

## Review Article

# Nutritional strategies in cancer patients. Oral supplementation and artificial nutrition

F.W. GUGLIELMI<sup>1</sup>, G. LEOGRANDE<sup>1</sup>, S. MAZZUOLI<sup>1</sup>, N. REGANO<sup>1</sup>, S. FREGNAN<sup>2</sup>, A. GUGLIELMI<sup>3</sup>, G. COLUCCI<sup>4</sup>,  
A. FRANCAVILLA<sup>2</sup>

<sup>1</sup>Section of Gastroenterology & Day Hospital of Artificial Nutrition, Hospital "San Nicola Pellegrino", Trani, (Bari)

<sup>2</sup>Section of Gastroenterology, Department of Emergency and Organ Transplantation, University of Bari, Bari

<sup>3</sup>Section of General Surgery, II University "Francesco Paccione", DETO, University of Bari, Bari

<sup>4</sup>Department of Medical Oncology, Oncologic Hospital "Giovanni Paolo II", Bari - Italy

**ABSTRACT:** *In the course of neoplastic disease, oncologic patients are frequently malnourished as a consequence of both cytokine hyperexpression due to cancer and the surgical or medical treatment they have undergone. The presence and stage of malnutrition depend on location, type and progression of cancer and often influence survival, efficacy of medical and radiation treatment, and also postsurgery morbidity and mortality. Research and clinical experience have shown to what extent artificial nutrition is able to prevent the negative effects of malnutrition on the course and prognosis of neoplastic disease and, most of all, on therapeutic efficacy. All of the above conditions show how important it is to adequately treat patients when they are suspected to be at risk of malnutrition. As a consequence, oncologists, nutritionists, and general practitioners should realize that the major targets of nutritional interventions in neoplastic patients are (a) to prevent further complications of their nutritional status, (b) to treat malnutrition, (c) to reduce postsurgery complications and mortality, and (d) to ensure a satisfying quality of life. (Nutritional Therapy & Metabolism 2007; 25: 101-12)*

**KEY WORDS:** *Cancer, Anorexia-Cachexia, Artificial nutrition, Oral supplementation, Enteral nutrition, Parenteral nutrition*

## INTRODUCTION

Malnutrition is a very common complication in the clinical history of neoplastic patients (1). Its prevalence varies according to site of tumor, stage of illness, type of treatment, and type of nutritional index used to identify malnutrition. According to DeWys et al (2), there is a slight variation in weight loss (from 25% to 65%) according to location (Fig. 1); and more recent reports, such as that by Stratton et al (3), seem to show malnutrition incidence rates to be higher: 9% for urologic cancer, 46% for lung cancer, and more than 85% for pancreatic cancer patients.

Many neoplastic patients face a gradual loss of weight, and some of them, especially in advanced stages of illness, develop the anorexia-cachexia syndrome, clinically characterized by a severe, chronic, and progressive reduction of fat and muscle mass (4).

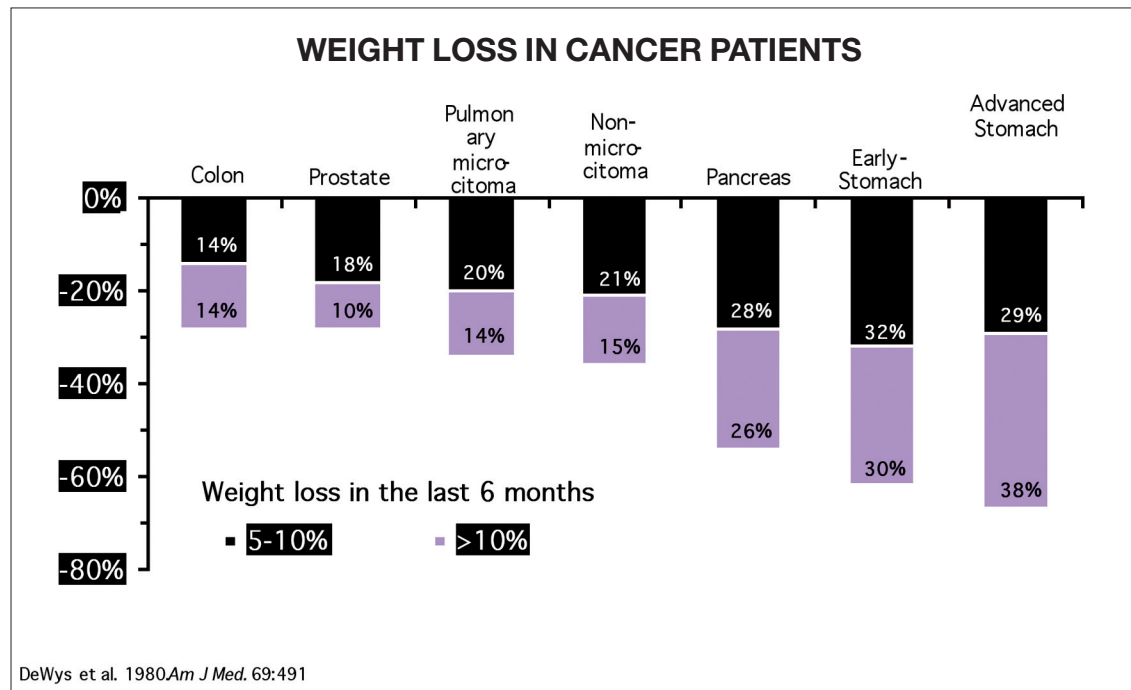
## ANOREXIA-CACHEXIA SYNDROME

The anorexia-cachexia syndrome (ACS) associated with cancer is considered to be one of the most widely

verified causes of death among cancer patients. It has a multifactorial etiopathogenesis, which has not been completely clarified: it is in part correlated to the same tumoral growth factor, to individual responses to the tumor and to chemotherapy and radiotherapy (5-22). Anorexia, early satiety, reduction of nutrient intakes, weight loss associated with decrease of muscle and fat mass, edema, alteration of immune functions, change in taste, and reduction of capacity for concentration are the principal clinical characteristics of the anorexia-cachexia syndrome (5-22).

The importance of the anorexia-cachexia syndrome and the subsequent necessity to plan a correct nutritional treatment have been proven by a number of studies which demonstrate a significant increase in morbidity and mortality in malnourished neoplastic patients compared with well-nourished neoplastic patients (23-26). The anorexia-cachexia syndrome plays a key role in the progression of neoplastic disease; its appearance represents in fact an important negative prognostic factor.

In conclusion, regarding what concerns cancer patients, the targets for the oncologist, nutritionist, and general practitioner should be (i) to prevent the appearance



**Fig. 1 - Weight loss for sites of neoplasia.**

of the anorexia-cachexia syndrome, (ii) to cure subjective and objective symptoms of the anorexia-cachexia syndrome, and (iii) to ensure a satisfying quality of life in patients for whom it is no longer possible to increase the length of their survival.

#### NUTRITIONAL ASSESSMENT IN NEOPLASTIC PATIENTS

The assessment of nutritional state seems to be fundamental for distinguishing among well-nourished patients, malnourished patients, and patients at risk of malnutrition. The nutritional parameters recommended to evaluate the nutritional state of cancer patients are the following: clinical assessment, nutrient intake analysis, anthropometric measurement, biological parameters, functional tests, Subjective Global Assessment (SGA), Mini Nutritional Assessment (MNA), Karnofsky Performance Status (KPS), the Quality of Life Questionnaire (QoLQ), and the Malnutrition Universal Screening Tools (MUST) (27). It is always advisable to carry out a complete nutritional assessment to identify malnourished patients and those at risk of malnutrition.

A clinical assessment is a simple but valid instrument for early detection of nutritional deficits suspected on the basis of specific symptoms: (a) pale face, ecchymosis, dermatitis, and skin desquamation; (b) fragility and striation of nails; (c) alteration of color and loss of hair; (d)

gingivitis and glossitis; (e) edema and ascites; (f) reduction of muscle and fat mass; and (g) lesion due to decubitus. This is an important step; however, it is not very reliable, because of its inability to quantify the degree of malnutrition.

A nutrient intake analysis is mandatory at the beginning of the evaluation of patients' nutritional status. This procedure is used to verify that the level of nutrient intake is not less than 50% of the total caloric intake, which would identify the patient to be at high risk of malnutrition. Therefore a nutritional anamnesis should be taken in detail stating both the number of meals and the quality of food intake.

Anthropometric measurements make use of parameters of 2 kinds: (a) global parameters: weight, height, usual weight, weight in the last 6 months, body mass index (BMI); and (b) local parameters (triceps, biceps, under scapular, upper iliac skinfolds, and mean arm circumference).

The most common biological parameters are albumin and transferrin. Transferrin is to be preferred.

Among functional tests, the assessment of muscle function has recently been indicated to be one of the most sensitive tests for the assessment of nutritional status (28). Handgrip strength (by means of a dynamometer) is, in our opinion, a suitable tool for testing the muscle function of cancer patients. It requires the patient's cooperation, is simple to use, and, as documented in literature (29), has a sensitiveness of 90% in preventing postoperative complications. It is important to highlight

that the assessment of muscle function not only represents an early index of malnutrition, but it is also an important parameter in the monitoring of the efficacy of the nutritional treatment.

The Subjective Global Assessment (SGA) is a simple, reliable, and well-documented malnutrition-screening tool validated in cancer patients. It is recommended to identify clinically relevant malnutrition in patients undergoing cancer surgery and to evaluate the role of preoperative nutritional intervention in preventing postoperative adverse outcomes.

In the complete nutritional assessment, the Mini Nutritional Assessment (MNA) (30) is used as a screening tool. It is articulated in 4 parts and allows for a more complete view of the patient: (a) anthropometric parameters: BMI, arm and leg circumferences, and loss of weight; (b) general evaluation: life-style, physical activity, and use of medicines; (c) dietary evaluation: number of meals, solid and liquid intake, and autonomy of nutrition; and (d) self-evaluation. The maximum score is 30. A score lower than 17 indicates malnutrition; a score between 17 and 23.5 indicates a risk of malnutrition; whereas a score higher than 24 indicates good nutritional status.

The Karnofsky Performance Status (KPS) is a simple questionnaire that allows us to assess the patient's level of autonomy (score between 20 and 100) considering parameters such as job, daily activities, personal care, symptoms, and healthcare support.

The Quality of Life Questionnaire (QoLQ) (specifically, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [EORTC QLQ-C30]) (31) is a questionnaire that has been validated in cancer patients, and that is able to define quality of life considering health through 9 parameters: 5 functional parameters (physical, cognitive, emotional, social, and real function), 3 symptomatic parameters (fatigue, pain, nausea and vomiting) and 1 parameter for global health status.

The Malnutrition Universal Screening Tools (MUST) is a recent method for nutritional screening (27) that not only allows an early identification of malnutrition but also defines the right indication for nutritional treatment. This method also allows us to avoid further and deeper nutritional assessment in well-nourished patients and to schedule the follow-up of patients at high risk of malnutrition.

MUST allows us to group patients into (a) patients at low risk for malnutrition; (b) patients at medium risk for malnutrition; (c) patients at high risk for malnutrition, using 3 parameters: BMI, weight loss, and loss of appetite in the last 5 days.

All the parameters previously mentioned are reported in the nutritional folder and are used to identify the typi-

cal clinical conditions characterizing patients with malnutrition and patients at risk of malnutrition:

Malnutrition: patients with BMI < 18.5 and weight loss > 10% in the last 3-6 months.

Risk of malnutrition: (a) patients who did not eat anything at all or almost anything for more than 5 days, (b) patients who are likely to fast or not to eat much for the following 5 days, (c) patients with bad intestinal absorption, and (d) patients with high loss of nutrients or high nutritional demands (hypercatabolism).

## NUTRITIONAL STRATEGIES

Nutritional strategies for the management of cancer patients include treatments of 2 kinds: nutritional support and pharmaconutritional therapy.

### Nutritional support

Nutritional support in neoplastic patients allows us to completely satisfy the personal demands for macronutrients and micronutrients, improving the clinical course of illness and, most of all, the patient's quality of life. The primary aim for the nutritionist is not only to intervene in case of malnutrition in neoplastic patients, but also to identify patients at risk for malnutrition, for whom eventual nutritional intervention would be able to prevent the worsening of nutritional state and to reduce clinical complications (32, 33). Nutritional therapy can be used, in the short term, as adjuvant treatment to chemotherapy or, in the long term, in all patients who are not able to maintain an adequate calorie intake with their diet.

Nutritional support in neoplastic patients consists of (a) dietary counselling, (b) oral supplementation, (c) enteral nutrition (EN), and (d) parenteral nutrition (PN) (25). These last 4 points we are going to cover in this review are based on the guidelines of the Società Italiana di Nutrizione Artificiale e Metabolismo (Italian Society of Artificial Nutrition and Metabolism; SINPE) (34) and the Royal College of Surgeons of England (35).

### Pharmaconutritional therapy

Cancer anorexia-cachexia is characterized by a shift in nutrient use. Associated metabolic changes result from changes in intake of the main nutrients and are all oriented toward a hypermetabolic status. An increased rate of muscle protein degradation and a progressive depletion of lean body mass cause cachexia. Considerable data from the literature (11, 36-42) demonstrate that in cancer patients, nutritional therapy using formulations enriched with n-3 polyunsaturated fatty acids (PUFA) and, partic-

ularly, eicosapentaenoic acid (EPA) is able to prevent and improve the anorexia-cachexia syndrome and its complications through mechanisms of interactions with inflammatory cytokines.

In fact, PUFA, EPA, and docosahexaenoic acid (DHA) have been shown to inhibit the production of proinflammatory cytokines such as interleukin-6 (IL-6), IL-1, and tumor necrosis factor (TNF) in healthy individuals and in patients with cancer. These nutrients positively act on cancer cachexia blocking cyclooxygenase-2 (COX-2) and lipoxygenase production (11). EPA has also been shown to have inhibitory effects on the growth of human pancreatic cancer cell lines *in vitro* and to have antitumor and anticachectic effects in a chemoresistant murine MAC-16 colon adenocarcinoma model (36-40), thus prolonging the survival of patients. Barber et al demonstrated that an EPA-enriched supplement to the diet may reverse cachexia in advanced pancreatic cancer patients (41).

## ORAL SUPPLEMENTATION

Oral supplementation (OS) is indicated for all patients whose nutrient intake is not sufficient to cover their needs for macronutrients and micronutrients, notwithstanding

preceding dietotherapy interventions (43). OS represents a simple, natural, and noninvasive method to increase calorie intake in all patients. The benefits of OS include increase of appetite, regain of weight, reduction of gastrointestinal toxicity, and improvement of performance status (44-47). Moreover, it was demonstrated that while improving the calorie-protein intake, OS allows a significant increase in the immune response (46-50).

OS should provide adequate quantities of all nutrients, including proteins, vitamins, and minerals, aiming at fully satisfying the patient's nutritional needs. In this regard, fiber intake is also important, because as is known, fibers play an important role in modulating both the absorption of nutrients and the time of intestinal transit, thus improving immune functions (51). The efficacy of OS depends on the quantity of nutrients introduced and on the duration of treatment. It was demonstrated (51) that malnourished patients who are subjected to oral supplementation enriched with EPA at recommended dosages (1.5-2 g/day), showed an increase of lean mass, compared with patients who did not reach the recommended caloric intake. Moreover, this fact confirms the importance of the patient's compliance for the efficacy of the treatment (52). Therefore, the acceptability and palatability of OS have a key role in its efficacy: taste, solidity, and quantity are particularly important (53, 54). Lack of palatability

TABLE I - RECOMMENDATIONS FOR ORAL SUPPLEMENTATION

- Healthcare professionals should consider oral supplementation\* an efficacious support for increasing the intakes of all patients who are able to receive normal oral nutrition but are malnourished• or at risk of malnutrition= (A).
- Moreover, it is necessary to ensure an adequately balanced nutritional support in terms of calorie, protein, fibres, electrolytes, vitamins and minerals intake (D (GPP)). For what concerns micronutrients intake, a complete oral supplementation should satisfy the intake of all vitamins and of all trace elements (D(GPP)).
- Oral supplementation can be suspended only when patients have reached an adequate nutritional intake with diet (D(GPP)).
- Preoperation oral supplementation is recommended in malnourished surgical patients.
- In gynecological surgical patients who are able to receive normal oral nutrition, a nutritional intake within 24 hours after the operation should be ensured (B).
- Oral supplementation should be ensured within 24 hours from the intervention in those patients who underwent major abdominal surgery and are able to receive normal oral nutrition and who show integrity of the intestinal function (A).
- Patients should be monitored in the eventual case of nausea and vomit (A).

Codes for the strength of the evidence supporting each guideline as described in the "Classification of Recommendations on Interventions by the NICE guideline for Nutrition support in adults" (35):

(A) recommendation based on the following evidence: (a) at least 1 meta-analysis, systematic review, or randomized controlled trial (RCT) that is rated as 1<sup>++</sup> and is directly applicable to the target population; (b) a systematic review of RCTs or body of evidence that consists principally of studies rated as 1<sup>+</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (c) evidence drawn from a UK National Institute for Health and Clinical Excellence (NICE) technology appraisal.

(B) recommendation based on the following evidence: (a) a body of evidence that includes studies rated as 2<sup>++</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (b) extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>.

(D) (GPP) recommendation based on the following evidence: (a) a good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group.

\* Oral supplementation includes each of the following procedures, which are useful to improve nutritional intake: food rich in proteins, carbohydrates and/or fats, mineral salts and vitamins, snacks; oral supplementation modifies the type of meal and dietary advice.

• Malnutrition: patients with BMI < 18.5 (calculated as kg/m<sup>2</sup>), together with weight loss > 10% in the last 3-6 months, or with BMI < 20 together with a weight loss > 5% in the last 3-6 months.

= At risk of malnutrition: patients who have not eaten much or at all for more than 5 days, patients who are likely not to eat much for the following 5 days, patients with a bad intestinal absorption capacity, or patients with high losses or high nutritional needs because of catabolism.

should be considered the inconvenience that most limits the efficacy of OS (25).

In some randomized studies of cancer patients, OS made using formulations enriched with EPA showed an increase in their survival and performance status (55, 56). Moreover, a reduction of gastrointestinal and infective complications and an improvement of renal and hepatic functions were observed (57, 58).

Table I shows the relative levels of scientific evidence which support OS recommendations.

## ENTERAL NUTRITION

Enteral nutrition (EN) is indicated for all patients with normal or sufficient function in the gastrointestinal tract but who are unable to fulfill their nutritional re-

quirements with diet or OS. There are different indications for EN: dysphagia, anorexia, and central nervous system diseases. EN is further indicated in cases of nutrient loss due to alterations of the digestive process and of intestinal absorption (low-delivery fistulas and Crohn's disease) (5, 33, 59, 60). In these cases, partial enteral nutrition is indicated that enables supplementation for the remaining amount of necessary calories. Total enteral nutrition is indicated for those cases when the patient is not able to achieve normal oral nutrition.

It has been demonstrated that home enteral nutrition (HEN) is safe and efficacious in neoplastic patients (61, 62). EN in cancer patients is able to increase appetite and so to improve anorexia; moreover, it enables patients to increase their protein and energy intakes, with a resulting improvement in nutritional status (50, 63, 64).

A number of studies have demonstrated that EN in

**TABLE II - SUMMARY OF ORAL SUPPLEMENTATION**

Nutritional strategy	Medical indications	Surgical indications	Access
Oral supplementation	Malnourished patients Patients at risk for malnutrition who can swallow	Preoperative: patients who can swallow but are malnourished. Postoperative: patients with former abdominal intervention who can swallow within 24 hours and who do not show any specific involvement in intestinal efficiency and integrity. Oral intake should begin within 24 hours after the operation.	Oral

**TABLE III - RECOMMENDATIONS FOR ENTERAL NUTRITION**

- EN is indicated for malnourished patients or patients at risk of malnutrition who show:
  - inadequate nutritional intake with diet;
  - normal function in the gastrointestinal tract (D(GPP)).
- Contraindications to the use of EN are characterized by the loss of an adequate absorption function or by the compromising of the intestinal tract (A).
- Preoperative enteral nutrition is indicated for all malnourished patients who are eligible for a major abdominal surgical intervention, who show an inadequate intake of nutrients with diet, and whose gastrointestinal tract is efficient (B).
- In those patients who have undergone general surgery, postoperative enteral nutrition (within 48 hours after the operation) is indicated only in presence of malnutrition and if a period of inadequate intake of nutrients with diet is expected and clearly always in presence of an efficient and accessible gastrointestinal tract (A).
- Dysphagic patients
  - In acute diseases, patients who are unable to swallow and with a subsequent inadequate nutritional intake, should have a preparatory phase of 2-4 weeks of EN through a nasogastric tube.
  - Qualified healthcare professionals with skilled and experienced in diagnosis, evaluation, and control of swallowing disorders should subsequently evaluate the prognosis and alternatives for future nutritional support (A).

Codes for the strength of the evidence supporting each guideline as described in the "Classification of Recommendations on Interventions by the NICE guideline for Nutrition support in adults" (35):

(A) recommendation based on the following evidence: (a) at least 1 meta-analysis, systematic review, or randomized controlled trial (RCT) that is rated as 1<sup>++</sup> and is directly applicable to the target population; (b) a systematic review of RCTs or body of evidence that consists principally of studies rated as 1<sup>+</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (c) evidence drawn from a NICE technology appraisal.

(B) recommendation based on the following evidence: (a) a body of evidence that includes studies rated as 2<sup>++</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (b) extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>.

(D(GPP)) recommendation based on the following evidence: (a) a good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group.

neoplastic patients is efficacious for (i) reducing gastrointestinal toxicity, with its impact on the immune system; (ii) improving the response to chemotherapy; (iii) improving the patients' quality of life; and (iv) reducing healthcare costs (61, 63, 65, 66). Some randomized studies have shown that severely malnourished neoplastic patients who receive EN have a better clinical course in the postoperative period.

Postoperative EN reduces complications (67), increases nitrogen balance, reduces protein catabolism (68), increases immune response (69), and reduces infections and hospital stay (70). Moreover, EN in severely

malnourished patients with head-neck tumors improves their quality of life in the period preceding surgical intervention (71).

In a recent survey, the potential benefits and efficacy of enteral treatment in patients with cancer (supplementation or total EN) have been defined (1). When compared with parenteral nutrition, EN greatly reduced hospital stays and risk of complications (infective and non-infective). However, no impact on mortality was observed, probably because short-term enteral supplementation (7 to 10 days on average) was not adequate to improve the survival period.

**TABLE IV - RECOMMENDATIONS FOR EN ACCESS**

- 
- Malnourished patients or patients at risk of malnutrition with indication to enteral nutrition (patients under general medicine, intensive therapy, and surgery) should be fed through tubes (nasogastric or nasojejunal) or through stomas (endoscopic or surgical) (A).
  - In case of alterations of the superior gastrointestinal tract, tubes or stomas for EN should be positioned respectively in the postpylorus or jejunum (D(GPP)).
  - Enteral nutrition through surgical openings (gastrostomy, jejunostomy) should be considered in cases of long-term enteral treatment (more than 30 days) (D(GPP)).
  - Percutaneous endoscopic gastrostomy (PEG) is the most widely used access for EN and can be efficient from about 4 hours after insertion (A).
- 

Codes for the strength of the evidence supporting each guideline as described in the "Classification of Recommendations on Interventions"

(A) recommendation based on the following evidence: (a) at least 1 meta-analysis, systematic review, or randomized controlled trial (RCT) that is rated as 1<sup>++</sup> and is directly applicable to the target population; (b) a systematic review of RCTs or body of evidence that consists principally of studies rated as 1<sup>+</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (c) evidence drawn from a NICE technology appraisal.

(D(GPP)) recommendation based on the following evidence: (a) a good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group.

---

**TABLE V - RECOMMENDATIONS FOR THE MANAGEMENT OF EN**

EN as method of infusion:

- The supply of EN to the stomach can be given in bolus or continuously (B).
- For those patients who are undergoing intensive therapy, EN through a nasogastric tube should be supplied continuously for 16-24 hours. If it is necessary to supply insulin, it is more practical to manage EN continuously after 24 hours (D(GPP)).

Factors that increase motility:

- For those patients who are undergoing intensive therapy with a lessened gastric emptying and who do not tolerate EN, the supply of prokinetic drugs that stimulate motility is indicated (A). The supply of these drugs is not indicated in cases of suspected intestinal occlusion (D(GPP)).
- Also for all other patients receiving EN, with a delayed gastric emptying and who do not tolerate enteral nutrition, prokinetics should be supplied (except for suspected intestinal obstruction) (D(GPP)).
- In conditions of lessened gastric emptying in spite of the use of prokinetics, with subsequent difficulty in continuing the enteral supply to the stomach, postpyloric enteral nutrition and/or parenteral nutrition is indicated (D(GPP)).

Management of tubes:

- In those patients who need EN, the positioning of the tube should be made by qualified and experienced personnel. The exact positioning of nasogastric tubes should be confirmed by the inhalation manoeuvre and by the measurement of pondus hydrogenii (PH) (by x-ray) as stated by the National Patient Safety Agency (NPSA). Local protocols should address clinical criteria that allow EN. These criteria require the ability to make continuous controls on the position of the tube, on the remaining gastric volume through inhalation, and on intragastric pH. Inability to take these parameters makes the method more dangerous.
  - Initial positioning of postpyloric tube should be confirmed by abdominal x-rays (unless radiologically positioned).
  - Protocols should be set before starting the process.
- 

Codes for the strength of the evidence supporting each guideline as described in the "Classification of Recommendations on Interventions by the NICE guideline for Nutrition support in adults" (35):

(B) recommendation based on the following evidence: (a) a body of evidence that includes studies rated as 2<sup>++</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (b) extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>.

(D(GPP)) recommendation based on the following evidence: (a) a good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group.

---

EN represents the best artificial nutritional technique because it is more physiological and so is able to maintain the anatomy and functional integrity of intestinal mucous; moreover, it presents lower risks and complications, is easier, safer, and not very expensive (1, 33).

Tables II, III, IV, and V report the levels of evidence that support the indications and choice of access for, and clinical management of, EN. Table VI summarizes indications for EN.

## PARENTERAL NUTRITION

Parenteral nutrition (PN) is rarely indicated for neoplastic patients, considering the higher numbers of com-

plications, infections, and longer hospitalization (1). PN is indicated for patients with acute and chronic intestinal insufficiency and in all the conditions where EN is impossible or inadequate (72-74). A few authors suggest that, according to their experience, home parenteral nutrition (HPN) may be able to improve the quality of life of neoplastic patients and of their relatives (75).

Once PN is indicated, it is necessary to identify (a) the formulation of the nutritional bag to cover the energetic needs of the patient, (b) the access for infusion (peripheral vein or central venous access), (c) the type of venous access, and (d) the duration of infusion.

The recommendations and relative levels of scientific evidence supporting the indications for, and management

**TABLE VI - SUMMARY OF ENTERAL NUTRITION**

Nutritional therapy	Clinical indications	Surgical indications	Dysphagic patients	Access options
Enteral Nutrition	Malnourished patients and those at risk of malnutrition, respectively with: - Inadequate oral intake or - documented risk for ab ingestis; - efficiency and accessibility of adequate gastrointestinal tract.	Preoperative: patients for whom major surgery of the abdominal tract is indicated.	Patients who are unable to swallow or receive adequate nutrients and calories orally.	- Gastrostomy is indicated in patients who need long-term enteral nutrition (4 weeks or more); nasogastric tube should be positioned during the previous weeks. In those patients with a disorder or inaccessibility of the superior gastrointestinal tract, postpyloric and enteral nutrition (duodenum or postpyloric) are indicated.

**TABLE VII - RECOMMENDATIONS FOR PARENTERAL NUTRITION**

PN is indicated in malnourished patients or those at risk of malnutrition in the following conditions:

- inadequate nutritional intake with diet or with EN;
- nonfunctioning, inaccessible, or perforated gastrointestinal tract (D(GPP)).
- PN should be progressively introduced and strictly monitored, usually at the beginning of the PN (during the first 24-48 hours) more than 50% of energy requirements should not be administered.
- Parenteral nutrition can be suspended when adequate oral nutrition takes place, when EN is tolerated and the patient's nutritional status is stabilized. Suspension of PN should be planned according to the clinical and nutritional conditions of the patient (D(GPP)).
- Prescription of PN should be made by qualified medical personnel who are able to assess the effective nutritional requirements of patients. In PN bags, according to the patient's clinical conditions, micronutrients, trace elements, and electrolytes can be added; however, these integrations should be made by qualified personnel who are able to detect any eventual pharmacological interaction (D(GPP)).
- PN can be suspended when nutrient intake with diet or EN is adequate to nutritional requirements. It is not possible to establish in advance a minimum period for PN (D(GPP)).
- Healthcare professionals should consider perioperative parenteral nutrition as a support for surgical, malnourished patients who have an inadequate or insufficient oral or enteral nutritional intake or who show a nonfunctioning, inaccessible, or perforated gastrointestinal tract (B).
- PN is indicated during the preoperative period in malnourished patients or patients at risk of malnutrition whose gastrointestinal tract is inaccessible and nonfunctioning. (B)
- For all other patients, parenteral nutritional treatment perioperatively is not indicated. PN should be used in critical or surgical patients who are intolerant of EN (B).

Codes for the strength of the evidence supporting each guideline as described in the "Classification of Recommendations on Interventions by the NICE guideline for Nutrition support in adults" (35):

(B) recommendation based on the following evidence: (a) a body of evidence that includes studies rated as 2<sup>++</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (b) extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>.

(D(GPP)) recommendation based on the following evidence: (a) a good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group.

of, parenteral nutrition; the manners and methods of infusion; and the management of central venous catheters are reported in Tables VII and VIII.

It is important to highlight the fact that the passage from parenteral to enteral feeding requires a careful evaluation. Furthermore, in relation to the general condition of the patient, it is possible to use other nutritional supports in combination with parenteral nutrition (artificial mixed nutrition). The indications and the choice of access for PN are reported and summarized in Table IX.

We should also specify that, although early enteral nutrition significantly reduces the complication rates and duration of postoperative stay in cancer patients, parenteral nutrition is better tolerated and more frequently

used by oncologists than enteral nutrition (76). Finally, since there has been considerable debate about the potential stimulation of tumor metabolism induced by a glucose-based total parenteral nutrition (TPN) in cancer patients, some authors have demonstrated that its disproportionately high uptake even in fasting conditions prevents parenteral glucose consumption from being modulated by a further supply of glucose or lipids (77).

## CONCLUSIONS

The anorexia-cachexia syndrome associated with cancer precedes and is one of the most widely document-

**TABLE VIII - RECOMMENDATIONS FOR THE MANAGEMENT OF PN**

Access for infusion:

- In hospital, PN can be administered by means of a central catheter which is inserted through a peripheral vein as an alternative to a central vein. In multilumen central catheters, 1 lumen should be used for PN (B).
- In those patients for whom short-term PN is scheduled (less than 14 days), the use of a peripheral venous access is indicated; whereas for long-term PN, a central venous catheter is indicated. Also the different formulation of the nutritional bag (in terms of caloric intake and osmolarity) influences the choice of access for infusion (B).
- Tunnelization of the subclavian vein for long-term PN (more than 30 days) is recommended (D(GPP)).
- Catheters should not be tunnelized for just a short period (less than 30 days) (B).

Method of infusion:

- PN in continuous infusion is indicated for those patients with an illness at an advanced stage (B).
- Cyclical infusion of PN should be considered when the use of a peripheral vein with i.v. cannula requires a routine change of the catheter (B).
- A gradual change from continuous to cyclical infusion should be considered in those patients who need PN for more than 2 weeks (D(GPP)).

Management of catheter:

- The setting and monitoring of the venous access for PN should be made by qualified medical personnel, who are able to ensure adequate control (D(GPP)).

Codes for the strength of the evidence supporting each guideline as described in the "Classification of Recommendations on Interventions by the NICE guideline for Nutrition support in adults" (35):

(B) recommendation based on the following evidence: (a) a body of evidence that includes studies rated as 2<sup>++</sup>, is directly applicable to the target population, and demonstrates overall consistency of results; (b) extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>.

(D(GPP)) recommendation based on the following evidence: (a) a good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group.

**TABLE IX - SUMMARY OF PARENTERAL NUTRITION**

Nutritional therapy	Medical indications	Surgical indications	Access options
Parenteral Nutrition	Malnourished patients and those at risk of malnutrition, with: <ul style="list-style-type: none"> <li>- Inadequate oral intake or at risk for ab ingestis.</li> <li>- Inadequate enteral nutrition</li> <li>- Nonfunctioning, inaccessible, or perforated gastrointestinal tract</li> </ul>	In the perioperative period, malnourished patients or patients at risk of malnutrition whose gastrointestinal tract is inaccessible and nonfunctioning. In critical or surgical patients who are intolerant to EN.	<ul style="list-style-type: none"> <li>- Peripheral venous access in patients for whom short-term PN (less than 14 days) is indicated.</li> <li>- Central venous access (in patients for whom long-term PN is indicated).</li> <li>- The different formulations of the nutritional bag, in terms of caloric intake and osmolarity, influence the choice of access for infusion.</li> </ul>

ed causes of death among cancer patients. From a clinical point of view, cachexia manifests itself in a loss of weight, essentially due to a considerable and significant reduction of lean mass. It has been shown that 80% of neoplastic patients lose weight during illness, and it is known that about 20% of them die because of malnutrition and not because of the disease per se (2).

Weight loss negatively influences a series of clinic variables, such as response to and/or tolerance of the therapy, quality of life, frequency of hospitalization, and infective complications. Therefore, the nutritional state of oncologic patients should be assessed at the beginning of the diagnostic-therapeutic procedure and monitored afterward to identify early those patients who need a specific nutritional support.

In this regard, some methods of nutritional screening used in a specific way in the neoplastic setting for a complete nutritional evaluation are now available. Oral supplementation and enteral and parenteral nutrition represent the therapies available nowadays to improve the nutritional status of patients. Nutritional support is able to prevent further compromising of the nutritional state in cancer patients and, most of all, to improve quality of life. As reported in the literature, nutritional formulations enriched with specific micronutrients (e.g., omega-3 fatty acids) are able to help reestablish lean mass in neoplastic patients.

SINPE has published guidelines (34) for artificial nutritional treatment in neoplastic patients, identifying some typologies of cancer patients who are eligible for the different kinds of nutritional support.

In conclusion, to summarize and underline the “take home messages” of this review:

1) the anorexia-cachexia syndrome represents the cause

of death for some neoplastic patients in an advanced stage;

- 2) it is advisable to assess the nutritional state of cancer patients, both those subjected to medical therapy (chemotherapy and/or radiotherapy) and those eligible for surgical interventions, to identify early malnourished patients and patients at risk for malnutrition;
- 3) the assessment of the nutritional state includes an anamnesis, clinical assessment, and a record of some anthropometric and biochemical parameters;
- 4) the nutritional strategies that should be used in the management of cancer patients include 2 kinds of treatments: (i) nutritional support, including oral supplementation (48, 49) and enteral and parenteral nutrition and (ii) pharmaconutritional therapy. The addition of particular micronutrients (e.g., omega-3) to the standard nutritional formulations is necessary to make the nutritional treatment of malnourished oncologic patients more efficacious;
- 5) SINPE guidelines enable clinicians to define the most appropriate and adequate nutritional intervention for each neoplastic patient.

#### Conflict of interest statement

None declared.

Address for correspondence:

Prof. Francesco William Guglielmi

Section of Gastroenterology & Day Hospital of Artificial Nutrition

Hospital “San Nicola Pellegrino”

70059 Trani (Bari), Italy

e-mail: [guglielmifw@libero.it](mailto:guglielmifw@libero.it); [william@gastro.uniba.it](mailto:william@gastro.uniba.it)

## REFERENCES

1. Elia M, Van Bokhorst-de van der Schueren MA, Garvey J, et al. Enteral (oral or tube administration) nutritional support and eicosapentaenoic acid in patients with cancer: a systematic review. *Int J Oncol* 2006; 28: 5-23.
2. DeWys WD, Begg C, Lavin PT, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. *Am J Med* 1980; 69: 491-7.
3. Stratton RJ, Green CJ, Elia M. Prevalence of disease-related malnutrition. In: Stratton RJ, Green CJ, Elia M, eds. *Disease-related malnutrition: an evidence-based approach to treatment*. Wallingford (UK): CABI Publishing, 2003; 35-92.
4. Fearon KC, Barber MD, Falconer JS. Pancreatic cancer as a model: inflammatory mediators, acute-phase response, and cancer cachexia. *World J Surg* 1999; 23: 584-8.
5. Mutlu EA, Mobarhan S. Nutrition in the care of the cancer patient. *Nutr Clin Care* 2000; 3: 3-23.
6. Nitenberg G, Raynard B. Nutritional support of the cancer patient: issues and dilemmas. *Crit Rev Oncol Hematol* 2000; 34: 137-68.
7. Fearon KC. Nutritional support in cancer. *Clin Nutr* 2001; 20: 187-90.
8. Tisdale MJ. Loss of skeletal muscle in cancer: biochemical mechanisms. *Front Biosci* 2001; 6: D164-74.
9. Laviano A, Meguid MM, Preziosa I, Fanelli FR. Oxidati-

- ve stress and wasting in cancer. *Curr Opin Clin Nutr Metab Care* 2007; 10: 449-56.
10. Laviano A, Meguid MM, Guijarro A, et al. Antimyopathic effects of carnitine and nicotine [review]. *Curr Opin Clin Nutr Metab Care* 2006; 9: 442-8.
  11. Mantovani G, Maccio A, Madeddu C, et al. A phase II study with antioxidants, both in the diet and supplemented, pharmaconutritional support, progestagen, and anti-cyclooxygenase-2 showing efficacy and safety in patients with cancer-related anorexia/cachexia and oxidative stress. *Cancer Epidemiol Biomarkers Prev* 2006; 15: 1030-4.
  12. Uomo G, Gallucci F, Rabitti PG. Anorexia-cachexia syndrome in pancreatic cancer: recent development in research and management [review]. *JOP* 2006; 7: 157-62.
  13. Laviano A, Meguid MM, Inui A, Muscaritoli M, Rossi-Fanelli F. Therapy insight: cancer anorexia-cachexia syndrome – when all you can eat is yourself [review]. *Nat Clin Pract Oncol* 2005; 2: 158-65.
  14. Maltoni M, Caraceni A, Brunelli C, et al; Steering Committee of the European Association for Palliative Care. Prognostic factors in advanced cancer patients: evidence-based clinical recommendations – a study by the Steering Committee of the European Association for Palliative Care [review]. *J Clin Oncol* 2005; 23: 6240-8.
  15. Laviano A, Muscaritoli M, Cascino A, et al. Branched-chain amino acids: the best compromise to achieve anabolism? [review]. *Curr Opin Clin Nutr Metab Care* 2005; 8: 408-14.
  16. Mantovani G, Madeddu C, Maccio A, et al. Cancer-related anorexia/cachexia syndrome and oxidative stress: an innovative approach beyond current treatment. *Cancer Epidemiol Biomarkers Prev* 2004; 13: 1651-9.
  17. Lelli G, Montanari M, Gilli G, Scapoli D, Antonietti C, Scapoli D. Treatment of the cancer anorexia-cachexia syndrome: a critical reappraisal [review]. *J Chemother* 2003; 15: 220-5.
  18. Mantovani G, Maccio A, Madeddu C, Massa E. Cancer-related cachexia and oxidative stress: beyond current therapeutic options [review]. *Expert Rev Anticancer Ther* 2003; 3: 381-92.
  19. Maltoni M, Nanni O, Scarpi E, Rossi D, Serra P, Amadori D. High-dose progestins for the treatment of cancer anorexia-cachexia syndrome: a systematic review of randomised clinical trials. *Ann Oncol* 2001; 12: 289-300.
  20. Mantovani G, Maccio A, Massa E, Madeddu C. Managing cancer-related anorexia/cachexia [review]. *Drugs* 2001; 61: 499-514.
  21. Mantovani G, Maccio A, Madeddu C, et al. Immunotherapy (recombinant interleukin 2), hormone therapy (medroxyprogesterone acetate) and antioxidant agents as combined maintenance treatment of responders to previous chemotherapy. *Int J Oncol* 2001; 18: 383-91.
  22. Mantovani G, Maccio A, Lai P, et al. Results of a dose-intense phase 1 study of a combination chemotherapy regimen with cisplatin and epidoxorubicin including medroxyprogesterone acetate and recombinant interleukin-2 in patients with inoperable primary lung cancer. *J Immunother* 2000; 23: 267-74.
  23. Dewys WD, Begg C, Lavin PT, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. *Am J Med* 1980; 69: 491-7.
  24. Andreyev HJ, Norman AR, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer* 1998; 34: 503-9.
  25. Rivadeneira DE, Evoy D, Fahey TJ, Lieberman MD, Daly JM. Nutritional support of the cancer patient. A: A Cancer Journal for Clinicians 1998; 48: 69-80.
  26. Van Bokhorst-de van der Schueren MA, vanLeeuwen PA, Kuik DJ, et al. The impact of nutritional status on the prognoses of patients with advanced head and neck cancer. *Cancer* 1999; 86: 519-27.
  27. Malnutritional Advisory Group, BAPEN 2002; Empfohlen von der Eur. Gesellsch. Fur Klinische Ernährung und Stoffwechsel. ESPEN Screening auf Mangelernährung im ambulanten Bereich. Malnutrition Universal Screening Tool (MUST) für Erwachsene. *Clinical Nutrition* 2003; 22: 415-21.
  28. Esther LH, Gonzalo MP, Julian RG. Handgrip dynamometry in healthy adults. *Clin Nutr* 2005; 24: 250-8.
  29. Mahalakshmi VN, Ananthakrishnan N, Kate V, et al. Handgrip strength and endurance as a predictor of postoperative morbidity in surgical patients: can it serve as a simple bedside test? *Int Surg* 2004; 89: 115-21.
  30. Guigoz Y, Vellas B, Garry PJ. Mini Nutritional Assessment: a practical assessment tool for grading the nutritional state of elderly patients. *Facts Res Gerontol* 1994; 4 (Suppl 2): S15-59.
  31. Fayers PM, Aaronson NK, Bjordal K, Curran D, Groenvold M; on behalf of the EORTC Quality of Life Study Group. EORTC QLQ-C30 scoring manual. Brussels: EORTC, 1999.
  32. Ottery FD. Supportive nutrition to prevent cachexia and improve quality of life. *Semin Oncol* 1995; 22 (Suppl 3): 8-111.
  33. Mercadante S. Parenteral versus enteral nutrition in cancer patients: indications and practice. *Support Care Cancer* 1998; 6: 85-93.
  34. Società Italiana di Nutrizione Parenterale ed Enterale (SINPE) – Gruppo di studio per la Nutrizione Artificiale Domiciliare (GNAD). Registri italiani di Nutrizione enterale e parenterale domiciliare. Valutazione dei risultati - Dicembre 2001 Area epidemiologica SINPE, 2002.
  35. National Collaborating Centre for Acute Care at the Royal College of Surgeons of England. Nutrition support at home in nutritional support in adults: oral supplements, enteral and parenteral feeding [draft for second consultation]. London: Royal College of Surgeons of England, 2005; 212-21.
  36. Barber MD, Ross JA, Fearon KC. Changes in nutritional,

- functional, and inflammatory markers in advanced pancreatic cancer. *Nutr Cancer* 1999; 35: 106-10.
37. Wigmore SJ, Plester CE, Richardson RA, Fearon KC. Changes in nutritional status associated with unresectable pancreatic cancer. *Br J Cancer* 1997; 75: 106-9.
  38. Falconer JS, Ross JA, Fearon KC, Hawkins RA, O'Riordain MG, Carter DC. Effect of eicosapentaenoic acid and other fatty acids on the growth in vitro of human pancreatic cancer cell lines. *Br J Cancer* 1994; 69: 826-32.
  39. Beck SA, Smith KL, Tisdale MJ. Anticachectic and anti-tumour effect of eicosapentaenoic acid and its effect on protein turnover. *Cancer Res* 1991; 51: 6089-93.
  40. Todorov P, Cariuk P, McDevitt T, Coles B, Fearon K, Tisdale M. Characterization of a cancer cachectic factor [letter]. *Nature* 1996; 379: 739-42.
  41. Barber MD, Ross JA, Voss AC, et al. The effect of an oral nutritional supplement enriched with fish oil on weight-loss in patients with pancreatic cancer. *Br J Cancer* 1999; 81: 80-6.
  42. Dewey A, Baughan C, Dean T, Higgins B, Johnson I. Eicosapentaenoic acid (EPA, an omega-3 fatty acid from fish oils) for the treatment of cancer cachexia. *Cochrane Database Syst Rev* 2007; 1: CD004597.
  43. Ravasco PM, Monteiro-Grillo I, Camilo ME. Does nutrition influence quality of life in cancer patients undergoing radiotherapy? *Radiother Oncol* 2003; 67: 213-20.
  44. Bounous G, Gentile JM, Hugon J. Elemental diet in the management of the intestinal lesion produced by 5 fluorouracil in man. *Can J Surg* 1971; 14: 312-24.
  45. Nayel H, el-Ghoneimy E, el-Haddad S. Impact of nutritional supplementation on treatment delay and morbidity in patients with head and neck tumors treated with irradiation. *Nutrition* 1992; 8: 13-8.
  46. Ovesen L, Allingstrup L. Different quantities of two commercial liquid diets consumed by weight-losing cancerpatients. *JPEN, J Parenter Enteral Nutr* 1992; 16: 275-8.
  47. Barber MD, Ross JA, Fearon KC. The anti-cachectic effect of fatty acids. *Proc Nutr Soc* 1998; 57: 571-6.
  48. Arnold C, Richter MP. The effect of oral nutritional supplements on head and neck cancer. *Int J Radiat Oncol Biol Phys* 1989; 16: 1595-9.
  49. McCarthy D, Weihofen D. The effect of nutritional supplements on food intake in patients undergoing radiotherapy. *Oncol Nurs Forum* 1999; 26: 897-900.
  50. Bozzetti F, Cozzaglio L, Gavazzi C, et al. Nutrition support in patients with cancer of the esophagus: impact on nutritional status, patient compliance to therapy and survival. *Tumori* 1998; 84: 681-6.
  51. Green CJ. Fibre in enteral nutrition. *Clin Nutr* 2001; 20 (Suppl 1): S23-39.
  52. Fearon KC, Von Meyenfeldt MF, Moses AG, et al. Effect of a protein and energy dense N-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer cachexia: a randomised double blind trial. *Gut* 2003; 52: 1479-86.
  53. Bolton J, Shannon L, Smith V, et al. Comparison of short-term and long-term palatability of six commercially available oral supplements. *J Hum Nutr Diet* 2003; 3: 317-21.
  54. Bell EA, Roe LS, Rolls BJ. Sensory-specific satiety is affected more by volume than by energy content of a liquid food. *Physiol Behav* 2003; 78: 593-600.
  55. Gogos CA, Ginopoulos P, Salsa B, Apostolidou E, Zombos NC, Kalfarentzos F. Dietary omega-3 polyunsaturated fatty acids plus vitamin E restore immunodeficiency and prolong survival for severely ill patients with generalized malignancy: a randomized control trial. *Cancer* 1998; 82: 395-402.
  56. Takatsuka H, Takemoto Y, Iwata N, et al. Oral eicosapentaenoic acid for complications of bone marrow transplantation. *Bone Marrow Transplant* 2001; 28: 769-74.
  57. Kenler AS, Swails WS, Driscoll DF, et al. Early enteral feeding in postsurgical cancer patients: fish oil structured lipid-based polymeric formula versus a standard polymeric formula. *Ann Surg* 1996; 223: 316-33.
  58. Swails WS, Kenler AS, Driscoll DF, et al. Effect of a fish oil structured lipid-based diet on prostaglandin release from mononuclear cells in cancer patients after surgery. *J Parenter Enteral Nutr* 1997; 21: 266-74.
  59. Laviano A, Meguid MM. Nutritional issues in cancer management. *Nutrition* 1996; 12: 358-71.
  60. Bloch AS. Cancer. In: Matarese LE, Gottschlich MM, eds. *Contemporary nutrition support practice: a clinical guide*. Philadelphia (USA): WB Saunders, 1998; 475-95.
  61. Roberge C, Tran M, Massoud C, et al. Quality of life and home enteral tube feeding: a French prospective study in patients with head and neck or oesophageal cancer. *Br J Cancer* 2000; 82: 263-9.
  62. Schattner M, Barrera R, Nygard S, et al. Outcome of home enteral nutrition in patients with malignant dysphagia. *Nutr Clin Pract* 2001; 16: 292-5.
  63. Tandon SP, Gupta SC, Sinha SN, Naithani YP. Nutritional support as an adjunct therapy of advanced cancer patients. *Indian J Med Res* 1984; 80: 180-8.
  64. den Broeder E, Lippens RJ, van't Hof MA, et al. Effects of naso-gastric tube feeding on the nutritional status of children with cancer. *Eur J Clin Nutr* 1998; 52: 494-500.
  65. Heys SD, Walker LG, Smith I, Eremin O. Enteral nutritional supplementation with key nutrients in patients with critical illness and cancer: a meta-analysis of randomized controlled clinical trials. *Ann Surg* 1999; 229: 467-77.
  66. Pietsch JB, Ford C, Whitlock JA. Nasogastric tube feedings in children with high-risk cancer: a pilot study. *J Pediatr Hematol Oncol* 1999; 21: 111-4.
  67. Beier-Holgersen R, Boesby S. Influence of postoperative enteral nutrition on postsurgical infections. *Gut* 1996; 39: 833-5.
  68. Hochwald SN, Harrison LE, Heslin MJ, Burt ME, Brennan MF. Early postoperative enteral feeding improves whole body protein kinetics in upper gastrointestinal cancer patients. *Am J Surg* 1997; 174: 325-30.
  69. Aiko S, Yoshizumi Y, Sugiura Y, et al. Beneficial effects of immediate enteral nutrition after esophageal cancer

- surgery. *Surg Today* 2001; 31: 971-8.
70. Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. *BMJ* 2001; 323: 773-6.
71. Van Bokhorst-de van der Schueren MA, Langendoen SI, Vondeling H, Kuik DJ, Quak JJ, van Leeuwen P. Perioperative enteral nutrition and quality of life of severely malnourished head and neck cancer patients: a randomized clinical trial. *Clin Nutr* 2000; 19: 437-44.
72. Wengler A, Micklewright A, Hebuterne X, et al; ESPEN-Home Artificial Nutrition Working Group. Monitoring of patients on home parenteral nutrition (HPN) in Europe: a questionnaire based study on monitoring practice in 42 centres. *Clin Nutr* 2006; 25: 693-700. Epub 2006 May 15.
73. Bozzetti F, Bozzetti V. Efficacy of enteral and parenteral nutrition in cancer patients. *Nestle Nutr Workshop Ser Clin Perform Programme* 2005; 10: 127-39 [discussion 139-42].
74. Bozzetti F. Home total parenteral nutrition in incurable cancer patients: a therapy, a basic humane care or something in between? *Clin Nutr* 2003; 22: 109-11.
75. Orrevall Y, Tishelman C, Permert J. Home parenteral nutrition: a qualitative interview study of the experiences of advanced cancer patients and their families. *Clin Nutr* 2005; 24: 961-70. Epub 2005 Aug 15.
76. Bozzetti F, Braga M, Gianotti L, Gavazzi C, Mariani LT. Postoperative enteral versus parenteral nutrition in malnourished patients with gastrointestinal cancer: a randomised multicentre trial. *Lancet* 2001; 358: 1487-92.
77. Bozzetti F, Gavazzi C, Mariani L, Crippa F. Glucose-based total parenteral nutrition does not stimulate glucose uptake by human tumours. *Clin Nutr* 2004; 23: 417-21.

Received: April 24, 2007

Accepted: September 14, 2007