editorial

Malnutrition in Cancer Care: Time to Address th Elephant in the Room

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The Clinical Problem

In 1974, *The Skeleton in the Hospital Closet* highlighted unrecognized hospital malnutrition (MN).[1] In general medicine, moderate or severe MN is associated with greater illness severity, longer hospital length of stay, and higher total costs. This prompted some screening protocols to identify those at risk on hospital admission with automatic nutritional evaluation and intervention. However, there is no national or international consensus about minimum standard nutrition interventions.

MN in Cancer

Cancer-related MN is a broad term that encompasses complex poorly understood processes. People with specific tumors (esophagus, head and neck, pancreas) or those who have treatment plans with high symptom burden (hematopoietic transplantation, mediastinal radiation) appear to be at greater risk. Multiple factors, including cancer-related symptoms (eg, anorexia, early satiety, and fatigue), treatment complications (eg, mucositis, nausea, taste changes), and psychologic distress, contribute to MN. The reported prevalence of (often ill-defined) cancer-related MN ranges from 20% to 80%. It varies by age, disease site, and stage. Conventionally, cancer-related MN was evidenced by weight loss (WL).

Unexplained WL is a common presenting cancer symptom and often signifies progressive disease. WL alone predicts cancer survival independent of primary site, stage, or performance status. Shorter survival is also related to greater percentage WL and a lower body mass index (BMI).[2] Up to 80% of patients have WL before treatment. It is well established that a third of these have lost more than 10% of their preillness body weight.[3] WL is usually associated with other multiple, highly prevalent, and poorly understood symptoms (eg, early satiety, fatigue, depression) that also impair quality of life.

Cancer Cachexia

Cancer-related MN is classically recognized as part of cancer cachexia (CC). CC, an inflammatory driven complex disorder, includes skeletal muscle loss (with or without fat) and progressive functional impairment.[4] It appears to be directly responsible for 20% to 30% of cancer deaths, perhaps more than 150,000 deaths in the United States alone each year.[5] A provisional definition was proposed in 2011 and included either WL greater than 5% during the past 6 months (absent simple starvation), BMI less than 20 kg/m^2 and any WL greater than 2%, or an appendicular skeletal muscle index consistent with sarcopenia and any WL greater than 2%.[4] As CC progresses, interventions seem less effective and are inherently difficult to study. Certain pharmaconutrients (eg, n-3 polyunsaturated fatty acids) seem to have positive effects on body weight; however, the overall benefits of oral nutritional supplements are unclear. Enteral and parenteral nutrition seem ineffective. Multimodal approaches that incorporate inflammation control, nutrition, and physical activity are under investigation, as are pharmacologic interventions.

CC has profound negative effects on patient-reported and therapeutic outcomes. Despite the high prevalence and associated morbidity and mortality, CC appears to be systematically underdiagnosed in clinical oncology practice. Underdiagnosis and failure to intervene are not surprising, because only 25% of medical schools have a dedicated nutrition curriculum, and few meet the 25 hours recommended by the National Academy of Science.[6] The Maintenance of Certification of the American Board of Internal Medicine (for Medical Oncology Fellows) dedicates only 11% to supportive care and, notably, nothing to cachexia or nutrition. The 2017 Cancer Moonshot entirely ignored the role of nutrition in either cancer prevention or recovery. For example, there was no registered dietitian on the Blue-Ribbon Panel.

Obesity and Sarcopenic Obesity

As a result of the obesity epidemic, 40% to 60% of new cancer diagnoses now present in those who are overweight or obese (BMI $\geq$ 25 kg/m^2). This has complicated the traditional CC diagnosis. For example, loss of lean body mass can be masked by adiposity (and/or fluid retention). Diagnosis of CC in the overweight and obese requires more formal screening to identify MN.

The obesity epidemic raises the more recent concept of sarcopenic obesity. Sarcopenia is defined as an appendicular skeletal muscle index two standard deviations less than a reference standard as measured by either dual-energy x-ray absorptiometry or

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Accepted on April 12, 2019 and published at jop.ascopubs.org on June 12, 2019: DOI https://doi.org/10.1200/JOP.19.00165

TABLE 1. Recommended Actions

Category	Action
Health policy	Collaboration among organizations, such as the American Society of Clinical Oncology, National Cancer Institute, and National Comprehensive Cancer Network, should create a nutrition consensus statement and a call to action for early systematic screening, diagnostic criteria, targeted interventions, and better education for all oncology professionals.
	Registered dietitians/nutritionists should be recognized and supported as critical in cancer care. Regulatory agencies should facilitate nutrition staffing. Currently, there is no staffing for a condition that affects most patients with cancer.
Clinical practice	Cancer centers must create screening protocols and nutrition care pathways to ensure monitoring with validated tools throughout cancer care. Standard assessment should include current or secondary nutrition impact symptoms.
	Effective pain and symptom management are needed to increase and optimize nutritional intake.
	The optimal diet at diagnosis and during active anticancer therapy must be explicitly established.
	A treatment protocol for malnutrition and cachexia must be prioritized. Interventions should be individualized and updated along the continuum of care.
Research	Nutritional status is arguably as important as performance status and should provide another prognostication and outcomes metric. It should be included routinely in the demographics of all cancer studies and guidelines for standard treatment recommendations.
	Consensus definitions for optimal endpoints and outcome measures are needed to test the efficacy and the safety of both new and available drugs.
	Standard research metrics, like caloric needs and handgrip strength, must be established.
	Increased funding mechanisms should focus on the evaluation and treatment of cancer cachexia.
Education	All clinical oncologists should be trained in screening and diagnosis of malnutrition as part of their specialist training and postgraduate continuing medical education.

computed tomography. Sarcopenia alone has been associated with greater chemotherapy toxicity and more treatment breaks. This is evident with both targeted and conventional cytotoxic therapies and, again, has negative oncologic outcomes.[7,8] Both CC and sarcopenia are common and independent of BMI.

Screening

Early identification of MN should allow for interventions to reduce morbidity and mortality. Inadequate screening has, however, resulted in poor recognition of (potentially) preventable MN; it is a major national and international problem. Both the American Society for Parenteral and Enteral Nutrition and the European Society for Clinical Nutrition and Metabolism recommend initial screening and frequent rescreening for MN in general medical practice. Many, if not most, cancer centers in the United States have not adopted such universal screening protocols, despite the high morbidity and mortality from MN. Currently, the Malnutrition Screening Tool,[9] the Malnutrition Universal Screening Tool,[10] and the Patient-Generated Subjective Global Assessment[11] are the only validated tools in inpatient and outpatient oncology. None of these tools can adequately detect sarcopenia.

It is notable that accredited cancer centers must screen for psychosocial distress but not for MN. Screening guidelines in the outpatient setting are vague. Bodies like the Association of Community Cancer Centers and the Commission on Cancer recommend that at-risk patients have dietitian access throughout their care. Most US patients with cancer receive ambulatory care in which nutrition is the individual responsibility of each health care facility. If a single dietitian covers multiple treatment centers, those accreditation guidelines are met, but effective intervention and follow-up are likely limited and/or delayed. Financial barriers are also evident. Dietitians compete for limited cancer resources with those that are either mandatory (eg, psychosocial support) or revenue generating (eg, rehabilitation), and dietitian services are often not reimbursed by private insurance.

Diagnosis

Currently, the American Society for Parenteral and Enteral Nutrition and the European Society for Clinical Nutrition and Metabolism have different MN diagnostic criteria. The Global Leadership Initiative on Malnutrition recognized the need for a global consensus on MN.[12] A two-step model was proposed. First, a validated tool should be used for screening; screening should be followed by assessment for diagnosis and severity. Criteria are divided into phenotypic (WL, low BMI, reduced muscle mass) and etiologic (reduced food intake/assimilation, disease burden/inflammation) types. Both types are required for an MN diagnosis, and severity is based on the phenotype. Neither type is oncology specific.

The percentage of WL considered clinically significant in oncology practice varies. It typically is not calculated automatically within the electronic medical record except for the purpose of chemotherapy administration. Patients often are not weighed regularly or appropriately. Some centers use a WL cut point (often 5% or 10%) to initiate dietitian referrals. However; WL of as little as 2.4% is clinically significant and is associated with poor survival independent of BMI.[2]

Treatment

Organizations like the American Cancer Society and American Institute for Cancer Research have post-treatment (survivorship) guidelines but, notably, no cohesive evidence-based nutritional approach during treatment. Of 21 National Comprehensive Cancer Network Web sites reviewed, few had (varied) nutritional recommendations, and many links to external Web sites.[13] Available dietary and nutritional advice varies. It often is limited to generalities about healthy eating. These generalities are particularly challenging for underserved populations. Ideally, nutrition interventions should be individualized, because the specific nutrition needs of patients with cancer likely vary by cancer type, stage, and treatment modalities (including immunotherapies). Because of the limited numbers of rigorously conducted trials of nutritional interventions, current web site information is based largely on expert opinion.

Nutrition supplements (eg, fish oil, omega-3 fatty acids) and macronutrients have been investigated to counter MN, but results are disappointing. Little is known about the role of micronutrients. The gut microbiome is emerging as a new avenue for understanding the natural history of cancer and the investigation of CC. Various studies have examined pharmacologic interventions. These interventions include anamorelin, cannabis, corticosteroids, ghrelin, megestrol acetate, psychotropic medications, testosterone, and thalidomide; no studies have been conclusive. Off-label use of some of these medications (eg, dronabinol, megestrol acetate) seems to stimulate appetite but has minor effects on WL. This lack of data limits clinical use of nutrition support in an evidence-based manner. Efforts to evaluate novel multimodality interventions in larger randomized, controlled trials are underway.

Next Steps

It is incomprehensible that severe body wasting in patients with cancer is ignored or viewed as inevitable. It is important to better understand CC. Not only does it cause much suffering, treatment toxicity, and early death, but also its clinical and biochemical characteristics may reveal important lessons about the natural history of cancer and allow more effective management of individual cancers. MN in patients with cancer is a ubiquitous but neglected problem and should be (but is not) a strategic priority in cancer care (Table 1).

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI https://doi.org/10.1200/JOP.19.00165.

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Data analysis and interpretation: All authors
Administrative support: Declan Walsh
Manuscript writing: All authors
Final approval of manuscript: All authors
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ACKNOWLEDGMENT

We thank Derek Raghavan, Egidio G. Del Fabbro, and Vickie E. Baracos for commenting on the manuscript.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Leadership: Nualtra
Stock and Other Ownership Interests: Nualtra
Research Funding: Nualtra

No other potential conflicts of interest were reported.