was 36.34€ for HPN and 7.90€ for HEN, paid by National Health System.

A



B

	N	Estimated survival time (weeks) Mean (St.Dev.)	Median (95% C.I.)	B coefficient	Hazard ratio Odds ratio (95% C.I.)	p
Pre-cachexia	199	28.7 (35.9)	19.3 (16.0-22.6)	-	-	-
Cachexia	453	17.1 (20.3)	11.3 (10.3-12.3)	.480	1.6 (1.4-1.9)	<.001
Refractory cachexia	238	11.9 (13.8)	7.8 (7.2-8.5)	.865	2.4 (1.9-2.9)	<.001

Fig. 5. Survival according to the degree of cachexia at the beginning of the HAN. (A) Kaplan–Meier survival curves for patients in pre-cachexia, cachexia and refractory cachexia; (B) Estimated survival time expressed as mean (St. Dev.) and median (95% Confidence Interval, C.I.). The association between the degree of cachexia and survival has been analyzed by a Cox regression adjusted for age and gender. Patients in pre-cachexia were considered as the reference group.

Discussion

Different studies [19–23] investigated the influence of caloric intake and energy expenditure on the nutritional status of cancer patients at different stages and typologies of the disease, detecting a strong correlation between weight loss and decreased survival. Malnutrition negatively affects muscle strength and performance status, reducing the patient's autonomy in daily functions with consequent fatigue, malaise and depression. The consequences of malnutrition include impairment of immune functions, decreased responses to chemotherapy, increased chemotherapy-induced toxicity and complications. Besides, cancer-related malnutrition is associated with significant healthcare-related costs [24–26]. Cancer-related malnutrition risk is sometimes overlooked or undertreated by clinicians [27], patients or their families [28]. In this context, a nutritional support can help to reduce the consequences of a cancer-associated nutritional decline to potentially improve the prognosis [15].

To prevent death from malnutrition and to improve the quality of life of cancer patients with hypophagia, a nutrition counseling service started in Bologna (Italy) in July 1990 in the framework of the home palliative care program provided by the non profit organization National Tumor Assistance (ANT) Foundation [5]. Founded in 1978, the ANT Foundation assists cancer patients at home, completely free of charge [8,29]. The ANT Foundation is present in 11 Italian regions with 23 multidisciplinary teams and has assisted 130.000 since 1985 representing the greatest experience of free home care for cancer patients in Italy and Europe.

The decision to start the artificial nutrition in advanced cancer patients depends not only on the presence of malnutrition, but it should include bioethical considerations [30–32] on the need to feed patients who are expected to survive weeks or days. At the same time, the decision to skip artificial nutrition or to suspend it should be considered only in an end-of-life setting [33–35]. Artificial nutrition may be integrated into palliative care programs when a benefit on quality of life is expected, and the risk of dying from malnutrition is higher than that due to cancer progression [5,15,36]. The use of a nutrition flow chart and valid selection criteria for HAN eligibility assumes a central role to identify patients who can benefit from HAN and to decrease the risk of excessive and indiscriminate use of nutritional therapy, which could lead to a therapeutic obstinacy.

In this study, the prediction of survival has been considered as one of the most important criteria for the eligibility to HAN. Whereas death by malnutrition occurs after about 60–75 days in prolonged fasting of a healthy adult, in patients with advanced cancer the starvation associated with underlying cachexia, a protein hypercatabolism and the consequences of cancer reduces survival to about 35–40 days [37]. In patients with a prognosis lower than 6 weeks, the HAN would not prevent death from cachexia, would be useless, expensive and would probably worsen the quality of life. The results of the present analysis showed that the survival of patients in HAN was more than 6 weeks in 73% of cases. These data, although encouraging, show that about 1/4 of the patients died within 6 weeks. This is partly due to the unpredictability of the disease trend, partly to the not always sufficient reliability of the PPS in predicting life expectancy and partly to the ethical choice of satisfying the patient's desire to be nourished, even artificially. The KPS is highly associated with survival in these patients, confirming its usefulness as a prognostic index in the decision-making process for the start of the HAN. The different estimated survival time between patients nourished by HPN and HEN should be ascribed to the indications for starting the specific nutritional therapy. The most of patients starting HPN showed gastrointestinal obstruction due to peritoneal carcinomatosis while the most of HEN patients were dysphagic and in a less advanced stage of disease.

The effect of HAN on the quality of life is still a controversial topic [38–40] and the assessment of quality of life in advanced cancer patients is challenging even using validated instruments [41–43]. Since literature data have shown a good correlation between the quality of life and KPS in these patients [44], we analyzed the impact of HAN on the performance status by using KPS changes after one month of HAN. In the present study, KPS showed an increase in 23%, no change in 67% and an impairing in 10% of patients. The improvement of KPS is associated with higher survival, showing that life expectancy increases proportionally to the improvement of performance status. Our results are in agreement with the conclusions of Bozzetti drawn from three papers about the effect of parenteral nutrition on quality of life evidencing that half of the patients showed no change, a quarter to fifth deteriorated and a quarter to a third improved [45].

According to international consensus conferences, cancer cachexia can be described as a multifactorial syndrome defined by an ongoing loss of skeletal muscle mass, accompanied or not with a loss of fat mass, that cannot be fully reversed by conventional nutritional support and that leads to progressive functional impairment [12,46]. This definition differentiates cancer cachexia from simple starvation or age-related loss of muscle mass. Since the body weight loss due to cancer cachexia has a multifactorial origin, an appropriate nutritional therapy, such as artificial nutrition, is not always able to correct the malnutrition [13]. At present, there is no accepted specific therapy for the treatment of cancer cachexia [13,14,47]. This often produces a sense of resignation, both in the patient and in the nutritionist, toward an inevitable loss of weight. Although most studies in the literature showed mixed reviews of HAN effectiveness on improving the quality of life and survival in cancer patients [15,48–51], some authors believe that artificial nutrition should be integrated into the contest of simultaneous care and the appropriate nutritional support should be guaranteed for all cancer patient [5,6,36].

Our results highlights the importance of the evaluation of the cachexia degree before starting HAN in cancer patients: the performance status improved after a month of HAN and the survival was higher in patients with pre-cachexia and cachexia at the entry. Patients starting HAN in a refractory cachexia status showed a shorter survival and maintained/worsened their KPS after one month. This results confirm the poor benefit of HAN in advanced cancer patients with refractory cachexia, in which the decision to start the HAN must therefore be based on more ethical than clinical/nutritional reasons.

The possibility of implementing artificial nutrition at home has a positive impact on the cost/benefit analysis: it reduces the costs of the National Health System (a hospital day only to carry out artificial nutrition costs 700€) and it allows the patients to spend the last months of life in their own environment and family. There were few cases of aversion to HAN, anyhow always felt as "necessary" and then prolonged, in almost all the cases, until the last days of life. In the small percentage of patients who have suspended HAN for worsening of conditions in the last days of life, this choice, directed by both clinical and ethical reasons, has been agreed and accepted by the patient and/or the family members.

Conclusions

The selection criteria allow the early and correct identification of patients who can take advantage of HAN. Data analysis shows that the HAN can be effective in avoiding death from malnutrition in 73% of treated patients, and in maintaining and improving the KPS at one month in 90% of cases. The benefits obtained by the HAN on survival and performance status depend on the degree of the cachexia detected at the start of artificial nutrition. Though the mean survival of patients in refractory cachexia is higher than 6 weeks, the slight benefit of HAN on the performance status and quality of life make the choice to start HAN in a very advanced stage of the disease a more ethical than clinical/nutritional question.

Limitations

Despite the many strengths, the present paper has some limitations. First of all, this study is a retrospective observational study without a control arm. In this research field, a randomized clinical trial is not ethically possible [45].

This study misses an assessment of the quality of life by a validated questionnaire. Indeed, quality of life questionnaires are demanding for these patients and not specific to capture the changes potentially due to HAN.

The first evaluation of the nutritional status was performed by the ANT home palliative physician without the regular use of a validated nutritional screening.

A better determination of the state of cachexia would require the analysis of Bioelectric Impedance Analysis (BIA), which was not carried out in all patients but it has become part of our investigative background only in the last two years.

Informed consent

Informed consent for the treatment and the data collection was obtained from all individual participants included in the study.

Ethical approval

Being a retrospective observational study, the Italian Legislation does not require any approval by a Research Ethical Committee.

Statement of authorship

ER, RO and LP contributed to the conception and design of the current work. ER and RO contributed to data analyses and data interpretation. ER drafted the manuscript, coordinated the NST of ANT Foundation and the data collection. ER, MG and FA substantially contributed to the data collection. RP was the responsible for project administration and supervision. All authors contributed to interpretation of data, critically revised, and approved the final version of this manuscript.

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Conflict of interest

The authors declare that they have no conflict of interest.

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