ESPEN expert group recommendations for action against cancer-related malnutrition

J. Arends[a], V. Baracos[b], H. Bertz[c], F. Bozzetti[d], P. C. Calder[e], N. E. P. Deutz[f], N. Erickson[g], A. Laviano[h], M. Lisanti[i], D. N. Lobo[j], D. McMillan[k], M. Muscaritoli[l], J. Ockenga[m], M. Pirlich[n], F. Strasser[o], M. de van der Schueren[p], A. Van Gossum[q], P. Vaupel[r], and A. Weimann[s]

[a] Department of Medicine I, Medical Center - University of Freiburg; Faculty of Medicine, University of Freiburg, Freiburg, Germany

[b] Department of Oncology, University of Alberta, Edmonton, Canada

[c] Department of Medicine I, Medical Center - University of Freiburg; Faculty of Medicine, University of Freiburg, Freiburg, Germany

[d] Faculty of Medicine, University of Milan, Milan, Italy

[e] Faculty of Medicine, University of Southampton and NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust and University of Southampton, Southampton, UK

[f] Center for Translational Research in Aging & Longevity, Department of Health and Kinesiology, Texas A&M University, College Station, TX, USA

[g] Comprehensive Cancer Center, Ludwig-Maximilian-University Hospital, Munich, Germany

[h] Department of Clinical Medicine, Sapienza University, Rome, Italy

[l] Department of Translational Medicine, University of Salford, Salford, UK

[j] Gastrointestinal Surgery, Nottingham Digestive Diseases Centre, National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust and University of Nottingham, Nottingham, UK

[k] Department of Surgical Science, University of Glasgow, Glasgow, UK

[l] Department of Clinical Medicine, Sapienza University, Rome, Italy

[m] Department of Gastroenterology, Endocrinology and Clinical Nutrition, Klinikum Bremen Mitte, Bremen, Germany

[n] Department of Internal Medicine, Elisabeth Protestant Hospital, Berlin, Germany

[o] Department Internal Medicine and Palliative Center, Cantonal Hospital St Gallen, St Gallen, Switzerland

[p] Department of Nutrition and Dietetics, VU University Medical Center, Amsterdam, Netherlands; Department of Nutrition and Health, HAN University of Applied Sciences, Nijmegen, the Netherlands

[q] Gastroenterology Service, Hospital Erasme, Brussels, Belgium

[r] Department of Radio-oncology and Radiotherapy Clinic, Technical University, Munich, Germany

[s] Department of General, Visceral, and Oncological Surgery, Hospital St Georg, Leipzig, Germany

Corresponding Author

Dr. med. Jann Arends
University of Freiburg
Department of Medicine, Hematology, Oncology, and Stem Cell Transplantation
Hugstetter Str. 55
79106 Freiburg, Germany
Tel: +49 761 270-31284
jann.arends@uniklinik-freiburg.de

Abstract

Patients with cancer are at particularly high risk for malnutrition because both the disease and its treatments threaten their nutritional status. Yet cancer-related nutritional risk is sometimes overlooked or under-treated by clinicians, patients, and their families. The European Society for Clinical Nutrition and Metabolism (ESPEN) recently published evidence-based guidelines for nutritional care in patients with cancer. In further support of these guidelines, an ESPEN oncology expert group met for a *Cancer and Nutrition Workshop* in Berlin on October 24 and 25, 2016. The group examined the causes and consequences of cancer-related malnutrition, reviewed treatment approaches currently available, and built the rationale and impetus for clinicians involved with care of patients with cancer to take actions that facilitate nutrition support in practice. The content of this position paper is based on presentations and discussions at the Berlin meeting. The expert group emphasized 3 key steps to update nutritional care for people with cancer: (1) screen all patients with cancer for nutritional risk early in the course of their care, regardless of body mass index and weight history; (2) expand nutrition-related assessment practices to include measures of anorexia, body composition, inflammatory biomarkers, resting energy expenditure, and physical function; (3) use multimodal nutritional interventions with individualized plans, including care focused on increasing nutritional intake, lessening inflammation and hypermetabolic stress, and increasing physical activity.

Keywords: Cancer; malnutrition; sarcopenia; cachexia; anorexia; nutritional intervention

Introduction

Patients with cancer are at particularly high risk for malnutrition because both the disease and its treatments threaten their nutritional status. It is estimated that the deaths of 10 to 20% of patients with cancer can be attributed to malnutrition rather than to the malignancy itself [1-3]. Thus, nutrition is an important aspect of multimodal cancer care. Yet, recent studies in European hospitals found that only 30% to 60% of patients with cancer who were at risk of malnutrition actually received nutritional support (i. e., oral supplements and/or parenteral nutrition and/or enteral nutrition) [4, 5]. In another European study, physicians misclassified the severity of cancer-related malnutrition in 40% of cases; as a result, many severely malnourished patients did not get necessary nutritional interventions [6]. Even when physicians recognized cancer-related malnutrition, the patients and their relatives often underestimated its presence [7].

To address cancer-related malnutrition in contemporary practice, the European Society for Clinical Nutrition and Metabolism (ESPEN) recently published evidence-based guidelines for nutrition care in patients with cancer [8]. In further support of these guidelines, an ESPEN oncology expert group met for a *Cancer and Nutrition Workshop* in Berlin on October 24 and 25, 2016. Here, they examined the causes and consequences of cancer-related malnutrition, reviewed currently available treatment approaches, and built the rationale and impetus for clinicians involved with care of the patient with cancer to take actions that facilitate nutrition care in practice. The content of this position paper is based on presentations and discussions at the Berlin meeting.

Talking about cancer and nutrition: the terminology

Critically important work has been done to build universally accepted definitions for malnutrition, cachexia, and sarcopenia. These definitions are intended to help clinicians identify and treat the underlying metabolic and nutritional issues associated with both aging and with chronic or acute diseases, including cancer (Figure 1) [9, 10]. Despite efforts to clearly differentiate these conditions, there is some overlap in the working definitions, as there is some overlap in the conditions themselves. Notably, the need to be absolute on the definitions is surpassed by the necessity of recognizing the negative impact of cancer on nutrition. While definitions are important, this paper focuses on identifying and treating the metabolic and nutritional alterations that impede recovery and survival of patients with cancer.

Disease-related malnutrition has been defined as a condition that results from the activation of systemic inflammation by an underlying disease such as cancer [9]. The inflammatory response causes anorexia and tissue breakdown that can, in turn, result in significant loss of body weight, alterations in body composition, and declining physical function [9].

Cachexia is a multifactorial wasting syndrome characterized by involuntary weight loss with ongoing loss of skeletal muscle mass with or without loss of fat mass; such wasting cannot be reversed by conventional nutrition care and may lead to functional impairment [10-14].

In **precachexia**, early clinical and metabolic signs precede extensive involuntary loss of weight and muscle. Risk for cachexia and its worsening depends on factors such as cancer type and stage, extent of systemic inflammation, and degree of response to anticancer therapy [10, 13].

Sarcopenia is low lean body mass (mostly muscle); fatigue is common, strength may be lessened, and physical function limited [11, 13]. As functionality is lost, patients with cancer may no longer be able to live independently, and they often report lower quality of life [8, 13].

Sarcopenic obesity is low lean body mass in obese individuals [9]. In such patients, clinicians frequently overlook muscle loss due to the presence of excess fat and extracellular water [12]. In fact, the presence of sarcopenic obesity is an important predictor of adverse outcome, which can be further worsened by surgical interventions [15].

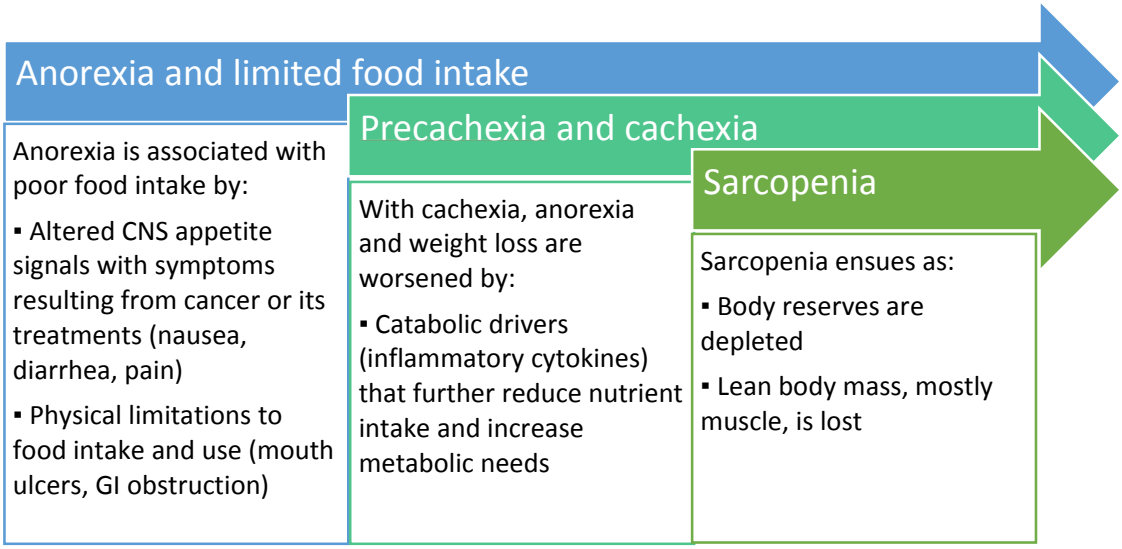

Figure 1. Malnutrition in patients with cancer: anorexia, cachexia, and sarcopenia. Anorexia, with poor food intake and consequent weight loss, commonly occurs in disease-related malnutrition, especially cancer. These harmful changes are driven by proinflammatory cytokines and tumor-derived factors. The associated conditions of cachexia and sarcopenia may also be present or may develop as cancer advances—cachexia due to inflammation, and sarcopenia due to fatigue and low physical activity and to other causes of declining muscle mass and function.

Abbreviations: Central nervous system, CNS; gastrointestinal, GI

The high prevalence of malnutrition in patients with cancer

Patients with cancer are more likely to be malnourished than patients treated in many other specialties [13]. The prevalence of malnutrition in patients with cancer has been reported to range from about 20% to more than 70% in worldwide studies, with differences related to patient age, cancer type, and cancer stage (Table 1). Patients with gastrointestinal tract, head and neck, and liver and lung cancers are at high risk for malnutrition [2, 4, 16, 17]. Malnutrition is more highly prevalent in older adults than in younger ones, and, and not surprisingly, in those with cancer at advanced stages rather than early stages [18, 19]. Malnourished patients with cancer may be cared for in hospitals, in nursing homes, or at home, and care must be adjusted to the setting. One report described the general prevalence of malnutrition as 30% in hospitals, 11% in nursing homes, and 23% in home care for adults <60 years old and as 39%, 20%, and 23% respectively for those ≥60 years [18].

Table 1. Reports of malnutrition prevalence in hospitalized patients with cancer

Study, country	Cancer type	Malnutrition prevalence
Attar et al., 2016 [6] France	Upper gastrointestinal	52% of patients on chemotherapy
Planas et al., 2016 [5] Spain	Multiple types	34% at hospital admission, 36% at discharge
Fukuda et al., 2015 [20] Japan	Gastric	19% of those hospitalized for gastrectomy
Maasberg et al., 2015 [21] Germany	Neuroendocrine	25% at risk or actually malnourished
Silva et al., 2015 [17] Brazil	Multiple types	71%, with 35% moderate and 36% severe
Hebuterne et al., 2014 [4] France	Multiple types	39% overall prevalence, varying by cancer type
Aaldriks et al., 2013 [19] Netherlands	Advanced colorectal	39% in patients >70 years, prior to chemotherapy
Freijer et al., 2013 [18] Netherlands	Multiple types	30% in patients >18 and <60 years old 39% in patients ≥60 years
Pressoir et al., 2010 [1] France	Multiple types	31%, with 12% rated as severely malnourished
Wie et al., 2010 Korea [2]	Multiple	61% of all patients, varying by cancer type and stage

High health and financial costs of malnutrition in patients with cancer

Numerous studies have highlighted the consequences of malnutrition in patients with cancer, including adverse impact on health and survival and added healthcare costs. We list recent and representative publications to illustrate the wide range of negative effects that have been reported (Table 2). In terms of poor health outcomes, malnutrition was associated with loss of weight and muscle [22], reduced immune competence and more infections [1, 20, 23], psychosocial stress [24], lower quality of life [25], treatment toxicity[19], and greater risk of mortality [1, 21, 22]. In terms of outcomes that affect healthcare costs, length of stay in hospital was longer in malnourished patients with cancer [1, 5, 21], and overall costs were increased by as much as €2000 per hospitalization episode [5]. In the Netherlands, disease-related malnutrition accounts for an excess €2 billion healthcare spending in a year with 1 of every €7 (about €300 million total) attributed to excess healthcare spending on patients with cancer [18].

Table 2. Health and financial impacts of malnutrition in patients with cancer reported in selected publications

Study, country	Cancer type	Negative impacts of malnutrition
Planas et al., 2016 [5] Spain	Multiple types	Significantly **longer LOS** (>3 days more) and **higher costs of care** (+ €2000) for patients with malnutrition risk
Fukuda et al., 2015 [20] Japan	Gastric	Significantly **higher risk of surgical site infections** in malnourished compared to well-nourished patients (36% vs 14%, P<0.0001)
Gellrich et al., 2015 [25] Switzerland	Oral	Malnourished patients had significantly **lower scores on QoL scales** related to physical function
Maasberg et al., 2015 [21] Germany	Neuroendocrine	Significantly **longer LOS** and **higher risk for mortality** in malnourished patients
Martin et al., 2015 [22] Canada	Multiple types	Weight-stable patients with BMI ≥25.0 kg/m^2 had the longest survival while **high % weight loss values associated with lowered categories of BMI were related to shortest survival**
Aaldriks et al., 2013 [19] Netherlands	Advanced colorectal	Malnutrition predicted **lower tolerance to chemotherapy** and was associated with greater **risk of mortality**
Freijer et al., 2013 [18] Netherlands	Multiple types	Disease-related malnutrition accounted for an excess €2 billion healthcare spending in a year; 1 of every €7 (about €300 million total) could be attributed to **excess healthcare spending on patients with cancer**
Pressoir et al., 2010 [1] France	Multiple types	Compared with adequately nourished patients, malnourished patients required **more antibiotic treatments** (36% vs 23%, P<0.0001) and had significantly **longer LOS** Severely malnourished patients were at **4-fold higher risk of 2-month mortality** than well-nourished patients

Abbreviations: length of stay, LOS; body mass index, BMI; quality of life, QoL

Mechanisms underlying cancer-related impairment of nutritional status

Cancer-related malnutrition is a multimodal process because many factors collude to impair food intake, increase energy and protein needs, decrease anabolic stimuli such as physical activity, and alter metabolism in different organs or tissues. The multimodal drivers of malnutrition form a rationale for use of multiple therapeutic strategies to prevent, delay, or treat malnutrition in people with cancer.

Immune response, systemic inflammation, and symptoms

Patients with cancer report clusters of symptoms that can be related to poor nutrient intake, weight loss, and declining physical function, as well as fatigue, pain, and depression [26]. Such symptoms have also been associated with reduced quality of life and survival in patients with advanced disease [27, 28]. In fact, there is a consistent association between symptoms, the presence of inflammatory markers, and upregulated immune responses (Figure 2) [26-30]. Poor cancer outcomes are predicted by markers of the systemic inflammatory response—altered acute phase proteins (elevated C-reactive protein, hypoalbuminemia, and their combination as the Glasgow Prognostic Score [29]) and changes in white cell counts (elevated neutrophil counts, low lymphocyte counts, high neutrophil-to-lymphocyte ratio) [26, 29, 31].

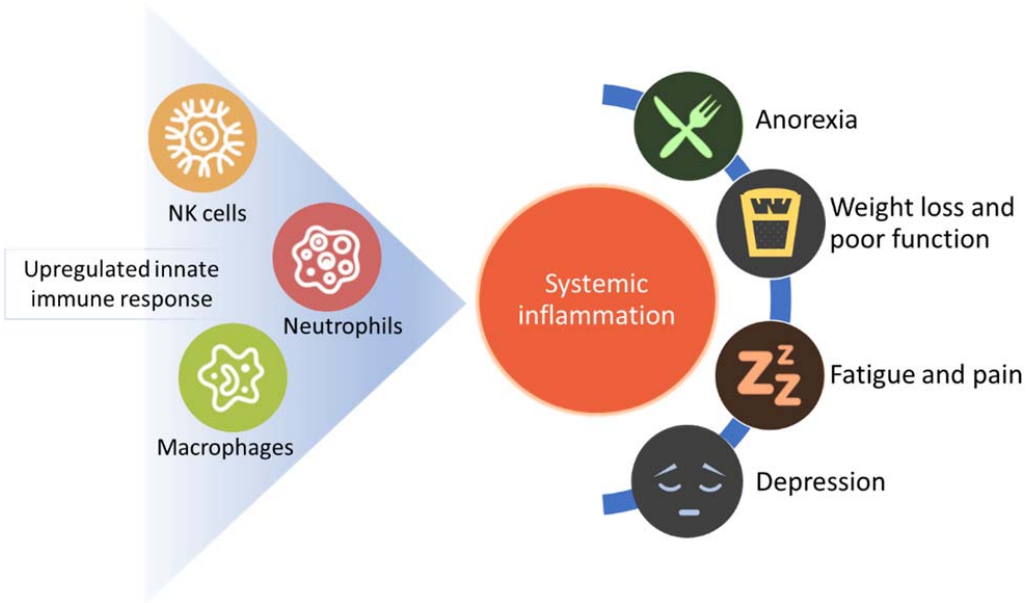

Figure 2. Association of immunologic, metabolic, and clinical phenomena in cancer. In patients with cancer, systemic inflammation is associated with the host's innate immune response and with clinical symptoms. Abbreviation: natural killer, NK.

Spillover of tumor-derived cytokines worsens systemic inflammation

Further systemic inflammation can be provoked by spillover of proinflammatory cytokines produced by the tumor [13, 23, 32, 33]. In turn, these proinflammatory cytokines disrupt metabolism of carbohydrates, fats, and proteins throughout the body (Figure 3) [32-36]. There is considerable evidence to support the roles of signaling by way of tumor-derived cytokines, e.g., interleukin 1 (IL-1), IL-6, and tumor necrosis factor-α (TNF-α) [37, 38]. Cytokines can affect the neuroendocrine control of appetite, leading to anorexia [23]. As well, tumor-derived cytokines can cause muscle wasting, resulting in fatigue and impaired physical activity [33]. Cytokine-regulated loss of adipose tissue, due to increased lipolysis and defective lipogenesis, depletes fat depots that normally serve as energy reserves [39]. Circulating cytokines can also alter production of acute-phase proteins by the liver, which can suppress drug clearance pathways and lead to risk for toxicity of anticancer agents [36].

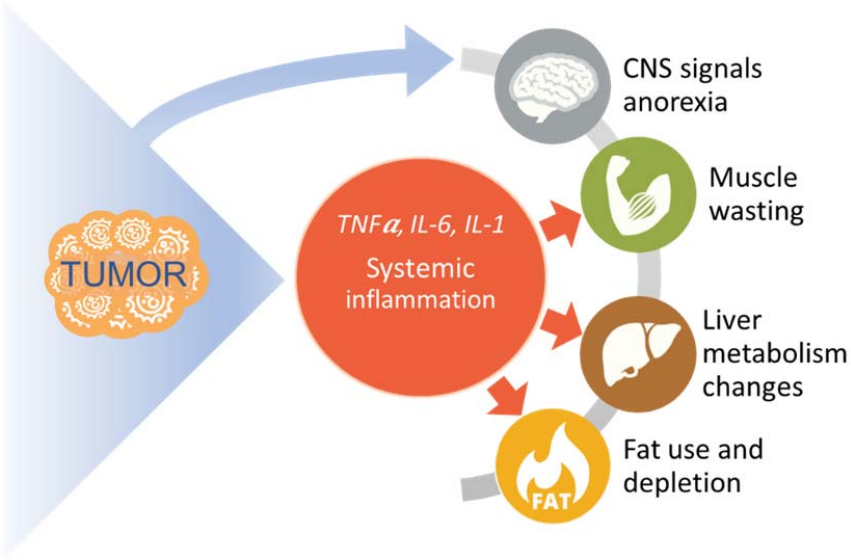

Figure 3. Pathophysiology and metabolism in the presence of a tumor: the mechanisms.
The tumor itself releases inflammatory and other factors that affect the brain, muscle, liver, and fat function. **Brain –** altered appetite signals from the CNS cause anorexia, resulting in reduced caloric intake; **Muscle –** an anabolic/catabolic imbalance leads to muscle wasting, reducing muscle mass and

strength, and increasing fatigue; **Liver –** in the liver, acute-phase protein production is stimulated, repressing drug clearance and raising the risk for cancer treatment toxicity; **Fat –** energy stores in fat deposits are depleted as cytokines stimulate increased lipolysis and cause defective lipogenesis, a maladaptive and wasteful response to low food intake. Abbreviations: central nervous system, CNS; IL, interleukin; TNF, tumor necrosis factor.

Hypoxic stress in the tumor microenvironment

Tumor hypoxia occurs when tumor cells have been deprived of oxygen. A tumor growing rapidly may outpace its blood supply, resulting in regions of the tumor where the partial pressure of oxygen is significantly lower than in healthy tissues [40]. When such hypoxia develops, complex maladaptive mechanisms are initiated; tumor metabolism is altered to rely more on glycolysis and less on oxidative phosphorylation, and protection against harmful reactive oxygen species is reduced [41]. These changes are associated with enhanced tumor growth, malignant progression, and even resistance to anticancer therapy [40-45]. Nutritional interventions, by modulating the local generation of reactive oxygen species might potentially interfere with these processes. Given the pathophysiological effects of tumor hypoxia, researchers are seeking new techniques to assess tumor hypoxia (e. g., oxygen electrodes, endogenous markers of hypoxia, magnetic resonance imaging-based measurements) with hopes that such information can potentially be used to improve the course of treatment [43].

Indirect effects of cancer or its treatments

Beyond anorexia, poor food intake will often result from side-effects of cancer treatments (drug- or radiation-therapy, surgery) or tumor-related local effects like tissue infiltration or physical obstruction. Such conditions include pain, fatigue, dry mouth or mouth ulcers, difficulty chewing, thick saliva, dysphagia, abdominal pain, nausea, intractable vomiting due to intestinal blockage, constipation, and diarrhea due to infections or malabsorption [8, 13, 15, 24, 46, 47].

Addressing malnutrition in patients with cancer: diagnosis and treatment

ESPEN's evidence-based nutrition guidelines for adult patients with cancer raise awareness by drawing attention to the high prevalence of malnutrition and its adverse impacts on response to treatment, prognosis, and survival [8]. The Academy of Nutrition and Dietetics (AND) has also developed guidelines on nutritional management for patients with cancer in acute care and ambulatory settings [48]. Such updates help clinicians keep pace with advances in the science behind cancer and nutrition, and advise them how to translate information into practice. Of similar importance are well-argued calls for action to effectively couple oncologic and nutritional approaches throughout the patients' journey [49]. As we will discuss in this paper, many strategies are available to update nutritional care in patients with cancer (Box 1). For example, most patients with cancer experience some degree of metabolic stress, which can now be quantified by measures of inflammatory biomarkers. Also, today's patients with cancer may be either underweight or overweight, but both groups are at high risk for cachexia and sarcopenia and its adverse effects. Sensitive new methods facilitate early and accurate measures of body cell and muscle mass [12]. Medical nutrition care strategies have been updated, including recommendations for energy and protein requirements and the use of immune modulators and specialized nutrients to lessen adverse inflammatory and catabolic effects [8].

Box 1.

New strategies to update nutritional care in cancer

- Screen each patient's nutritional status early in the course of his or her cancer treatment.
- Identify signs or symptoms of anorexia, cachexia, and sarcopenia as early as possible.
- Measure body cell or muscle mass precisely by sensitive imaging technologies (computed tomography and others) for early detection of malnutrition/sarcopenia.
- Use specific biomarkers to assess severity of cancer-related systemic inflammation, e.g. CRP and albumin.
- Use indirect calorimetry to estimate resting energy expenditure (REE) in order to personalize energy and protein needs.
- Use nutrition and metabolic support as a vital part of cancer care; some new strategies show promise for reducing inflammation and restoring lean body mass.
- Assess physical function routinely to monitor and guide physical rehabilitation.

Importance of early nutrition screening

For care of patients with cancer, nutritional guidelines consistently advise screening for nutritional risk as soon as the diagnosis of cancer is made, followed by full nutritional assessment when risk is present

[8, 48]. Specific studies have shown that such screening programs can be implemented for all patients with cancer [50].

Nutritional assessment and diagnosis of malnutrition

Practice changes for nutritional care in patients with cancer are based on progressing science and technology (Box 1). Identification of patients with cancer who are at risk for malnutrition relied traditionally on low body weight (or BMI) and a history of weight loss. An approach based on body weight alone has become increasingly ineffective in the face of the global obesity epidemic and the new understanding of the metabolic alterations that occur prior to any measurable change in body weight. Anorexia is now recognized as an early risk indicator for malnutrition, and appetite change can occur regardless of a patient's initial weight. Weight loss is a signature sign of advancing malnutrition, thus it needs to be detected and recognized. Inadequate nutritional intake is confirmed if patients cannot eat for a week or if their energy intake is less than 60% of estimated requirements for 1-2 weeks [8].

Evolving definitions of cachexia and sarcopenia aim to identify and quantify signs/symptoms of malnutrition or its risk, including evidence of inflammation as well as loss of muscle mass and function [10, 22]. The Glasgow Prognostic Score (GPS), based on serum concentrations of C-reactive protein and albumin as markers of inflammation, is an easy-to-use and highly predictive tool for the assessment of inflammation in patients with cancer [29]. Importantly, GPS has been thoroughly validated in clinical practice to predict prognosis and mortality [29, 51]. While imaging techniques have long been used for the diagnosis of cancer, these techniques are becoming forefront strategies for nutritional evaluation. Retrospective reviews of computed tomography images in patients with cancer have shown that such imaging can detect loss of muscle mass as well as fatty muscle infiltration (myosteatosis) [13, 52]. It is now recognized that sarcopenia can occur concurrently with obesity [12, 53, 54]. In under- and overweight patients alike, sarcopenia is associated with higher incidence of chemotherapy-related toxicity, shorter time to tumor progression, physical disabilities, poorer surgical outcomes, and reduced survival [12, 53-56]. A recent study found a relationship between loss of physical function and cancer survival [57]; additional studies are needed to identify tools that best assess function in patients with cancer and to use assessment results to guide prescription of physical rehabilitation.

Treatment: needs, counseling, support, specific ingredients

The form of medical nutrition care depends on the patient's medical history, appetite, type of cancer, stage of cancer, and his or her response to treatment [10]. Some patients with cancer may experience a progression through worsening stages of cachexia, from precachexia to cachexia to refractory cachexia close to end of life (Figure 4). The burden of cachexia can be lowered or alleviated by comprehensive nutrition care tailored to meet the needs of the patient during different stages of the disease.

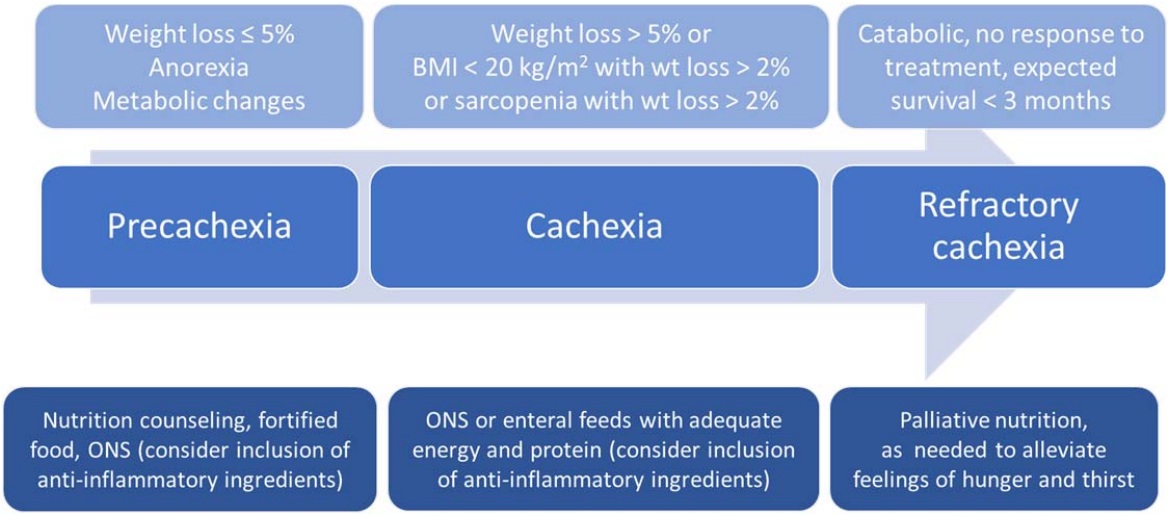

Figure 4. Medical nutrition care depends on a patient's nutritional and metabolic needs, which are related to cancer stage and nutritional status. Some nutritional strategies can be used across multiple cancer stages. In general, worsening cachexia (with intensifying inflammation) necessitates adjustments in nutritional care. Abbreviations: oral nutritional supplements, ONS

Nutritional needs

Initiating effective nutritional treatment of the patient with cancer depends on an estimation of total energy expenditure (TEE), which is the sum of resting energy expenditure (REE) plus activity-associated energy expenditure. The use of standard formulas for the calculation of energy needs may be inaccurate given the altered energy metabolism and metabolic differences in patients with different cancer types [35, 58, 59]. REE tends to be elevated in patients with advanced stages of cancer, but such patients also experience increasing fatigue and decreasing physical activity, thus limiting TEE [60]. Indirect calorimetry appears to be the most accurate in predicting the patient's REE and may be considered for all at-risk patients with cancer [58]. If REE and or TEE cannot be measured directly, 25 to 30 kcal/kg/day with 1.2

to 1.5 g protein/kg/day serve as a target range to help maintain or restore lean body mass; it has been proposed that even higher doses of protein may be necessary when depletion is severe [8, 61, 62]. However, in severely depleted patients, feeding is initiated slowly and over several days (while carefully monitoring phosphate and electrolytes) to avoid potentially harmful refeeding syndrome [63].

Nutritional counseling and nutritional support

Nutritional counseling is the first and most commonly utilized intervention for the management of malnourished patients with cancer and a functioning gastrointestinal tract [64]. A dietitian-nutritionist can provide individualized advice to achieve energy and nutrient balance based on the patient's estimated REE, lifestyle, disease state, current intake, and food preferences. Counseling needs to address the presence and severity of symptoms such as anorexia, nausea, dysphagia, abdominal bloating or cramping, diarrhea, and constipation. Critical components of nutrition counseling are to: (1) convey to the patient the reasons and goals for nutritional recommendations, and (2) motivate the patient to adapt to altered nutritional demand of their disease.

Oral nutrition support includes regular food or fortified foods as meals or snacks and oral nutritional supplements (ONS) to fill nutritional gaps when patients are at nutritional risk. Some studies evaluating nutrition counseling with and without the use of ONS have shown improvements in nutrition outcomes when including ONS: weight gain, BMI increase, and improved scores on a validated nutrition assessment test (Patient-generated subjective global assessment, PG-SGA) [65]. Studies have been limited, however, and remain inconclusive with respect to the effectiveness of oral nutrition strategies for the management of weight loss in patients with cancer [66]. The limitations are likely due to the wide range of pathophysiological alterations that occur in cancer, which require complex and individually targeted strategies such as adaptations to gastrointestinal deficiencies and modulations of metabolic components of cachexia in order to allow nutrition interventions to be effective [23].

Anti-catabolic and anti-inflammatory ingredients

In patients with cancer, systemic inflammation inhibits nutrient utilization and promotes catabolism, thus leading to muscle breakdown. Calorie and protein fortification of regular foods, even with standard ONS, does not reduce systemic inflammation. Updated nutritional strategies now suggest considering nutrition with anti-catabolic and inflammation-suppressing ingredients.

Studies have indicated that ONS with addition of essential amino acids (EAA) or high-dose leucine may improve muscle protein synthesis even within the context of inflammation, although results have not been fully consistent [67, 68]. More research is needed in this area to confirm roles of nutrition with EAA and leucine in the management of patients with cancer.

Fish oil, a source of long chain omega-3 fatty acids, is currently suggested to improve appetite, oral intake, lean body mass, and body weight in patients with advanced cancer and at risk of malnutrition [8]. The mechanism of fish oil to downregulate the systemic inflammation related to cancer cachexia is still under investigation. Results of a randomized study in patients with advanced colorectal cancer who were given 2 g fish oil daily during the first 9 weeks of chemotherapy showed time-to-tumor-progression was significantly longer for patients receiving fish oil [69]. Two studies with a complete oral nutritional supplement containing the omega-3 fatty acid eicosapentaenoic acid (EPA) given to patients with lung cancer showed improvement in quality of life and physical function [70, 71]. While studies are still needed to confirm improvement in clinical outcomes, fish oil remains promising as an important part of overall nutrition management.

Arginine and nucleotides are being studied as immune-supporting ingredients in enteral feeding formulas in surgical and radiation patients. When immunomodulatory enteral formulas were given to patients undergoing cancer surgery, there were positive trends toward enhancing the immune response and reducing post-operative infections [72-77]. A study in cancer patients receiving radiation therapy showed enhanced immune cell responses in the group treated with immune-enhancing enteral therapy [74]. Meta-analyses of randomized controlled studies have shown that patients undergoing major surgery (including for cancer) have reduced infectious complication rates and lengths of stay in hospital when given an immune enhancing feed rather than a standard isocaloric, isonitrogenous feed [78-81]. This is a promising area of nutritional research; however, further study is needed to provide definitive and clinically meaningful results.

Realizing the importance of exercise training and physical rehabilitation

Physical activities are included in the new ESPEN guidelines on nutrition and cancer [8]. Endurance and resistance exercises of varying intensities are increasingly recognized as essential anabolic stimuli for maintaining body resources in patients undergoing anticancer treatment, as well as for recovery in survivors of cancer. Activities may be in the form of usual daily grooming, chores, and errands as well as

aerobic exercise and resistance training. A systematic review reported evidence supporting aerobic and resistance exercise as effective strategies to improve upper and lower body muscle strength more than usual care [82]. Most of the reviewed studies were done in patients with early stage cancers, in breast and prostate cancers or in tumor-free survivors, so further work is needed to examine effects in more advanced stages.

Multimodal therapy: putting it all together

Body resources in patients with cancer are endangered by a complex and varying pattern of physical and functional derangements. Therefore, nutritional therapy by itself could be clinically ineffective if other current needs are not addressed. Nutritional therapy should be part of a more comprehensive supportive care, including psychological counseling, optimal pain control, among others. Following this understanding, Fearon et al. introduced the concept of multi-modal therapy for optimal care in patients with cancer [23]. The adverse nutritional effects of tumors (and their treatments) represent potential primary sites for therapeutic intervention—(1) increasing and optimizing nutritional intake, limiting systemic inflammation, and engaging in exercise and activities (Figure 5) [23]. In the future, nutrition programs will need to be merged with metabolic concepts, exercise programs and other approaches. As multi-modal strategies evolve, we anticipate interactions that will enhance individual effects of each individual treatment modality.

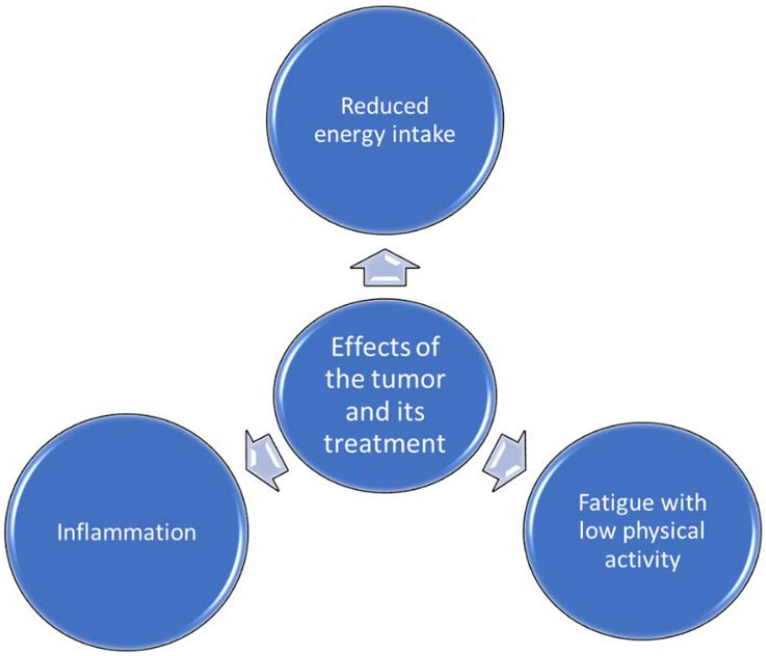

Figure 5. Three major negative effects of tumors and their treatment. The 3 principal adverse effects represent 3 potential targets for interventions by (1) nutritional support, (2) physical rehabilitation, and (3) anti-inflammatory nutrients or medications.

Specific nutritional strategies for cancer subgroups

Two subgroups of patients with cancer pose specific nutritional challenges, which call for additional treatment strategies—those undergoing surgery and those nearing end-of-life.

For all patients with cancer who are undergoing either curative or palliative surgery, management according to an enhanced recovery after surgery (ERAS) program is advised [83]. Within this program, every patient should be screened for malnutrition, and if deemed at risk, given additional support such as enteral or parenteral nutrition [83, 84]. The ERAS strategy has been shown to improve survival in some patients with cancer [85]. Because patients with cancer are at particularly high risk for malnutrition, preoperative nutritional support can even be used for non-malnourished patients, as it has been shown to maintain better nutritional status and reduce the number and severity of postoperative complications [86].

For patients with cancer who are nearing end of life, dedicated palliative care is appropriate [87]. In end-of-life care, nutrition is tailored to the patient's symptomatic needs and is primarily intended to support

comfort and quality of life. While many earlier goals for care are no longer valid (e.g., maintaining energy intake, physical activity), patient feelings of hunger and thirst must still be met [88]. In some settings, patients feel connected to others by the thread of sharing food and drink, even if only in small or in a symbolic way. Optimal patient management in these settings requires sensible education and respectful counseling for patients and families. To this end, meaningful interactions between the patient, caregivers, and the medical team are important to help fulfil each patient's specific needs and thus improve quality of life. There are many ethical considerations concerning food and hydration, so feeding decisions are made with and for each patient in the context of cultural, personal, and religious practices for the patient and his or her family members [88].

Take-home messages for cancer nutrition practice and research

Despite numerous advances in treatments and care for people with cancer, malnutrition remains an unresolved issue. In recent guidelines on nutritional care in patients with cancer, ESPEN experts advised practice updates and summarized evidence supporting such advice [8]. At the *Cancer and Nutrition Workshop,* Berlin 2016, our ESPEN expert study group underscored the importance of putting the guidelines into full practice and offered key recommendations for improving nutrition care (Box 2).

Box 2. Call-to-action: improved nutritional care for patients with cancer

- Screen all patients with cancer for nutritional risk early in their course of care, regardless of body mass index and weight history; regularly rescreen nutritional status.
- Increase nutrition assessment to include measures of anorexia, body composition, inflammatory biomarkers (e. g., Glasgow prognostic score), resting energy expenditure, and physical function.
- Use nutritional intervention with individualized plans, including care focused on increasing nutritional intake, decreasing inflammation and hypermetabolic stress, and increasing physical activity.

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