

Nutritional support for cancer patients

Patients who are receiving adequate nutrition have a better prognosis, respond better to chemotherapy and can tolerate higher doses of anticancer treatments. It is therefore important for oncologists to assess and manage malnutrition.

Malnutrition, which is easily identified during clinical examination by weight loss and hypophagia, is an independent negative prognostic factor for cancer patients. Nutritional health can be considered based on a person's protein status. This is very important because there is no store of protein in the body, yet each protein has a specific function, for example as an enzyme, antibody, or contracting muscle protein or transport protein. The severity of malnutrition is often related to the degree of the protein depletion.

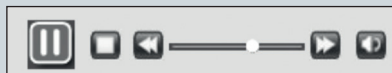
Nutritional health can be defined as having 100% of body protein (see figure overleaf). Depending on the duration of starvation or the cause of malnutrition, protein depletion leads to loss of organ function. This starts with decreased muscle mass (skeletal, cardiac and smooth muscle), followed by decreased visceral proteins, including albumin, transferrin and transport protein. Further protein malnutrition results in impaired



European School of Oncology e-grandround

ESO presents fortnightly e-grandrounds which offer participants the chance to discuss a range of cutting-edge issues with leading European experts. One of these is selected for publication in each issue of *Cancer World*.

In this issue Federico Bozzetti, from the University of Milan, Italy, reviews malnutrition as an independent negative prognostic factor in cancer, and looks at how to identify which patients are at risk and how to support them. The material is based on a recent review (*Crit Rev Oncol Hematol* 87:172–200). Nada Kozjek, from the Institute of Oncology in Ljubljana, Slovenia, poses questions raised by participants during the live online presentation. Edited by Susan Mayor.



The recorded version of this and other e-grandrounds is available at www.e-eso.net

immune response, which is compromised with the decrease of lymphocytes and synthesis of antibodies and acute phase proteins. This can be seen in a surgical patient, with impaired wound healing. The next step in protein depletion is impairment of organ function – gut, liver and heart. Finally, further protein depletion leads to a poor adaptation to any minimal biologic stress, which can prove to be fatal. Nitrogen death was defined thirty years ago as when 30% of body nitrogen has been lost. This depletion is incompatible with survival.

So-called secondary malnutrition (the type commonly associated with a serious infectious or neoplastic disease) leads to protein depletion, and differs from pure starvation, such as in anorexia nervosa, where visceral proteins are

maintained and remain stable until weight loss is extreme. In cancer or sepsis, where there is an inflammatory status, the decrease of visceral proteins is common.

Several studies have identified malnutrition as an independent negative prognostic factor for survival in patients with a variety of malignancies. We have very extensive evidence to show that malnutrition plays a major role in predicting poor prognosis, based on measuring weight loss,¹ low bioelectric phase angle^{2–10} or depletion of body protein or fat with sophisticated laboratory methods.^{11,12} On clinical grounds, the Prognostic Nutritional Index^{13,14} and the Glasgow Prognostic Score¹⁵ are very effective in identifying patients with a poor prognosis.

Malnutrition not only compro-

mises survival, but also has a major adverse effect on the quality of life. Studies have shown that malnourished cancer patients have:

- higher rates of hospital readmissions and longer hospital stays^{16,17}
- increased symptom distress¹⁸
- reduced quality of life, based on usual questionnaire for cancer patients^{19–24}
- reduced muscle strength and functional status⁸

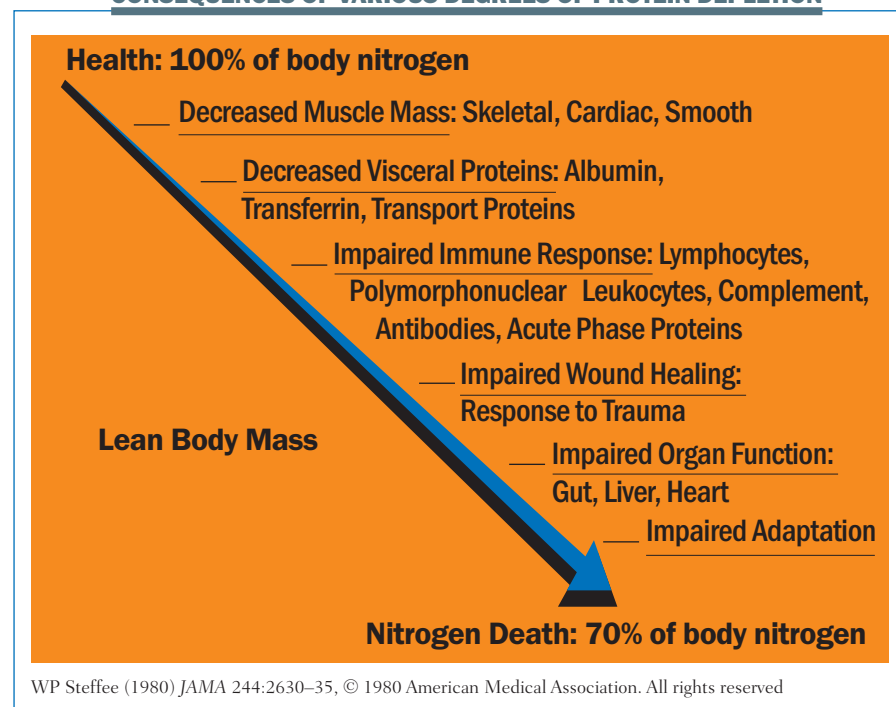
All of these studies have identified malnutrition as an independent factor that adversely affects the quality of life.

Importantly for oncologists, malnutrition increases chemotherapy toxicity. This has been demonstrated for weight loss and hypoalbuminemia²⁵ and low total body nitrogen as a predictor of neutropenia.²⁶ It has also been demonstrated for sarcopenia as a significant predictor of toxicity, based on CT scan.²⁷ It is also true for patients with a body mass index (BMI) lower than 25kg/m².²⁸ All of these factors have been found to be associated with poor adherence to chemotherapy, and high toxicity.

Malnourished cancer patients also have poorer responses to chemotherapy, both in terms of the percentage of patients responding to chemotherapy and the duration of response to treatment.^{29,30} The fact that malnourished patients have a poor prognosis, are more likely to have poor responses to chemotherapy, and have increased toxicity means that it is important for oncologists to assess and manage malnutrition.

Question: We have so much data, going back more than 40 years, so why are people still trying starvation

CONSEQUENCES OF VARIOUS DEGREES OF PROTEIN DEPLETION



diets to kill their cancer and why is the awareness of the negative impact of malnutrition still so low among oncologists?

Answer: When patients die because of cancer there is often a combination of cachectic status due to the inflammatory reaction that we know is a major contributor to the weight loss, metabolic derangement and poor nutrient intake. For oncologists and other clinicians it is not clear whether a cancer patient has died because of tumour progression or starvation. Some patients with a slowly progressing tumour or a tumour not involving vital organs could survive for some months, but they die sooner because they do not eat enough. The problem is related to the fact that it is difficult to separate the morbidity and mortality that is due to the simple deficiency of macronutrients from the alteration of metabolism that is due to inflammation, which is a major cause of cachexia. So many oncologists have a nihilistic approach and do not try to feed cancer patients in an optimal way. In contrast, I suggest that these patients should be supported in the best possible way with nutrition.

How can we identify cancer patients at nutritional risk?

There are several nutritional screening tools, but the most important and most commonly used in hospitals are shown in the table above. The Malnutrition Screening Tool (MST) relies mainly on unintentional weight loss and appetite, so it is very simple to use this score if a hospital has limited resources. The Nutritional Risk Screening includes more parameters: unintentional weight loss, BMI, severity of disease, age, and impaired general condition, with



COMPARISON OF MALNUTRITION RISK SCREENING TOOLS

| Malnutrition Risk Screening Tools | Description | Parameters Used |
|---|--|---|
| Malnutrition Screening Tool (MST) | MST is a simple, quick-to-administer, 2-question tool. | Unintentional weight loss ^a Appetite ^a |
| Nutritional Risk Screening-2002 (NRS-2002) | Developed by ESPEN, this is a preferred tool to screen for malnutrition in European hospital settings. | Unintentional weight loss ^a BMI ^a Disease severity Age Impaired general condition |
| Malnutrition Universal Screening Tool (MUST) | Developed for screening in the community, MUST is widely used in the United Kingdom and Europe. | Unintentional weight loss ^a BMI ^a Disease severity Food intake ^a |
| Short Nutritional Assessment Questionnaire (SNAQ) | A simple, easy-to-administer, 3-question screening tool developed in the Netherlands for hospital screening. | Unintentional weight loss ^a Appetite ^a Use of oral supplement or tube feeding |

It is important to screen patients for nutritional status; the choice of screening tool is less important

BMI – body mass index; ESPEN – European Society for Clinical Nutrition and Metabolism

^a Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition diagnostic characteristic

scores ranging from 0 to 7. An important point about this screening tool, which is commonly used in Europe, is that it was developed to identify not only malnourished patients but also those who may improve with nutritional support.

The Malnutrition Universal Screening Tool (MUST) is widely used in the UK and Europe, and includes unintentional weight loss, BMI, severity of disease and food intake. The Short Nutritional Assessment Questionnaire (SNAQ) asks questions about unintentional weight loss, appetite and use of oral supplements or tube feeding. A very interesting and comprehensive review on screening tools by Marian van Bokhorst³¹ found there is no perfect screening tool, and none of the tools are better than the others, but concluded that the important thing is to use a tool to assess patients from a nutritional point of view.

Question: Which malnutrition risk screening tool would you recommend?

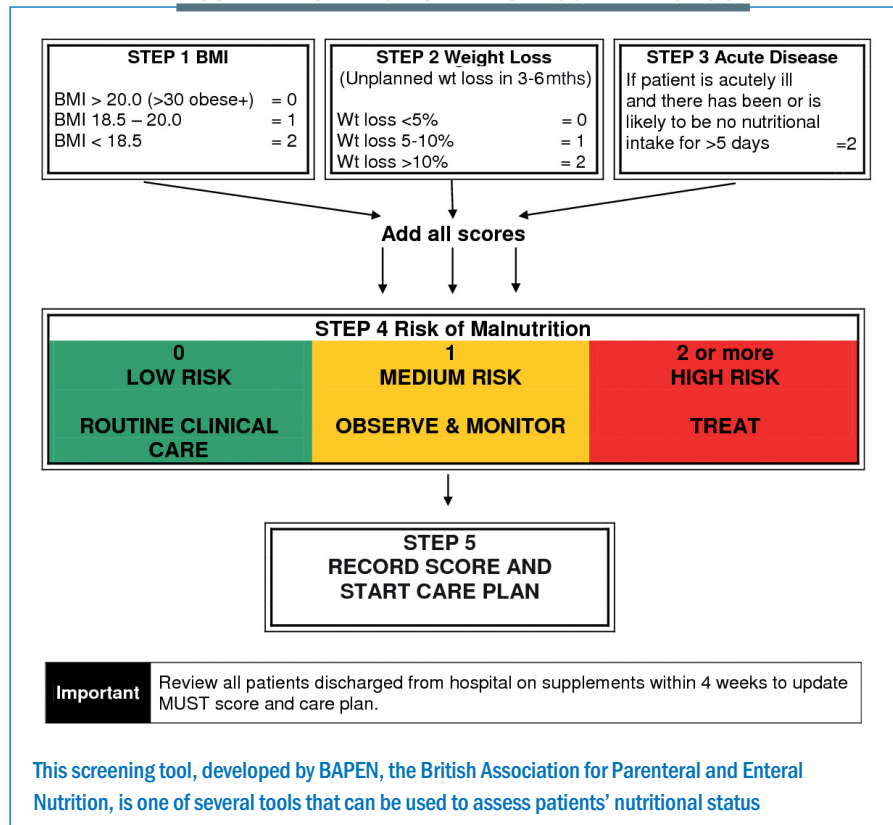
Answer: It depends on the situ-

ation. I used the Nutritional Risk Screening 2002 tool (NRS-2000) for my studies, and we published at least two studies demonstrating that nutritional risk is correlated to the type and stage of a patient's tumour. In routine clinical practice, if I realise that a patient is anorexic because they say they have no appetite, relatives report that the patient is not eating and the patient has lost weight, this information is enough to consider nutritional support. However, if you want to stratify for trials of nutritional support, I would recommend the NRS-2002, though this is not because it has been demonstrated to be better than the others. Ideally in routine practice a patient's chart should include a space to report their nutritional risk.

Ways to provide nutritional support to cancer patients

The approach to nutritional support depends on the availability of a working/accessible gastrointestinal (GI) tract. Very simply, we can consider nonsurgical cancer patients identified

MUST MALNUTRITION UNIVERSAL SCREENING TOOL



improve the muscle protein fractional synthesis rate compared to a standard diet.³⁸ A study giving amino acids rapidly in high quantity (40 g), given as a bolus, increased the mixed muscle fractional synthesis rate in cancer patients undergoing intense chemotherapy.³⁹ These studies show that giving amino acids as a bolus or an enriched leucine diet can improve muscle synthesis in cancer patients, despite chemotherapy or inflammatory status.

There is some controversy over supplements enriched with omega-3 fatty acids, according to four systematic reviews and two meta-analyses.^{40–45} One meta-analysis concluded that omega-3 supplementation increased lean body mass in cancer patients, while the other found no improvement.

Recent non-randomised clinical trials have shown that omega-3 fatty acids increased lean body mass in patients with head and neck cancer⁴⁶ and increased the muscle mass, body weight and response to chemotherapy in patients with lung cancer.⁴⁷

Recent randomised controlled trials, not included in the previous meta-analyses, demonstrated improved quality of life in patients with lung cancer,⁴⁸ as well as reduced leukopenia in patients on neoadjuvant chemotherapy for oesophageal cancer,⁴⁹ and reduced weight loss and higher remission rates in leukaemic patients receiving omega-3 fatty acids.⁵⁰

How can we optimise the use of oral nutritional supplements? An excellent systematic review⁵¹ found greater adherence to higher-energy-density supplements (91% with 2 kcal/ml). Adherence was probably better with liquid oral nutritional supplements. This sort of energy

as malnourished at nutritional risk in three broad groups:

- patients with the whole GI tract working
- patients with the upper GI tract inaccessible
- patients with the whole GI tract inaccessible or not working.

In patients with the whole GI tract working, I think the first approach is oral nutritional intervention with supplements, which are better if enriched with omega-3 or leucine, with or without dietetic counselling and megestrol. However, sometimes we may also consider supplementary intravenous nutrition. In patients who already have a central line it is sometimes easier

to give nutritional supplementation by vein than forcing oral intake or using a tube.

What are the effects of oral supplementation?

Dietary counselling alone does not ameliorate quality of life, but dietary counselling plus nutritional supplements improves weight more than dietary counselling alone or usual care.^{32–34} Dietary counselling plus nutritional supplements improves quality of life, according to two studies.^{35–37} However, oral nutritional intervention has no effect on cancer mortality.

An experimental diet high in protein and enriched with 10% free leucine was found to significantly

supplement should be in addition to food, with clinical benefits when the intake was in the range of 300–600 kcal/day for more than five weeks.

Dietary energy density was positively associated with energy balance. Survival was positively associated with energy balance while systemic inflammation had a negative association. The review recommended using omega-3 fatty acids and/or leucine-enriched oral nutritional supplements. When amino acids are used, they should be given as a bolus.

Patients with inaccessible upper GI tract

Options for patients with an inaccessible GI tract are tube feeding using either a nasogastric tube or percutaneous endoscopic gastrostomy, where the tube feeds directly into the patient's stomach, passing through their abdominal wall.

There is a lot of experience in patients with head and neck cancer, during radiation with or without chemotherapy, and many non-randomised trials report better weight maintenance and quality of life, as well as better adherence to therapy and fewer hospital admissions, compared with oral feeding.

A randomised clinical trial comparing percutaneous endoscopic gastrostomy with use of a nasogastric tube found that percutaneous endoscopic gastrostomy was associated with better weight maintenance and a longer duration of enteral nutrition^{52,53} as well as a similar⁵² or better⁵³ quality of life. The results are quite limited so we cannot recommend percutaneous endoscopic gastrostomy over nasogastric feeding.

Patients whose whole GI tract is inaccessible or not working

You are obliged to use parenteral (intravenous) nutrition in patients whose GI tract is inaccessible or not working. There is little scientific experience and very few randomised trials, but the approach is very practical and well accepted by those patients who already have a central venous catheter and may not be able to differentiate between therapy and nutritional support. This may be important from a psychological point of view, as the patients do not realise that they are so compromised that they require nutritional support to survive. Small-volume high-density emulsions can cover a large part of the patient's energy requirement, so they can be used easily in home environments.

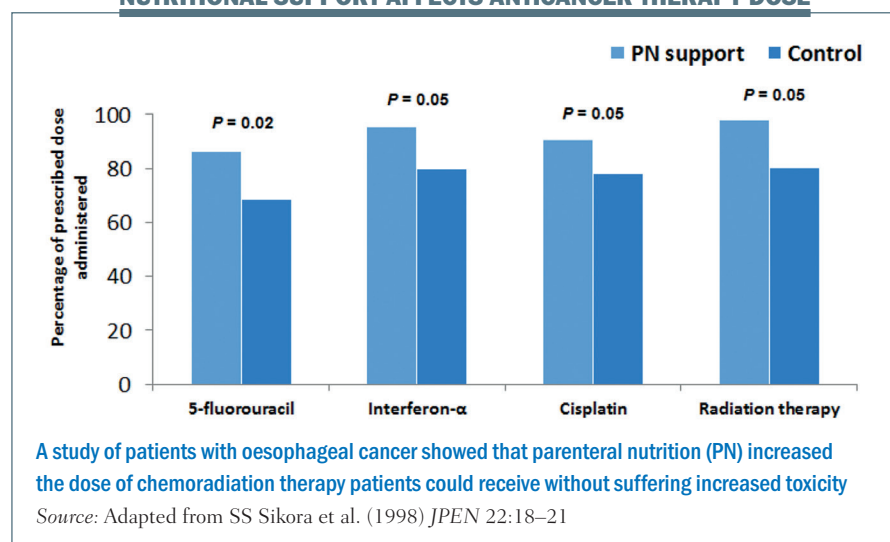
Supplemental parenteral nutrition can be useful in patients whose GI tract is only partially obstructed or who are partially aphagic (have a reduced ability to swallow), because delivery via a vein may be more comfortable for them and is easier than putting a tube in the stomach or forcing

oral nutrition. A randomised study in patients with cancer of the oesophagus showed those fed by parenteral nutrition were able to receive higher doses of chemoradiation therapy (see figure below) without increased toxicity, compared to controls.⁵⁴

A recent Chinese study identified malnourished cancer patients using a nutritional screening tool and treated them with enteral or parenteral nutrition. In comparison with patients who did not receive any nutritional treatment, those who received enteral or parenteral nutrition had a significantly reduced risk of developing adverse events. The authors concluded that undernutrition and nutritional risk are common problems that impact on outcomes of hospitalised cancer patients.⁵⁵

There are few studies on the use of supplemental parenteral nutrition at home, but one study showed giving supplemental parenteral nutrition intravenously in cachectic patients who were not totally aphagic when their oral intake dropped to 21–24 kcal/kg/day was

NUTRITIONAL SUPPORT AFFECTS ANTICANCER THERAPY DOSE



associated with an increase in energy balance, longer survival and improved maximum exercise capacity.⁵⁶ A further study demonstrated an increase in lean body mass in cancer patients receiving supplemental parenteral nutrition.⁵⁷

We conducted a study in 414 incurable cancer patients who were cachectic and almost aphagic using parenteral nutrition at home. Results showed a six-month survival of 28% and a three-month survival of 57%.⁵⁸ In contrast, according to the literature, without nutritional support these patients would have survived less than three months.

We were also able to identify some simple biochemical/clinical prognostic factors that predict a higher rate of three-or six-month survival

in patients on home total parenteral nutrition. A randomised trial cannot be carried out for ethical reasons, but comparison with evidence in the literature suggests that survival can be prolonged with parenteral nutrition at home. Home parenteral nutrition may therefore prolong survival in selected incurable cancer patients who are cachectic and aphagic, usually with malignant obstruction, and who do not have jaundice or major liver, renal or respiratory insufficiency.

According to the guidelines of both the American Society for Parenteral and Enteral Nutrition and the European Society for Clinical Nutrition and Metabolism, the routine use of enteral or parenteral supplementation during chemotherapy is not recommended. However, if

patients are malnourished or facing more than a week of starvation, then oral nutritional supplements and/or enteral nutritional support should be considered (grade B recommendation, with supporting evidence in the literature). If this is not feasible, then parenteral nutrition is recommended.

If patients develop GI toxicity from chemotherapy or radiation therapy, short-term parenteral nutrition may be better tolerated (and more efficient) than enteral nutrition to restore intestinal function, prevent nutritional deterioration and allow full adherence with therapy (general consensus statement). ■

The references cited in this article can be accessed online at www.cancerworld.org

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