REVIEW

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Frailty in older adults: Insights and interventions

ABSTRACT

Frailty is a state of vulnerability that carries an increased risk of poor outcomes in older adults. Common signs and symptoms are fatigue, weight loss, muscle weakness, and progressive decline in function. Frail older adults are among the most challenging for medical management. However, awareness of this syndrome and its risks can help us care for these patients more confidently and decrease their risk for adverse outcomes.

KEY POINTS

Frail older adults are less able to tolerate the stress of medical illness, hospitalization, and immobility.

The geriatric evaluation and management model uses an interdisciplinary team to follow the patient and manage specific issues. In the comprehensive geriatric assessment approach, the interdisciplinary team makes recommendations to the patient's primary care physician.

Acute Care for Elders hospital units are designed to prevent functional decline and improve functional independence if decline has occurred. Such units typically feature a more home-like environment; patient-centered medical care to prevent disability; and comprehensive discharge planning and management.

SOME OLDER ADULTS are frail. This is not news. The news is that we are getting better at systematically predicting who is frail and hence more vulnerable to poor health outcomes. Our understanding of the biologic basis of this vulnerability is improving, which should lead to the development of interventions to improve health outcomes in these patients.

Frailty, a progressive physiologic decline in multiple body systems, is marked by loss of function, loss of physiologic reserve, and increased vulnerability to disease and death. Frailty increases susceptibility to acute illness, falls, disability, institutionalization, and death.[1] Caring for frail older patients is challenging because they have an increased burden of symptoms, are medically complex,[1,2] and often have increased social needs.

In this review, we discuss the clinical spectrum of frailty, its potential biologic basis, and clinical interventions. A heightened awareness by physicians may help improve the quality of life for this most vulnerable subset of older adults.

FRAILTY AS A SYNDROME

Geriatricians have long been aware of a syndrome of multiple coexisting conditions, weakness, immobility, and poor tolerance to physiologic or psychologic stressors.[3] People so affected are often characterized as "frail" and are known to be more vulnerable to poor health outcomes, including disability, social isolation, and institutionalization. Although frailty is more prevalent in older people and in those with multiple medical conditions,[1,2] it can exist independently of age, disability, or

disease, and may be an independent physiologic process involving multiple systems.[1,4]

THE SPECTRUM OF FRAILTY: SAMPLE CASES

Frailty and the inherent vulnerability of frail older adults can be subtle and easily overlooked. The following examples illustrate the range in vulnerability to adverse health outcomes in frail older patients.

A 75-year-old woman with osteoarthritis and congestive heart failure lives with her son and daughter-in-law, who notice that she has been losing weight over the past year and that she often says she feels tired. Although she can perform most activities of daily living, these are becoming more difficult for her and take more time to complete. She now needs help bathing and uses a walker. Complaints of progressive dyspnea on exertion lead to hospitalization for worsening congestive heart failure. The hospital course is prolonged, complicated by acute renal failure and delirium. She is unable to return to her previous level of functioning and develops urinary incontinence. She needs help transferring to a bedside commode or chair and can no longer walk. Her daughter-in-law becomes her primary caregiver.

Frailty: loss of function and strength, increased vulnerability to sickness and death

A 75-year-old widower with hypertension and cerebrovascular disease undergoes carotid endarterectomy after a transient ischemic attack and diagnosis of significant stenosis. Over the next 3 years he is active in his church but must gradually decrease his volunteer activities because of increasing fatigue. He presents to his primary care physician with complaints of dyspnea and productive cough. He is treated as an outpatient with oral antibiotics for presumed community-acquired pneumonia, but he reports worsening fatigue and weakness and falls twice at home within the next 6 months.

A 75-year-old man has well-controlled hypertension, benign prostatic hypertrophy, and diabetes mellitus, which he manages with diet and metformin. He is active and plays golf and walks for exercise. After consultation with his urologist, he decides to undergo transurethral resection of the prostate. While in the hospital, he experiences some postoperative nausea, treated with promethazine. He also requires assistance getting to the bathroom, but he remains continent. After being sent home, he returns to all of his usual activities within 2 weeks.

DEFINITIONS OF FRAILTY

Frailty is often clinically apparent to geriatricians, especially in its end stages. However, although a number of definitions have been proposed, none is considered the gold standard.[4] Most definitions describe a freestanding syndrome marked by loss of function, strength, and physiologic reserve, and by increased vulnerability to sickness and death. Most definitions include declines in mobility, strength, endurance, nutrition, and physical activity as the clinical components,[1,5,6] and others include cognitive impairment and depression.[5,7,8]

Many definitions of physical frailty use measures of function and performance as markers of the changes in mobility and strength found in frail older adults.

Studenski et al,[8] for example, found that a measure combining gait speed, ability to rise from a chair, and balance skills independently predicted decline in function, hospitalization, and global decline in health in older patients seen in primary care. This correlation persisted even after adjusting for age, baseline functional status, a validated estimator of hospitalization, and the primary care physician's estimate of risk for decline.

Chin et al[6] compared three different definitions of frailty: inactivity plus low energy intake, inactivity plus weight loss, and inactivity plus low body mass index. In 450 independently living older men, the combination of inactivity and weight loss was the most predictive of death and functional decline over 3 years. In addition, men with this combination had poorer health profiles (self-rated and physician-rated health, number of diseases) and functional capacity (disability, grip strength, walking speed) compared with more active men whose weight was stable or who were gaining weight.

The Cardiovascular Health Study[1] tested the validity of its own definition of frailty in a prospective cohort of men and women age 65

and older. That definition was based on the concept that frailty is a syndrome with a critical mass of signs and symptoms. Subjects who had three out of five conditions (slow walking speed, poor hand grip, exhaustion, weight loss, and low energy expenditure) were at significantly higher risk for falls, disability, hospitalization, and death. These findings persisted after adjusting for health status, socioeconomic status, and disability at baseline, supporting the concept that frailty is not the same as disability or disease. Furthermore, the incidence of these outcomes increased in stepwise fashion from non-frail (no factors) to intermediate (one or two factors) to frail people (three or more factors).

Other studies used clinical information to identify those at risk for poor outcomes.

Rockwood et al[9] compiled a frailty index based on impairments in cognitive status, mood, motivation, communication, mobility, balance, bowel and bladder function, activities of daily living, instrumental activities of daily living, nutrition, and social resources, as well as a number of comorbidities. This index was found to be highly predictive of death or institutionalization.

PHYSIOLOGIC CORRELATES OF FRAILTY

Weakness and fatigue are central to almost all definitions of frailty. Sarcopenia (loss of skeletal muscle mass) is likely a key component of these symptoms. Building on models from specific diseases such as cancer or rheumatoid arthritis in which systemic weakness and fatigue are common, investigators have tested several hypotheses regarding specific physiologic systems thought to contribute to these symptoms.

Effects of endocrine changes

Changes in the endocrine system likely play a role in the accelerated decline in muscle mass and strength seen in frail older adults.[10]

In women, sex hormone levels decline fairly abruptly with the onset of menopause; in men testosterone levels also decline, but less abruptly.[11,12]

Growth hormone levels also decrease with age.[13,14] Compared with non-frail older adults, frail older adults have lower levels of the sex hormone dehydroepiandrosterone sulfate and insulin-like growth factor-1 (IGF-1), a messenger molecule stimulated by growth hormone.[15] Lower levels of IGF-1 have been shown to be associated with lower strength and decreased mobility in a cohort of community-dwelling older women.[16]

Many other hormones and nutrients, including vitamin D, have been shown to preserve muscle strength and hence may play a role in preventing or treating frailty.[17] More studies on this topic are needed.

Effects of inflammation

Markers of inflammation are also associated with the frailty syndrome. Serum levels of interleukin 6 (IL-6) and C-reactive protein have been found to be elevated in community-dwelling frail older adults.[18,19] IL-6 is strongly associated with adverse physiologic effects such as sarcopenia, weight loss, and an increased susceptibility to infection.[20]

In addition, IL-6 may contribute to anemia by directly inhibiting production of erythropoietin or by interfering with normal iron metabolism.[21] In a cohort of community-dwelling older adults, subclinical normocytic anemia was observed in those who were frail, and an inverse correlation was found between serum IL-6 and hemoglobin levels.[19]

This chronic inflammatory state likely also contributes to other hematologic effects such as activation of the clotting cascade. Indeed, frail older adults have been found to have significantly elevated levels of factor VIII, fibrinogen, and D-dimer.[18]

Frailty likely results from endocrine, inflammatory, and other changes

Interaction of systemic changes is likely

The physiologic findings and other features that characterize frailty are not likely to be the result of changes in a single system, but rather of the interaction of several systems resulting in a global process (**FIGURE 1**).

For example, the combination of low IGF-1 and high IL-6 levels in a cohort of community-dwelling older women conferred a high risk for progressive disability and death that was greater than the effect of either of these two factors alone, suggesting an additive effect.[16] Similarly, Roubenoff et al[22] showed that increased cellular production of tumor necrosis factor alpha and IL-6 and decreased

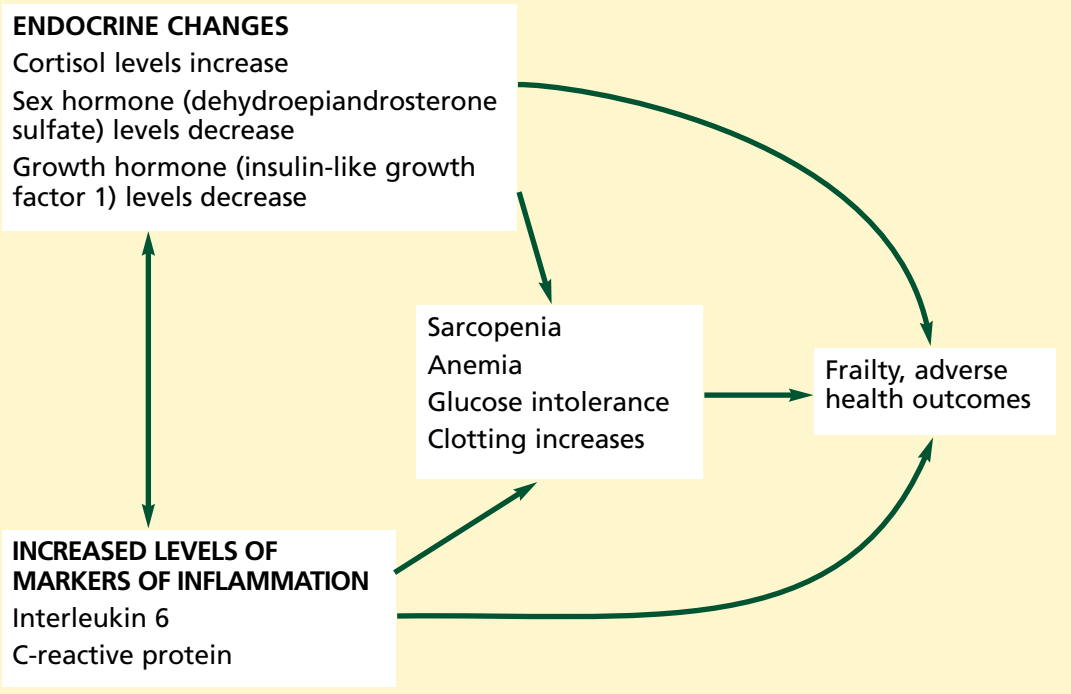

FIGURE 1. Hypothesized interactions in physiologic systems, with inflammatory and endocrine systems influencing changes in red blood cell production, muscle, clotting, and metabolism. All of these physiologic changes are then hypothesized to contribute to the symptoms experienced by frail older adults and ultimately to their known vulnerability to adverse health outcomes.

Evaluate to determine the patient's place on the spectrum of frailty

cellular production of IGF-1 were associated with increased death rates over 4 years in a cohort of community-dwelling older adults. These findings persisted after adjusting for potential confounders such as chronic disease.

INTERVENTIONS AND MODELS OF CARE

Developing interventions is a critical next step in decreasing adverse health outcomes in frail older adults. **FIGURE 2** plots potential interventions according to where the patient fits along the spectrum of frailty. We will discuss these interventions in terms of how they may be useful in the three examples presented earlier.

Exercise

Muscle mass and strength decrease with age, and the trend is even more pronounced in the frailty syndrome.[23] Numerous studies have shown that exercise is beneficial in older adults along the full spectrum of health status, even in the frailest subset. The benefits include increased mobility, enhanced performance of activities of daily living, improved gait, fewer falls, increased bone mineral density, and improvements in general well-being.[24–27]

Exercise is likely to benefit even the frailest of older adults. In a group of nursing home patients whose average age was 87, Fiatarone et al[28] showed that a program of resistance training increased muscle strength more than 100%, muscle size in the lower extremities by 3%, and gait velocity by 12%. These findings were all statistically significant compared with those of a control group, which showed either marginal increases or declines in these areas. Training was also associated with increased mobility and spontaneous physical activity.

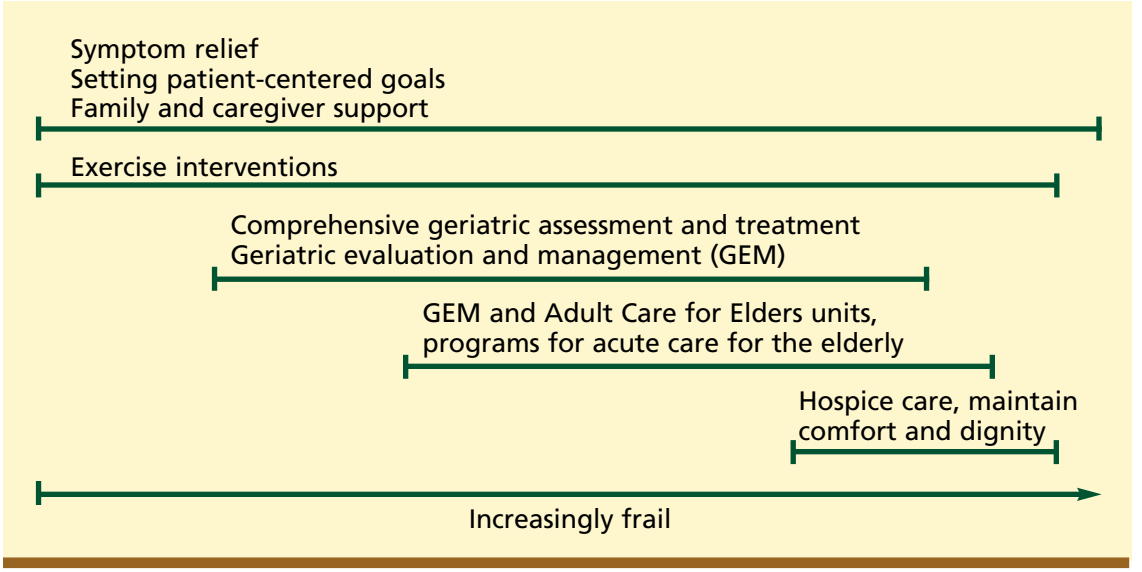

FIGURE 2. Potential interventions along the spectrum of frailty in older adults

Even low levels increase muscle strength. Although the perfect prescription for exercise in frail older adults is not known, studies have shown benefit from programs of resistance training on as few as 2 days per week.[29] Miller et al[30] found that the ability to walk about 1 mile per week was associated with a slower progression of functional limitations over a follow-up of 6 months.

Hormonal or anti-inflammatory interventions

Supplementation of sex hormones and growth hormone is a potential intervention to improve muscle mass and strength, in the hope of improving function. However, to date, no hormonal therapy is recommended for frail older adults unless a clear clinical deficiency is found.

Side effects also limit the use of hormonal therapy. For example, although testosterone replacement can increase muscle mass and strength in hypogonadal and eugonadal men, especially in combination with exercise, it may unfavorably affect lipid levels, and it has unpredictable effects on the size of the prostate gland.[31,32]

Similarly, while growth hormone replacement has been shown to be beneficial in pituitary deficiency, no study has yet proven the efficacy of growth hormone or growth hormone-releasing factor at improving function or other clinical outcomes in older adults with age-related declines.[33]

Further intervention studies are needed to determine the effectiveness and the potential harm of hormonal treatments in frail older adults.

Comprehensive geriatric assessment and treatment

Once an elderly patient is determined to be vulnerable or frail, the risk of adverse outcomes may be reduced via a comprehensive geriatric assessment with the development and implementation of an interdisciplinary treatment plan.[34] The overall goals are to improve physical and psychological function, decrease the need for nursing home placement and hospitalization, reduce the risk of death, and improve patient satisfaction.[35]

To date, no hormonal therapy is recommended for frail older adults

The interdisciplinary care team usually includes a geriatrician or other medical practitioner knowledgeable in the care of older adults, a nurse, a social worker, and an occupational or physical therapist, if available.

In some cases, the geriatric assessment interdisciplinary team follows the patient and manages his or her specific issues, a model or approach referred to as *geriatric evaluation and management*. In other cases the team makes recommendations to the patient's primary care physician, a model referred to as *comprehensive geriatric assessment*.[35] Although com-

prehensive geriatric assessment is not always targeted at frailty per se, vulnerable older adults are thought to be most likely to benefit.

Boult et al[36] conducted a randomized controlled trial of intervention with geriatric evaluation and management, specifically targeting outpatients at increased risk for repeated hospitalization. Intervention resulted in decreased health care utilization, improved depressive symptoms, and, most importantly, slowed functional decline. The study also showed the importance of ensuring that specific recommendations are implemented. In this study, the intervention group received continued primary care from the interdisciplinary team until the patient's significant issues had resolved or until a stable management plan had been established.

In general, poor implementation of recommendations from the comprehensive geriatric assessment team is the main reason that a single visit without continued management by an interdisciplinary team is less effective.[37] Patient adherence to treatment plans also determines the effectiveness of comprehensive geriatric assessment.[38] Physicians are more likely to implement the plan and patients are more likely to adhere to it if the patient and primary care physician share a collaborative relationship.[39]

A team better ensures implementation of recommended treatments

All-inclusive care for the elderly

The most frail older adults may benefit from a model known as the "program for all-inclusive care for the elderly," in which community-dwelling older adults receive primary care from an interdisciplinary team in a day clinic.[40] The team includes a practitioner knowledgeable in geriatric medicine, nurses, physical and occupational therapists, and social workers. Patient-centered services include home nursing, physical and occupational therapy, transportation, home health aide service, and adult day care. The goals are to improve function, overcome environmental challenges, and keep older adults living in their communities by preventing institutionalization. However, once participants enter the program, they receive complete long-term care and are followed until the end of their lives, even if they should eventually require placement in an assisted-living facility or nursing home.

Although it is not yet clear that these all-inclusive programs offer clear monetary or health outcome advantages over traditional care, the model provides interdisciplinary team care that has proven effective in other health care models for older adults.

The Acute Care for Elders model

Hospitalization puts frail older patients at risk of significant morbidity. Change in environment, exposure to new medications, and immobility combined with acute illness can have devastating outcomes for these vulnerable patients. Often, a decline in level of function and ability to care for oneself occurs during hospitalization and persists after discharge.[41,42] This can lead to a decrease in quality of life and an increased risk of institutionalization.

The Acute Care for Elders model is designed to prevent functional decline and improve functional independence if decline has already occurred. The model typically includes a specially designed, more home-like environment; patient-centered medical care to prevent disability; and comprehensive discharge planning and management.[43] In a randomized controlled trial of 1,531 community-dwelling adults age 70 and older, this model was shown to decrease the likelihood of decline in the ability to perform activities of daily living or a decline in nursing home placement both at hospital discharge and at 12 months, without an increase in hospital length of stay or hospital costs.[43]

CASES REVISITED: TAILORING INTERVENTIONS

For robust elderly patients, a practitioner would likely incorporate treatment of known chronic diseases with appropriate screening measures and preventive medicine.[44]

For example, the most robust of the patients in the sample cases we presented above—the active 75-year-old man with well-controlled hypertension and diabetes—was able to return to full function quickly after a brief hospitalization for an elective procedure, and is an example of a robust patient who would benefit from preventive medical care such as cancer screening and lifestyle modifi-

cation counseling (eg, smoking cessation, if applicable). However, during his brief hospitalization he required assistance to the bathroom, which may be an indication of susceptibility to future disability that could be amenable to an intervention such as exercise therapy to strengthen the lower extremities.

Moderately frail patients. The widower with hypertension and cerebrovascular disease who underwent carotid endarterectomy displays signs of frailty, especially when stressed. The two falls after his hospitalization and worsening fatigue and weakness are indications of probable further decline. This patient would be an excellent candidate for physical therapy, comprehensive geriatric assessment, and admission to an Acute Care for Elders unit in case of future hospitalization. A primary care provider knowledgeable about geriatric conditions such as falling, iatrogenic illness, polypharmacy, atypical presentation of depression, complex chronic disease care, and social networks should be able to continue to effectively manage such high-risk patients.

In moderately to severely frail patients, a good rule of thumb is "less is more," as aggressive screening for diseases may bring about unnecessary burden and risk to a patient already at great risk of further illness and death.[45]

This is most certainly the case in the first patient we described, who depends almost completely on her daughter-in-law for mobility and personal care. However, many of the mentioned interventions are also applicable. She would still likely benefit from exercise, as it may improve her level of function and independence. She would also be a good candidate for comprehensive geriatric assessment and an Acute Care for Elders unit if she should need to be hospitalized again.

However, if discussions with the patient and family indicate that the most important goals of her medical care are to maintain comfort and dignity and if her overall condition should continue to decline, the practitioner might decide not to hospitalize her for acute illness if she has indicated a desire to remain at home. She may also benefit from a program of all-inclusive care, in which she would be managed by an interdisciplinary team and would likely benefit from the added social support this model provides. Alternatively, she and her family may decide on primarily palliative and hospice services to ease symptom burden and facilitate end-of-life care.

Because the increased disability and lack of social support seen in frail older adults is a challenge to care, an interdisciplinary team approach is often required to meet their needs. As vulnerable older adults become more frail and develop more severe disease and disability, a medical care plan that is tailored to the needs of these vulnerable patients—and that keeps their personal values and goals in mind—will help maintain dignity and quality of life for these patients.

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