Review Article

Frailty: An overview

Rahmath Kalladi[1], Sujitha Elavally[2], Rojan P. M.[3], Usharani E. N.[1]

[1]Government College of Nursing, Thrissur, Kerala, India, [2]PAAET College of Nursing, Kuwait, [3]Kerala Veterinary and Animal Science University, Wayanad, Kerala, India

Abstract

Frailty is an emerging global health concern driven by population aging and rising prevalence of multimorbidity. It is a multidimensional geriatric syndrome characterized by reduced physiological reserve and increased vulnerability to stressors, leading to adverse outcomes such as disability, falls, hospitalization, and mortality. The prevalence of frailty varies across settings and populations, ranging from 4% to 16% among community-dwelling older adults to over 40% in clinical subgroups, with higher rates observed in women and the oldest-old. The etiology is multifactorial, involving sarcopenia, chronic inflammation, endocrine dysregulation, nutritional deficits, psychosocial stressors, and environmental influences. Pathophysiological mechanisms, such as inflammaging, mitochondrial dysfunction, and metabolic alterations, create a self-perpetuating cycle of decline across physiological domains. Diagnosis relies on clinical tools like the fried frailty phenotype, frailty index, and clinical frailty scale, supported by comprehensive geriatric assessment. Management requires a holistic, multidisciplinary approach that integrates exercise, nutritional optimization, medication review, fall prevention, cognitive and psychological support, and social engagement. Early identification and tailored interventions are essential to mitigate the burden of frailty, preserve independence, and improve quality of life. This review highlights current understanding of frailty's prevalence, mechanisms, clinical features, and evidence-based management strategies, underscoring the urgent need for integrated care models and context-specific interventions, particularly in low- and middle-income countries.

Keywords: Clinical frailty scale, comprehensive geriatric assessment, frailty, frailty index, frailty management, frailty phenotype, inflammaging, multimorbidity, sarcopenia

Introduction

Population aging is a pressing global health problem. By 2030, 17% of the world's population will be aged 60 or older, a figure projected to surge from 1 billion in 2020 to over 2 billion by 2050. The most rapid growth is among the oldest-old (aged ≥80 years), whose numbers are expected to triple to 420 million, placing extraordinary demands on health systems.[1] This trend underscores the challenge of multimorbidity—the coexistence of multiple chronic conditions—which drives steep healthcare costs, particularly when frailty is involved.[2,3] Biologically, aging erodes resilience, a process reflected in changes such as sarcopenia (muscle loss). These changes are accelerated by modifiable factors such as inactivity and poor nutrition[4,5] and are compounded by chronic diseases, which heighten the risk of frailty.[1]

Frailty is the clinical expression of this accumulated vulnerability, rendering individuals susceptible to adverse health outcomes.[6] It develops from interacting factors and creates a downward spiral, where recovery becomes difficult, leading to disability.[7] Thus, frailty shifts the focus from chronological age to biological resilience as the key measure of health in later life. This review provides an actionable guide for clinicians to better identify and manage frailty, improving patient outcomes. For patients and families, it reframes frailty as a manageable condition, empowering them with knowledge to maintain independence and quality of life through proactive strategies.

Address for correspondence: Mrs. Rahmath Kalladi, Government College of Nursing, Thrissur, Kerala, India.
E-mail: rahmathkalladi@gmail.com

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Definition of frailty

Frailty represents a state of critically depleted physiological reserve, fundamentally compromising an older adult's capacity to respond to physical and psychological stressors. This syndrome extends beyond simple aging to encapsulate a specific clinical vulnerability that significantly elevates the risk of adverse outcomes, including falls, hospitalization, functional decline, and mortality.[1]

While conceptual definitions emphasize this overarching vulnerability, operational tools are essential for its clinical identification. The most widely recognized model is the physical phenotype of frailty, pioneered by Fried *et al*.[7] This framework defines frailty as the presence of three or more of the following five measurable criteria: Unintentional weight loss (e.g. >5% of body weight in the past year), self-reported exhaustion, low physical activity levels, slowed walking speed, and weak grip strength

The presence of these signs indicates dysregulation across multiple physiological systems such as energy metabolism, neuromuscular function, and neuroendocrine signaling.[1] Therefore, frailty is best understood not merely as a description of high risk but as a distinct clinical syndrome signifying a state of multisystem impairment and heightened vulnerability to stressors.[1,6]

Prevalence of frailty

The prevalence of frailty is not a fixed figure but varies significantly across populations and is influenced by key demographic and clinical factors. Consistently, studies have shown that frailty is more common in older adults, women, and individuals burdened by chronic diseases.[6,8,9]

Reported prevalence rates differ substantially based on the assessment tool and population sampled. Among community-dwelling older adults (aged ≥65 years) in the United States, estimates typically range from 4% to 16%.[6,10,11] This range highlights the impact of the different diagnostic criteria. The condition is markedly more common in clinical subgroups; for instance, up to 43% of older oncology patients meet the criteria for frailty.[5] Perhaps more critical from a public health perspective is the high prevalence of pre-frailty, a precursor state identified in 28% to 44% of older adults, which represents a large population at an imminent risk of functional decline.[2,3,5]

The choice of frailty definition dramatically influences prevalence estimates. A 2012 systematic review demonstrated that models based purely on physical criteria yielded a prevalence of 9.9%. However, when the definitions incorporated psychosocial dimensions, the estimated prevalence rose to 13.6%, underscoring the multidimensional nature of the syndrome.[12] This variability is further illustrated by a large European study (SHARE), which found that applying eight different frailty scales to the same population produced prevalence rates ranging from 6% to 44%.[13] This confirms that frailty is a spectrum and that its measured prevalence is highly sensitive to the instrument used.

The prevalence escalates sharply with extreme age. Research on the "oldest-old" in the United States found that frailty affected 24% of those aged 90–94 and nearly 40% of those aged 95 and above,[14] illustrating the cumulative impact of age-associated decline.

Data on frailty from low- and middle-income countries (LMICs), such as India, are emerging and reveal a significant public health burden. Evidence from the first wave of the nationally representative Longitudinal Aging Study in India (LASI) indicates a substantial prevalence of functional impairment and frailty among older adults. The study, which assessed frailty using a multidimensional deficit accumulation approach, found that approximately 27% of Indians aged 60 and above were frail, while an additional 49% were in the pre-frail stage.[15] This means that a combined 76% of the older population showed signs of vulnerability. Studies conducted in clinical settings, which capture individuals with higher morbidity, report even more pronounced rates.[16-18] For instance, a study of older patients in a tertiary care hospital in New Delhi found a frailty prevalence of 33.2% using Fried's phenotypic criteria.[19] The variation between the community-based LASI estimate and the hospital-based figure reflects differences in the assessment tools and populations. Nonetheless, these findings consistently highlight the large and concerning burden of frailty in India, underscoring the urgent need for targeted public health strategies.

Etiology and contributing factors of frailty

Frailty is best understood not as a consequence of a single cause but as a multifactorial syndrome arising from the complex interplay of physiological, medical, psychosocial, and environmental factors. The etiology of frailty can be conceptualized within a biopsychosocial framework, where age-related physiological decline creates a baseline vulnerability that is significantly modulated by disease burden, lifestyle, and social context.[1]

The physiological substrate—Age-related decline: The foundational element of frailty is the progressive decline in physiological reserve across multiple organ systems that accompanies aging. This includes sarcopenia (loss of muscle mass and strength) and osteopenia/osteoporosis, which directly undermine mobility and resilience. These changes result from a combination of cellular senescence, reduced protein synthesis, and hormonal shifts, leading to a diminished capacity to maintain homeostasis in the face of stressors.[20]

The amplifying role of chronic disease and inflammation: The presence of chronic diseases acts as a powerful accelerator of frailty. Conditions, such as cardiovascular disease, diabetes, chronic kidney disease, and COPD, contribute to a state of chronic, low-grade inflammation ("inflammaging") characterized

by elevated levels of pro-inflammatory cytokines such as IL-6 and TNF-α. This inflammatory milieu promotes muscle catabolism, anemia, and neuroendocrine dysfunction, thereby exacerbating the core physiological deficits of frailty. Furthermore, chronic conditions often lead to reduced physical activity, creating a vicious cycle of decline.[21]

- **Lifestyle and Nutritional Drivers:** Lifestyle factors critically influence the trajectory of frailty. Physical inactivity is a primary driver, directly leading to muscle atrophy, decreased aerobic capacity, and poor balance.[22] Similarly, inadequate nutrition, particularly deficient intake of protein, vitamin D, and antioxidants, compromises muscle integrity, immune function, and energy levels, preventing recovery from illness or injury.[23] These factors are often intertwined, as poor health can lead to poor appetite and reduced mobility, further exacerbating nutritional deficits.
- **Psychosocial and Environmental Determinants:** The risk of developing frailty is profoundly shaped by psychosocial and environmental contexts. Depression, cognitive impairment, and social isolation are not merely consequences but potent risk factors for frailty.[24] These can lead to apathy, poor self-care, and reduced adherence to medical regimens. Socioeconomic factors, including low education, poverty, and poor access to healthcare, create barriers to maintaining healthy behaviors and managing chronic conditions, thereby increasing vulnerability.[25]
- **Underlying Biological and Genetic Mechanisms:** Emerging research points to the role of genetic predisposition and fundamental biological processes. Certain genetic polymorphisms related to inflammation, muscle metabolism, and cellular repair may influence an individual's susceptibility to frailty. At the subcellular level, mitochondrial dysfunction and increased oxidative stress are believed to contribute to the cumulative cellular damage that underpins frailty syndrome.[18]

Pathophysiological mechanisms of frailty

Understanding these interconnected mechanisms is paramount for moving beyond symptomatic management to developing interventions that target the root biological causes of frailty syndrome.

The pathophysiology of frailty involves a progressive loss of physiological reserve across multiple interconnected systems, leading to heightened vulnerability. This decline stems from the dysregulation of core biological mechanisms, including chronic inflammation, endocrine dysfunction, and cellular stress, which create a self-perpetuating cycle of decline.[1]

A central feature is chronic, low-grade inflammation, or "inflammaging," marked by elevated pro-inflammatory cytokines like IL-6, TNF-α, and CRP.[21] This state promotes muscle breakdown and suppresses anabolic pathways. Concurrent immunosenescence—the aging of the immune system—impairs responses to new antigens, increasing infection risk and further fueling inflammation.[26]

Endocrine dysregulation is also critical. Declines in anabolic hormones, like testosterone, growth hormone, and IGF-1, reduce muscle mass and strength. Simultaneously, dysregulation of the HPA axis leads to chronically elevated cortisol, creating a catabolic state that accelerates sarcopenia and cognitive decline.[27]

At the cellular level, mitochondrial dysfunction causes inefficient energy production and increased reactive oxygen species (ROS). The resulting oxidative stress damages cellular components, contributing to fatigue, weakness, and impaired tissue repair.[20]

Metabolic alterations, particularly insulin resistance and dyslipidemia, are common. These shifts promote an unfavorable body composition—increased visceral fat and loss of lean mass—which worsens both metabolic and inflammatory dysfunction.[28]

These pathways interact synergistically. For example, inflammation can induce insulin resistance, while mitochondrial dysfunction amplifies oxidative stress. This interplay creates a vicious cycle where decline in one system accelerates dysfunction in others, explaining the disproportionate functional decline seen after minor stressors. Understanding these mechanisms is crucial for developing interventions that target the root causes of frailty.

Clinical presentation, identification, and burden of frailty

Frailty is a recognizable clinical syndrome of multisystem impairment, marked by a decline in robustness and increased vulnerability. Its identification requires a holistic assessment, looking beyond individual diseases to identify a pattern of diminished physiological reserve.[7]

The most salient features include physical decline, such as diminished muscle strength (dynapenia), profound fatigue, and markedly slowed walking speed, and functional decline, often progressing from difficulty with instrumental activities of daily living (IADLs) to basic activities of daily living (ADLs). This picture is frequently compounded by unintentional weight loss and cognitive or mood impairment.[29]

This clinical presentation directly drives a cascade of adverse effects. The core lack of resilience translates into a high risk of functional dependence, falls, and fractures. These events often trigger a cycle of hospitalization, complications such as delirium, institutionalization, and significantly increased mortality.[30]

Comprehensive geriatric assessment and frailty-specific tools

Effective frailty management requires a meticulous, multidimensional evaluation. The comprehensive geriatric assessment (CGA) provides the essential framework, moving beyond a simple medical history to holistically appraise the physical, functional, psychological, and social domains integral to

the syndrome.[31-33] It is crucial for diagnosing frailty, identifying reversible contributors, and formulating a personalized care plan.[34]

The assessment's cornerstone is a detailed evaluation of functional capacity, encompassing basic and instrumental activities of daily living (ADLs/IADLs). This is complemented by objective measures like gait speed and grip strength, which are powerful predictors of adverse outcomes.[16] A thorough medical review covers comorbidity burden, polypharmacy, and nutritional status. Standardized cognitive and mood assessments are also conducted, given the strong bidirectional relationship between cognitive impairment, depression, and frailty.[24] Finally, evaluating psychosocial factors and the living environment is indispensable for contextualizing vulnerability.

Within the CGA structure, specific instruments operationalize the diagnosis. The choice of tool depends on the clinical setting and goal.[35,36] The two principal paradigms are the physical phenotype model and the deficit accumulation model. The fried frailty phenotype, a key example of the former, defines frailty by the presence of three or more of five physical criteria: unintentional weight loss, exhaustion, low activity, slowness, and weakness.[7] While valuable for research, its reliance on performance measures can limit clinical feasibility. Simpler tools, like the FRAIL scale, offer practical alternatives for rapid screening in primary care.[37]

The second paradigm, the deficit accumulation model, is exemplified by the frailty index (FI). It quantifies frailty as a continuous variable based on the proportion of accumulated health deficits.[7] The FI is a robust predictor of mortality but requires extensive data. Bridging these models is the clinical frailty scale (CFS), which uses clinical judgement to categorize patients on a nine-point scale, providing a rapid global assessment highly useful in acute care for prognostic stratification.[38] For holistic screening, tools, like the Groningen Frailty Indicator (GFI) and the PRISMA-7 questionnaire, incorporate physical, cognitive, and psychological domains, thereby facilitating holistic care planning.[39,40]

Management of frailty

Frailty is increasingly recognized as a multidimensional geriatric syndrome characterized by reduced physiological reserve, increased vulnerability to stressors, and a higher risk of disability, hospitalization, and mortality. It significantly impairs independence and quality of life in older adults, making its management a global priority.[41] Because frailty involves interconnected domains, including physical, nutritional, cognitive, psychosocial, and medical factors, its management must adopt a holistic and individualized approach.

Comprehensive assessment

The cornerstone of frailty management is an early and comprehensive assessment. Tools, such as the Fried's frailty phenotype and the clinical frailty scale, allow clinicians to determine severity and guide personalized interventions.[42] A multidimensional evaluation, covering physical function, cognition, comorbidities, and social support, ensures a targeted care plan.

Physical activity and exercise

Exercise is one of the most effective interventions for treating frailty. Age-related sarcopenia accelerates weakness and functional decline; however, research has shown that resistance, balance, and aerobic training improve strength, mobility, and cardiovascular health.[43] Even moderate activity enhances independence and reduces the risk of falls while supporting psychological well-being. Exercise prescriptions should be tailored, progressive, and safe, with supervision as necessary.

Nutritional optimization

Nutritional support is equally important. Older adults with frailty frequently experience weight loss and malnutrition, which exacerbates physical decline.[44] Evidence suggests that a protein intake of 1.0-1.2 g/kg/day, alongside adequate calories, micronutrients, and hydration, supports muscle preservation and recovery.[45] Vitamin D, calcium, omega-3 fatty acids, and vitamin B12 are particularly important in this population. Oral supplements and texture-modified diets may be required in cases of difficulty swallowing or inadequate intake.

Medication review and optimization

Polypharmacy is highly prevalent among frail older adults and increases the risk of adverse drug events.[46] Regular medication reviews help identify potentially inappropriate medications (PIMs) and simplify the regimens. Tools, such as the Beers Criteria and STOPP/START guidelines, assist in identifying high-risk drugs and improving prescribing practices.[47] Medication optimization must consider comorbidities, life expectancy, and the patient's goals of care.

Fall prevention

Falls are common in frailty and can lead to serious injuries.[48] Multifactorial prevention programs that combine exercise, home safety modifications, sensory optimization, and medication review effectively reduce fall risk.[7] Appropriate footwear, mobility aids, and education for patients and caregivers also play important roles.

Cognitive and psychological support

Frailty often coexists with cognitive decline and poor mental health. Cognitive stimulation therapy, reminiscence activities, and structured training programs help preserve cognitive function. Social interaction and psychological support interventions, including mindfulness and counseling, address depression, anxiety, and loneliness.[49] Caregiver support and respite care are equally vital for the long-term sustainability of the program.

Social support and community engagement

Social networks and community involvement protect against frailty progression. Participation in community programs, peer support groups, intergenerational activities, and volunteer opportunities fosters a sense of belonging and purpose.[50] Accessible transportation and age-friendly environments are required to reduce isolation and enhance engagement.

Multidisciplinary care and advance planning

Optimal management relies on interdisciplinary collaboration among geriatricians, nurses, physiotherapists, occupational therapists, dietitians, pharmacists, and social workers. Coordinated care ensures continuity across hospitals and community settings.[51] Advance care planning respects patient autonomy by aligning interventions with individual preferences and end-of-life goals.

Conclusion

Frailty is a complex condition that requires multidimensional management. Comprehensive assessment, exercise, nutrition, medication review, fall prevention, cognitive stimulation, social engagement, and multidisciplinary coordination are the central strategies. Early identification and proactive intervention can slow the progression, enhance independence, and improve the quality of life of older adults living with frailty. Further research, particularly in low- and middle-income countries such as India, is needed to adapt evidence-based interventions to the local context.

Limitations and future recommendations

This review is limited by heterogeneous frailty definitions, a research base dominated by high-income countries, and a scarcity of longitudinal and interventional studies. Future work must prioritize standardized, practical assessment tools and large-scale studies to clarify causal pathways. Developing culturally adapted, resource-sensitive management strategies for low- and middle-income countries is essential. Ultimately, integrating frailty screening into primary care, leveraging technology, and enacting supportive policies are critical to reducing the global burden of frailty and improving outcomes for older adults.

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Conflicts of interest

There are no conflicts of interest.

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