
Assessment of Malnutrition and Nutritional Therapy Approaches in Cancer Patients

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2.1 Definition

Malnutrition can be defined as a state of altered nutritional status that is associated with increased risk of adverse clinical events such as complications or death. Nutritional care is fundamental to cancer treatment (Davies M). Malnutrition specific to cancer patient populations has been observed to negatively impact patient's response to therapy; increase the incidence of treatment-related side effects; interrupt serial treatment regimens; extend hospital stay; impair muscle function, performance status, immune function, and quality of life; and ultimately affect survival [1–5]. Depression, fatigue, and malaise also significantly impact on patient well-being. In addition, cancer-related malnutrition is associated with significant health-care-related costs [5, 6]. In a recent study to evaluate the role of malnutrition and mortality in patients undergoing surgery for renal cell carcinoma, Morgan et al. [7] reported that malnutrition is associated with a higher mortality, independent of key clinical and pathological factors. On the other hand, proactive intervention to comprehensively assess and correct malnutrition early has been shown to reduce patient costs and length of hospital stay, improve response to treatment and, most importantly, improve functional status and quality of life in the patient [3]. For example, improvement of nutritional status over time is associated with better survival in ovarian cancer patients [8]. These effects were observed to be independent of age, stage at diagnosis, and prior treatment history and tumor response as determined by CA 125. Others have shown that significantly lower postoperative 30-day mortality after colorectal cancer resection was observed in cases less than 70 years of age, and absence of synchronous liver metastasis, malnutrition, and respiratory and vascular comorbidity were significantly reduced. With continuously evolving treatment modalities and novel agents for the treatment of cancer, it has also become critical to address nutritional care in the entire continuum of cancer (pretreatment, treatment, and posttreatment) to reduce GI toxicities and improve clinical outcomes and to ultimately improve morbidity and mortality in this patient population [8–12].

2.2 Prevalence of Malnutrition in Cancer Patients

Malnutrition is the most common comorbidity in cancer patient populations. Studies have demonstrated that anywhere from 30% to 87% of cancer patients are diagnosed with malnutrition [51], with 30–60% of cancer patients diagnosed with protein-calorie malnutrition with higher rates of as much as 80% observed in esophageal cancer patients. The prevalence of malnutrition as high as 67% has been observed on ovarian cancer patients, while only 6% of endometrial cancer patients were malnourished [13, 14]. Others have observed that more than 64% of cancer patients were malnourished, increasing to 81% for patients undergoing palliative care [9, 10]. In clinical observations studies, over 95% of cancer patients indicate one or more symptom involving the gastrointestinal (GI) tract contributing to compromised nutritional status. Malnutrition is thus a frequent manifestation of cancer and a significant contributor of morbidity and mortality.

2.3 Etiology of Malnutrition

The etiology of malnutrition in a cancer patient is multifactorial and can be contributed to several factors: local effects of a tumor, the host response to the tumor, and anticancer therapies resulting in chronic or acute malnutrition. Other causes include reduced food intake (due to systemic effects of the disease, local tumor effects, psychological effects or adverse effects of treatment) and alterations in nutrient metabolism and resting energy expenditure (REE) [5]. Results of inadequate intake or absorption or increased metabolic requirements imposed by disease, including excessive loss of nutrients and drug-nutrient antagonisms, increased demands, inadequate intake, increased losses, relative intake of other nutrients, as well as symptoms of cancer and cancer treatment, can contribute to malnutrition. Figure 2.1 summarizes the multifactorial etiology of malnutrition in cancer.

2.3.1 Tumor-Related Etiology

Nutritional deficits are frequently observed in cancers of the gastrointestinal tract that can physically obstruct nutritional intake or produce metabolic and physiological disturbances that result in poor assimilation or reduction of nutritional intake. Stenosis of the GI tract, dysphagia, and previous surgery may affect the digestive capacity, or an abdominal tumor mass, disturbance of the motility, or repeated (sub) ileus may contribute to nausea and vomiting and therefore to reduced nutrient intake [15]. Pancreatic as well as gastric resections can result in pancreatic exocrine and endocrine insufficiency, creating major nutrition problems such as steatorrhea and hyperglycemia that may impede nutritional intake. Extensive resection of the small bowel can lead to malabsorption, whereas small resections of the bowel usually do not lead to major nutrition problems [16]. Liver cancer patients are confronted with the additional risk of malnutrition because the disease is often associated with hepatitis, liver cirrhosis, and metabolic disturbances [17]. Several agents produced by

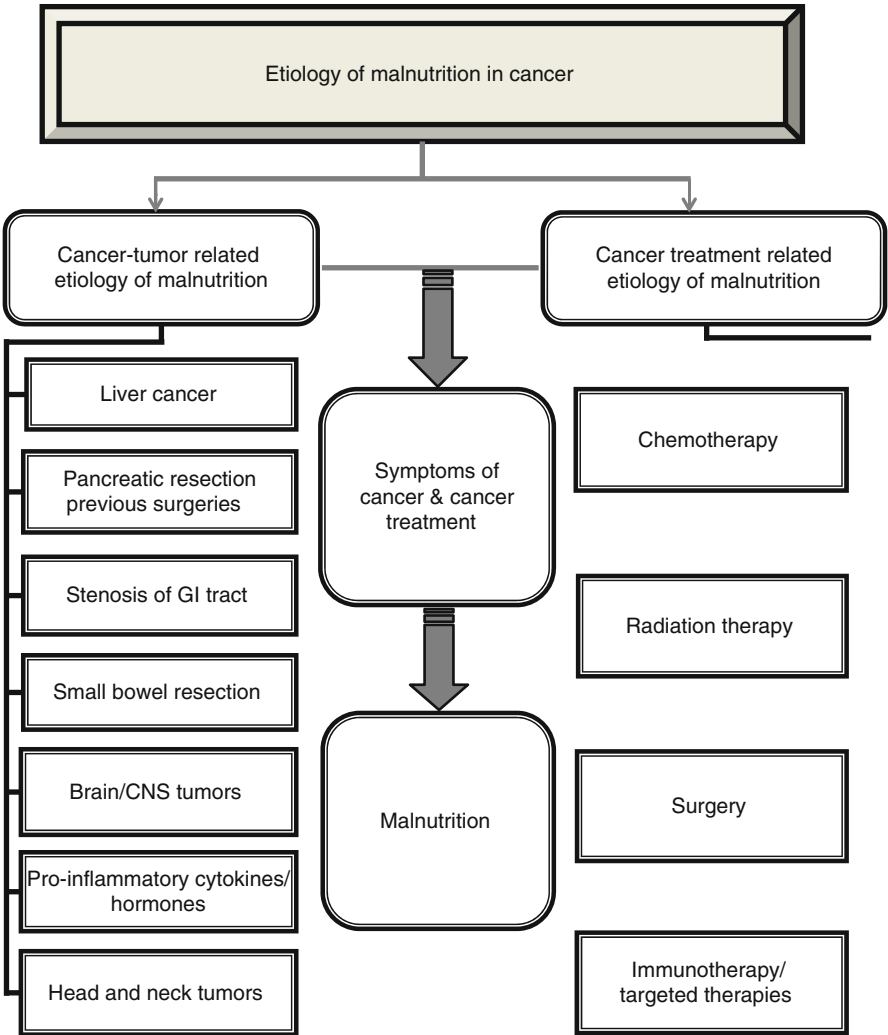


Fig. 2.1 Etiology of malnutrition in cancer

the tumor directly, or systemically in response to the tumor, such as proinflammatory cytokines and hormones, have been implicated in the pathogenesis of malnutrition and cachexia. A recent ASPEN and ESPEN guidelines group examined the pathophysiology of malnutrition and agreed that an etiology-based approach that incorporates a current understanding of inflammatory response would be most appropriate. The committee proposes the following nomenclature for nutrition diagnosis in adults in the clinical practice setting. “Starvation-related malnutrition,” when there is chronic starvation without inflammation; “chronic disease-related malnutrition,” when inflammation is chronic and of mild to moderate degree; and “acute disease or injury-related malnutrition,” when inflammation is acute and of

severe degree [18]. Although the recommended classification needs to be validated in future studies, they provide the basis for a mechanism-based approach to the treatment of malnutrition in the cancer patients.

2.3.2 Treatment-Related Etiology

Patients with cancer have increased nutritional needs due to hypermetabolism, impaired organ function, increased nutrient losses, and therapy-related symptoms of dysphagia, mucositis, pain, cachexia, anorexia, fatigue, and radiation enteritis, all contributing to malnutrition. In addition, patients with cancer may also have increased requirements for both micro- and macronutrients due to the prolonged period of deficits prior to diagnosis [19]. Intensive therapy for multiple myeloma was significantly associated with decline in nutritional status [20], although these returned to pretherapy levels 6 months posttreatment. Nausea, vomiting, loss of appetite, weight loss, and poor quality of life were all reported by this patient population. Decrease in grip strength and triceps skin fold, as well as decline in hepatic proteins, testosterone, and gonadotropin in intensive treatment of patients with acute myeloid leukemia (AML) have been observed, suggesting a catabolic metabolism leading to impaired nutritional status [20]. Malnutrition is commonly associated to head and neck cancer patients, especially aggravated by radiotherapy or concurrent chemoradiation therapy [21–23]. In a study to characterize the effect of radiotherapy for head and neck cancer and GI cancers on nutritional status, Mahdavi et al. [24] observed that after treatment, the incidence of malnutrition increased significantly in patients in both groups with significant weight loss and decreased energy and protein intake in addition to decreases in serum zinc, copper, and albumin levels. Significantly lower antioxidants and selenium were found in lung cancer patients compared to healthy controls. Those patients with lower functional scores using the Eastern Cooperative Oncology Group (ECOG) performance scales had significantly lower levels of β -carotene and selenium compared to those with higher functional scores [25]. Similarly, we and others have observed lower serum levels of antioxidants lycopene in prostate cancer patients compared to disease-free men [26]. Thus, irrespective of baseline nutritional deficits, cancer patients experience a progressive decline in nutritional symptoms as they go through cancer treatment. Although some cancer patients recover from these nutritional consequences over time, significant variability in individual response to both disease and treatment makes this recovery to baseline nutritional status a complex, unpredictable, and challenging endeavor for the health-care team.

2.4 Assessment of Malnutrition in Cancer Patients

Nutritional care process that encompasses nutritional assessment and therapy of cancer patients in a clinical setting is accomplished in six basic steps: nutritional screening, initial comprehensive nutritional assessment, planning and implementation

of nutritional therapy, education of the patient and family, communication with multidisciplinary team and reassessment to monitor response, and change in nutritional status as evaluation of efficacy of therapy. Timely nutritional screening to identify current and potential challenges to maintaining nutrition status and assessment and early nutritional therapy to replenish, improve, and manage exacerbation of symptoms may provide the best opportunity to prevent the debilitating consequence of cancer and cancer treatment. Figure 2.2 below provides a model for an integrated nutritional care process in the cancer continuum.

2.4.1 Nutritional Screening

The goal of screening is to identify patients who present with malnutrition or, due to recent diagnosis, comorbidities, and planned treatment approaches may be at high risk for malnutrition. Validation of these screening tools have been completed utilizing objective markers of malnutrition such as serum hepatic proteins and anthropometrics including body density measurements, weight loss history, and total body potassium. Instruments such as patient-generated subjective global assessment (PG-SGA) [13], SGA [27], and simple screeners using the nutritional risk index or NRS 2000 with more objective variables have been found to be valid for use in cancer patient populations [28]. Other screening tools such as Mini Nutritional Assessment have shown good correlation with laboratory parameters related to inflammation markers such as albumin, CRP, adiponectin, and leptin and were independently associated with survival [29]. In a study of 300 cancer patients to determine whether the Mini Nutritional Assessment (MNA) could effectively rate the nutritional status of patients with liver cancer in Taiwan, Tsai et al. [17] evaluate two modified versions of the MNA in short and long forms. MNA-Taiwan version 1 adopted population-specific anthropometric cut points, whereas version 2 replaced mid-arm and calf circumferences in place of body mass index. Results showed that both versions of the MNA were effective in predicting nutritional status, with nutritional scores correlating well with hemoglobin, serum albumin, C-reactive protein, γ -glutamyl transpeptidase, TNM (tumor, node, metastasis) staging, and severity of cirrhosis [17]. Some of the practical variables used in clinical settings for nutritional screening are (a) hepatic proteins (prealbumin <10 mg/dL, albumin <2.1 g/dL, transferrin <100 mg/dL), (b) weight loss compared to percentage of usual weight, (c) body mass index (<20 kg/m²), (d) lymphocyte counts, and (e) anticipated time to resolution of symptoms that impede nutritional intake (and gastrointestinal function not expected to resolve within 7–10 days or nutritional intake less than 50% of needs >7 days) – all of which form the basis to inform the medical team of the patient's initial nutritional status. Pretreatment weight loss has been documented as a predictor of poor survival, irrespective of type of tumor [30]. Since abnormalities in immune function have been associated with malnutrition, measures of total lymphocyte count may be useful on initial evaluation of the newly diagnosed patient with a solid tumor. However, the application of these parameters during treatment is limited due to the immunosuppressive effects of steroids and

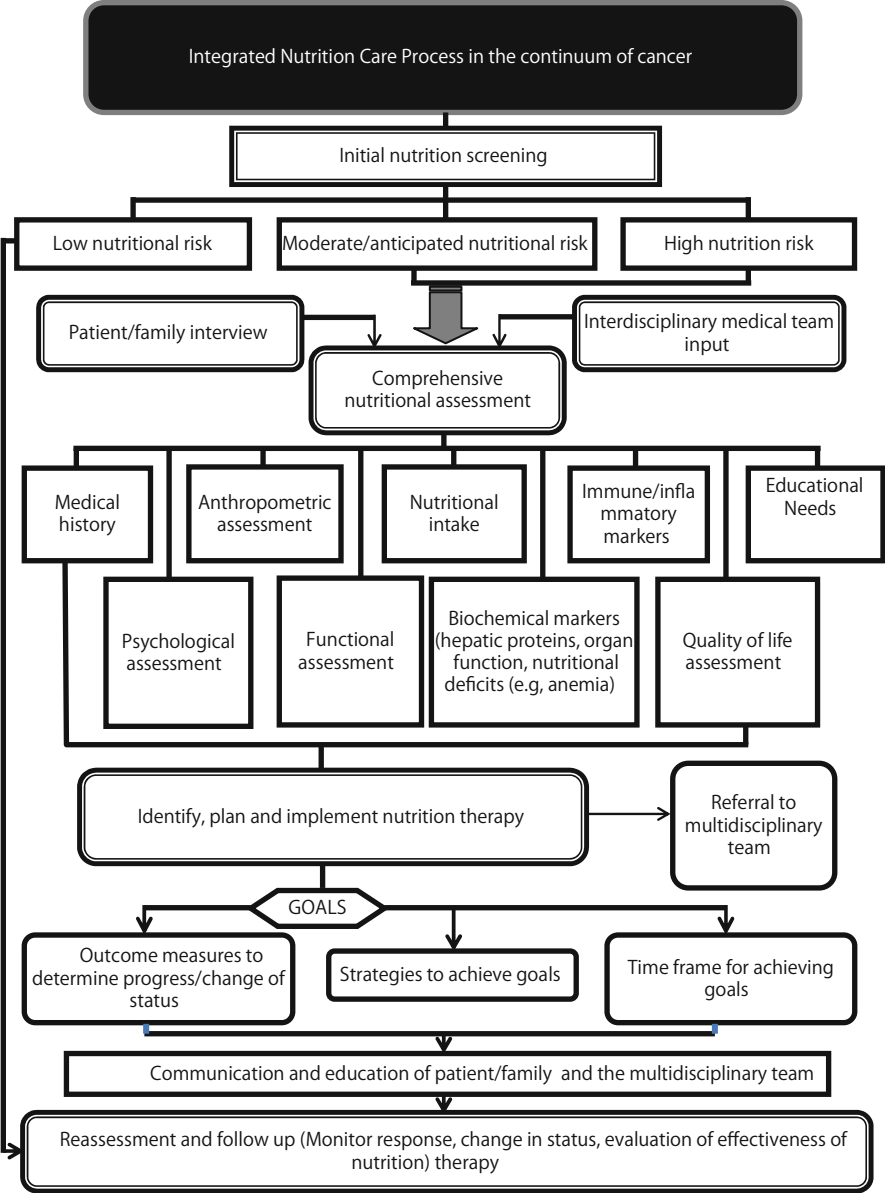


Fig. 2.2 Integrated nutrition care process in the continuum of cancer

many chemotherapy agents. Also, some hematological cancers are known to cause depression of bone marrow function resulting in leukopenia. Combinations of these indicators can stratify patients into low-, moderate-, and high-risk categories for nutrition-related surgical complications [2, 31–33]. Although these specific variables

have been consistently shown to correlate to and predictive of malnutrition and poor prognosis, no one individual variable has contributed to identifying a patient at risk for malnutrition. Combinations of these indicators have been used to stratify cancer patients at clinical presentation into no risk, mild, moderate, and severe malnutrition [34–37]. Although a patient is screened initially with the diagnosis of mild or moderate malnutrition, based on the cancer and treatment trajectory, this condition can progress from moderate to severe malnutrition, requiring frequent rescreening and assessment. It is also critical that the initial screening tool must be simple and uncomplicated for application in a clinical setting [38], with readily available objective data [39]. The goal of the nutritional screen originated to identify and prioritize those patients at highest nutritional risk that needed to be evaluated and triaged for nutrition intervention. In most settings, all health professionals including nurses and intake specialists must be trained to screen patients for malnutrition. Whether screening in an acute-care setting or in an ambulatory clinical setting, all newly diagnosed cancer patients are screened on first contact with the health professional. Once patients are identified at high or moderate risk, a comprehensive nutritional assessment follows. Those at mild malnutrition or no risk must be under surveillance for change in condition or treatment. Several tools to screen cancer patients have been developed and validated [13, 40]. Assessment tools have included simple, objective, easily obtainable indicators, while some combine objective and subjective parameters to screen cancer patients.

2.4.2 Nutritional Assessment

The primary aim of assessing a cancer patient comprehensively is to design and implement optimal nutritional therapy, taking into consideration baseline nutritional status, current diagnosis, and comorbidities; planned cancer treatment and anticipated symptoms; and increased nutritional needs. Nutritional assessment is used to guide and inform the planning of nutritional therapy with the goal of improving treatment outcomes, managing symptoms, and improving function and quality of life. A comprehensive assessment of nutritional status is usually based on demographics (specific consideration to age); anthropometric measures; biochemical or laboratory tests; medical history including comorbidities, clinical indicators, and assessment of cancer and cancer-related symptoms; dietary assessment; oral assessment; current and planned medications; psychosocial assessment; swallowing ability; functional assessment including physical activity; and most importantly an assessment of patient and family cultural and religious belief systems. A comprehensive nutritional assessment is performed with objective data available in the patient's medical records and information provided by patients and their families in addition to information gleaned from other members of the multidisciplinary team.

2.4.2.1 Medical History

In addition to current diagnosis and stage of cancer, information regarding the patient's past medical history, presence of complications such as infection or sepsis,

present and past antineoplastic therapy, prior surgeries especially gastrointestinal, treatment and physical manifestations of disease, or nutrient deficits are essential to assessment of nutritional status and development of plan for nutrition therapy. Information on other comorbidities such as diabetes; heart disease; renal, hepatic, or inflammatory bowel disease; and current medications used to treat these illnesses can be useful. Other history of symptoms including toxicities from treatment including mucositis, nausea, vomiting, diarrhea, steatorrhea, constipation, or recent unintentional weight loss; oral or dental disease; or limitations should be obtained from patient or family. Constitutional, dermatological, gastrointestinal (GI), metabolic, and pain symptoms can be obtained using the NCI-CTG Common Toxicity Criteria Checklist

2.4.2.2 Psychosocial History

Social risk factors can also be identified at this time such as smoking history, alcohol or drug use, socioeconomic status [41–43], and availability of social support system. Emergent programs taking into consideration the need for psychosocial support for management of cancer and symptoms have shown to benefit both patients and their family members [44–46]. The need for a support system consisting of family, peers, and friends is a common thread in every culture and has been quantitatively assessed and equated with hope. Factors such as impediments due to personal, family, caregiver, or insurance issues that could interfere with symptom management must be discussed and resolved [47]. On the other hand, emotional suppression and distress through helplessness/hopelessness and stress can increase distress and depression with cancer diagnosis. Information on religious, cultural, and social support systems that can mediate and impact nutritional intake is essential to plan individualized nutritional therapy. Individuals who live alone have been shown to be at risk of having a poor intake [44]. Social deprivation or isolation also increases risk and has been associated with weight loss [45]. Social networks play a role in the maintenance of adequate food intake, and socialization results in increased food intake during a meal. Research has drawn attention to the challenges that patients receiving treatment for head and neck cancers experience, including the physical and emotional impact of diagnosis and treatment, weight loss, challenges related to eating, and strategies used by patients to address nutritional problems. It is clear that patients experience physical, emotional, and social losses associated with a changed meaning of food. Acknowledging the significance of eating problems and the changed meaning of food is required in order to provide patients with the appropriate support, strategies, and interventions to manage with the changes and losses [46]. The goal of psychosocial support is thus to provide tools to manage stress, encourage social interaction during meal times, and proactively educate patients with regard to anticipated symptoms that they may experience while providing strategies to cope with these scenarios. Approaches to education of patient and family, enhanced problem solving skills, stress management, psychosocial support, group support to improve mood and coping response, psychotherapy, and tailored behavioral interventions have shown promise in reducing symptoms of cancer.

2.4.2.3 Anthropometric Data
Body Weight and Body Mass Index

Anthropometric measurements such as patient’s height, weight, and body mass index are considered relevant and objective measures of a cancer patient’s nutritional status, with few potential errors in measurement in a clinical setting [48, 49]. Body weight and weight history are essential components of the initial nutritional assessment due to the significant impact of weight loss and underweight on morbidity and mortality. Unplanned weight loss occurs more commonly in more aggressive lymphomas, colon and lung cancers. Greatest weight loss is observed in gastric and pancreatic cancer patients [30]. In many forms of cancer, weight loss is an independent predictor of shorter overall survival even prior to chemotherapy, and individuals with weight loss are found to suffer more severe toxicity from chemotherapy [30, 50]. Unintentional weight loss with cancer is found in up to 80% of patients with pancreatic cancer and up to 60% of patients with NSCLC [51, 52]. Current weight is only useful as an indicator of nutritional risk or depletion if it is evaluated in comparison to the patient’s usual weight. Weight loss must also be assessed in relation to its duration and whether it is unintentional or intended weight loss. Unintentional weight loss can be expressed as a percentage of usual body weight. Current weight that is 20% below ideal body weight is also an indication of nutritional risk. Similarly, a weight of 20% or less below ideal body weight is also indication of potential nutritional risk. In most cases, measurement of body weight and information regarding recent weight loss are important indicators of the presence of malnutrition upon initial screening and assessment; however, it has serious limitations as an outcome measure or monitoring tool since weight is a dynamic variable and is confounded by hydration and use of medications such as corticosteroids. The relevance of rapid and unplanned weight loss (10% of usual body weight in the past 6 months or 5% weight loss in the past 3 months) has been observed consistently to be associated with poor prognosis [30] and thus is an excellent indicator for screening cancer patients for nutritional risk. It is recommended that weight and weight change be assessed in combination with other parameters. Table 2.1 provides the formula used to calculate percent change from usual body weight.

In addition to weight loss, decreasing body mass index (18.5 kg/m²) has continued to be informative for nutritional assessment of a cancer patient in clinical practice as an indicator of malnutrition [14, 30]. Patients undergoing nephrectomy for localized renal tumors with a BMI of less than 23–25 kg/m² have worse outcomes compared to those patients with a BMI >25 kg/m² [50, 51], demonstrating that BMI continues to be an important prognostic marker in cancer. Pretreatment body weight has also been shown to be a risk factor for locoregional failure in patients receiving

Table 2.1 Calculation of percent change from usual body weight

$$\% \text{ Weight change} = \frac{\text{Usual weight} - \text{Present weight}}{\text{Usual weight}} \times 100$$

Table 2.2 Body mass index (BMI) calculations and categories

$\text{BMI} = \frac{\text{Mass (lb)} \times 703}{(\text{Height (in)})^2}$
Underweight = <18.5
Normal weight = 18.5–24.9
Overweight = 25–29.9
Obesity = BMI of 30 or greater

concurrent chemoradiation therapy for head and neck cancer [23]. Anorexia and weight loss are associated with increased mortality [4]. Studies showing inconsistencies in the relationship between BMI and malnutrition can be attributed to criteria used to determine normal versus obese or undernutrition ranges for BMI. For example, Marin Caro et al. [3] used <20 kg/m² for their definition of malnutrition, while others used up to 25 kg/m² to define malnutrition. Other parameters such as skinfold and circumference measurements and bioelectrical impedance technology have been used in clinical settings to measure lean body mass as well as body fat distribution. However, these methods suffer from errors due to measurement, unless performed by well-trained clinical staff and do not provide meaningful data of efficacy on nutritional therapy. Table 2.2 provides methods for calculating BMI and the categories to estimate under weight to obesity.

Body Composition

Although body weight, unplanned weight loss, and weight as a parameter as it relates to body mass index are valid measures to evaluate malnutrition, weight as an indicator to response to treatment has serious limitations since it is a dynamic variable and confounded by hydration and use of medications such as corticosteroids. Body composition measurements, both total lean body mass (LBM) changes and total bone mineral density (BMD), are relatively better markers that can be applied in order to tailor nutritional treatment to patients’ individual requirements [52] as well as to monitor progress in a clinical setting. At present, body composition (BC) is rarely measured in the clinical setting because it is thought to be too unmanageable and time-consuming and burdensome to the patient. Skeletal muscle function is a central determinant of functional capacity in humans. Loss of muscle as seen in cancer patients results in poor function and decreased survival rate following critical illness [53]. Muscle size is therefore considered an important marker of functional status in studies of sarcopenia/cachexia [54–56]. Measurements of body composition combined with physical assessment for signs of obvious muscle wasting may help to identify significant losses in somatic protein stores; however, a more objective and sensitive measure of protein nutriture is the biochemical assessment of visceral protein stores. Using new technologies, the estimation of fat, lean body mass, and body fluids that are significant in the management of nutrition therapies in oncology has improved.

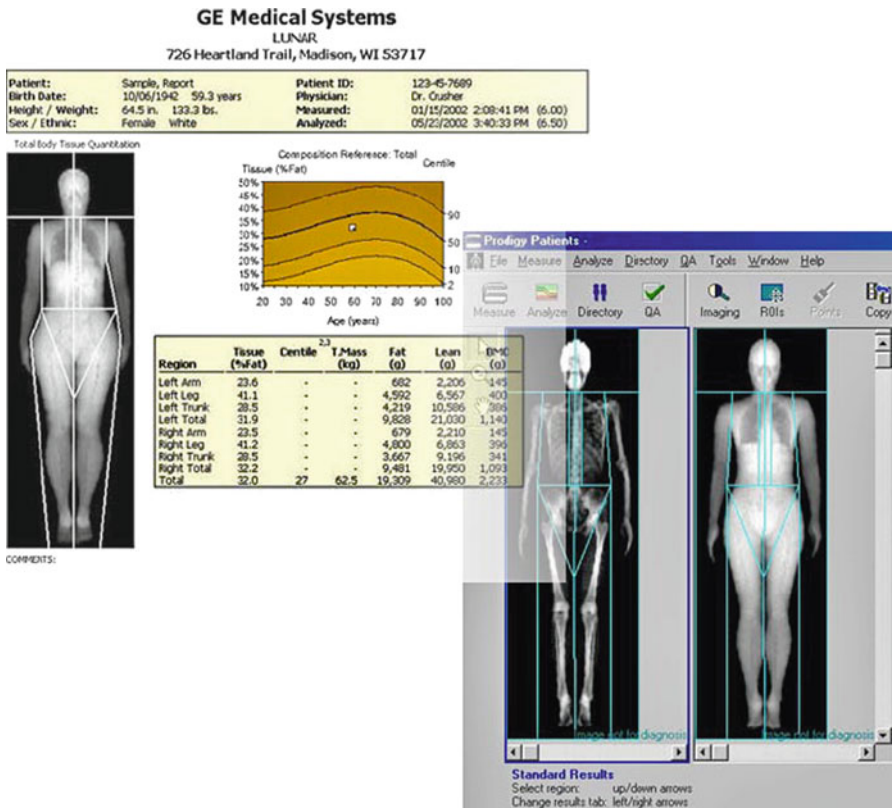


Fig. 2.3 Sample report of body composition as measured by DXA

Dual-Energy X-Ray Absorptiometry (DXA)

Figure 2.3 Sample report of body composition as measured by DXA (Body Composition Center, 77 Birch St., Suite A, Redwood City, CA 94062) has been used to measure human body composition on a high-speed fan-beam scanner. High- and low-energy attenuation pairs, produced by the various combinations of fat mass and fat-free mass in the human body, were compared to attenuation values produced by standard materials (aluminum and acrylic). These standards were measured in various combinations to construct calibration curves for fat and fat-free mass. Primary calibration of the aluminum/acrylic combinations was achieved by direct comparison to the dual energy attenuation produced by stearic acid and pure water. Whole body examinations were accomplished using three 45-s longitudinal passes of the fan beam. These passes were acquired and assembled to create a giant, isocentric fan beam with a single center of focus. In vivo precision was 0.009 g/cm² for bone mineral density (BMD) and 425 g for fat mass and fat-free mass (s.d.) [55]. DXA technology is now considered the most valid measure used to assess both total

lean body mass (LBM) changes and total bone mineral density (BMD) in a clinical setting without increasing the burden to the cancer patient. Total bone mineral density (BMD) can also be followed as an indirect measure of muscle and patient activity. Total LBM is sometimes called total fat-free mass (FFM) depending upon specific DXA manufacturer. Total lean body mass changes can be calculated with total LBM values taken directly from most current DXA compared to total LBM from baseline DXA. DXA instruments use an X-ray source that generates or is split into two energies to measure bone mineral mass and soft tissue from which fat and fat-free mass are estimated. The exam is quick (1–2 min), precise (0.5–1%), and noninvasive. DXA scanners have the precision required to detect changes in muscle mass as small as 5%. Radiation exposure from DXA scans is minimal. The National Council of Radiation Protection and Measurements (NCRP) has recommended that the annual effective dose limit for infrequent exposure of the general population is 5,000 μSv and that an annual effective dose of 10 μSv be considered a negligible individual dose. The effective dose of a dual-energy X-ray absorptiometry whole body scan on an adult is 2.1 μSv

(a) *MRI of Thigh Muscle*

To obtain accurate measures of change in skeletal and fat mass with nutritional therapy, other direct measure of thigh muscle volume (TMV) may be obtained by MRI scan [56]. However, this is not always a practical option at this time as it not only increases patient burden but also the economic burden to the cancer patient. Subjects will be imaged using an MRI scanner (Siemens) at 1.5 T and a Q-body coil. Caution will be taken to ensure minimal patient motion during scanning (e.g., by placing folded pads/sheets under the legs) and using same positioning used for all subsequent scans. After a rapid survey scan, thigh images will be acquired using a 3D fast-gradient echo Dixon technique sequence (VIBE-Dixon) to cover the entire thigh (knee to hip). The total sequence time will be approximately 25 s. This sequence is superior for intramuscular fat quantitation. The 3D sequences yield automated separate fat images and images of water signal (almost all of which is in skeletal muscle), as well as combined (in-phase T1-weighted) and combined opposed phase images (Fig. 2.4). Muscle and fat compartments will be segmented. Muscle volume will be determined from the segmented calculation and will be made of (a) volume of subcutaneous fat and fat between muscle groups, (b) intramuscular fat volume, and (c) muscle volume. Muscle mass in kilograms will be determined by multiplying muscle volume by density. A density value of 1.0597 g/cm^3 as described in literature from unfixed rabbit and canine muscle tissue will be used for this calculation. Similarly, intermuscle fat content and subcutaneous adipose tissue will be obtained in kilograms by multiplying fat volume by the density of adipose tissue (0.9196 g/mL). Our primary endpoint will be defined by TMV based on MRI [56]. In addition to TMV, MRI will also allow exploratory outcomes (e.g., T2 and ADC) to assess metabolic impact of $N - 3$ FA on skeletal muscle and adipose tissue in the upper leg. This assessment can be related to the metabolic and functional abnormalities of the skeletal muscle in muscle wasting. The MRI pulse sequence used will allow for lipid quantification in the thigh muscle region

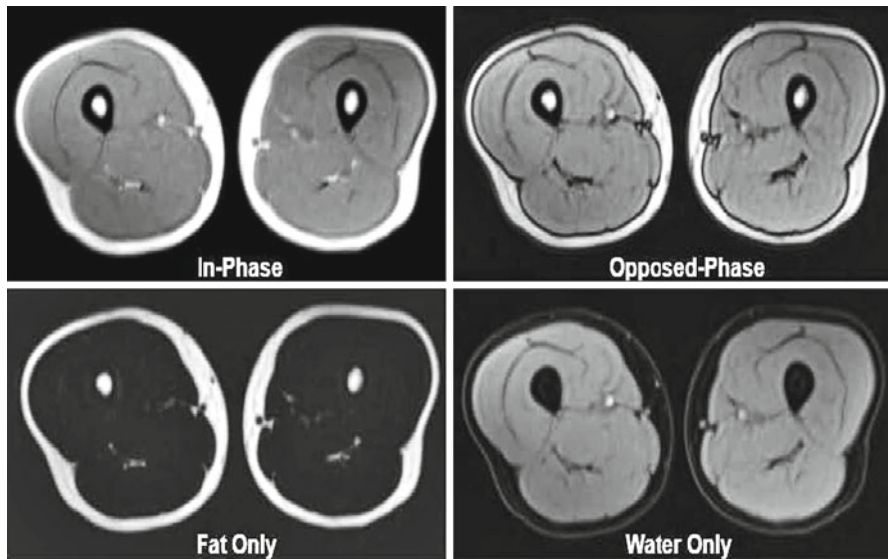


Fig. 2.4 Segmentation of fat and water images of the thigh using a single whole volume 3D gradient echo sequence

(i.e., subcutaneous adipose and intermuscular fat content or intermuscle adipose tissue) Fig. 2.4.

2.4.2.4 Measurements of Function and Strength

(a) *Handgrip Strength Dynamometry Assessment*

Figure 2.5 shows a sample of the Jamar dynamometers used to measure grip strength in a clinical setting. Muscle strength has been shown to be positively associated to muscle mass but negatively associated with inflammatory activity. Handgrip strength is also correlated with serum albumin levels [27]. A validated tool commonly used to assess handgrip strength is the Jamar dynamometer, which is a fast, reliable, and easy-to-perform device commonly used by our team to measure improvements in functional strength [57]. The Jamar dynamometer has a lower percent coefficient of variation and is thus a more precise device than other handgrip dynamometers (Fig. 2.5).

(b) *Functional Markers*

Evaluation of patient's functional status and barriers to obtaining adequate nutrients are also necessary. A physical exam combined with personal interview should include the evaluation of functional status such as the ability to chew and swallow, dental or oral problems causing odynophagia or dysphagia, signs of muscle wasting or anasarca, presence of edema, presence of skin or mouth lesion, and ability to perform instrumental activities of daily living (IADLs) such as cooking, shopping, and feeding self. It is critical to assess activities of daily living, physical activity, exercise, sleep, and ability to work and perform other functional roles. Limitations in the activities of daily living have been



Fig. 2.5 Jamar dynamometers

identified secondary to and as a cause of weight loss in cancer patients. Cancer and other chronic diseases pose difficulties specifically for the cancer patient receiving treatment and the elderly in carrying out activities of daily living. A loss of postural and locomotive muscle mass has been observed within 7 days of inactivity [58]. The Karnofsky Performance Scale Index allows patients to be classified as to their functional impairment. This has been used to compare effectiveness of different therapies and to assess the prognosis in individual patients and has been validated in cancer patient populations [59].

2.4.2.5 Nutritional Intake

A vital component in the assessment of a patient's nutritional status is a detailed diet history and the collection of information regarding the patients eating behavior. This is extremely important in order to identify factors which may result in diminished nutrient intake. Nutritional intake is best assessed by conducting random weekly, 2 weekdays + 1 weekend day, 24-h dietary recalls (gold standard for collecting dietary data) using a five-step multipass procedure [32, 33] (which has been found to assess mean energy intake within 10% of actual intake). Food portion visuals should be provided to the patient to assist with documenting portions of food consumed [44, 60]. Nutritional history should include habitual diet and any change in diet pattern, frequency of meals or snacks, quantity of food at meals, self-imposed food restrictions, use of supplements, and other complementary therapies and vitamin/mineral use. Other symptom-related assessment must include ability to chew or swallow, specific intolerance to texture or type of food, presence of mechanical obstruction, poor dentition or pain with swallowing, recent or prolonged food or smell aversions, taste changes, early satiety, nausea or vomiting, pain, fatigue, appetite loss, and food allergies or intolerance. Questions should be open-ended to allow for accurate recall of diet history. After diet history is obtained, current nutrient intake should be compared to predicted requirements to determine adequacy of intake and need for intervention. Several nutritional analysis software are available

today which range from free to the more the frequently updated University of Minnesota Nutrition Data System for Research (NDSR) version database for analysis of nutrient composition.

2.4.2.6 Biochemical Markers

- (a) *An Objective Evaluation of Organ Function Can Be Determined Using Standard Comprehensive Metabolic Profile (CMP) and Complete Blood Count (CBC)*

Complete Blood Count (CBC): The CMP is performed using electronic cell sizing sorting cytometry/microscopy are recommended at baseline and periodically. Tests performed as part of the CBC panel include the following: WBC, RBC, HgB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, absolute neutrophils, absolute bands, absolute lymphs, absolute monocytes, absolute eosinophils, and absolute basophils.

Comprehensive Metabolic Panel, Direct: The CMP is performed using spectrophotometry, ion selective electrode (ISE), and hexokinase. Tests performed as part of the CMP panel will include the following: albumin, total bilirubin, alkaline phosphatase, AST, ALT, total protein, calcium, serum glucose, creatinine, urea nitrogen (BUN), BUN-to-creatinine ratio, sodium, potassium, chloride, and carbon dioxide.

- (b) *Protein Status (Serum Albumin, Prealbumin, and Transferrin)*

Serum hepatic protein (albumin, transferrin, and prealbumin) levels have historically been linked to nutritional status. Nutritional status and protein intake are the significant correlates with serum hepatic protein levels. Evidence has consistently suggested that serum hepatic protein levels correlate with morbidity and mortality and thus are useful indicators of severity of illness. Although serum hepatic proteins do not measure nutritional repletion (with the exception of prealbumin), it has been shown to be useful in identifying those who are the most likely to develop malnutrition, even if well nourished prior to onset of illness [61]. Serum proteins provide indirect information about visceral protein levels, indicating less hepatic synthesis which is usually a consequence of intake deficits. In cancer patients who are provided nutrition therapy including protein-sparing diets supplemented with proteins, an increase in serum hepatic proteins could signify an anabolic response. With half-lives of prealbumin (2–3 days) and serum transferrin (8 days) being relatively much shorter compared to serum albumin (15–20 days), changes in response to nutritional therapy can be observed within days of repletion [62]. Serum prealbumin and transferrin are thus considered relatively more sensitive parameters of the efficacy on nutrition interventions.

Serum albumin is the most validated as a prognostic index and readily available biochemical parameter used to assess protein status. However, its relatively long half-life (14–20 days) makes it slow to respond to dietary interventions. Since the intervention period is 12 weeks, we have selected this to measure change in visceral protein stores. Perioperative serum albumin has also been observed to predict prognosis and survival in colorectal cancer patients undergoing surgical treatment [63]. In a comprehensive review of epidemiological data investigating

the prognostic value of serum pretreatment albumin levels and survival in a heterogeneous group of cancers, Gupta and Lis [8] demonstrated that this was an excellent prognostic marker and may be used to better define baseline nutritional risk in cancer patients. Marin Caro et al. [3] observed a significant association between patients with low serum albumin levels and nutritional intake.

Prealbumin changes to short-term interventions are best indicated by prealbumin since it has a 2-day half-life versus albumin, making it a good indicator for early monitoring. Prealbumin is also unaffected by hydration status and, together with transferrin, predictive of changes in serum albumin [62, 64]. Prealbumin levels may be reduced with hepatic dysfunction, acute catabolic stress, sepsis, surgery, trauma, or severe enteritis or ulcers which may result from cancer treatment or progression of disease versus inadequate intake.

Transferrin is a serum beta globulin protein synthesized primarily in the liver, but unlike albumin it is located intravascularly as a transporter of iron, has a shorter half-life (8–10 days), and responds more rapidly to changes in protein status. Although transferrin levels are affected by iron status, serum transferrin, either singly or as part of a multiparameter index, is the *strongest predictor of cancer patient mortality and morbidity* [62, 64, 65]. Serum transferrin receptor is a marker of severe iron deficiency only when iron stores are exhausted. Clinical studies indicate that serum transferrin is less affected by inflammation [65]. The limitation of using transferrin as an indicator of nutritional status in cancer patients is that serum levels will decrease in chronic infections, acute catabolic states, surgery, and with renal impairment.

It may be important to recognize the challenge that patients with a syndrome like cachexia or with multiple, confounding symptom clusters may have inconsistencies in hepatic protein levels. Other potential confounding factors include stage of disease and impact of prospective concurrent anticancer therapies including surgery, chemotherapy, and radiation therapy. There is substantial evidence of the correlation between serum hepatic proteins and inflammation, making these the most relevant biomarkers in CC. Serum transferrin, prealbumin, and albumin have been observed as intermediate endpoint biomarkers and independently associated with worse outcome in cachexia [66, 67]. Measurements of body composition combined with more objective and sensitive measure of protein nutriture is ideal for the biochemical assessment of intravascular and visceral protein stores. Over 70% of patients of both genders with advanced cancer receiving palliative care have been shown to consistently have below normal serum hepatic protein levels [30]. Plasma levels of proteins (prealbumin, albumin, and transferrin) have been consistently used as indicators of protein-calorie malnutrition in the general population [62–70].

2.4.2.7 Immune and Inflammatory Markers

Unlike anorexia, in CC, there is a range of metabolic responses triggered by inflammatory and immunological responses. It is believed that the putative mediators of CC are cytokines, and increased expression of tumor necrosis factor and interleukin-6 has been observed in patients with CC. Cytokines will be measured in a panel including IL-1, IL-4, IL-6, IL-8, IL-10, GM-CSF, IFN- γ , TNF- α , and CRP (BioRad-Bioplex). All of these biomarkers have been shown to increase with disease, aging,

and cytotoxic agents. Though we realize these intermediate endpoint biomarkers of cytokines cannot be reliably interpreted, as over 70% of the subjects as observed in our preliminary studies were on active treatment with cytotoxic agents, these variables are important to determine as they may provide useful information and contribute to the better understanding of the mechanistic process.

With our knowledge of the basis for some of symptoms such as cachexia observed in cancer, other novel markers of inflammation such as elevated C-reactive proteins and systemic inflammation-based scores such as Glasgow prognostic score, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio are being evaluated for use with cancer patients [71]. In addition to identifying patients at risk, these inflammation-based scores can potentially provide therapeutic targets in future intervention trials for the treatment of nutritional decline.

2.4.2.8 Quality of Life

Nutritional related symptoms such as cachexia, anorexia, weight loss, fatigue, cognitive impairment, and gastrointestinal manifestations such as mucositis and diarrhea are not only reflective of nutritional status but, in most cases, also reflective of social isolation and nonprogressive or declining functional status, ultimately impacting quality of life. The evaluation of nutritional status should include an assessment of quality of life in order to optimize nutritional treatment for patients' individual requirements. Because of the potentially clinically relevant impact of nutritional intervention on quality of life, nutritional care should be included in any antineoplastic strategy [72]. Other factors such as depression and distress have also been correlated to poor nutritional intake and compromise nutritional status in the cancer patient [73]. The Rand Short Form (SF)-36 [74] (Medical Outcomes Study SF36) has been used extensively with both general, high-risk, and cancer populations and has available norms for mail and telephone versions and comparisons between group and individual scores. Scores are calculated and transformed to a 0–100 scale, with higher scores indicating increased health status. Reliability of the SF-36 scales was measured by Cronbach α coefficient, and the results ranged from 0.78 in general health perceptions to 0.91 in the physical functioning domain.

2.5 Nutrition Therapy

Once the nutritional needs have been assessed, the best mode of nutritional delivery must be determined in consultation with the multidisciplinary team, utilizing the expertise of clinical nutritionist and clinical pharmacists. Determinants for options of supportive nutrition in cancer patients include presence or absence of functional GI tract; treatment plans – surgery, hormonal therapy, radiation therapy, chemotherapy, or biological response modifier therapy; degree of baseline deficit; quality of life and prognosis; and cost effectiveness/utility [75]. The choice of nutritional support is dependent on the degree of function of the gastrointestinal tract, access, patient comfort and motivation, type of therapy, anticipated disease course, duration of therapy, anticipated toxicities [76], and, most importantly, the choice of the patient. The availability of caregivers, patient's performance status, and financial

resources should also be considered. In spite of the clear understanding of the effectiveness of nutritional therapy on intermediate markers of nutrition status [77], the ultimate effect on proven clinical outcomes such as morbidity, mortality, quality of life, tolerance to therapy, and cancer outcomes are all still limited [78]. Similarly, there is a clear correlation between degree of malnutrition and increased risk of perioperative complications in cancer patients undergoing surgery, although the beneficial effects of NST in perioperative patients have been difficult to demonstrate consistently [79]. This can be attributed to the complex effects of not only malignancies but also the continuously evolving treatment modalities with novel and targeted agents on the host's physiological, psychological, and metabolic milieu. In addition, these inconsistencies may be in part, due to methodological problems with trials performed in this setting, including the use of suboptimal feeding regimens and the inclusion of well-nourished patients unlikely to benefit from nutritional support regimens [79]. With our understanding of the metabolic and physiological mechanisms involved in the development of cancer and cancer-treatment related consequences, nutrition therapy for the cancer patient has now evolved to be an integrated, multimodality therapy that includes both pharmacological and nonpharmacological approaches that need to be individualized for specific patient populations. Nutritional support, addressing the specific needs of this patient group, is required to help improve prognosis and reduce the consequences of cancer-associated nutritional decline [5]. Nutritional intervention or therapy should be considered as a supportive measure within the global oncology strategy [72]. In curative oncology care, it contributes to reduced postoperative infection rate, better control of cancer-related symptoms, shortened length of hospital stay, and improved tolerance to treatment. In palliative care, the nutritional intervention focuses on controlling symptoms, thus improving quality of life [72]. If feasible, pretreatment nutritional therapy should be considered. Although earlier studies did not show the benefit of pretreatment nutritional support prior to head and neck radiation therapy [80], more recent studies have demonstrated benefit. Additionally, nutritional interventions adapted to diets modified based on side effects using oral route, combination of oral and tube feedings as with tube feeding only all resulted in improvement in increase in caloric and protein intake [21], demonstrating the benefits of nutritional therapy. Intensive nutrition interventions targeted specifically for head and neck cancer patients receiving radiation therapy improved intake of calories and proteins compared to standard interventions using nutritional education [81]. Furthermore, administration of the supplemented diet before and after surgery seemed to be the best strategy to reduce complications and length of hospital stay [82].

2.5.1 Estimation of Nutritional Needs

2.5.1.1 Calories

It is well accepted that many malignancies exert a metabolic effect on the host; however, the difficulty lies in predicting to what degree metabolic rate is affected due to the great variability in individual response as well as type of cancer and combination of therapies. Studies have measured the basal energy expenditure in a variety of cancer

Table 2.3 Calculating energy requirements

Basal energy expenditure (BEE)
For females: $55(9.6 \times \text{wt in kg}) + (1.7 \times \text{ht in cm}) - (4.7 \times \text{age})$
For males: $66.5(13.7 \times \text{wt in kg}) + (5 \times \text{ht in cm}) - (6.8 \times \text{age})$
For weight maintenance needs: $\text{BEE} \times 1.15 - 1.3$
For weight anabolism needs: $\text{BEE} \times 1.5$
Harris and Benedict [90]

patients. Cancer patients with pancreatic tumors, solid tumors, and liver carcinomas have been observed to be hypermetabolic [83–85]; however, other studies have not demonstrated a similar pattern in lung, colon, esophageal, and metastatic liver cancers [60, 86, 87]. Although others have demonstrated no differences in basal metabolic rate (BMR) between cancer patients and controls, the decrease in energy expenditure that is normally seen in starvation and weight loss in healthy men and women could not be demonstrated in weight-losing gastric or colorectal cancer patients [60]. Squamous cell carcinoma of the head and neck is associated with significant weight loss prior to, during, and after cancer diagnosis and treatment. A meta-analysis of effectiveness of nutritional intervention using appetite stimulants, dietary counseling, and prophylactic enteral tube feeding to meet compromised nutritional needs in patients receiving radiation and/or chemotherapy support the use of these proactive interventions to optimize nutrition in this population [88]. However, more randomized clinical trials are needed in this area. Caloric and protein supplementation has been shown to improve clinical outcomes in general populations, specifically in cancer patient populations too. Anorexia and weight loss are associated with increased mortality [4]. Oral supplementation is a simple, noninvasive option to increase nutritional intake in patients who are unable to meet nutritional requirements despite counseling [19] and modification of intake as per tolerance and has shown.

The best and most accurate method of determining calorie expenditure is by measuring metabolic rate via direct or indirect calorimetry under a variety of conditions. However, these methods are limited by the expense and availability of the necessary equipment and the added inconvenience of performing additional diagnostic testing on the already stressed and anxious patient. Another simpler method for calculating expected metabolic rate is with a formula developed by Harris and Benedict [89] (Table 2.3). This equation, used in combination with accepted activity and stress factors, is widely used for calculating basal energy expenditure in hospitalized patients. This method takes into account the patient’s gender, height, weight, and age, factors known to influence metabolic rate. The accuracy of this equation has been verified in validation studies comparing actual measurements and predicted values of healthy individuals with a mean difference of only 4% [89].

The calculations of predicted total energy expenditure (TEE) are derived using the Harris-Benedict equation multiplied by an activity factor or a stress factor (Table 2.4). These factors are based on data collected by Long et al. [91] measuring the metabolic

Table 2.4 Activity and stress factors for calculating total energy expenditure

Activity level	
Bedrest	1.2
Low activity	1.3
Moderate activity	1.5–1.75
Highly active	2.0
Injury factors:	
Minor surgery	1.1
Major surgery	1.3
Mild infection	1.2
Moderate infection	1.2–1.4
Sepsis	1.4–1.8
Skeletal trauma	1.2–1.4
Skeletal or head trauma (treated with steroids)	1.6–1.8

Source: From Long [89]

response to injury and illness. In order to determine an estimate of energy requirements, it is critical to obtain information regarding the patient’s nutritional status, treatment, and any additional metabolic stresses as identified in the nutritional assessment. To determine calorie needs in the absence of surgery or infection, as is often the case with cancer patients, a factor of $1.15 \times \text{BEE}$ can be used for weight maintenance or $1.5 \times \text{BEE}$, for repletion and anabolism [92] The average caloric deficit in weight-losing patients observed by us and other teams is approximately 250–400 kcal/day with significant variations based on stage and severity of disease. In most clinical settings, these deficits in nutritional intake have been compensated by providing caloric and protein supplementation with a goal of meeting nutritional needs of the individual patient. The average supplementation of 1 cal/mL supplements have not shown to improve nutritional status of patients on chemotherapy [93, 94]. However, recent studies using a more calorie-dense (1.5 kcal/mL) and higher protein supplementation have suggested that at least weight stabilization can be achieved [95], although improvements in lean body mass has not been observed in these studies. Our preliminary studies have also demonstrated that high-calorie and high-protein supplemental (calorie- and protein-dense) feedings result in substitution of regular meals and thus a reduction of caloric and protein intake in this patient population who experience early satiety as a symptom cluster with anorexia or cancer cachexia. It is important to take into consideration that these guidelines were established several decades ago and continue to be used for lack of alternate evidence-based guidelines. Because these calculations are an estimate and not based on actual measurement of caloric expenditure, the best indicator of adequacy is the patient’s response to the nutrition regimen. Monitoring of patient progress and adjustments of calorie goals as needed are essential parts of the nutrition care plan.

2.5.1.2 Protein

Injury and illness are known to produce marked losses of protein as indicated by increases in urinary nitrogen excretion [89]. Acceleration of protein turnover and

derangements in protein metabolism have also been seen in cancer patients [96]. Protein-calorie deficits have been shown to contribute to malnutrition in esophageal cancer patients. Provision of exogenous energy and protein has been shown to invoke an anabolic response as indicated by an increase in serum prealbumin and transferrin level in this patient population [62]. In contrast to simple starvation where the body attempts to spare protein, the opposite is true under conditions of metabolic stress such as the cancer process itself or combined with antineoplastic therapy. The most accurate method of determining protein requirements in a hypermetabolic patient is based on urinary nitrogen loss; however, this is impractical in most settings due to the labor intensity involved in collecting 24-h urine specimens and fecal specimens for total nitrogen output in addition to accurately calculating protein intake. The only setting in which this might be feasible is in critical care. The estimated protein requirement is determined based on the degree of protein depletion and the metabolic stress factors. For the well-nourished, mildly stressed individual, the protein needs may only be 0.8–1.0 g/kg IBW; however, with mild to moderate depletion combined with metabolic stress, 1.5–2.0 g/kg IBW may be required to achieve positive nitrogen balance and protein repletion. Another method of estimating protein requirements is by calculating the ratio of nitrogen to nonprotein calories. It is recommended to provide 1 g nitrogen (protein in grams divided by 6.25) per 120–150 nonprotein calories for anabolism in the moderately to severely malnourished or stressed patient [97, 98]. As with estimating calorie requirements, the best indicator of whether protein needs are being met is with monitoring and reassessment for weight gain and nitrogen retention in the malnourished patient and weight maintenance and nitrogen equilibrium in the well-nourished patient [99]. Initially, the pathophysiology of CC had two principle components – a failure of food intake and a systemic hypermetabolism/hypercatabolism syndrome. Additionally, diets adequate in calories from fats and carbohydrates were required in “protein-sparing” quantities for muscle anabolism [100]. Protein intake must also be sufficient for wound repair, resistance to infection, and synthesis of enzymes and plasma proteins [101, 102]. Supplementation with glutamine, arginine, and branched-chain amino acids appears to support improvement in reducing complications and improving treatment outcomes [103]. Future clinical trials should evaluate the impact of multimodal interventions using, in addition to nutrients and appetite stimulants, immune modulatory nutrients for the treatment of malnutrition in well-powered clinical trials. Guidelines for estimating protein requirements are provided in Table 2.5. However, as with total calories, these calculations are an estimate and not based on actual measurement of protein expenditure in cancer patient populations. Thus, the best indicator of adequacy is the patient’s response to the nutrition regimen. Monitoring of patient progress and adjustments of protein intake goals as needed are essential parts of the nutrition care plan.

2.5.1.3 Fats/Lipids

There are no recommended dietary allowances for lipids and carbohydrates in cancer patient populations.

Table 2.5 Calculating protein requirements

For calculating protein needs : Divide IBW by 2.2 = kg of IBW

For protein maintenance : Multiply 0.8 – 1.4× kg of IBW

For protein anabolism : Multiply 1.5× kg of IBW

2.5.1.4 Vitamins and Minerals

The need for vitamins and minerals is increased in this patient population. Oxidative stress and inflammation contribute to several organ toxicities, including neurotoxicities, after common cancer chemotherapy regimens. Doxorubicin and other platinum-based therapies have been documented to cause the generation of free radicals and the induction of oxidative stress, associated with cellular injury [104]. The debate continues as to the safety of antioxidant use *during* chemotherapy to reduce oxidative stress, other than a multivitamin-mineral supplement that meets the current USRDA. Increased doses higher than the USRDA may not be recommended based on the safety and nutrient-cytotoxic agent interaction concerns, if administered during active therapy. In September 2005, studies were published [105, 106] warning against the concurrent use of antioxidants with cytotoxic therapies. Supplementing with antioxidants and anti-inflammatory agents posttreatment may serve to “rescue” tissues from the effects of the oxidative damage, in addition to replenishing depleted status of these critical nutrients and reversing oxidative damage. However, these theories have not been tested in well-powered trials, in clinical trials targeting cancer patients.

2.5.1.5 Determining Hydration

Daily fluid replacement is essential, specifically in chronically or acutely ill patients who are on diuretics, laxatives, or other therapeutic regimens for cancer treatment. In addition, dehydration is commonly observed in the elderly as they have reduced thirst sensation and diminished water conservation by the kidneys. Nutritionally related symptoms as a result of cancer treatment such as diarrhea, inability to swallow liquids, or fever may also increase requirements contributing to clinical dehydration. Recurrent urinary tract infections have been documented in hospitalized elderly women. A minimum schedule of 30–35 mL fluid/kg of body weight or a minimum of 1,500 mL a day is recommended.

2.6 Route of Nutrition Intervention

2.6.1 Oral Intake

The preferred method of nutrition intervention, the least expensive and least invasive, is a standard or modified diet plus oral supplementation [107]. Several options of commercial and homemade recipes are recommended as tolerated and/or preferred by the patient. Several pharmacological and nonpharmacological strategies to improve appetite and nutritional intake and prevent early satiety are developed with individual

patients. However, if patients are unable to consume sufficient protein and calories for greater than 7–10 days with continued decline in nutritional status as indicated by serum hepatic proteins, weight loss, and anthropometrics, alternate means of support via enteral support or total parenteral nutrition (TPN) may be indicated. Table 2.4 provides general guidelines/criteria for selection of route of feeding.

2.6.2 Enteral Nutrition

Enteral nutrition involves the nonvolitional delivery of nutrients by tube into the gastrointestinal tract. Patients who cannot, should not, or will not eat adequately, in whom the benefits of improved nutrition outweigh the risk, and have a functional gastrointestinal tract are candidates for enteral tube feedings [108]. Enteral feeding provided through a tube, catheter, or stoma delivers nutrients distal to the oral cavity (Fig. 2.6). The chosen route for enteral feedings depends on the patient's clinical status, risk for aspiration, and anticipated duration of tube feeding. Short-term feedings (less than 3–4 weeks) usually are administered via nasogastric, nasoduodenal, or nasojejunal tubes. The nasoduodenal and nasojejunal (postpyloric) routes are preferable to the nasogastric route if the patient is at risk for aspiration. A decision to perform a tube enterostomy (esophagostomy, gastrostomy, jejunostomy) is usually made for long-term feedings (>3–4 weeks). Jejunostomy is the preferred approach when the patient is at risk for aspiration or is unable to consume adequate calories due to uncontrolled nausea or vomiting. If patient is critically ill, timely, early nutritional intervention using the enteral route may be beneficial. If oral intake is not feasible, early enteral nutrition may be instituted, especially in head and neck cancer patients [19, 109]. If enteral nutrition is insufficient or fails to alter nutritional status, parenteral nutritional therapy may be considered, taking into consideration the often-reduced demand for exogenous substrates, especially in the critically ill patient [110]. The impact of timing of PEG tube placement on clinical endpoints in patients undergoing concurrent chemoradiation therapy showed a significant clinical benefit from early placement for nutritional supplementation [111]. However, the effect of prophylactic GT placement on acute and long-term outcomes in patients treated with definitive chemoradiotherapy for head and neck cancer is still not certain, with recent reports demonstrating a higher rate of late esophageal toxicity and need for weighing the benefits to risk in this patient population [112]. In the ASPEN guidelines for surgical cancer patients, it is recommended that EN should not be used routinely in patients undergoing major cancer surgery. However, it is recommended that perioperative EN may be beneficial in moderately or severely malnourished patients if administered for 7–14 days preoperatively, but the potential benefits of EN must be weighed against the potential risks of the EN itself and of delaying surgical procedures [79].

Although concerns about PEG feeding have been documented, specific risk factors have been examined. Factors such as cirrhosis and radiation therapy were predictors of infection. Post-PEG bleeding and other complications were found to be a rare event in a large population-based study. Even in patients taking concurrent anticoagulants, no elevated risk was observed with PEG feedings [113]. Jejunostomy tubes (JT) which are usually placed at time of esophagectomy have also been

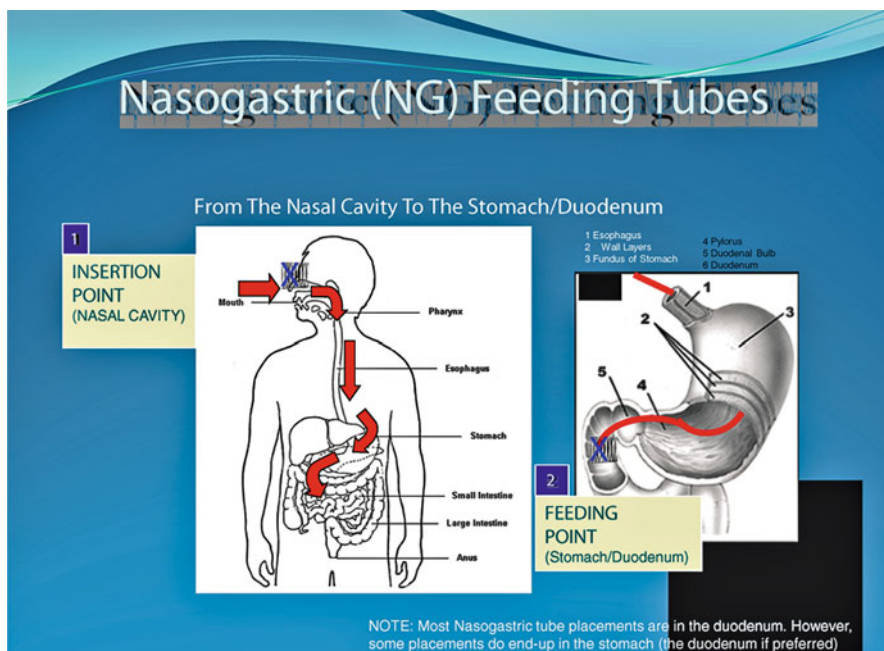


Fig. 2.6 Insertion and feeding points for nasogastric feeding tubes

associated with low morbidity. Although no major contraindications were observed, the only absolute indication for JT placement after esophagectomy was a BMI $<18.5 \text{ kg/m}^2$ or based on the surgeon's judgment [114]. More recently, several novel methodologies to insert PEGs for long-term feeding of cancer patient populations has received attention. The safety of pull-type and introducer-type insertion of PEG have been evaluated, and the introducer PEG procedure for long-term tube feeding has been found to produce significantly higher complications and mortality rates in patients with head/neck or esophageal malignancies treated with chemotherapy and radiation therapy compared to pull-type PEG placement [115, 116]. Techniques for PEG placement using the T-fastener gastropexy technique in head and neck cancer patients and esophageal cancer patients also resulted in lower overall complication rate compared to the pull method [117]. Enteral nutrition has been shown to reduce infectious complications and mortality compared to parenteral nutrition [118]. Although enteral nutrition is generally considered safe, gastrointestinal, metabolic, and respiratory complications have been documented [79]. Inappropriate formula advancement or feeding interruptions may result in underfeeding. Gastrointestinal intolerance is often due to improper methods of feeding, such as bolus delivery into the small intestine. The most common problems associated with enteral feedings can be minimized or prevented through proper formula preparation and equipment selection, controlled administration, and monitoring. A reduced incidence of metabolic abnormalities and other improved outcomes of enteral nutrition have been demonstrated when patients are managed by a multidisciplinary team. Figure 2.6 below provides examples of placement of nasogastric tube feedings (Table 2.6).

Table 2.6 General guidelines/criteria for selection of route of feeding

Criteria for enteral feeding via oral route.	Criteria for enteral feeding via tube feeding	Indications for parenteral nutrition	Ethically acceptable guidelines for nutritional support in end-stage disease
<p>(a) If the gastrointestinal tract is working- use this.</p> <p>(b) Evaluate risk for dysphagia, aspiration, nausea, vomiting, diarrhea, gastric motility or abdominal pain while eating.</p> <p>(c) Absent above symptoms or if above symptoms are anticipated to resolve in <7 days</p> <p>(d) Consider oral intake.</p>	<p>If patient's condition is not anticipated to resolve in <7 days, consider enteral tube feeding</p> <p>(a) Nutritional intake below 50% of needs</p> <p>(b) Functioning gastrointestinal tract</p> <p>(i) Nasogastric (NG) feeding (insertion point: nasal cavity, feeding point: stomach/duodenum)</p> <p>(ii) Percutaneous endoscopic gastrostomy (PEG): does not require general anesthesia</p> <p>(iii) PEG-J: jejunal extension in patients at risk for aspiration</p>	<p>In patient where enteral feeding is not feasible and the gastrointestinal problems are anticipated to persist – consider parenteral feeding if benefits outweigh other risks:</p> <p>(a) If problems with GI tract function is anticipated</p> <p>(b) Severely malnourished</p> <p>(c) GI problems will persist >7–10 days</p> <p>(d) Nutritional needs not met (<50%) over 7–10 days</p> <p>(e) Not at risk for sepsis or multiple, resistant infections</p> <p>(f) Unsuccessful enteral feedings</p> <p>(g) Aggressive malignancy and persistent obstruction – functioning GI tract – consider total parenteral nutrition</p> <p>(h) Monitor patient for</p> <p>(i) Serum glucose >300 mg/dL</p> <p>(ii) Serum phosphorous <2 mg/dL</p> <p>(iii) BUN >100 mg/dL</p> <p>(iv) Serum potassium >5.7 or <3.0 mEq/L</p> <p>(v) Catheter-related infection</p> <p>(vi) Malfunction of catheters due to clotted or clogged ports</p> <p>Wean to enteral as soon as patient consumes 50% of calories and protein based on need.</p>	<p>In cancer patients not receiving curative antineoplastic therapy/end-stage disease.</p> <p>(a) Nutritional support – viewed as a palliative measure</p> <p>(b) The goal is to support hydration</p> <p>(c) IV route for hydration may also serve as a route for delivering necessary medications</p> <p>(d) Decision must be made based on patients desire. Family preferences should be taken into account</p> <p>(e) Informed decision based on stage of cancer and prognosis</p> <p>(f) Anticipated consequences of not receiving hydration or nutrition should be communicated to patient and family</p> <p>(g) Risks involved in administering support: fluid overload, infection, malabsorption</p> <p>(h) Allow patients to eat for enjoyment</p> <p>(i) Quality of life is key</p> <p>(j) Educate family on nutritional care for the patient based on patient's wishes.</p> <p>(k) Patient will be unable to tolerate if intake is planned to meet increased needs.</p> <p>(l) Provide emotional support consulting with spiritual counselor, palliative care services when available.</p>

(continued)

Table 2.6 (continued)

Contraindications for enteral feeding using the gastrointestinal tract	Contraindications for enteral tube feeding using the gastrointestinal tract	Contraindications for parenteral feeding
(a) If patient is hemodynamically unstable (b) Malabsorption (c) Short-bowel syndrome (d) Pseudo obstruction (e) Gastrointestinal fistula (f) Mesenteric ischemia – interruption in blood flow to all or part of the small intestine or the right colon radiation enteritis (g) Paralytic ileus – either by a physical obstruction of the lumen such as a growing tumor, or by a loss of normal peristaltic function	(a) If patient is hemodynamically unstable (b) Malabsorption (c) Short-bowel syndrome (d) Pseudo obstruction (e) Gastrointestinal fistula (f) Mesenteric ischemia – interruption in blood flow to all or part of the small intestine or the right colon radiation enteritis. (g) Paralytic ileus – either by a physical obstruction of the lumen such as a growing tumor, or by a loss of normal peristaltic function	(a) End stage disease (b) Multiple organ failure (c) Sepsis (d) Resistant infections (e) Nutritional support – viewed as a palliative measure (f) The goal is to support hydration (g) Decision must be made based on patients desire. (h) Family preferences should be taken into account. Informed decision based on stage of cancer and prognosis

2.6.3 Parenteral Nutrition

In patients where enteral nutrition is not feasible nor tolerated, parenteral nutrition offers the possibility of increasing or ensuring nutrient intake [78]. The ESPEN guidelines [119] on enteral nutrition in oncology recommends that several of the indications for parenteral nutrition are similar to those for enteral nutrition (weight loss or reduction in food intake for more than 7–10 days), but only those who, for whatever reason, cannot be fed orally or enterally are candidates to receive parenteral nutrition. Other groups where short-term parenteral nutrition is recommended are in patients with CC using a high fat-to-glucose ratio may be advised because these patients maintain a high capacity to metabolize fats and in patients with acute gastrointestinal complications from chemotherapy and radiotherapy. Long-term (home) parenteral nutrition has been found to be critical in patients with subacute/chronic radiation enteropathy. Other patient populations that have shown to benefit from home PN are incurable cancer patients who are hypophagic/(sub)obstructed patients (if there is an acceptable performance status) if they are expected to die from starvation/undernutrition prior to tumor spread [119]. In a study to evaluate the effects of TPN and EN on biochemical and clinical outcomes in pancreatic cancer patients who underwent pancreaticoduodenectomy (PD), Liu et al. [120] observed that although there were no preoperative differences between the groups, significant differences in liver and kidney function parameters were observed with incidence of pancreatic fistulas and hemorrhages significantly greater in the TPN group compared to the EN group. Although the specific criteria for using TPN instead of PN in the first place are not indicated and the sample size of the target population was small, these studies demonstrate that EN is a better choice if the gut is functioning versus TPN in this patient population [120]. Others have examined if early preoperative enteral nutrition improved postoperative course, since most patients post-PD have symptoms of nausea, diarrhea, and abdominal distention presenting challenges to initiate PN. In a pilot trial to examine both EN and EN plus TPN in this target group, the rate of discontinuance was significantly greater in the EN group compared to the EN plus TPN group, with no differences in the infection rate between the two groups [121]. The ESPEN [119] guidelines recommend that perioperative parenteral nutrition only be used in malnourished patients if enteral nutrition is not feasible. In nonsurgical, well-nourished oncologic patients, routine parenteral nutrition is not recommended, since it has not offered any advantage and is associated with increased morbidity. A benefit, however, is reported in patients undergoing hematopoietic stem cell transplantation [119]. The benefit of administering TPN as means of support or for repletion of nutritional status continues to remain controversial due to the lack documentation for a favorable impact of TPN on response to therapy or survival. The decision to use TPN as an adjunct to therapy remains a matter of clinical judgment. However, malnourished patients unable to tolerate enteral feedings with a clear response or potential response to antineoplastic treatment are usually considered candidates for parenteral support, taking into consideration problems and challenges identified in patient populations with organ failure, circulatory disorders, and effects of other therapies used and tumor effects.

2.7 Reassessment and Follow-up Nutritional Care

Improved management of malnutrition with nutritional therapy may require a multimodal intervention by multidisciplinary teams using a comprehensive and integrated approach. Initial screening and knowledge of treatment trajectory of the cancer patient should guide a plan for reassessment of the cancer patient at regularly planned intervals. Subjective and objective data on progress and response to nutritional therapy may be assessed using the indicators used in the comprehensive nutritional assessment. Newly developed symptoms resulting from treatment or progression of disease may require additional monitoring or revision of nutritional therapy. Nutritional reassessment is also indicated in those patients initially identified at low or no risk for malnutrition. Criteria for reassessment in this group is indicated when treatment symptoms are anticipated or develop; a deficiency in nutritional intake is observed compared to assessed requirements; patient exhibits nutritional symptoms such as nausea, vomiting, and diarrhea; or patient is on serial treatment regimens that have been shown to increase nutritional risk. Reassessment/reevaluation for monitoring and evaluation of nutritional therapy must include monitoring of clinical, functional, dietary, and behavioral outcomes that were identified by the comprehensive nutritional assessment.

2.8 Patient and Family Communication/Education

The goals of nutritional therapy, the outcome measures planned, and strategies to achieve these goals, as well as a time frame within which these goals can be achieved, must be communicated both to the patient as well as the interdisciplinary medical team throughout the continuum of cancer care. Patient education may include information about the results of nutritional assessment, planned nutritional therapy and patient's role in planning this therapy, symptoms that can be anticipated based on treatment regimen, and strategies to manage symptoms. Patient and family education, proactively, has been the single most important component of managing nutrition therapy in cancer patients. Patients must be educated on reporting symptoms and not take for granted that these symptoms are a part of cancer treatment. Approaches to education of patient and family, enhanced problem solving skills, stress management, psychosocial support, peer group support to improve mood and coping response, psychotherapy, and tailored behavioral interventions have shown promise in reducing symptoms of cancer.

2.9 Communication with Interdisciplinary Team

Ongoing communication/education as to the rationale of nutritional therapy must be communicated to all members of the health-care team including the attending physician, social worker, speech therapist, physical therapist, dietitian, and nursing

staff, and the patient's family or caregiver is essential in developing and implementing the best possible care plan for the patient. Physician-nurse communication has been identified as one of the main obstacles to progress in patient safety. Breakdowns in communication between physicians, nurses, and members of the health-care team often result in errors, many of which are preventable [122]. Clear and complete communication between health-care providers is a prerequisite for safe patient management [123]. These studies have continued to support the development of structured communication interventions to improve quality of nurse-physician communication. Errors in dose of chemotherapy, medications, and other treatment are preventable if communication is structured, timely, and thorough. When referral is made to dental health, radiology, nutritionists, or other health professionals for pretreatment, specific information about patient's diagnosis, anticipated start date and restrictions to medications or therapeutic procedures, and contact information for further questions must be provided by the lead medical oncologist to maximize the effectiveness of service provided by other team members. With outstanding communication devices and systems in place, timely communication between team members should not present a challenge.

2.10 Future Directions

It is clear that patients with cancer and those who receive treatment for cancer are at a nutritional risk throughout the continuum of cancer. Nutritional screening, assessment, support, and reassessment should be considered a valuable measure within the overall oncology strategy. Despite extensive research in the field of clinical nutrition, examining the value of nutritional interventions in specific cancers and treatments, definite guidelines to base rational nutritional assessment and support in cancer patients are still debated. This may be attributed to a dynamic environment in oncology, where novel agents and treatment modalities—chemotherapeutic agents, radiation therapy, chemoradiation, immune therapies, and targeted therapies—have flooded the practice of clinical oncology. Although the focus of clinical oncologists continue to be in the treatment of cancers and improving morbidity and mortality in the cancer patient, they rely upon the expertise and partnership of their multidisciplinary teams to provide supportive care to their patients. Future research testing effectiveness of cancer treatment approaches should also include in parallel, an integrated evaluation of safety and effectiveness of supportive care approaches to manage symptoms and comorbidities. The results of these studies can inform the practice of nutritional and other supportive care that can significantly impact treatment outcomes and quality of survival in the cancer patient. The following chapters comprehensively examine some of the most common symptoms of cancer and treatments which have an implication on nutrition status and examine their significance, prevalence, etiology, current treatment strategies, and guidelines for management in a clinical setting using an integrated, multidisciplinary approach.

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