Tumori, 99: 218-224, 2013

Home artificial nutrition in advanced cancer patients

Enrico Ruggeri[1], Federica Agostini[1], Luana Fettucciari[1], Marilena Giannantonio[1], Loris Pironi[2], and Franco Pannuti[1]

[1]*ANT (Associazione Nazionale Tumori) Foundation;* [2]*Department of Internal Medicine and Gastroenterology, S Orsola-Malpighi Hospital, Bologna, Italy*

ABSTRACT

Aims and background. Malnutrition is over 50% in advanced cancer patients and is related to a decreased survival. Cachexia is the first reason for death in 4-23% of cases. The aim of the study was to estimate the appropriateness of the criteria to select patients for home artificial nutrition and its effectiveness to avoid death from cachexia and to improve quality of life in patients with advanced cancer assisted at home by the National Tumor Association (ANT) Foundation.

Methods and study design. The criteria for patient selection are: inadequate caloric intake ± malnutrition; life expectancy ≥6 weeks; suitable psycho-physical conditions; informed consent. The measured parameters were sex, age, tumor site, food intake, nutritional status, Karnofsky performance status, indication for home artificial nutrition, type of home artificial nutrition (enteral or parenteral), and survival after starting home artificial nutrition.

Results. The ANT Foundation assisted 29,348 patients in Bologna and its province from July 1990 to July 2012. Home artificial nutrition had been submitted to 618 patients (2.1%): enteral to 285/618 (46.1%) and parenteral to 333/618 (53.9%). Access routes for home artificial nutrition were: 39% nasogastric tube, 26% percutaneous endoscopic gastrostomy, 33% digiunostomy, and 2% gastrostomy. The central venous catheters used for home artificial nutrition were: 61% non-tunneled, 13 peripherally inserted, 8% partially tunneled, and 18% totally implanted. By July 2012, all the patients had died. Duration of life ≥6 weeks was 78% (484/618). Karnofsky performance status was related to survival ($P<0.0001$): one month after starting home artificial nutrition, it decreased in 73 patients (12%), was unchanged in 414 (67%), and increased in 131 (21%).

Conclusions. The low incidence of home artificial nutrition over all the patients assisted by the ANT Foundation and the achievement to avoid death from cachexia in 78% prove the efficacy of the criteria of patient selection in order to prevent its excessive and indiscriminate use. It was effective in maintaining and improving the performance status in 88% of patients. Karnofsky performance status is a reliable prognostic index to start home artificial nutrition.

Introduction

Cachexia is one of the most important causes of morbidity and mortality[1-2] in oncology. It occurs in more than 50% of patients, up to 80% when the cancer affects the head-neck region or the gastrointestinal tract[3], and is the primary cause of death in 4-23% of advanced cancer patients. Artificial nutrition is the appropriate nutritional treatment when the reduction of oral food intake is due to organic direct consequences of the cancer.

Home artificial nutrition (HAN) is indicated as a nutritional therapy in three specific types of cancer patients[4-6]: 1) patients without ongoing disease, in which the malnutrition state is due to nutritional consequences of specific therapy (chemo-radio-

Key words: advanced cancer patients, cachexia, home artificial nutrition, selection criteria.

Correspondence to: Enrico Ruggeri, via Fondazza 51, 40125 Bologna, Italy. Tel +39-348-3102998; email enrico.ruggeri@inwind.it

Received August 20, 2012; accepted October 23, 2012.

therapy and/or surgery); 2) patients with cancer disease, malnourished, who have to undergo curative or palliative treatment and in whom the correction of malnutrition is the *conditio sine qua non* for starting the treatment; 3) patients with advanced cancer, in which malnutrition and/or inadequate food intake represents the first cause of death.

Choosing to start a HAN in cancer patients with advanced disease represents one of the most critical decisions for the specialist, after having considered the nutritional and ethical questions. The use of selection criteria for the identification of the patient candidate to HAN reduces death from cachexia, avoiding the risk of excessive and indiscriminate use of nutritional therapy.

The following are the results of 22 years of nutritional counseling at the ANT Foundation in Bologna, Italy. The aim of the study was to evaluate the adequacy and effectiveness of the selection criteria for advanced cancer patients candidate to HAN in order to prevent death from cachexia and improve quality of life.

Materials and methods

Nutritional counseling and selection criteria

ANT nutritional counseling was started with two distinct modalities: a) in patients at home already in ANT home care; b) in hospitalized patients already in artificial nutrition who required ANT home care.

Patients at home. A questionnaire for the assessment of nutritional status with a modified Malnutrition Screening Tool[7] (Figure 1) was filled out for all patients in ANT home care. If the nutritional screening showed risk or the presence of a malnutrition state, the doctor filled out the Palliative Prognostic Score[8] (PPS) to assess life expectancy (Figure 2). If the 30-days survival probability was <30% (risk group C), the ANT doctor could choose not to use any nutritional therapy or only a water/calorie supplementation. If the expected survival was >70% (risk group A), nutritional counseling was sought. The nutritionist made his evaluation at home and verified the implementation of the following selection criteria.

1) Malnutrition and/or negative protein-energy balance. The nutritional status was assessed with the body mass index, calculated with the Quetelet formula (kg/m^2; n.v., ≥18.5) and the percentage of weight loss in the last 6 months [(initial weight - actual weight/initial weight) × 100; n.v., <10%]. Protein-energy malnutrition was present when both parameter were altered. The protein-energy balance was assessed by analysis of oral intake through food investigation and was considered negative when the caloric intake was <50% of basal energy expenditure, calculated using the Harris-Benedict formula.

2) Survival ≥6 weeks. Life expectancy of the patient was established with the Karnofsky performance status[9] (KPS) and other clinical and laboratory parameters reported in the PPS and was based on cancer histology and the presence and localization of metastases.

3) Psycho-physical and environmental conditions suitable for HAN. A patient was considered eligible if a)

Nutritional Screening (modified MST)

evaluation date ___/___/___

name-surname ______ age ______ sex ______
address ______ phone ______
ANT doctor ______ (ANT phone ______)

Have you lost weight recently (may be understood as "the last 2 weeks") without trying?

no	score	0
unsure	score	2

If yes, how much weight (kg) have you lost?

1-3	score	1
4-6	score	2
7-10	score	3
> 10	score	4
unsure	score	2

Have you been eating poorly because of a decreased appetite?

no	score	0
yes	score	1

TOTAL SCORE ______

Total score	Action
< 2 = no risk of malnutrition	[ ] revaluation monthly or when changing the clinical
≥ 2 = presence or risk of malnutrition	[ ] evaluate the Palliative Prognostic Score (PPS)

Figure 1 - Nutritional Screening (modified Malnutrition Screening Tool).

Palliative Prognostic Score (PPS)

Parameter	Criteria	Partial score
Dyspnea	SI / NO	1 / 0
Anorexia	SI / NO	1.5 / 0
Karnofsky Performance Status	≥ 30 ≤ 20	0 2.5
Clinical prediction of survival (weeks)	> 12 11-12 9-10 7-8 5-6 3-4 1-2	0 2 2.5 2.5 4.5 6 8.5
Total WBC/mm^3	4.800-8.500 8.501-11.000 > 11.000	0 0.5 1.5
Lymphocyte %	20-40 % 12-19.9 % 0-11,9 %	0 1 2.5
	Total score	

Risk group	PPS score	30 day survival
A	0 - 5.5	> 70 %
B	5.6 - 11.0	30 – 70 %
C	11.1 - 17.5	< 30 %

Figure 2 - Palliative Prognostic Score.

there was no organ failure, b) the pain was well controlled, c) the patient and/or the caregiver was able to understand and manage HAN independently, and d) the environmental and hygiene conditions were adequate.

4) Informed consent from the patient and/or caregiver.

Hospitalized patients. The doctor or the patient's family, when they requested ANT home care, indicated that there was an artificial nutrition in progress. The ANT nutritionist performed his counseling when the patient arrived at home, or directly in the ward, and verified the suitability of the selection criteria.

Home artificial nutrition

The choice of administration route of HAN was made in accord with the Guidelines of the Italian Society of Parenteral and Enteral Nutrition[6]. In patients with adequate intestinal function, the primary choice was home enteral nutrition (HEN), by nasogastric tube (at home), percutaneous endoscopic gastrostomy (ambulatory or day hospital), or jejunostomy (hospitalization). In patients with inadequate intestinal function, the main choice became home parenteral nutrition (HPN) by central venous catheter. For the placement of non-tunneled percutaneous catheters (subclavian, jugular, or peripherally inserted), partially tunneled, or totally implanted (Port-A-Cath), a "day hospital" regime was required.

HAN was performed by using commercial mixtures, and all the material (blends and infusion sets for HEN, nutritional bags and material for attaching-detaching the HPN, material for dressing the access routes) was provided by the Bologna Health System. The material for the HAN was delivered to the patient's home by the ANT Family Service, once a week.

Training for the correct and independent management of the infusion line of the HAN was always given at home, to the patient or a dedicated caregiver (a family member or someone outside the family). The caregiver must be present, necessarily, throughout the infusion period of HAN. For HEN, the training was carried out by nutritionist or specialized nutritional nurse and lasted about 1-3 days. For the HPN, the nurse trained the caregiver how to attach and detach the nutritional bag, and the training lasted about 4-5 days. The dressing of the access routes to HAN was always performed by the nurse, 1-2 times a week.

The monitoring of HAN was carried out regularly (1-2 times a week) by the nutritionist. The nurse, who was totally in charge of the patient, carried out the visits several times a week, as required. During examinations, clinical, nutritional and biochemical parameters were recorded. For any emergency related to HAN, patient and caregiver were able to contact by phone the nutritionist or nurse.

Statistics

Data are reported as mean ± standard deviation. To analyze the results, we used Pearson's correlation coefficient and Student's t test for unpaired data.

Results

From July 1990 to July 2012, the ANT Foundation assisted 29,348 advanced cancer patients at home, in Bologna and its province. HAN started in 618 patients (2.1% of all cared patients): 370 males, 248 females, age ranged from 6 to 95 years (65.5 ± 12.8).

Clinical and nutritional features

Table 1 shows the characteristics of the patients at the start of HAN. The main tumor site was the head-neck region and the gastrointestinal tract (81%), and the primary indication for starting HAN was dysphagia for enteral nutrition (67% of HEN) and gastrointestinal obstruction for parenteral nutrition (87% of HPN). The KPS (52 ± 9.6) was >40 (disable, requires special care and assistance) in 75.1% of HEN cases and 73.2% of HPN cases, and it was positively correlated (P <0.05) to the body mass index (19.1 ± 2.8), with no significant changes according to tumor site. Less than half of the patients were malnourished, and almost all had an oral caloric intake of less than 50% of basal energy expenditure, with no differences between HEN and HPN.

Table 1 - Clinical and nutritional characteristics of the patients at the start of artificial nutrition

Characteristic	HEN		HPN	
	(n=285)	(%)	(n=333)	(%)
Tumor site				
Head-neck	114	(40.0)	31	(9.3)
Gastrointestinal tract	128	(44.9)	226	(67.9)
Lung	22	(7.7)	10	(3.0)
Genitourinary tract	5	(1.8)	45	(13.5)
Other organs	16	(5.6)	21	(6.3)
HAN indications				
Anorexia	11	(3.8)	8	(2.4)
Dysphagia	190	(66.7)	33	(9.9)
High gastrointestinal occlusion	77	(27.0)	113	(33.9)
Low gastrointestinal occlusion	7	(2.5)	179	(53.8)
Karnofsky score				
30	5	(1.7)	2	(0.6)
40	66	(23.2)	86	(25.8)
50	101	(35.5)	142	(42.7)
60	85	(29.8)	72	(21.6)
70	26	(9.1)	30	(9.0)
80	2	(0.7)	1	(0.3)
Nutritional status				
Protein-energy malnutrition	127	(44.6)	162	(48.6)
Negative protein-energy balance	274	(96.1)	309	(92.8)

HEN, home enteral nutrition; HPN, home parenteral nutrition; HAN, home artificial nutrition.

Figure 3 summarizes the choice for HAN access routes. HEN was performed in 285/618 (46.1%) patients and HPN in 333/618 (53.9%) patients. Table 2 summarizes methodology and techniques used for patients in HAN. Training for the management of the HAN infusion line was given to a patient's family member or a specifically identified care giver, both for HEN (87.4%) and HPN (96.7%). The infusion mode required the use of a nutritional pump for most of the patients in HEN (78.2%), whereas for monitoring the HPN infusion a dial-flow was used in 100% of the cases. In our experience, the dial-flow was sufficient to allow an adequate control of the regularity of the infusion time, even when the HPN was performed during the night (68.8%), considering the nutritional pump more binding and not strictly necessary.

Complications (Table 3) involved 18.6% of HEN and 15.0% HPN. The most frequent were those involving the access route. The incidence of central venous catheter sepsis was 0.24 episodes/catheter year.

All patients were dead by the end of the observation period. HAN was prolonged until the end of life in almost all patients. In a small percentage (5.2%), the significant worsening of clinical conditions in the last days of life did not recommended the continuation of HAN. The choice, directed by both clinical and ethical reasons, was agreed upon and accepted by the patient and/or the family members.

The mean time of HAN was 20.4 ± 23.8 weeks (range, 1-217) for HEN and 15.8 ± 18.6 weeks (range, 1-130) for the HPN. Survival was ≥6 weeks in 484/618 patients (78%) (Figure 4). Table 4 shows the correlations between survival and quality of life, nutritional status and HEN. Duration of life was strongly related with the KPS evaluated at study entry (r = 0.291; P <0.0001).

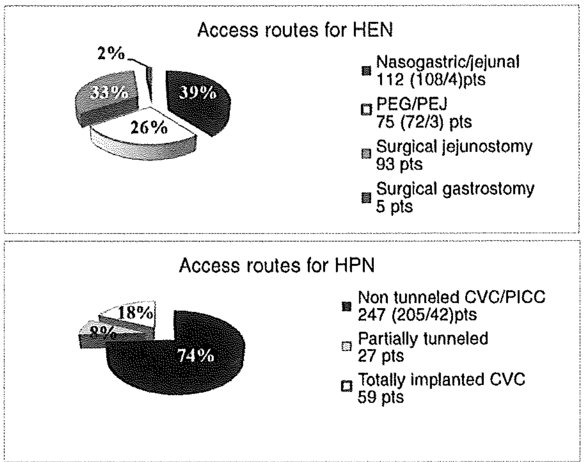

Figure 3 - Access routes for HAN.

Table 2 - Methodology of home artificial nutrition

	HEN		HPN	
	(n=285)	(%)	(n=333)	(%)
Training				
To the patient	36	(12.6)	11	(3.3)
To a family member or caregiver	249	(87.4)	322	(96.7)
Training time	1-3 days		5-7 days	
Infusion mode				
Nutritional pump	224	(78.2)	—	(0)
Gravity or dial-flow	48	(16.8)	333	(100)
"Gavage" (small bowls)	13	(4.6)		
Infusion duration				
Cyclic day	262	(91.9)	21	(6.3)
Cyclic night	23	(8.1)	229	(68.8)
Continuous (24/24 h)	—	(0)	83	(24.9)

HEN, home enteral nutrition; HPN, home parenteral nutrition.

Table 3 - Complications of home artificial nutrition

	No. of patients	(%)
HEN (n=285)		
Occlusion	26	(9.1)
Nasogastric tube ejection	12	(4.2)
External brackage	4	(1.4)
Gastrointestinal (diarrhea or severe constipation)	11	(3.9)
HPN (n=333)		
Sepsis	24	(7.2)
Deep vein thrombosis	3	(0.9)
Occlusion	13	(3.9)
External brackage	3	(0.9)
Significant electrolyte abnormalities	7	(2.1)

HEN, home enteral nutrition; HPN, home parenteral nutrition; HAN, home artificial nutrition.

Effectiveness of HAN on quality of life and nutritional status

Table 5 summarizes the changes in KPS one month from starting HAN. It was decreased in 73 patients (12%), unchanged in 414 (67%) and increased in 131

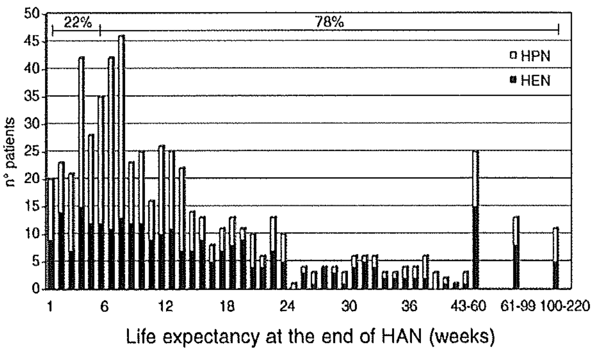

Figure 4 - Life expectancy of patients in HAN. HEN, home enteral nutrition; HPN, home parenteral nutrition; HAN, home artificial nutrition.

Table 4 - Correlations between survival and quality of life, nutritional status and home enteral nutrition

	Correlations with survival	P <
Quality of life	Karnofsky performance status (at study entry)	0.0001
Nutritional status	Body mass index (at study entry)	n.s.
	Body weight changes after 1 month of HEN	0.01
HEN	Total calories	0.005
	Calories/kg of body weight	0.02
	Total proteins	0.003
	Proteins/kg of body weight	0.02
	Total infused volume	n.s.

HEN, home enteral nutrition; n.s., not significant.

(21%), with no considerable differences between HEN or HPN. The KPS was significantly increased ($P < 0.05$) in the group of patients with cancer of the head-neck region. The mean survival was significantly higher in the group of patients with an increased KPS ($P < 0.0001$).

Intravenous energy intake was higher in patients on HPN (Cal/kg, 36.4 ± 8.7) than in those on HEN (Cal/kg, 30.4 ± 7.7), which resulted in an increase in body weight, which was most relevant in patients on HPN ($P < 0.05$). The increased body mass index was not correlated to an improvement of the KPS.

Discussion

Different studies[10-13] have 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. The Consensus Conference on Cachexia in 2006 defines cachexia as "a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle mass, regardless of fat loss"[14]. This definition differentiates cancer cachexia from simple starvation or age-related loss of muscle mass, indices that distract the oncologist from a correct differential diagnosis, since they also cause a marked reduction in body weight. In fact, a loss of body weight is present both in starvation and in cachexia. In cancer cachexia, the metabolic response is opposite to that originated by prolonged fasting, which is conservative.

Since the body weight loss due to cancer cachexia has a multifactorial origin[15], an appropriate nutritional therapy, such as artificial nutrition, is not always able to correct and improve the malnutrition state. At present, there is no accepted specific therapy for the treatment of cancer cachexia[16]. 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 show mixed reviews of HAN effectiveness on improving the quality of life and survival in cancer patients receiving radio-chemotherapy and surgery[17], HAN still seems to be the nutritional treatment of choice when the etiology of weight loss is represented by the direct nutritional consequences of cancer (dysphagia, bowel obstruction).

In order to avoid death from cachexia and improve quality of life in cancer patients who are unable to feed per os, a nutrition counseling service at the non-profit organization ANT-Italy Foundation[18-19] started in Bologna in July 1990. ANT is an association founded in 1978, assisting patients with advanced cancer, completely free of charge[20-21]. The ANT Foundation is present in 9 Italian regions and represents, with 20 home care oncology hospitals and 85,000 patients assisted, the greatest experience of free home care for cancer patients in Italy and Europe.

The systematic use of the Malnutrition Screening Tool[7] and PPS[8] for identification of the patient with the presence or risk of malnutrition started in July 2000. In the previous decade, this identification was related to the competence of the ANT doctors, who decided on

Table 5 - Changes in the performance status one month after starting the artificial nutrition

	HAN		Tumor site					
	HEN (285 pts)	HPN (333 pts)	HN (145 pts)	GI (354 pts)	Other (119 pts)	Survival (weeks) (m±SD)		
KPS (after one month of HAN)								
Decreased	33 (12%)	40 (12%)	12 (8%)	43 (12%)	19 (16%)	8.9 ± 11.7	^	
Unchanged	181 (63%)	233 (70%)	95 (66%)	237 (67%)	81 (68%)	16.3 ± 19.6		#
Increased	71 (25%)	60 (18%)	38 (26%)	74 (21%)	19 (16%)	28.1 ± 26.2	#	
				*				

HN, head-neck region; GI, gastrointestinal tract; HEN, home enteral nutrition; HPN, home parenteral nutrition; HAN, home artificial nutrition; KPS, Karnofsky performance status.
*$P < 0.05$; ^$P < 0.002$; #$P < 0.0001$.

their own whether the nutritional counseling was necessary. This may have partially influenced the low percentage of patients selected for the HAN (2.1% of all ANT home care patients), compared with the incidence of death by cachexia (4-23%) in the literature.

The decision to start artificial nutrition in advanced cancer patients depends not only on the presence of malnutrition, but sets ethical and moral issues, involving not only unnecessary and expensive treatment, but also a worsening of the previously compromised quality of life of the patient[22-23]. The search for valid criteria for patients candidate for HAN assumes a primary value to avoid the risk, always present, of an excessive and indiscriminate use of nutritional therapy, which could lead to a therapeutic obstinacy. The negative protein-energy balance was considered more important than the malnutrition in the decision-making process for starting artificial nutrition. Table 4 shows that not all of the patients on HAN had a negative protein-energy balance, as required by the nutrition flow chart. Of the patients on HEN and of those on HPN, 3.9% and 3%, respectively, had an adequate oral intake of energy but were malnourished. In these patients, HAN had been started in order to improve the nutritional status and to allow the patient to undergo curative and palliative treatment.

The main parameter of the decisional nutrition flow chart is the prediction of survival. In fact, whereas death by malnutrition occurs after about 60-75 days in a long-fasting healthy adult, in patients with advanced cancer the disability to feed is associated with an underlying cachexia, a protein hypercatabolism and the consequences of the cancer, reducing survival to about 35-40 days[24]. To avoid death from cachexia therefore means early intervention with artificial nutrition in cancer patients with advanced disease, malnourished and/or hypophagic for the consequences of cancer, whose life expectancy is more than 6 weeks. In patients whose death prognosis is <6 weeks, administering HAN would not prevent death from cachexia, it is useless, expensive and would worsen the quality of life. The results of our analysis showed that the survival of patients on HAN was ≥6 weeks in 78% of cases. Such data, although encouraging, demonstrate however that about 1/5 of the patients died within 6 weeks. It is therefore important to have accurate clinical and/or laboratory parameters related to survival[25-26]. In our nutritional protocol, we used the PPS[27] to guide the ANT doctor to the expected clinical prognosis. The results showed a highly significant correlation between survival and KPS at entry HAN, confirming the accuracy and usefulness of performance status as a prognostic index in the decision-making process for the start of HAN[28-29].

The literature data on the assessment of quality of life in cancer patients is still scarce and contradictory[30,31] and cannot be used in clinical nutrition. We analyzed the impact of HAN on the quality of life by using KPS changes after a month of HAN, which showed improvement in 21% of patients, a stationary status in 67%, and worsening in 12%. The data, related to the mean survival, showed that life expectancy of patients increases proportionally to the improvement of performance status due to HAN. The result supports the hypothesis of studies that have reported improved quality of life in patients with advanced cancer treated by HPN[32-33]. On the evaluation of the improvement of the quality of life, we felt it was important to consider the positive impact for the resolution of hypophagia and the resulting weight loss, which lead to psychological and physical comfort of the patient and the family, who describe this as one of the reasons for greater apprehension. Finally, the possibility of implementing HAN at home, during the night and independently, without having to spend the last months of life in a hospital only for carrying out artificial feeding, has been recognized by the patient and the family members as a considerable advantage. 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.

Conclusions

Data analysis showed the importance of a nutritional flow chart able to select patients candidate for HAN. The selection criteria were crucial in avoiding death from cachexia in 78% of patients treated with HAN. Furthermore, the low incidence of HAN in all the patients entering in ANT home care (2.1%) demonstrates that the nutritional protocol is a valid and decisive tool in reducing the risk of indiscriminate use of the technique.

HAN was effective in maintaining and improving the performance status in 88% of patients. The correlation between survival and the KPS at study entry confirmed the reliability of performance status as a prognostic index in the decision-making process for starting artificial nutrition in advanced cancer patients.

References

1. Inui A: Cancer anorexia-cachexia syndrome: current issues in research and management. CA Cancer J Clin, 52: 72-91, 2002.
2. MacDonald N, Easson AM, Mazurak VC, Dunn GP, Baracos VE: Understanding and managing cancer cachexia. J Am Coll Surg, 197: 143-161, 2003.
3. Hopkinson JB, Wright DNM, MacDonald JW, Corner JL: The prevalence of concern about weight loss and change habits in people with advanced cancer. J Pain Symptom Manag, 32: 322-331, 2006.
4. Bozzetti F: Guidelines on artificial nutrition versus hydration in terminal cancer patients. Report of an ad hoc Consensus Conference. Nutrition, 12: 163-167, 1996.
5. Staun M, Pironi L, Bozzetti F, Baxter J, Forbes A, Joly F, Jeppesen P, Moreno J, Hébuterne X, Pertkiewicz M, Mühlebach S, Shenkin A, Van Gossum A; ESPEN: ESPEN Guide-

lines on parenteral nutrition: home parenteral nutrition (HPN) in adult patients. Clin Nutr, 28: 467-479, 2009.
6. Commissione SINPE: Linee guida SINPE per la nutrizione artificiale ospedaliera 2002. RINPE, 20 (Suppl 5): S17-S22, 2002.
7. Ferguson M, Capra S, Bauer J, Banks M: Development of a malnutrition screening tool for adult acute hospital patients. Nutrition, 15: 458-464, 1999.
8. Pirovano M, Maltoni M, Nanni O, Marinari M, Indelli M, Zaninetta G, Petrella V, Barni S, Zecca E, Scarpi E, Labianca R, Amadori D, Luporini G: A new Palliative Prognostic Score. A first step for the staging for terminally ill cancer patients. J Pain Symptom Manage, 17: 231-239, 1999.
9. Karnofsky DA, Burchenal JH: The clinical evaluation of chemotherapeutic agents in cancer. In: Evaluation of Chemotherapeutic Agents, MacLeod CM (Ed), Columbia Univ Press, New York, 1949.
10. Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, Cohen MH, Douglass HO Jr, Engstrom PF, Ezdinli EZ, Horton J, Johnson GJ, Moertel CG, Oken MM, Perlia C, Rosenbaum C, Silverstein MN, Skeel RT, Sponzo RW, Tormey DC: Prognostic effect of weight loss prior to chemotherapy in cancer patients. Am J Med, 68: 491-497, 1980.
11. Vigano A, Bruera E, Jhangri GS, Fields AL, Suarez-Almazor ME: Clinical survival predictors in patients with advanced cancer. Arch Intern Med, 160: 861-868, 2000.
12. Bosaeus I, Daneryd P, Lundholm K: Dietary intake, resting energy expenditure, weight loss and survival in cancer patients. J Nutr, 132 (suppl 11): 3465S-3466S, 2002.
13. Laviano A, Meguid MM, Rossi-Fanelli R: Cancer anorexia: clinical implications, pathogenesis, and therapeutic strategies. Lancet Oncol, 4: 686-694, 2003.
14. Ewans WJ, Morley JE, Argiles J, Bales C, Baracos V, Guttrige D, Jatoi A, Kalantar-Zadeh K, Lochs H, Mantovani G, Marks D, Mitch WE, Muscaritoli M, Najand A, Ponikowski P, Rossi Fanelli F, Schambelan M, Schols A, Schuster M, Thomas D, Wolfe R, Anker SD: Cachexia: a new definition. Clin Nutr, 27: 793-799, 2008.
15. Mattox TW: Treatment of unintentional weight loss in patients with cancer. Nutr Clin Pract, 20: 400-410, 2005.
16. Gullett NP, Mazurak V, Hebbar G, Ziegler TR: Nutritional interventations for cancer-induced cachexia. Curr Probl Cancer, 35 (2): 58-90, 2011.
17. Bozzetti F, Cozzaglio L, Gavazzi C, Bidoli P, Bonfanti G, Montalto F, Soto Parra H, Valente M, Zucali R: Nutritional support in patients with cancer of the esophagus: impact on nutritional status, patient compliance to therapy, and survival. Tumori, 84 (6): 681-686, 1998.
18. Pironi L, Ruggeri E, Giordani S, Casadio M, Pannuti F, Miglioli M: Nutrizione artificiale domiciliare nei pazienti neoplastici in fase avanzata: attività di consulenza agli assistiti dell'Associazione Nazionale Tumori nell'area di Bologna e provincia. RINPE, 14 (1): 29-38, 1996.
19. Pironi L, Ruggeri E, Tanneberger S, Giordani S, Pannuti F, Miglioli M: Home artificial nutrition in advanced cancer. J R Soc Med, 90: 597-603, 1997.
20. Casadio M, Biasco G, Abernethy A, Bonazzi V, Pannuti R, Pannuti F: The National Tumor Association Foundation (ANT): a 30 years old model of home palliative care. BMC Palliative Care, 9: 12, 2010.
21. Pannuti R, Casadio M, Varani S, Pannuti F: Il progetto Eubiosia. Sintesi dell'esperienza assistenziale ANT 1985-2010. RICP, 4: 52-62, 2010.
22. Raijmakers NJH, van Zuylen L, Costantini M, Caraceni A, Clark J, Lundquist G, Voltz R, Ellershaw JE, van der Heide A, OPCARE9: Artificial nutrition and hydration in the last week of life in cancer patients. A systematic literature review of practices and effects. Ann Oncol, 22: 1478-1486, 2011.
23. Bozzetti F: La nutrizione del paziente afagico con malattia incurabile: una voce fuori dal coro. Nutri Ther Metabol - SINPE News, aprile-giugno: 2-6, 2006.
24. August D, Thorn D, Fisher R, Welchek C: Home parenteral nutrition for patients with inoperable malignant bowel obstruction. JPEN, 15: 323-327, 1991.
25. Maltoni M, Caraceni A, Brunelli C, Broeckaert B, Christakis N, Eychmueller S, Glare P, Nabal M, Viganò A, Larkin P, De Conno F, Hanks G, Kaasa S: Prognostic factors in advanced cancer patients: evidence-based clinical recommendations – A study by the Steering Committee of the European Association for Palliative Care. J Clin Oncol, 23: 6240-6248, 2005.
26. Tanneberger S, Malavasi I, Mariano P, Pannuti F, Strocchi E: Planning palliative of terminal care: the dilemma of doctors' prognoses in terminally ill cancer patients. Ann Oncol, 13: 1320-1322, 2002.
27. Tassinari D, Fantini M, Modenesi C, Maltoni M: La caratterizzazione prognostica della malattia oncologica in fase avanzata. RICP, 1: 37-42, 2005.
28. Bruera E, Miller MJ, Kuehn N, MacEachern T, Hanson J: Estimate of survival of patients admitted to a palliative care unit: a prospective study. J Pain Symp Manag, 7: 82-86, 1992.
29. Morita T, Tsunoda J, Inoue S, Chihara S: The Palliative Prognostic Index: a scoring system for survival prediction of terminally ill cancer patients. Support Care Cancer, 7: 128-133, 1999.
30. Finlay IG, Dunlop R: Quality of life assessment in palliative care. Ann Oncol, 5: 13-18, 1994.
31. Shang E, Weiss C, Post S: The influence of early supplementation of parenteral nutrition on quality of life and body composition in patients with advanced cancer. JPEN, 30: 222-230, 2006.
32. Cozzaglio L, Balzola F, Cosentino F, DeCicco M, Fellagara P, Gaggiotti G, Gallitelli L, Giacosa A, Orban A, Fadda M, Gavazzi C, Pirovano F, Bozzetti F: Outcome of cancer patients receiving home parenteral nutrition. JPEN, 21: 339-342, 1997.
33. Bozzetti F, Cozzaglio L, Biganzoli E, Chiavenna G, De Cicco M, Donati D, Gilli G, Percolla S, Pironi L: Quality of life and length of survival in advanced cancer patients on home parenteral nutrition. Clin Nutr, 21: 281-288, 2002.