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Assessment of Cancer-Associated Cachexia — How to Approach Physical Function Evaluation

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Abstract

Purpose of review Cachexia is a devastating syndrome that impacts a majority of cancer patients. Early assessment of cachexia is critical to implementing cachexia treatments. Our aim was to summarize the existing cachexia assessment tools for their utility in both symptom and function evaluation.

Recent Findings Several tools now exist that provide a symptom-based approach for evaluating weight change, appetite, and nutrition impact symptoms in cancer patients with cachexia. However, current instruments used to assess physical function changes related to cachexia are limited in depth and breadth. Instead, we recommend a tiered approach to cachexia-related functional assessment that involves evaluation of activities of daily living, general mobility, and exercise tolerance in a prioritized sequence.

Summary Current tools for cancer-associated cachexia assessment are adept at symptom evaluation. New approaches to physical function evaluation are needed that efficiently and broadly evaluate the diverse functional needs of cachexia patients.

Keywords Cancer · Cachexia · Rehabilitation · Physical function

Introduction

Cachexia is a devastating clinical syndrome hallmarked by muscle loss in the setting of chronic disease. It has a 50% prevalence across all cancer types, rises to 80% in patients with advanced stage cancer, and accounts for 30% of all cancer related mortalities [1]. Distinct from other muscle wasting syndromes such as primary sarcopenia and disuse atrophy, cachexia is typically recognized in the clinical setting by weight-based criteria [2]. However, the clinical approach to cachexia is evolving. While the historical approach to cachexia in cancer prioritized primary disease treatment, several studies across distinct cancer populations have shown that cachexia is an independent risk factor for negative clinical outcomes, even at early stage disease [1]. Clinical experts, particularly in the palliative care field, have consequently advocated for management that approaches cachexia as a parallel and independent clinical diagnosis [3]. Basic science studies have shown that cachexia is driven by chronic inflammation that affects multiple organ systems [4], suggesting that while muscle is the primary output, cachexia is a truly systemic illness [5]. As a result, cachexia diagnosis, evaluation, and treatment have expanded to include the assessment of a variety of symptoms and pathologies [6], and this in turn has led to improvement in cachexia related quality of life and symptom burden [7].

For cancer patients with cachexia, a key turning point in their clinical progression is physical functional decline [8]. Change in physical function is a critical symptom in cachexia diagnosis and recognition that it should be directly

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addressed in treatment has prompted the development of multi-disciplinary and rehabilitation strategies for the cachexia population [9, 10]. Efforts to implement physical activity and exercise measures in the cachexia population have also grown [11]. However, the precise strategy for implementation of function-focused therapies in cachexia patients is unclear. In part, this is due to the lack of a systematic approach to precisely evaluating and categorizing functional decline using existing cachexia assessment tools [8, 12]. Compared to other muscle wasting disorders, there is no agreement between existing cachexia assessment tools on an approach to assessing multiple distinct levels of physical or cognitive function [13–16]. Additionally, there is no guidance for prioritizing specific functional complaints from patients. Thus, there is a clear need to develop a programmatic approach to functional assessment in the cachexia population before function targeted cachexia therapies can be designed and implemented at either the clinical trial level or in clinical practice.

Rehabilitation clinicians, which include physicians (physiatrists), physical therapists/physiotherapists, occupational therapists, and speech therapists, are trained to assess the function-based needs of patients across a wide spectrum of diseases and disabilities. While there has been some prior engagement of the rehabilitation community in cachexia treatment [10, 11], commonly used approaches in rehabilitation medicine have yet to be applied consistently in the cachexia population. Given our collective experiences as rehabilitation physicians at an inpatient rehabilitation facility that receives a high volume of functionally debilitated cancer patients who are significantly impacted by muscle wasting [17], the objectives of this narrative review are the following:

1. Summarize and discuss current approaches to diagnosis and assessment of cancer patients with cachexia
2. Propose a framework for assessment of functional decline in cachexia patients that can be adapted for both current cachexia clinicians and for future studies that incorporate function focused therapies.

History of Defining and Diagnosing Cachexia

One of the first descriptions of *cachexia* (in Greek "bad condition") is widely touted to be by Hippocrates in 460–377 BCE when he observed patients with advanced heart failure: "[T]he flesh is consumed and becomes water, …the abdomen fills with water, the feet and legs swell, the shoulders, clavicles, chest and thighs melt away. …This illness is fatal" [18]. This description was also an early indicator that cachexia is a multi-organ system condition. In the nineteenth century, the term became linked with cancer, portending poor prognosis [19]. And by the early twentieth century, cachexia was recognized less as a muscle disease and more as a syndrome that involved a distinct pattern of symptoms across multiple organ systems [20]. Clinicians had also begun to describe the clear link between cachexia and decline in physical function through reports of fatigue, "adynamia," and asthenia [21].

The first decade of the twenty-first century saw dramatic gains in the pathophysiologic characterization of cachexia, clarifying that it is a syndrome with combined clinical appearance and biochemical derangements. In parallel, several cachexia focused clinical researchers had begun to establish cachexia definitions that overlapped in both clinical and pathophysiological priorities but also left opportunity for confusion. Prompted by the need for consensus in clinical trials and at a practical level, Fearon et. al. reported, "The agreed diagnostic criterion for cachexia was weight loss greater than 5%, or weight loss greater than 2% in individuals already showing depletion according to current bodyweight and height (body-mass index [BMI] < 20 kg/m2) or skeletal muscle mass (sarcopenia)" [2]. Moving forward, this clinical definition has remained the gold standard for the clinical setting. However, many have recognized that this definition continues to omit several key pathophysiological and systemic features of cachexia-anorexia syndrome and several instruments and measures have been subsequently developed in the hope of more precisely identifying patients with cachexia [12, 22].

Current Cachexia Assessment Approaches: Weight Criteria and Beyond

The goal of assessment is to recognize cachexia as early in the course of disease as possible and to elucidate the patient-specific mechanisms of cachexia in order to inform the development of a targeted multimodal intervention. Evaluation for cancer cachexia spans many domains due to the multifactorial and variable nature of this pathology. Patient assessment should include evaluation of nutritional status, intake, body composition, systemic inflammatory and metabolic markers, impact of co-morbidities, and characterization of the clinical significance of cachexia including symptoms, functional impairments, and impact on quality of life.

The existence of multiple criteria for diagnosis can make recognition of cachexia challenging [23]. The overlap of cachexia, malnutrition, primary sarcopenia (age related), and disuse-related muscle atrophy can further complicate diagnosis [24]. Screening begins with assessment for unintentional weight loss, a key feature of cachexia. Weight loss may be present before cancer diagnosis and is associated with reduced survival, treatment tolerance, HRQOL, and functional impairment in several cancer types [25, 26]. A

2018 retrospective study including 3190 patients with lung or gastrointestinal cancer determined that pretreatment cancer-associated weight loss was present in 32.1% of patients and was associated with reduced overall survival [27]. Body mass index is a modifying factor in the assessment of cachexia. The Weight Loss Grading Scale (WLGS), developed by Martin et al., incorporates both degree of weight loss and BMI as continuous variables to categorize cachexia severity [22]. The scale features five grades based on percent weight loss and BMI deciles that have been stratified by overall survival rates, independent of age, cancer type, cancer stage, and performance status. Multiple studies have demonstrated that the WLGS is associated with additional cachexia-related features including appetite loss, fatigue, decreased dietary intake, and physical function [28, 29]. Additional analysis also has revealed that the predictive value of WLGS can be enhanced by additional performance status, physical function, or emotional function assessment [29].

Physical exam and diagnostic testing can play a role in muscle wasting assessment. Salient exam findings include fluid retention, subcutaneous adipose tissue loss, muscle atrophy, and weakness. Prominent muscle wasting may be notable in the temporal region or thenar eminence, though these often do not present until later stages. Although not routinely used in clinical practice, determination of body composition using imaging techniques is feasible and can provide more specific information than anthropometric measures or clinical exam, identifying individuals at risk for cachexia and sarcopenia who may be missed with screening based on weight loss or body mass index [30, 31]. Imaging options include body impedance analysis (BIA), dual-energy X-ray absorptiometry (DEXA), and computerized tomography (CT) scans of the lumbar region. CT scans have the benefit of being a routine part of oncologic care and reliably differentiating between fat and muscle content. Several studies in multiple cancer populations have highlighted the association between decreased muscle mass identified on CT and survival, tolerance of therapy, and physical function measures [25, 32, 33]. BIA measures body composition based on the electrical properties of tissues and represents a low cost and low radiation technique for assessment in cancer patients [34]. However, BIA may underestimate fat free mass when compared to CT and DEXA [35, 36]. Conversely, BIA technology is frequently used in clinics that also monitor cancer-related lymphedema [37], making it more accessible for rapid assessment of body composition compared with CT or DEXA.

Serum-based markers capitalize on the importance of inflammation and metabolic disturbances in cachexia. C-reactive protein (CRP) is widely used as a marker of inflammation and has been linked to poor prognosis in several cancers [38]. The modified Glasgow prognostic score (mGPS) incorporates both CRP and albumin to predict survival and has been validated for cachexia assessment in several cancer types [39, 40]. However, CRP is not routinely collected in most cancer populations, and additional emerging tools based on routine laboratory parameters include neutrophil lymphocyte ratio (NLR) [41–43], which is calculated by comparing the absolute neutrophil count and absolute lymphocyte count from a peripheral blood count, and prognostic nutritional index, derived from the serum albumin concentration and total lymphocyte counts [44–46]. Both NLR and PNI are alternatives for detecting systemic inflammation that are easily accessible through frequently collected lab panels compared to CRP. Multiple additional serum markers that are associated with cachexia and inflammation during cancer in distinct populations have been developed [47], but currently, there is no mechanism for implementing these novel biomarkers in clinical practice.

Initial assessment of nutritional intake should include patient perception of intake change, presence of anorexia (appetite loss), and a quantitative assessment of caloric intake, with special attention to protein content. Appetite loss is a particularly important symptom that has been linked to shorter survival in patients with cancer [48]. Cancer and cancer therapies frequently result in nutrition impact symptoms (NIS), which are symptoms that lead to decreased oral intake and often represent therapeutic targets for increasing oral intake [49]. Examples of NIS include nausea, vomiting, diarrhea, constipation, change in taste or smell, and mouth sores. Of note, screening for endocrine abnormalities, including hypothyroidism, hypogonadism, and adrenal insufficiency, is recommended given that many of these processes are easily reversible with pharmacologic intervention [50]. Similar to anorexia, NIS burden is associated with weight loss and poor survival [51, 52]. Beyond NIS burden, symptoms associated with cancer cachexia and cancer should be investigated. This can be aided by the Edmonton Symptom Assessment Scale (ESAS) and by the functional assessment of anorexia-cachexia therapy (FAACT) scale, which are both symptom batteries that investigates frequent symptoms experienced by persons with cancer and have previously been successfully implemented in cachexia focused clinics [51, 53, 54]. Serum screening for endocrine abnormalities, including hypothyroidism, hypogonadism, and adrenal insufficiency, is recommended given that many of these processes can impact muscle metabolism and are easily reversible with pharmacologic intervention [50].

Numerous validated composite tools have been developed to facilitate screening for malnutrition and may be useful is cachexia identification. These tools and the diagnostic domains they address are summarized in Table 1. Although tools mentioned above, such as the ESAS or the serum-based tools, explore particular features of malnutrition, cachexia, and cancer, the Cachexia Score (CASCO)

Table 1 Coverage of signs, symptoms, and serum markers by cachexia assessment instruments

Instrument	Body composition	Anorexia/reduced food-intake	Metabolic and inflammatory abnormalities	Psychosocial impairment and quality of life
CT [25]	x			
BIA [34]	x			
DEXA [35]	x			
mGPS [39]			x	
Neutrophil to lymphocyte ratio [43]			x	
Prognostic nutritional index [45]			x	
NIS [52]		x		
ESAS [51]		x		x
FAACT [54]		x		x
CASCO [13]	x	x	x	x
PG-SGA [55]	x	x		x

is the most comprehensive and only cachexia specific validated screening tool [12, 13]. It includes laboratory testing, physical exam, and patient questionnaire, however does not include measurement of body composition. Of the common screening tools for malnutrition, the Patient-Generated Subjective Global Assessment (PG-SGA) is the most comprehensive instrument, exploring domains of weight history, food intake, symptoms, function, and provider assessment [3, 55, 56]. Although literature has supported their feasibility and role in screening for nutritional risk, there is no consensus upon the best screening tool for routine clinical practice and no single item has been used widely in clinical practice [13, 57].

Fatigue has been established as one of the most prevalent side effects of both cancer and its treatments [58] and has also been tied to cachexia syndrome [59]. While cancer-related fatigue is defined by inability to resolve with rest, it can further be distinguished by central versus peripheral etiology and symptom clusters. Central fatigue is the dysfunction of cortical mechanisms proximal to the neuromuscular junction, while peripheral muscle fatigue is the result of metabolic derangements within the muscle [60, 61]. Approaches to assessment of fatigue are evolving [62] and patient reported tools are being developed that can distinguish peripheral and central fatigue symptoms clusters [63]. At the practical level, we recommend taking a history of the context of the patient's fatigue complaints, including if they are task specific, involve cognition, or associated with mood symptoms. Distinguishing these features is important as recent studies suggest that exercise is helpful in decreasing fatigue levels in subsets of patients [64]. While physical therapist and occupational therapists can help address task specific issues and mobility, speech therapy is needed in a subset of patients for optimizing their attention, memory, and cognitive planning. Additionally, speech and swallow therapy becomes particularly important in patients with head and neck cancers, given the link between cancers in this region and speech/swallow impairments.

How to Define Cachexia Related Function in Clinic and Research

It is important to distinguish between the terms "function," "physical activity," and "strength," which are often used interchangeably to describe physical function related to cachexia. Herein, we adhere to the definition of physical function as the "ability to perform both basic and instrumental activities of daily living" [65]. This is consistent with the definition that rehabilitation clinicians apply in daily clinical practice and the framework for function and disability established by the World Health Organization (WHO) [66]. By comparison, physical activity is defined by the WHO as "any bodily movement produced by skeletal muscles that requires energy expenditure" [67], and strength is defined as "ability to exert force against resistance" [68]. While each of these three concepts are correlated and may act as proxy measures for one another in the research setting, they are distinct. One measure does not necessarily provide specific and clinically actionable details about the others.

Thus, it is important to analyze whether one is assessing function "at the level of body or body part, the whole person, and the whole person in a social context" as has been outlined by the WHO [66]. Holistic and individualized assessment of physical activity and function may recognize functional decline that broad categories addressed by currently used tools do not identify. For example, a previously independent person who works full-time with lung cancer who cannot walk up several flights of stairs may feel like this activity is drastically different, but an immunocompromised person who works from home may not notice much change in their daily life with cancer diagnosis. Matching assessment of function to each patient's stated functional goals might be difficult to implement on a large scale; however, it may be more practical for the patient as we think of that individual's quality of life and specific living environment.

To approach patient's functional goals from a practical perspective, rehabilitation clinicians prioritize evaluating tasked based functional independence rather than general mobility. Functional independence evaluation starts with examining their activities of daily living (ADLs) and instrumental activities of daily living (IADLs). ADLs are fundamental tasks that a patient is required to do to care for oneself and are eating, bathing, toileting, personal hygiene, and transferring [69]. The next layer of functional independence is IADLs, which include managing finances, meal preparation/cooking, shopping for necessities, taking medications, using communication tools, and cleaning the house. A focus on functional independence is more likely to improve patient sense of self-worth and quality of life, as has been shown in a variety of debilitating conditions [70]. It is also important to note that prior reports in the cancer population, in particular, have shown that lack of functional independence often goes ignored by oncologic health care providers until patients are hospitalized [71]. Thus, an emphasis on evaluation of ADLs and IADLs in the outpatient setting could not only improve patient well-being but also improve health care resource utilization, an approach that has already shown significant benefits in cancer patients with pain [72, 73]. Once function at the ADLs and IADL levels has been addressed, then function at the general mobility and exercise tolerance levels could be further evaluated. It should also be noted that patients may stop performing certain ADLs or IADLs due to changing family/social supports — for example, if a family member has to help with assisting their loved one to the bathroom or commode/hygiene after toileting, the patient may choose to wear diapers in bed to limit perceived caregiver burden.

Current Function Instruments in Use with Cachexia Patients

In the context of functional independence, we performed a literature review of the current function assessment tools commonly used specifically in the cachexia population in prior studies. This survey revealed the limitations of the current instruments to effectively and comprehensively reflect function at the levels of ADLs, IADLs, general mobility, and exercise tolerance levels. Herein are examples of the limitations of the existing patient-reported outcomes, physical tests, and performance status scales (Table 2).

Several patient-reported outcome (PRO) measures are currently in use in cachexia trials but have mixed value for practical application in the clinic setting beyond research. The functional assessment of anorexia-cachexia therapy (FAACT) scale has been validated previously in the cachexia population and consists of a functional assessment of cancer therapy general (FACT-G) scale and an anorexia-cachexia subscale. The FACT-G scale includes physical, emotional, social, and functional domains [54]. While the sum of 39-item score correlates well with quality of life [74], the major drawback is that the scale does not offer details on functional independence in specific activities or tasks. Therefore, the function information from the FAACT is not necessarily clinically actionable in terms of subsequent function focused rehabilitation. The Short Form Health Survey (SF-36) and European Organization for the Treatment and Research of Cancer-Quality of Life Questionnaire (EORTC QLQ-C30) are both PROs that are validated for detecting quality of life and health related changes that contain more specific items on functional independence. Both instruments are widely applicable to many cancer patients, and in use by clinicians in the research setting [75, 76]. However, the functional independence items in these surveys are limited to a subset of daily activities of living and therefore do not provide a high degree of detail or breadth. By comparison, Cancer Rehabilitation Evaluation System (CARES) has a more comprehensive approach to function and is unique among common clinical oncology measures for asking about a cancer patient's sexual wellbeing and function [77].

Table 2 Function levels assessed by select instruments previously suggested for cachexia related functional change

Instrument	Number of items	ADL + IADLs	Mobility	Exercise tolerance	Sexual Function	Strength
FACT-G + FAACT [54]	39		x			
SF-36 [75]	36	x				
QLQ-C30 [76]	30	x	x			
CARES/CARES-SF [77]	139/59	x	x		x	
Grip strength [78]	1					x
6MWT [80]	1		x	x		
30CST/TUG [81]	2		x			x

However, the long form CARES has 139 questions and the short form has 59 items, making it particularly burdensome to implement.

Several measures of strength or specific physical activities have been used in both the clinical and research settings in cancer cachexia populations, including hand grip strength (GS), the 6-min Walk Test (6MWT), 30-s sit to stand (30CST), and timed-up-and-go test (TUG). Each of these measures has been recognized as a screening tool that correlates with health, morbidity, and mortality, with GS being the most widely cited across a spectrum of conditions, including in cancer-associated cachexia [78]. While grip strength may often be used as a screening tool for overall health status, its utility as a metric for specific functional change is less clear. As result, use of GS as an outcome to track functional independence or general mobility over time is not recommended compared to other approaches [79]. 6MWT, 30CST, and TUG are each more useful in assessing general mobility, have been evaluated in cancer cachexia populations [80, 81], and can act as proxy measures for assessing general physical functional ability [82], but again are unable to provide specific detail on functional tasks.

Additional measures used to approximate function include the Karnofsky Performance Status (KPS) and Eastern Cooperative Oncology Group Performance Status (ECOG) scales, which are widely in use to determine patient eligibility for specific cancer treatment regimens. While performance status can inform prognosis and quality of life in the cachexia population [83, 84], there is a high degree of subjectivity and bias in the application of these scales. Others have also suggested that the performance status scores do not accurately reflect a patient's perception of their functional status or provide clinically actionable information that is function focused [85].

Thus, the path forward for a systematic approach to assessing the physical function of cachexia patients is unclear based on the current literature. The current instruments are limited in either their ability to comprehensively assess functional independence and mobility, or are burdensome in number of items needed for comprehensive evaluation.

Practical and Research Approaches to Functional Assessment in Cachexia

Given our collective experience in the functional evaluation of cancer patients at the practical level, herein, we propose a general approach to assessing function of patients with cancer-associated cachexia. In addition, given the limitations in functional evaluation of current tools commonly used in cachexia studies, we have made suggestions on functional tools used widely in other clinical research settings that could be translated to future cachexia studies. Additionally, we recommend that non-rehabilitation trained cachexia providers, who may not feel comfortable with prescribing individualized functional interventions, use the information gathered from this tiered approach to consult with rehabilitation clinicians in a more focused manner. We hope to spur the adoption of a more objective approach to cachexia-specific function assessment. This approach highlights the importance of recognizing functional impairments [86]. Identification of these impairments can expedite the involvement of cancer rehabilitation clinicians who are experienced in specifically addressing these impairments, and therefore prevent cachexia related disability.

Practical Approach

At the practical level, history and physical exam remain critical components of any functional evaluation of a cancer patient with cachexia. The aforementioned tools for monitoring nutritional intake symptoms remain relevant for function evaluation, as they are also tightly linked to overall functional independence. For example, patient history regarding GI symptoms such as constipation or diarrhea, are important for both nutrition intake and bowel function independence. Regarding assessment of functional history, it is clear that no one algorithm will be applicable to all clinical settings, given the diversity of stages, health statuses, and functional abilities of cancer patients with cachexia.

Instead, we propose a tiered approach meant to help clinicians assess a patient's functional history (Fig. 1). As outlined above, beginning functional assessment at the ADL and IADL levels ensures that the most vital physical functional tasks are prioritized for cachexia patients. If specific ADL or IADL tasks are deficient for patients, and have some capacity for rehabilitation, then interventions can focus on these items rather than being directed at higher level tasks. Importantly, ADL or IADL tasks can be addressed using both supportive (adaptive aids and techniques) and restorative approaches (muscle strength and coordination), and lead to improvement in functional quality of life independent of medical prognosis or primary disease status [87]. If patients are functionally independent, then assessment can shift to general mobility, which we define as a deficiency in physical activity that does not impact ADLs or IADLs. This often presents with patients who remain functionally independent but complain of fatigue during their daily life. Often, patients with deficits in general mobility have begun to selectively function at the community level, thereby limiting their overall physical activity. Beyond general mobility, patients with cachexia who are at higher levels of function are most likely to present for evaluation with a desire to improve and restore their exercise tolerance or return to work. Questions regarding a patient's changing ability to participate in exercise or

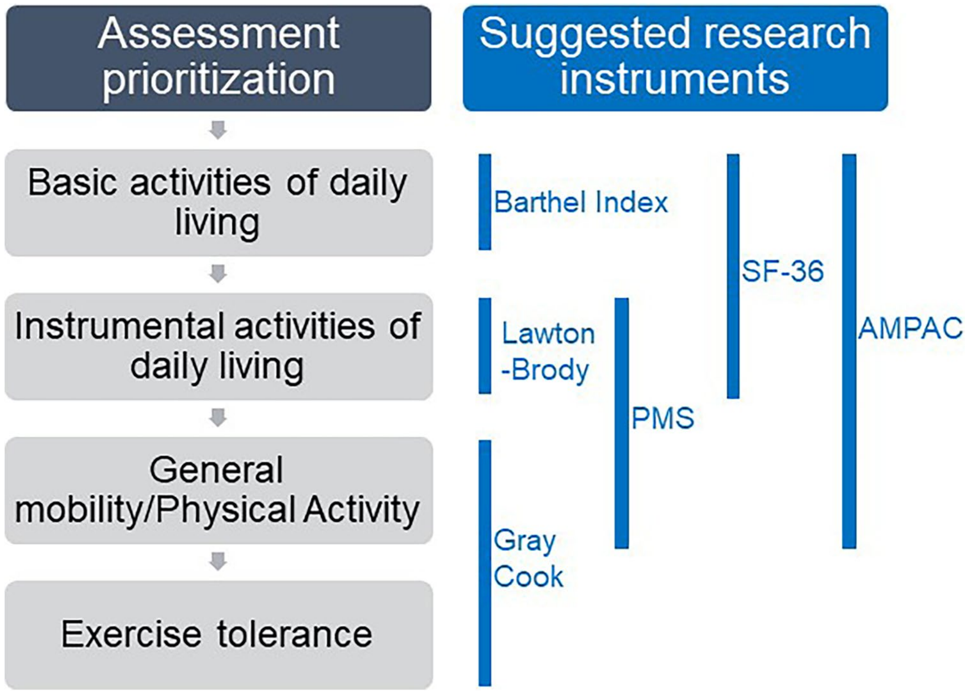

Fig. 1 Prioritization of function assessment through acuity levels and select instruments. Functional assessment can begin at the basic activities of daily living level (ADL), next in the hierarchy is instrumental activities of daily living (IADL), followed by general mobility that is not already assessed through ADLs or IADLs, and last in the hierarchy would be tolerance of exercise or occupational/employment level activities. The Barthel index is appropriate for ADL assessment, Lawton-Brody for IADL assessment, and SF-36 includes item that cover some of both levels. The physical mobility scale (PMS) covers both IADLs and general mobility. The basic mobility AMPAC addresses elements of ADLs, IADLs, and general mobility. The seven-item Gray Cook Functional movement screen is one example of an instrument for higher level function assessment that is modifiable depending on the patient's abilities and can be used for mobility and exercise/occupational tolerance

the occupation specific tasks are appropriate at this level. In our experience, these patients still have opportunities for functional improvement but often require careful evaluation by rehabilitation specialized clinicians.

For objective assessment, we recommend a neurologic exam that includes strength assessment of all extremities, brief sensory screening in extremity peripheral dermatomes, and muscle stretch reflex testing. Focal weakness or neurologic symptoms can become a target for rehabilitation interventions, but should also raise the possibility of additional clinical investigation. Focal symptoms could be suggestive of super-imposed clinical diagnoses (e.g., peripheral neuropathy) that will remain as a barrier to functional recovery from cachexia or cancer unless directly addressed. Serum, radiological, and electrophysiological investigation of neurologic symptoms should be pursued when deemed clinically appropriate. Likewise, as mentioned above, screening for endocrine abnormalities through serum testing is also recommended, given the link between sex hormone levels and both physical and cognitive function.

Future Tools for Function Focused Research

At the research level, at each tier of function mentioned above, we have suggested examples of instruments that are commonly used in the rehabilitation field, have not commonly been used in the cachexia population, and may be of use in both the research and practical clinical setting for cachexia-affected patients.

While the function independence measure (FIM) scale is the gold standard for recognizing changes in ADLs and some IADLs in the inpatient setting, even for cancer patients [88], it is too burdensome to use more broadly, since it requires the involvement of multiple rehabilitation trained clinicians. In the outpatient setting, detection of disability at the ADL level can be effectively assessed using measures such as the Barthel Index [89], which has previously been applied in one prior cachexia study and been shown to be a sensitive harbinger of cachexia related morbidity [90]. For IADLs, we recommend following the categories covered by the Lawton-Brody questionnaire, which has been applied in a wide variety of populations with chronic disease and critical illness [91]. Though less ideal due to lack of comprehensive coverage of functional tasks, the SF-36 also can act as a proxy for screening assessment of both ADLs and IADLs [92].

For general mobility, there is no one specific scale that is a sensitive measure of functional status at this level that does not also overlap with other levels of function. For example, Physical Mobility Scale (PMS) and the Activity Measure for Post-Acute Care (AMPAC) are both tools that cover function across multiple levels but also provide specific information regarding general mobility beyond basic function [93, 94]. Additionally, the AMPAC has been validated as a tool in patients with cancer at multiple stages and may be less burdensome to implement as a computer adaptive test (CAT) [95]. PROMIS is additional option for cancer rehabilitation–related populations, and also includes multiple short and long versions that can be computer adapted. However, which version of PROMIS has the most utility in the cachexia population and is the most implementable in clinical studies is not clear [96]. Additionally, there are more advanced movement assessment metrics that can be applied to these populations. For example, variations of the Gray Cook functional movement screening tool are used in a variety of outpatient clinical settings and have been adapted to specific populations [97, 98], though not within cancer. A major feature of these tools is a graded approach to testing core and proximal strength. This customized approach allows careful assessment of body strength in anatomical regions that have implications on overall physical health and activity tolerance [99, 100].

In taking this tiered approach, cachexia-focused health care providers will be able to prioritize the most clinically significant deficits in function for patients. The functional tools mentioned above can be used as outcome measures in future studies of cachexia focused function. In addition, in formal prescriptions for physical therapy, occupational therapy, or exercise therapy, these tools can be included as metrics for rehabilitation professionals to track through a rehabilitation course for a cachexia patient.

Conclusion

As a multifactorial disease that impacts multiple distinct organ systems, cachexia is a syndrome that is difficult to comprehensively assess. In the past few decades, the cachexia research community has made tremendous strides in establishing tools for symptom-based assessment of cachexia. However, less guidance exists in the context of physical function assessment in cachexia patients. Herein, we have briefly reviewed several existing instruments for the assessment of physical function in cachectic patients. Instead, we recommend a tiered approach to functional assessment that covers multiple levels including, ADLs, IADLs, general mobility, and exercise tolerance. We have also given examples of several distinct instruments for assessment at these function levels that can be applied by cachexia and cancer providers.

Declarations

Conflict of Interest The authors declare no competing interests.

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