From guidelines to clinical practice: a roadmap for oncologists for nutrition therapy for cancer patients

Maurizio Muscaritoli1, Jann Arends and Matti Aapro

Abstract: Tackling malnutrition in cancer patients remains one of the most challenging tasks in clinical practice. Even though robust evidence exists stressing the role of nutritional status in relation to treatment outcome, its appropriate consideration in clinical practice is often lacking. In this review, we discuss the significance of nutritional status and of malnutrition for the cancer patient. Drawn from experience and from current recommendations of the European Society for Clinical Nutrition and Metabolism (ESPEN), we propose concrete and manageable steps to routinely incorporate nutritional aspects in today’s oncological clinical practice.

Keywords: cachexia, clinical nutrition, ESPEN guidelines, malnutrition, nutritional status, oncology

Highlights
Malnutrition, the result of a poor nutritional status, has a well-documented negative effect on treatment outcome in cancer patients.

(1) Although high-quality randomized controlled trial (RCT)-based evidence is still scarce, data exist showing that timely intervention can lead to improved treatment outcomes.

(2) Comprehensive therapies should include strategies for cancer treatment while maintaining the nutritional status of the patient.

(3) Measures and tools proposed in this article can help to determine the nutritional status and detect and treat malnutrition in a timely manner.

Cancer: an unparalleled challenge for treating physicians
Today, malignant disorders represent the second leading cause of death worldwide.1 Progressively aging populations, especially in western countries, together with an anticipated global increase of cancer incidence2 pose new challenges to screening procedures, as well as to diagnosis, treatment, monitoring, and reimbursement.

Recent therapeutic advances have profoundly changed cancer treatment options and outcomes for the better.3 New substance classes target immune cells, reactivating anticancer-directed immune activities, as well as tumor cells, reducing their burden and leading to increased survival rates.3 However, tolerability of treatment regimes and outcome of therapy depend on several aspects, one of the most important being the nutritional status of the patient. In this review, we have summarized the current knowledge of nutritional status in oncology in an attempt to provide oncologists involved in the care of patients with cancer with a roadmap for nutritional therapy in their everyday clinical practice.

Based on the recent guidelines from the European Society for Clinical Nutrition and Metabolism (ESPEN) we propose possible nutritional interventions, from diagnosis to treatment and monitoring.

Nutritional status in cancer treatment: current understandings, future challenges
Among hospitalized patients, cancer patients present with the highest prevalence of malnutrition, with 30–50% of hospitalized cancer patients...
found to be malnourished or at risk of malnutrition, in large European surveys.4–7 Weight loss arises early in the course of disease and may develop at any time throughout the patient’s cancer journey.3 A recent study in 22 medical oncology centers in Italy with almost 2000 patients showed that 51% had nutritional impairment and 9% were overtly malnourished.7 Furthermore, the authors found a clear correlation between severity of malnutrition and stages of cancer.7 A French study evaluating the prevalence of malnutrition in cancer patients (n = 1903) in 154 French hospital wards found that 39% of patients were malnourished. This study also reported that 42.5% of the patients identified as malnourished did not receive any nutritional support.4 Patient groups at particular high risk of malnutrition include those with head-and-neck cancer and esophageal cancer, undergoing esophageal resection.9,10 It has been reported that malnutrition develops in ~80% patients with esophageal cancer, with dysphagia and weight loss frequently being already present at the time of diagnosis.11 In patients with pancreatic cancer, both the disease-related impairment of exocrine and endocrine pancreatic function and anticancer treatment effects contribute to the development of malnutrition.12 More than 80% of patients with pancreatic cancer suffer from significant weight loss already by the time of diagnosis.13 Malnutrition has a negative impact on clinical outcome and mortality in cancer patients,8,14–17 with adverse consequences, including impaired quality of life,14 higher rates of complications and worse postoperative outcomes,19 longer duration of hospitalization, and poorer anticancer treatment tolerance due to increased toxicity, poorer compliance and decreased response.21,22 Severity of malnutrition is an independent predictor of shorter survival.23 Therefore, the need for adequate nutritional interventions in cancer has been stressed for decades.24,25 In the oncologist’s clinical practice, however, awareness for the nutritional status in cancer patients remains scarce, demonstrated by the fact that it is not regularly assessed in hospitals or ambulatory oncology services as part of standard procedures.26–29 This is even more surprising, since the negative impact of malnutrition on oncological patients’ outcomes has been extensively demonstrated. The pathogenesis of malnutrition in cancer patients is multifactorial in origin.30 Causes can be both disease or therapy related; for example, anorexia, oral ulceration, intestinal obstruction, xerostomia, diarrhea, nausea, vomiting, cramping, or bloating.8,31–36 Cancer-related loss of skeletal muscle mass, often referred to as sarcopenia,30,37,38 driven by enhanced intramuscular proteolytic systems and triggered by the complex interaction between reduced food intake, possible increased energy expenditure, systemic inflammation, tumor growth, but also through targeted therapies,39 leads to further deterioration of the patient’s clinical and functional status and to poorer overall prognosis.30 General consequences of muscle loss in cancer can be physical impairment, as well as increased postoperative complications and elevated chemotherapeutic toxicity.8,37,38,40–44 Loss of muscle mass is a hallmark of cancer cachexia, a cancer comorbidity which has been defined as ‘a multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment.’45 Since cancer cachexia syndrome can develop progressively through various stages, it can be classified, according to its severity (i.e. degree of depletion of energy stores and body protein), into precachexia, cachexia and refractory cachexia.45 While patients with refractory cachexia are less likely to respond to nutritional therapy,45 the stages of precachexia and cachexia represent unique and unmissable windows of opportunity for nutritional intervention,8,30 with measurable impact on clinical outcomes, including survival. Indeed, consolidated evidence suggests increased mortality rates associated with cancer cachexia.8,30,46–48

**Under-recognition of cancer-related nutritional impairment: a matter of terminology?**

One possible obstacle in the daily prevention, recognition, and treatment of cancer-associated malnutrition and cachexia is the current lack of consistent nomenclature (Box 1).

Malnutrition (synonym ‘undernutrition’) is defined as ‘a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat-free mass) and body cell mass leading to diminished physical and
When malnutrition is caused by an underlying disease, be it acute or chronic, it is classified as disease-related malnutrition (DRM). Systemic inflammation plays a major role in the pathogenesis of DRM, but DRM may also occur in the absence of a clinically significant inflammatory response (DRM without inflammation). In this light, cancer cachexia may be considered a form of DRM with inflammation, brought about by a complex and peculiar pathophysiology.

Despite the recognized negative impact of DRM on patients’ prognosis and healthcare costs, during recent decades, there has been a fundamental lack of consensus on diagnostic criteria for malnutrition to be applied in clinical settings. As a consequence, DRM remains frequently unrecognized, underdiagnosed and untreated, with its prevalence being extremely variable, depending on the assessment method used.

A combined task force commissioned by four major international clinical nutrition societies (ESPEN, the American Society for Parenteral and Enteral Nutrition, the Parenteral and Enteral Nutrition Society of Asia, and Federación Latino Americana de Terapia Nutricional, Nutrición, Clínica y Metabolismo) has recently proposed a consensus scheme for diagnosing malnutrition in adults in clinical settings, on a global scale. Briefly, the panel of experts has suggested that diagnosis of malnutrition is based on three phenotypic criteria (unintentional weight loss, low body mass index (BMI), and reduced muscle mass) and two etiologic criteria (reduced food intake or assimilation, and inflammation or disease burden). To diagnose malnutrition, at least one phenotypic criterion and one etiologic criterion should be present. Severity of malnutrition may also be assessed based on the degree of deviation of these criteria from normality.

**Box 1.** Malnutrition, cachexia and sarcopenia: definitions and differentiation (according to Cederholm et al., Cruz-Jentoft et al., Baracos et al., Arends et al., and Fearon et al.).

**Malnutrition**
- A state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat-free mass) and body cell mass;
- Leading to diminished physical and mental function and impaired clinical outcome from disease.

**Disease-related malnutrition**
- Malnutrition caused by an underlying acute or chronic disease;
- Can occur with or without the presence of systemic inflammation;
- Reduced food intake or assimilation will cause tissue breakdown that can, in turn, result in significant loss of body weight, alterations in body composition, and declining physical function.

**Cachexia**
- Multifactorial syndrome characterized by involuntary weight loss, with ongoing loss of skeletal muscle mass with or without loss of fat mass;
- May be considered a form of disease-related malnutrition with systemic inflammation as an important contributing factor;
- Staging according to nutritional status/severity of catabolism and response to nutritional intervention:
  1. Precachexia: onset of low-grade weight loss (≤5% body weight):
     - Early initiation of preventive nutritional intervention is key;
     - Measurable impact on clinical outcomes, for example, mortality.
  2. Cachexia: progressing weight loss (>5% or BMI <20 kg/m²) with weight loss >2% body weight or sarcopenia with weight loss >2%:
     - Adequate nutrition support as a mainstay of a multimodal treatment approach;
     - Measurable impact on clinical outcomes, for example, mortality.
  3. Refractory cachexia: extensive weight loss/catabolism close to the end of life (expected survival <3 months):
     - Low emphasis on nutritional intervention except for palliative nutrition to alleviate hunger and thirst;
     - Low likelihood of response to any type of treatment intervention.

**Sarcopenia**
- Progressive and generalized loss of skeletal muscle mass and function associated with increased likelihood of adverse outcomes, including falls, fractures, physical disability and mortality;
- Can be age related (primary sarcopenia) or due to other causes such as disease, inactivity, or malnutrition (secondary sarcopenia);
- Sarcopenia is a hallmark of cancer cachexia.

BMI, body mass index.
Lastly, inconsistencies also exist regarding sarcopenia. The term sarcopenia is commonly and still largely used to define the loss of skeletal muscle mass and function associated with aging. More recently, the European Working Group on Sarcopenia in Older People has defined sarcopenia as ‘primary’ (or age related) and ‘secondary’ (when other causes other than, or in addition to, aging are present, such as chronic diseases; reviewed in the work of Muscaritoli and colleagues). However, the term sarcopenia is being increasingly used in cancer clinical practice to indicate decreased muscularity as assessed by computed tomography (CT) scan, irrespective of the loss of muscle function. Consensus concerning meaning and use of different terms is warranted in order to harmonize terminology, as well as diagnosis and treatment algorithms of sarcopenia.

**Effectiveness of nutritional therapy in oncology: where is the evidence?**

Another barrier preventing the implementation of structured clinical nutrition pathways in oncology is the lack of high-quality RCT-based evidence of nutritional therapy efficacy. This has considerably weakened the interest of oncologists toward clinical nutrition. Indeed, it must be acknowledged that while the negative impact of cancer-related malnutrition and cachexia is striking, the results on the effects of nutrition on patients’ overall prognosis are weak or inconsistent. Nutritional care and therapy in cancer patients encompass dietician-aided dietary counseling (aimed at improving patients’ spontaneous food intake), oral supplementation with industry-prepared oral nutritional supplements (ONS), enteral nutrition (EN) and parenteral nutrition (PN). The term ‘nutritional therapy’ is used when active interventions are implemented with ONS, EN or PN. ‘Medical nutrition’ utilizes ONS, EN and PN to prevent or correct DRM, depending on the clinical indications and patient’s clinical condition.

Growing evidence supports active nutritional interventions in the oncological patient. In cancer patients who were malnourished or at risk of malnutrition, oral nutritional support or dietary counseling were shown to improve energy intake and body weight but had no effect on clinical outcomes of oncological relevance, such as survival and treatment toxicity. In patients with colorectal cancer undergoing radiotherapy, individual dietary counseling and ONS improved nutritional status and reduced early and late radiotherapy-induced toxicity. The long-term follow up of this study showed the longest survival rates in patients with intensified nutritional counseling compared with usual diet plus supplements and usual diet alone.

Nutritional interventions in head-and-neck cancer patients yielded more consistent results. Early nutritional intervention ranging from counseling (for patients with low nutritional risk) to ONS or EN via tube (for those with higher nutritional risk) reduced weight loss, frequency and duration of treatment interruptions, as well as rehospitalizations. In high-risk patients, for example, with hypopharyngeal primary site, T4 tumor, female sex, or receiving combined radiochemotherapy, prophylactic percutaneous endoscopic gastrostomy (PEG) was associated with fewer malnourished patients over time and higher quality of life. Early nutritional intervention with either counseling ONS or EN was associated with reduction of treatment interruption and duration of hospitalization.

In selected cancer patient populations, mainly in those whose gastrointestinal function is partially or totally impaired, PN may play an essential role in maintaining nutritional status. In patients with advanced pancreatic cancer, supplemental parenteral nutrition improved nutritional status. Two studies focusing on the impact of home parenteral nutrition (HPN) in cancer patients could show that HPN is associated with an improvement in nutritional status, as well as quality of life. In summary, the available studies addressing the effects of nutrition care or therapy on cancer patients’ outcomes is still insufficient or inconsistent. Further high-quality RCT-based evidence is needed to better identify the categories of cancer patients in whom nutritional therapy may be cost effective in impacting outcomes of oncological relevance.

**Simultaneously targeting the tumor and nutritional and metabolic derangements: the oncological parallel pathway**

Because of their high incidence and prognostic relevance, screening for and assessment, treatment and follow-up evaluations of nutritional deficits should be implemented as a standard second pillar in cancer therapy (Figure 1). The nutritional and metabolic (e.g. inflammation-driven
impaired glucose tolerance, muscle hypercatabolism, anabolic resistance) changes should be attended to in parallel to all oncological treatments and during all stages of a patient in cancer disease. Thus, the aim is to start nutritional management early in the course of the disease, beginning with the assessment of nutritional status at the time of diagnosis, and starting nutritional interventions in parallel with cancer therapies. Nutritional strategies should be adapted to different cancer stages and treatments, and all options of nutritional therapy should be explored, including ONS, EN or PN, as appropriate, in patients who are not able to fully meet their nutritional requirements by the oral route, according to existing clinical practice guidelines and recommendations on nutrition in cancer patients.

Multifactorial patient needs require a multidisciplinary team approach: the role of the oncologist
Cancer treatment represents a continuum of care, from diagnosis to treatment and follow up. Addressing stage- and condition-dependent patient needs should be at the center of all treatment decisions. To be optimized, such individualized approaches cannot be shouldered by the treating oncologist alone, but should best be performed by a closely collaborating multidisciplinary team, led by the hematologist/oncologist and including other medical (e.g. surgeon, gastroenterologist, pain expert, supportive and palliative care expert) and allied specialists (e.g. nurses, dieticians/nutritional therapists, psychologists, and physiotherapists; Figure 2). A comprehensive treatment plan should be designed by the
treatment team and regularly reviewed for necessary modifications.

Cancer diagnosis and treatment should be accompanied by a comprehensive screening for and assessment of possible malnutrition. The plan should consider key aspects (e.g., nutritional status, pain management, and coping strategies) to be adapted throughout the patient’s cancer journey by a team consisting of different professions, for example, oncologists, surgeons, psychologists, nutritional therapists, nurses, and physiotherapists.

Translating clinical knowledge into practice: recommendations of the ESPEN board
Since 1997, ESPEN publishes guidelines and position papers in the field of clinical nutrition. Recent ESPEN guidelines for nutritional care in cancer offer a comprehensive overview and recommendations authored by 22 experts from 13 countries.8 The guidelines are based on evidence of clinical practice, as well as on personal experience of the experts in the field and provide a set of recommendations for screening, assessment, treatment, and monitoring of malnutrition in oncological patients. In the following sections, the most important guideline recommendations and their implementation into clinical practice are presented.

Integration of nutritional management into cancer care: the role of early screening and assessment
Historically, nutritional intervention in cancer has often been associated mainly with the setting of advanced cancer stages as part of a palliative treatment regimen. This has been, and still frequently is, due to a low awareness for nutritional and metabolic problems in clinical oncology and has resulted in underdiagnosing the gradual development of malnutrition of patients during anticancer treatment.

However, nutritional therapy, if applied in a timely fashion, can contribute to maintaining or
regaining a normal nutritional and functional status of the patient, which is associated with better tolerability of anticancer treatment and better clinical outcome.8,16,17,25,26,37,38,40–44

Therefore, timely screening (Figure 2, Table 1) of the nutritional status should be seen as a hallmark of care for the patient, and as good clinical practice. Early detection of nutritional needs and appropriate intervention programs are critical in cancer treatment (Figure 2). Key drivers for later complications like malnutrition and cachexia can be detected and treated at an early stage, thus helping to prevent treatment interruptions caused by impaired physical status. Such timely screening of the nutritional status can lead to better tolerability of therapy, higher completion rates of treatment cycles and an optimized treatment outcome. A number of screening tools are available; ESPEN8 suggests using validated nutrition screening tools, for example, Nutrition Risk Screening 2002, the Malnutrition Universal Screening Tool, the Malnutrition Screening Tool, or the Mini Nutritional Assessment Short Form Revised.69 The Patient-Generated Subjective Global Assessment has been highly recommended due to its high sensitivity, specificity and predictive value in the oncological setting,70–72 but also other validated tools may be used.

Prior to chemotherapy, patients should undergo an intensive risk assessment, including disease staging, medical condition of the patient, as well as specific examination of pre-existing cachexia or further metabolic disturbances. Valid methods for determination are depicted in Table 2. CT-aided examination already used for cancer
### Table 1. Screening for (risk of) malnutrition.

| Criteria to build and select screening tools (Mini Nutritional Assessment and ESPEN criteria) | Reliable detection of nutritional deficits requiring intervention |
|---|---|
| | Easily performed by non-nutrition expert |
| | Minimally invasive |
| | Brief |
| Nutritional aspects evaluated by most screening tools | Food intake |
| | Loss of body weight |
| | Body mass index |
| | Metabolic changes (e.g. glucose intolerance, inflammation) |
| | Nutrition Risk Screening 2002 |
| | Malnutrition Universal Screening Tool |
| | Mini Nutritional Assessment |
| | Patient-Generated Subjective Global Assessment, specifically designed for oncology patients |

**ESPEN, European Society for Clinical Nutrition and Metabolism.**

### Table 2. Quantitative or semiquantitative assessment of relevant nutritional and metabolic parameters at present and as expected for the near future.

| Domain | Parameter |
|---|---|
| Energy and protein intake | e.g. Food diary, dietary recall |
| Barriers to food intake | Gastrointestinal problems |
| | Nutrition impact symptoms (nausea, anorexia, dysphagia, diarrhea) |
| | Chronic pain |
| | Psychosocial distress |
| Physical appearance | Low body weight, BMI |
| | History of weight loss/change |
| Muscle mass/function | e.g. Anthropometry, bioelectrical impedance analysis, dual-energy X-ray absorptiometry, computed tomography, handgrip strength |
| Physical activity | e.g. ECOG score/performance index, step counter/accelerometry (when available) |
| Systemic inflammation | e.g. C-reactive protein, serum albumin, modified Glasgow Prognostic Score |

**BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.**

Screening can be applied to identify body composition and muscle mass.

Patients with abnormal screening should undergo a comprehensive assessment of nutritional imbalance. This includes nutritional intake, assessment of symptoms potentially interfering with food intake (e.g. anorexia, nausea, vomiting, dysphagia, dysgeusia), assessment of muscle mass, determination of physical performance, and degree of systemic inflammation. Key domains for this assessment should comprise dietary intake, body composition, physical activity, and underlying metabolic abnormalities (e.g. glucose intolerance, liver failure, kidney failure) in the patient (Table 2).

### How to enable food intake and support metabolism

Results of the assessment procedures need to be compared with the individual aims for the patient. If the present condition deviates from these aims, interventions need to be planned to diminish or remove the observed deficits. Aims include the intake of adequate amounts of energy and nutrients, the absence of nutrition impact symptoms (e.g. nausea anorexia, dysphagia, abdominal pain,
diarrhea), a functioning gastrointestinal tract, the absence of chronic pain and psychosocial distress, adequate physical activity, and the absence of systemic inflammation. Specialists of the multidisciplinary team are to be assigned to alleviating specific barriers according to their specializations (Table 3).

Table 3. Tasks and contributions of the multidisciplinary team.

| Task                           | Health Care Specialist                                                                 |
|--------------------------------|----------------------------------------------------------------------------------------|
| Food intake                    | Dietician, clinical nutritionist                                                        |
| Dysphagia                      | Speech therapist, ear–nose–throat specialist, dentist, head-and-neck surgeon, neurologist |
| Gastrointestinal problems      | Dietician, clinical nutritionist gastroenterologist, surgeon                           |
| Chronic pain                   | Pain expert                                                                            |
| Psychosocial distress          | Psychologist, social worker, palliative care specialist                                 |
| Muscle loss, fatigue, inactivity| Clinical nutritionist, physiotherapist, exercise physiologist, dietician                 |

Nutritional goals are summarized in Table 4. In patients with malnutrition or risk of malnutrition, the use of dietary restrictions is not recommended and even considered dangerous. Theoretical arguments that nutrients would primarily benefit the tumor lack scientific evidence and thus, should not lead to interruption, decrease, or cessation of nutritional intervention in cancer patients.\textsuperscript{8,15} Energy intake should initially aim to be from 20–25 to 35 kcal/kg body weight, choosing the higher range for ambulatory, younger, underweight, and male patients, while choosing the lower range for bedridden, older, obese, and female patients. During follow up, energy provisions need to be adapted according to the nutritional status and the metabolic condition. Protein intake should be above 1 g/kg and aiming for 1.2–1.5 g/kg body weight per day.

Nonprotein energy may be provided by fat and carbohydrates, with each nutrient group providing a similar amount of energy. Vitamins and essential trace elements should be provided daily in doses analogous to recommended daily allowances for healthy subjects\textsuperscript{81} either \textit{via} habitual diet or in cases of inadequate food intake, as a daily oral, enteral or intravenous supplement.\textsuperscript{8}

For patients with nutritional need, the route of administration should be tailored to the patient’s physical condition. Patients with inadequate food intake who are able to eat should receive adequate dietary counseling, including fortification of foods as well as ONS. If oral nutrition remains inadequate or is not feasible, EN is recommended. Should EN not be feasible or fail to improve the nutritional status of the patient, PN should be implemented,\textsuperscript{8} either as supplemental, or, if not otherwise possible to supply adequate nutrition, as total or complete PN.

Table 4. Nutritional goals in cancer treatment.\textsuperscript{8,15}

| Nutritional Intakes                  | Amount                                                                 |
|-------------------------------------|------------------------------------------------------------------------|
| Energy                              | 20–25 kcal/kg/d for bedridden patients                                 |
|                                     | 25–30 kcal/kg/d for ambulatory patients                               |
| Protein                             | >1 g/kg/day and, if possible, up to 1.5 g/kg/day                       |
| Micronutrients, i.e. vitamins and essential trace elements | Vitamins and minerals to be supplied in amounts approximately equal to the RDA. Use of high-dose micronutrients in the absence of specific deficiencies is discouraged |

RDA, recommended daily allowance.
Figure 3 shows a treatment algorithm for nutritional management of malnutrition in oncological patients, including screening and assessment, as well as treatment and monitoring.

**Nutritional considerations during different modes of anticancer treatments: surgery, radiotherapy, anticancer drug treatment**

Nausea, anorexia, dysphagia, diarrhea and other nutritional-impact symptoms may and do occur during most anticancer treatments. Recent data show better clinical outcome in patients undergoing chemotherapy by use of standardized web-based monitoring of patient-reported symptoms. Comparatively, the patients using the electronic symptom monitoring had a 5-month-longer survival (31.2 months (95% confidence interval (CI), 24.5–39.6) versus 26.0 months (95% CI, 22.1–30.9); \( p = 0.03 \)).

In all situations, the general rule is to ensure an adequate intake of energy and nutrients. This may require early placement of an enteral tube in patients with obstructing tumors of the upper gastrointestinal tract, or if radiation of the head-and-neck region or the esophagus is planned. In cases with severe dysfunction of the small bowel (e.g. mucositis induced by high-dose chemotherapy, intestinal graft versus host disease after allogeneic stem cell transplantation, short bowel syndrome after surgical resections), PN may be required and tailored to the individual need. The primary goal of nutritional intervention in all these settings is to keep patients fit for, and to avoid dose reductions or interruptions of, anticancer therapy.

**Role of physical activity**

Muscle activity initiates essential anabolic stimuli. Increasing or maintaining muscle mass may be hampered or made impossible by inactivity. Indeed, inactivity prevents optimal incorporation and utilization of nutrients by muscle. Therefore, muscle training should accompany every nutritional intervention and should be an essential component of the parallel supportive pathway. The benefits of exercise reported in patients with cancer include increased exercise capacity, improved activity levels, and reduced fatigue, the latter of which is the most frequent and burdensome side effect of chemotherapy. Exercise has also been shown to preserve physical well-being.

Thus, early, continuous, and multimodal interventions with a range of approaches, including endurance training and aerobic exercises (e.g. walking, treadmill walking, stationary cycling, resistance training) is recommended, aiming at improving muscle mass and function. Oncologists should favor implementation of multimodal therapeutic approaches, including controlled physical activity for their patients, even in those complaining of asthenia and fatigue.

**Nutrition in oncology: time for a change of perspective**

Historically, treatment advances in cancer have predominantly focused on the introduction of new substances. Lately, patient-centered treatment approaches are gaining momentum, progressively including patient’s performance status, interindividual variability in drug pharmacokinetics and genetic background. This has led to an increased variety of treatment options, but results (compared with just a few years ago) in longer treatment durations for cancer patients. This may expose the patient to the prolonged risk of nutritional impairment and progressive depletion of body resources. Counteracting such depletion with nutritional interventions represents a major supportive goal in modern oncology. Still, in current clinical practice, nutritional status receives little attention. Standard evaluation focuses rather on disease-specific parameters to determine treatment procedure. Awareness is needed of how a deteriorated nutritional status or a high risk of malnutrition is an important prognostic factor for later treatment success or failure.

Incorporation of the nutritional status evaluation and monitoring should therefore be regarded as a hallmark of good clinical practice in cancer treatment. From diagnosis onward, meeting individual requirements of each cancer patient should be at the center of every treatment approach. A close collaboration of experts is the cornerstone of a state-of-the-art cancer treatment. This requires profound changes in today’s hospital infrastructure, including diagnosis and treatment criteria; however, such implementations will strongly benefit the patient, and therefore poses an ethical responsibility for treating physicians and associated clinical staff.

**Funding**

The project received funding from Fresenius Kabi Deutschland GmbH. Medical writing assistance, supported financially by Fresenius Kabi.
Deutschland GmbH, was provided by Medizin und Markt, a medical agency, during the preparation of this article. The sponsor had no role in the writing process of the publication. The authors are fully responsible for all content and editorial decisions, were involved at all stages of manuscript development and have compiled and approved the final version.

**Conflict of interest statement**
The authors declare that there is no conflict of interest.

**ORCID iD**
Maurizio Muscaritoli https://orcid.org/0000-0003-1955-6116

**References**

1. Carruba G, Cocciadiferro L, Di Cristina A, et al. Nutrition, aging and cancer: lessons from dietary intervention studies. *Immun Ageing* 2016; 13: 13.

2. World Health Organization. Cancer, http://www.who.int/mediacentre/factsheets/fs297/en/ (accessed October 2019).

3. American Society of Clinical Oncology. Cancer progress timeline, https://www.asco.org/research-progress/cancer-progress-timeline/major-milestones-against-cancer (accessed October 2019).

4. Hebuterne X, Lemarie E, Michallet M, et al. Prevalence of malnutrition and current use of nutrition support in patients with cancer. *JPEN J Parenter Enteral Nutr* 2014; 38: 196–204.

5. Planas M, Alvarez-Hernandez J, Leon-Sanz M, et al. Prevalence of hospital malnutrition in cancer patients: a sub-analysis of the PREDyCES® study. *Support Care Cancer* 2016; 24: 429–435.

6. Pressoir M, Desne S, Berchery D, et al. Prevalence, risk factors and clinical implications of malnutrition in French comprehensive cancer centres. *Br J Cancer* 2010; 102: 966–971.

7. Muscaritoli M, Lucia S, Farcomeni A, et al. Prevalence of malnutrition in patients at first medical oncology visit: the PreMiO study. *Oncotarget* 2017; 8: 79884–79896.

8. Arends J, Bachmann P, Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr* 2017; 36: 11–48.

9. Low DE, Allum W, De Manzoni G, et al. Guidelines for perioperative care in esophagectomy: enhanced recovery after surgery (ERAS®) society recommendations. *World J Surg* 2019; 43: 299–330.

10. Alberda C, Alvadj-Korenic T, Mayan M, et al. Nutrition care in patients with head and neck or esophageal cancer: the patient perspective. *Nutr Clin Pract* 2017; 32: 664–674.

11. Jordan T, Mastnak DM, Palamar N, et al. Nutritional therapy for patients with esophageal cancer. *Nutr Cancer* 2018; 70: 23–29.

12. Gilliland TM, Villafane-Ferriol N, Shah KP, et al. Nutritional and metabolic derangements in pancreatic cancer and pancreatic resection. *Nutrients* 2017; 9: pii: E243.

13. Gartner S, Kruger J, Aghdassi AA, et al. Nutrition in pancreatic cancer: a review. *Gastrointestinal Tumors* 2016; 2: 195–202.

14. Lee JL, Leong LP and Lim SL. Nutrition intervention approaches to reduce malnutrition in oncology patients: a systematic review. *Support Care Cancer* 2016; 24: 469–480.

15. Arends J, Baracos V, Bertz H, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr* 2017; 36: 1187–1196.

16. Ryu SW and Kim IH. Comparison of different nutritional assessments in detecting malnutrition among gastric cancer patients. *World J Gastroenterol* 2010; 16: 3310–3317.

17. Poziomyck AK, Fruchtenicht AV, Kabke GB, et al. Reliability of nutritional assessment in patients with gastrointestinal tumors. *Rev Col Bras Cir* 2016; 43: 189–197.

18. Caro MM, Laviano A and Pichard C. Nutritional intervention and quality of life in adult oncology patients. *Clin Nutr* 2007; 26: 289–301.

19. Shen Y, Hao Q, Zhou J, et al. The impact of frailty and sarcopenia on postoperative outcomes in older patients undergoing gastrectomy surgery: a systematic review and meta-analysis. *BMC Geriatr* 2017; 17: 188.

20. Saitoh-Maeda Y, Kawahara T, Miyoshi Y, et al. A low psoas muscle volume correlates with a longer hospitalization after radical cystectomy. *BMC Urol* 2017; 17: 87.

21. Arrieta O, De la Torre-Vallejo M, Lopez-Macias D, et al. Nutritional status, body surface, and low lean body mass/body mass index are related to dose reduction and severe gastrointestinal toxicity induced by afatinib in patients with non-small cell lung cancer. *Oncologist* 2015; 20: 967–974.

22. Bozetti F. Forcing the vicious circle: sarcopenia increases toxicity, decreases response to chemotherapy and worsens with chemotherapy. *Ann Oncol* 2017; 28: 2107–2118.
23. Martin L, Senesse P, Gioulbasanis I, et al. Diagnostic criteria for the classification of cancer-associated weight loss. J Clin Oncol 2015; 33: 90–99.

24. Caccialanza R, Pedrazzoli P, Cereda E, et al. Nutritional support in cancer patients: a position paper from the Italian society of medical oncology (AION) and the Italian society of artificial nutrition and metabolism (SINPE). J Cancer 2016; 7: 131–135.

25. Drasin H, Rosenbaum EH, Stitt CA, et al. The challenge of nutritional maintenance in cancer patients. West J Med 1979; 130: 145–152.

26. Caccialanza R, Cereda E, Pinto C, et al. Awareness and consideration of malnutrition among oncologists: insights from an exploratory survey. Nutrition 2016; 32: 1028–1032.

27. Pirlich M, Schutz T, Norman K, et al. The German hospital malnutrition study. Clin Nutr 2006; 25: 563–572.

28. Agarwal E, Ferguson M, Banks M, et al. Nutrition care practices in hospital wards: results from the nutrition care day survey 2010. Clin Nutr 2012; 31: 995–1001.

29. Muscaritoli M, Rossi Fanelli F and Molfini A. Perspectives of health care professionals on cancer cachexia: results from three global surveys. Ann Oncol 2016; 27: 2230–2236.

30. Baracos VE, Martin L, Korc M, et al. Cancer-associated cachexia. Nat Rev Dis Primers 2018; 4: 17105.

31. Nitenberg G and Raynard B. Nutritional support of the cancer patients: issues and dilemmas. Crit Rev OncolHematol 2000; 34: 137–168.

32. Bossola M. Nutritional interventions in head and neck cancer patients undergoing chemoradiotherapy: a narrative review. Nutrients 2015; 7: 265–276.

33. Tuca A, Guell E, Martinez-Losada E, et al. Malignant bowel obstruction in advanced cancer patients: epidemiology, management, and factors influencing spontaneous resolution. Cancer Manag Res 2012; 4: 159–169.

34. Kouhen F, Affi M, Benhmidiou N, et al. What nutritional management in patients with head and neck cancers undergoing radiotherapy? An overview. Bull Cancer 2015; 102: 874–879.

35. Marx W, Kiss N, McCarthy AL, et al. Chemotherapy-induced nausea and vomiting: a narrative review to inform dietetics practice. J Acad Nutr Diet 2016; 116: 819–827.

36. Grabenbauer GG and Holger G. Management of radiation and chemotherapy related acute toxicity in gastrointestinal cancer. Best Pract Res Clin Gastroenterol 2016; 30: 655–664.

37. Prado CM, Baracos VE, McCargar LJ, et al. Body composition as an independent determinant of 5-fluorouracil-based chemotherapy toxicity. Clin Cancer Res 2007; 13: 3264–3268.

38. Prado CM, Cushen SJ, Orso CE, et al. Sarcopenia and cachexia in the era of obesity: clinical and nutritional impact. Proc Nutr Soc 2016; 75: 188–198.

39. Schiessel DL and Baracos VE. Barriers to cancer nutrition therapy: excess catabolism of muscle and adipose tissues induced by tumour products and chemotherapy. Proc Nutr Soc 2018; 77: 1–9.

40. Aapro M, Arends J, Bozzetti F, et al. Early recognition of malnutrition and cachexia in the cancer patient: a position paper of a European school of oncology task force. Ann Oncol 2014; 25: 1492–1499.

41. Biolo G, Cederholm T and Muscaritoli M. Muscle contractile and metabolic dysfunction is a common feature of sarcopenia of aging and chronic diseases: from sarcopenic obesity to cachexia. Clin Nutr 2014; 33: 737–748.

42. Ciuni R, Biondi A, Grosso G, et al. Nutritional aspects in patient undergoing liver resection. Updates Surg 2011; 63: 249–252.

43. Schutte K, Schulz C and Malfertheiner P. Nutrition and hepatocellular cancer. Gastrointestinal Tumors 2016; 2: 188–194.

44. Prado CM, Baracos VE, McCargar LJ, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clin Cancer Res 2009; 15: 2920–2926.

45. Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011; 12: 489–495.

46. Baracos V and Kazemi-Bajestani SM. Clinical outcomes related to muscle mass in humans with cancer and catabolic illnesses. Int J Biochem Cell Biol 2013; 45: 2302–2308.

47. Martin L, Birdsell L, Macdonald N, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. J Clin Oncol 2013; 31: 1539–1547.

48. 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: 491–497.

49. Cederholm T, Barazzoni R, Austin P, *et al.* ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr* 2017; 36: 49–64.

50. Cruz-Jentoft AJ, Bahat G, Bauer J, *et al.* Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019; 48: 16–31.

51. Cederholm T, Jensen GL, Correia M, *et al.* GLIM criteria for the diagnosis of malnutrition - a consensus report from the global clinical nutrition community. *Clin Nutr* 2019; 38: 1–9.

52. Muscaritoli M, Lucia S, Molfino A, *et al.* Muscle atrophy in aging and chronic diseases: is it sarcopenia or cachexia? *Intern Emerg Med* 2013; 8: 553–560.

53. Argiles JM and Muscaritoli M. The three faces of sarcopenia. *J Am Med Dir Assoc* 2016; 17: 471–472.

54. Spiro A, Baldwin C, Patterson A, *et al.* The views and practice of oncologists towards nutritional support in patients receiving chemotherapy. *Br J Cancer* 2006; 95: 431–434.

55. Baldwin C, Spiro A, Ahern R, *et al.* Oral nutritional interventions in malnourished patients with cancer: a systematic review and meta-analysis. *J Natl Cancer Inst* 2012; 104: 371–385.

56. Bourdel-Marchasson I, Blanc-Bisson C, Doussau A, *et al.* Nutritional advice in older patients at risk of malnutrition during treatment for chemotherapy: a two-year randomized controlled trial. *PLoS One* 2014; 9: e108687.

57. Ravasco P, Monteiro-Grillo I, Vidal PM, *et al.* Dietary counseling improves patient outcomes: a prospective, randomized, controlled trial in colorectal cancer patients undergoing radiotherapy. *J Clin Oncol* 2005; 23: 1431–1438.

58. Ravasco P, Monteiro-Grillo I and Camilo M. Individualized nutrition intervention is of major benefit to colorectal cancer patients: long-term follow-up of a randomized controlled trial of nutritional therapy. *Am J Clin Nutr* 2012; 96: 1346–1353.

59. Odelli C, Burgess D, Bateman L, *et al.* Nutrition support improves patient outcomes, treatment tolerance and admission characteristics in oesophageal cancer. *Clin Oncol (R Coll Radiol)* 2005; 17: 639–645.

60. Paccagnella A, Morello M, Da Mosto MC, *et al.* Early nutritional intervention improves treatment tolerance and outcomes in head and neck cancer patients undergoing concurrent chemoradiotherapy. *Support Care Cancer* 2010; 18: 837–845.

61. Silander E, Nyman J, Bove M, *et al.* Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer: a randomized study. *Head Neck* 2012; 34: 1–9.

62. Salas S, Baumstarck-Barrau K, Alfonsi M, *et al.* Impact of the prophylactic gastrostomy for unrespectable squamous cell head and neck carcinomas treated with radio-chemotherapy on quality of life: prospective randomized trial. *Radiother Oncol* 2009; 93: 503–509.

63. Assenat E, Thezenas S, Flori N, *et al.* Prophylactic percutaneous endoscopic gastrostomy in patients with advanced head and neck tumors treated by combined chemoradiotherapy. *J Pain Symptom Manage* 2011; 42: 548–556.

64. Pelzer U, Arnold D, Goevercin M, *et al.* Parenteral nutrition support for patients with pancreatic cancer. Results of a phase II study. *BMC Cancer* 2010; 10: 86.

65. Richter E, Denecke A, Klapdor S, *et al.* Parenteral nutrition support for patients with pancreatic cancer–improvement of the nutritional status and the therapeutic outcome. *Anticancer Res* 2012; 32: 2111–2118.

66. Culine S, Chambrier C, Tadmouri A, *et al.* Home parenteral nutrition improves quality of life and nutritional status in patients with cancer: a French observational multicentre study. *Support Care Cancer* 2014; 22: 1867–1874.

67. Cotogni P, De Carli L, Passera R, *et al.* Longitudinal study of quality of life in advanced cancer patients on home parenteral nutrition. *Cancer Med* 2017; 6: 1799–1806.

68. Muscaritoli M, Molfino A, Gioia G, *et al.* The “parallel pathway”: a novel nutritional and metabolic approach to cancer patients. *Intern Emerg Med* 2011; 6: 105–112.

69. Isenring E and Elia M. Which screening method is appropriate for older cancer patients at risk for malnutrition? *Nutrition* 2015; 31: 594–597.

70. Mendes NP, Barros TA, Rosa COB, *et al.* Nutritional screening tools used and validated for cancer patients: a systematic review. *Nutr Cancer* 2019; 71: 49–64.

71. Du H, Liu B, Xie Y, *et al.* Comparison of different methods for nutrition assessment in patients with tumors. *Oncol Lett* 2017; 14: 165–170.

72. Abbott J, Teleni L, Mckavanagh D, *et al.* Patient-generated subjective global assessment short form (PG-SGA SF) is a valid screening tool in chemotherapy outpatients. *Support Care Cancer* 2016; 24: 3883–3887.
73. Kondrup J, Rasmussen HH, Hamberg O, et al. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr* 2003; 22: 321–336.

74. Boléo-Tomé C, Monteiro-Grillo I, Camilo M, et al. Validation of the malnutrition universal screening tool (MUST) in cancer. *Br J Nutr* 2012; 108: 343–348.

75. Vellas B, Guigoz Y, Garry PJ, et al. The mini nutritional assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition* 1999; 15: 116–122.

76. Open.edu. Nutritional module: 5. Nutritional assessment, http://www.open.edu/openlearncreate/mod/oucontent/view.php?id=318&printable=1.

77. Lee Y, Kwon O, Shin CS, et al. Use of bioelectrical impedance analysis for the assessment of nutritional status in critically ill patients. *Clin Nutr Res* 2015; 4: 32–40.

78. Genton L, Hans D, Kyle UG, et al. Dual-energy X-ray absorptiometry and body composition: differences between devices and comparison with reference methods. *Nutrition* 2002; 18: 66–70.

79. Kavanagh JJ and Menz HB. Accelerometry: a technique for quantifying movement patterns during walking. *Gait Posture* 2008; 28: 1–15.

80. mGPS Calculator, https://www.mdcalc.com/modified-glasgow-prognostic-score-mgps-cancer-outcomes (accessed October 2019).

81. Food and Nutrition Board IoM. *Dietary Reference Intakes*. Washington D.C.: National Academic Press, 2015. http://nationalacademies.org/hmd/Activities/Nutrition/SummaryDRIs/DRI-Tables.aspx (accessed September 2019).

82. Basch E, Deal AM, Kris MG, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. *J Clin Oncol* 2016; 34: 557–565.

83. Basch E, Deal AM, Dueck AC, et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *JAMA* 2017; 318: 197–198.

84. Admsen L, Quist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial. *BMJ* 2009; 339: b3410.

85. Cheville AL, Kollasch J, Vandenberg J, et al. A home-based exercise program to improve function, fatigue, and sleep quality in patients with stage IV lung and colorectal cancer: a randomized controlled trial. *J Pain Symptom Manage* 2013; 45: 811–821.

86. Cheville AL, Girardi J, Clark MM, et al. Therapeutic exercise during outpatient radiation therapy for advanced cancer: feasibility and impact on physical well-being. *Am J Phys Med Rehabil* 2010; 89: 611–619.