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Geriatrics for oncologists

How should older adults with cancer be evaluated for frailty?

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ABSTRACT

Traditionally used as a descriptive term, frailty is now a recognized medical syndrome identifying individuals with decreased physiologic reserve. Frailty is characterized by diminished strength, endurance, and reduced physiologic function. Several valid frailty screening tools exist in the literature, and these measures have been used to relate frailty to outcomes important to the older patient with cancer. Frail adults are at increased risk of adverse surgical outcomes and early findings suggest that frailty predicts poor chemotherapy tolerance. While much research is needed to explore the biologic relationships between frailty and cancer, there is an urgent need to implement frailty screening and management into the care of the older patient with cancer in order to improve outcomes in this vulnerable subset. The purpose of this paper is to provide an introduction of frailty to oncologists including a review of the definition, frailty screening tools, its clinical relevance to older patients with cancer, and a brief guide to frailty management.

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1. Introduction

Historically, “frail” was a term used to describe a patient who appeared shrunken, weak and vulnerable, someone with clear fragility, evident to even the untrained eye. In the last several years of geriatric oncology literature, the word “frailty” has been used broadly to define any high risk older adult whether marked by disability, functional deficits, multimorbidity, advanced age, poor nutritional status, polypharmacy, cognitive impairment, or mood disorders. The broad use of this term has contributed to some confusion about the definition of frailty. With increasing numbers of medical and surgical interventions in an aging population, there is a need to more accurately quantify age-related physiologic risk to help identify appropriate candidates for these therapies. In response to this need, aging research experts have worked to develop more formal conceptualizations and definitions of frailty. In parallel, they have worked to develop and validate multiple assessment tools to differentiate between frail and vulnerable versus more robust older adults. As such, two prominent conceptualization theories of frailty have evolved over the past decade with the majority of frailty tools developed around these two theories. These methodologies and assessments described below are increasingly utilized to identify patients at high risk of adverse outcomes in many medical, oncological, and surgical settings. Indeed, the importance of frailty screening in older patients with cancer can be appreciated in several studies relating frailty to important oncology outcomes. The purpose of this paper is to provide an introduction of frailty to oncologists including a review of the definition, frailty screening tools, its clinical relevance to older patients with cancer, and a guide to frailty management.

2. Frailty Definitions: Conceptualization and the Development of Assessment Tools

In general, frailty has been defined as a state of vulnerability to adverse outcomes in older adults. Frailty represents a loss of physiologic reserve to maintain (or regain) homeostasis in the face of a stressor. Motivated by a growing demand to quantify reserve, aging experts have long sought to create a more formal, medical definition of frailty. A consensus conference held in 2013 suggested a medical definition around the concept of physical frailty. Physical frailty was defined as “a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death.”¹ While there is broad agreement around this definition of frailty, there is less agreement around the most appropriate tools or assessments to identify frail older

adults. Hence, this definition allows for much flexibility in measuring frailty as described below.

Two leading theories of frailty’s pathophysiology exist in the literature: the frailty phenotype and the accumulated deficit theories.^{2,3} The phenotypic frailty theory has been conceptualized around an observed condition of weakness, weight loss, and physical decline. It supposes that frailty arises from aging-related cellular and physiological changes that lead to a condition of vulnerability.^{4,5} The accumulated deficit frailty theory has been conceptualized as a vulnerability that results from accumulated medical, physical and social conditions that in turn drive the increased vulnerability observed in frailty.⁶ The phenotypic frailty theory is grounded in an evidence-based biologic pathway of altered energetics, declining physiologic complexity, and loss of homeostatic capability.⁴ The accumulated deficit frailty theory is based on the conceptual framework that a global system loses robustness as it develops various illnesses or functional declines, termed “deficits.” This theory asserts that, at a certain threshold of deficits, the system fails completely (e.g., dies).⁶ As such, an accumulated deficit index tool has been developed that combines between 20 and 70 age-related indicators of health including comorbidities, disability, functional impairments, and symptoms into a single index that can be cumulatively scored (e.g., the higher the number of co-morbidities, the higher the frailty score). The phenotypic frailty theory presupposes that an underlying physiological decline contributes to frailty and ultimately to a variety of co-morbidities. The accumulated deficit frailty theory presupposes that an accumulation of co-morbidities drives frailty. The phenotypic frailty theory argues that the presence of frailty, or age-related physiologic dysfunction, is not dependent on the presence of comorbidity or disability, though they can co-exist, and is therefore assessed using markers other than comorbidity and disability. The accumulated deficit frailty theory intentionally includes comorbidities and disability as “deficits” of age.

3. Measuring Frailty

Many frailty screening tools have been developed and reported in the literature; a subset of these has been validated as well (Table 1).^{1,4,6,10,72-82} The tools generally align with one of the two predominant frailty pathophysiology theories described above although to varying degrees.³ The original measures selected for phenotypic frailty were chosen for their ability to assess various points along the proposed central biologic pathway: weak grip strength, unintentional weight loss, low physical activity, slow gait, and exhaustion. It was operationalized by Fried et al. into a validated screening exam whereby those below a population-based cutoff receive a point.⁴ Those with 3–5 points are deemed frail, and those with

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