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FRAILTY SYNDROME IN OLDER ADULTS: PATHOPHYSIOLOGY, CONSEQUENCES, AND STRATEGIES FOR PREVENTION AND TREATMENT

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ABSTRACT

Introduction: Frailty syndrome is a common geriatric condition characterized by decreased physiological reserves and increased vulnerability to stressors, leading to adverse health outcomes such as disability, hospitalization, and mortality. With the rapid aging of the global population, frailty has become a major public health challenge requiring early identification and effective preventive strategies.

Objective: The aim of this article is to summarize current evidence on the pathophysiology, clinical consequences, prevention, and management of frailty syndrome in older adults, with particular emphasis on physical activity, nutritional interventions, and multidisciplinary care.

Methods: A narrative review of the literature was conducted using peer-reviewed articles, systematic reviews, clinical guidelines, and international recommendations, including those from the World Health Organization. Studies addressing frailty assessment tools, risk factors, preventive strategies, and therapeutic interventions in community-dwelling and institutionalized older adults were analyzed.

Results: Frailty syndrome is associated with an increased risk of falls, functional decline, chronic disease progression, cognitive impairment, and mortality. Evidence indicates that regular physical activity, especially resistance and balance training, significantly reduces frailty progression and improves functional capacity. Adequate nutritional intake, particularly sufficient protein, energy, and micronutrients, plays a crucial role in preventing sarcopenia and malnutrition-related frailty. Screening tools such as the Fried phenotype, Mini Nutritional Assessment, and Malnutrition Universal Screening Tool enable early identification of at-risk individuals and facilitate timely interventions.

Conclusions: Frailty syndrome is a potentially reversible condition when identified early and managed using a comprehensive, multidisciplinary approach. Integrating physical activity, individualized nutritional strategies, and holistic geriatric care is essential for improving quality of life, maintaining independence, and reducing adverse outcomes in older adults.

KEYWORDS

Frailty Syndrome, Aging, Older Adults, Pathophysiology Of Frailty, Chronic Diseases, Mobility Disorders, Cognitive Impairment, Dementia

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Introduction

Aging is an integral part of human existence. As we age, the function of many systems and organs deteriorates, which in turn leads to general functional decline, slowing of movement and the development of cardiovascular diseases, cancer, and neurodegenerative disorders. Features of aging include genomic instability, telomere shortening, epigenetic changes, loss of proteostasis, mitochondrial dysfunction, cellular aging, stem cell depletion, and altered intercellular communication [1,2,3]. Frailty syndrome is defined as depletion of the body's physiological reserves and inability to maintain homeostasis in response to stressful stimuli from the environment, associated with aging [4,5]. One of the cornerstones of geriatric care should be early recognition of the features of frailty syndrome in the elderly, as it carries health and social consequences [6,7]. The onset of frailty is a dynamic, potentially reversible process, hence the importance of early recognition to prevent physical and mental dysfunction, falls, hospitalization and death [8]. It is assumed that frailty occurs in 7% of people over 65 years of age, in the group of 75-80 year olds in 30%, and over 80 years of age in more than 50% [9,10]. The most common are two models of frailty, which guide the diagnostic process. The most common is the model according to Fried, which treats frailty syndrome as a separate pathological process. The second model according to Rockwood assumes that it is a consequence of overlapping deficits and conditions. The model according to Fried considers five factors, of which the occurrence of three is indicative of frailty syndrome [11]. These include unintentional weight loss of 4-5 kilograms or 5% of body weight in a year (based on weight measurement), weakness (measured by handgrip strength, taking into account BMI), exhaustion and low energy levels (determined using the Center for Epidemiologic Studies Depression Scale (CES-D) [12,13], gait slowing measured by walking speed (15 ft. - approx. 4.6 m), taking into account the sex and height of the subject, reduced physical activity, assessed using a shortened version of the Minnesota Leisure Time Activity Questionnaire. The CES-D scale, originally developed to measure depressive symptoms, is commonly applied in frailty assessment to quantify exhaustion, which correlates with decreased physical resilience. The Rockwood model conceptualizes frailty as the accumulation of deficits, including chronic disease, malnutrition, disability, cognitive impairment, and social or emotional factors, which collectively disrupt homeostasis [14,15].

Materials and Methods

This narrative review was based on a literature search conducted in electronic databases, including PubMed and Google Scholar. The search strategy used the following keywords and their combinations: frailty syndrome, aging, older adults, diabetes, cardiovascular disease, falls and fractures, and nutrition.

Diagnostic criteria

Reviewing data from publications in the diagnostic process can be based on a number of criteria, which in fact are components of both models. The scales used and their results vary depending on which group of people they are applied to. It is noted that a given patient, depending on the scale used, may be classified into different groups [16]. Some of the most commonly used tools for diagnosing frailty syndrome will be presented below. The Fried criteria take into account the five factors mentioned above. If a patient meets 1–2 criteria, they are classified at risk for frailty syndrome, if he meets at least 3 he is classified as frail. Those without these factors are referred to as robust [17]. Another popular scale by which the risk of frailty can be assessed is the Frailty index (FI) developed by Rockwood, based on the Canadian Study of Health and Aging cohort study of 10000 older adults [18]. It took into account 92 factors including functional capacity, comorbidities, visual impairment, hearing impairment, laboratory test results, among others. The more factors present, the greater the risk of frailty [19].

Another tool is the Clinical Scale of Canadian Study of Health and Aging (CSHA), correlated with the frailty index, which classifies patients into 7 categories (1-high frailty, 2-good frailty, 3-good frailty, treated comorbidities, 4-partial frailty, 5-mild frailty, 6-moderate frailty, 7-severe frailty) [20]. People in groups 5-7 are classified as frail, people in groups 1-3 are classified as robust.

The Groningen Frailty Index (GFI) is used in primary care settings. It is a questionnaire with 15 questions on physical, psychological, cognitive, social problems [21]. A score of at least 4 indicates frailty syndrome. The GFI questionnaire sifts through self-reported limitations and is widely used in the Netherlands. According to data included in the study, those who scored less than 4 were older, more likely to require medical visits, mostly lived alone, had lower education, and were more likely to be female [22]. It was also proven that patients with a higher FI had a higher GFI in all spheres assessed.

A scale that has also been validated in Polish is the Triburg Frailty Indicator (TFI) [23]. It is filled out by elderly people in person. The TFI consists of two parts. Part A contains questions about 10 determinants of frailty such as gender, age, marital status, education, economic status, place of birth, lifestyle, stressful situations, chronic diseases and living environment [24]. Part B includes questions about 15 components of the frailty syndrome. The components of frailty refer to physical frailty (health status, body weight, mobility, imbalance, deterioration of vision, hearing, lack of strength in hands and physical fatigue), mental frailty (cognitive impairment, coping, depression, nervousness, anxiety), social frailty (loneliness, support from others, social relationships). Frailty syndrome is diagnosed with a total TFI score ≥ 5 [25].

The Edmonton Frail Scale assesses cognitive function (assessed by the clock-drawing test), general health status, hospitalizations, polypharmacy, functional independence, physical performance, social support, emotional status, nutritional status and continence [26]. This scale is one of several validated instruments used to assess frailty in community-dwelling older adults, as demonstrated in systematic reviews comparing frailty assessment tools. Assessment with this scale should take a maximum of 5 minutes. The score ranges from 0-17 points, where 0-5 means no frailty syndrome, 12-17 increased frailty syndrome [27].

Pathophysiology

As the aging process progresses, the function of many body systems and organs deteriorates, leading to impaired homeostasis in response to internal and external stressors [28]. Older adults exhibit reduced concentrations of growth hormone (GH) and sex hormones. Decreased GH secretion is associated with reduced synthesis of insulin-like growth factor 1 (IGF-1), which plays a crucial role in maintaining skeletal muscle mass and function, provides protection against oxidative stress, and serves as a marker of nutritional status [29].

Reduced concentrations of testosterone and estradiol negatively affect skeletal muscle mass, contributing to sarcopenia and the development of frailty syndrome. Lower levels of dehydroepiandrosterone (DHEA) are also associated with adverse effects on skeletal muscle [30]. Some studies report an association between higher DHEA concentrations and better health status in older age, as well as increased longevity. In contrast, aging is accompanied by increased concentrations of glucocorticosteroids, particularly cortisol [31].

The role of growth hormone in aging remains controversial. Some studies indicate potential benefits of GH deficiency, including prolonged lifespan, improved cognitive function, increased resistance to disease, and enhanced insulin sensitivity. Consequently, the role of GH in aging and cognitive function remains unclear [32]. Growth hormone influences anabolic processes, amino acid uptake, protein synthesis, and the synthesis of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Both GH and IGF-1 are believed to slow vascular and cerebral aging processes.

Vitamin D deficiency, which exerts multidirectional effects on the human body, plays a significant role in aging-related processes. Deficiency is associated with an increased risk of falls, fractures, osteoporosis, cardiovascular complications, and depressive disorders. Abnormal vitamin D levels may result from reduced intestinal absorption, impaired cutaneous synthesis, decreased renal and hepatic hydroxylation to the active form, and limited sun exposure [33].

Chronic low-grade inflammation plays a central role in the pathophysiology of frailty syndrome and is associated with dysfunction of the endocrine and immune systems, chronic diseases, and musculoskeletal disorders. Increased production of pro-inflammatory cytokines, particularly interleukin-6 (IL-6), a recognized biomarker of frailty syndrome, contributes to reduced skeletal muscle mass and muscle atrophy, primarily through inhibition of IGF-1 activity [34]. Elevated levels of C-reactive protein (CRP), leukocytes, neutrophils, monocytes, coagulation factor VII, fibrinogen, and D-dimer have also been observed, along with disturbances in iron metabolism and anemia [35].

The Polish PolSenior study demonstrated a significant association between increased IL-6 and CRP concentrations and poorer physical performance in older adults [36]. Age-related immune system dysfunction further contributes to reduced resistance to infections. Chronic inflammation is a well-established risk factor for cardiovascular disease, cancer, chronic kidney disease, and cognitive impairment [37], leading to multimorbidity, mobility limitations, and reduced independence in activities of daily living [38].

Emerging evidence also highlights the role of intestinal dysbiosis in inflammation and aging. A healthy gut microbiota has been shown to exert beneficial effects on metabolic, immune, and overall health in older adults [39,40].

Oxidative stress is another important mechanism implicated in the pathophysiology of frailty syndrome. Increased concentrations of reactive oxygen species (ROS) lead to damage of DNA, proteins, and lipids [41], resulting in alterations in intracellular signaling pathways, gene expression, and cellular survival mechanisms.

ROS contribute to impaired protein metabolism, telomere shortening, and apoptosis, promoting skeletal muscle damage and sarcopenia [42]. Frailty syndrome occurs more frequently in individuals with low antioxidant levels, particularly vitamins C and E, and in those with insufficient consumption of vegetables and fruits [43].

Consequences of frailty syndrome

Frailty syndrome is a dynamic, reversible process, which means that some people will experience deterioration during the follow-up period, while some people classified as frail may improve and in reclassification may be classified as pre-frail. A number of studies have shown that elderly people with frailty syndrome are more likely to be hospitalized, require more medical consultations and are more likely to be placed in nursing facilities [44]. According to Polish data, up to 50% of geriatric patients in inpatient care facilities have been diagnosed with frailty syndrome [45]. Endocrine disorders, chronic inflammation, sarcopenia, and reduced bone mineral density significantly increase the risk of falls and bone fractures, which leads to reduced mobility and loss of independence, contribute to increased frailty [46]. Reduced physical activity and fitness is a significant risk factor for falls and bone fractures, often leading to permanent disability [47]. Disruption of homeostasis and lack of normal immune response in response to even minor infections, not infrequently lead to significant deterioration of health and even death [48]. Increasing attention is being paid to the impact of frailty on the onset and treatment of cardiovascular disease and the diagnosis of subclinical cardiovascular disease. It is accepted that chronic inflammation influences the development of atherosclerosis, poorer blood pressure control, increases the risk of heart failure exacerbations, and is more likely to cause acute coronary syndromes [49]. Death is more common in patients after myocardial infarction and coronary revascularization [50]. Elderly patients with frailty syndrome are more likely to be deemed unsuitable for surgical procedures, and recovery takes longer and carries more postoperative complications. According to data from medical publications, hyperglycemia is also important, contributing to the development of frailty on the one hand, while on the other hand, the pathophysiological changes of frailty syndrome affect the faster development, unstable course and vascular and organ complications caused by diabetes [51].

In people with multimorbidity, taking multiple medications, the compensation of chronic metabolic diseases such as diabetes is not optimal. It is also worth noting hypoglycemia, which affects the deterioration of the general condition, and is often unrecognized, the symptoms of hypoglycemia are mistakenly attributed to other conditions of the body, combined with dementia[52]. A number of studies that have been conducted note the higher prevalence of cognitive impairment in frail individuals. A 3.5-year study conducted in Italy found that frailty independently of other factors has an impact on dementia in people between the ages of 65 and 84 [53,54], proving that frail people, compared to healthy people, were eight times more likely to have dementia and almost eight times more likely to have cognitive impairment [55].

Prevention and treatment

Recently, frailty syndrome has attracted a lot of interest from researchers, due to increasing life expectancy and increasing numbers of elderly people. Many studies are looking for the association of frailty with quality of life, independence, motor activity, cognitive ability and susceptibility to disease in old age. Great attention is paid to identifying susceptible individuals already at the primary care level, as many of the consequences of frailty syndrome can be prevented or even reduced [56]. Prevention of frailty syndrome is multifaceted. A key role in maintaining fitness is played by systematic, proper physical activity, which improves physical fitness, prevents sarcopenia, falls, and affects gait speed and balance [57]. After age 25, physical capacity decreases by an average of 1% per year, and after age 50, muscle mass decreases by 1-2% per year. In addition, physical activity supports the treatment of lifestyle diseases, sensitizes tissues to insulin, and has a beneficial effect on muscles. A sedentary lifestyle has an adverse effect on health. WHO recommends a minimum of 150-300 minutes of moderate physical activity or at least 75-150 minutes of vigorous activity per week for people over 65 [58].

Recommended exercise includes walking, swimming, cycling, and resistance and balance exercises. The Health ABC study examined the association of gait speed and ability to stand up from a chair, with impaired physical function. These factors were found to have adverse health effects, including disability, impact on placement of elderly people in nursing facilities, and increase mortality. Data has been presented that the inability to get up from a chair increased the risk of developing dependence on daily activities by more than twofold in 1 year in 563 community-dwelling elderly people [59].

Malnutrition is another cause that has a huge impact on the functioning of the elderly. The Universal Malnutrition Screening Tool (MUST), classifies the risk of malnutrition as low, medium or high based on three components: Body Mass Index (BMI), history of unexplained weight loss and impact of acute illness [60]. The MUST tool was developed primarily for use in the community, but has also been shown to have high predictive accuracy in hospital settings.

The Mini Nutritional Assessment (MNA) scale was developed to assess the risk of malnutrition in the elderly in home care programs, nursing homes and hospitals. It is hypothesized that it should be better at identifying frail elderly patients at risk of malnutrition because it includes physical and mental aspects of health, plus it detects the risk of malnutrition while albumin levels and BMI are still normal [61]. The MNA has predictive value for adverse health outcomes, social functioning, mortality and frequency of general practitioner (GP) visits, as well as length of hospital stay, likelihood of discharge to a nursing home and mortality. A score above 11 indicates that malnutrition is not present.

Attention is paid not only to caloric requirements, but also to nutrients. Data from the InChianti study report that low intake of more than three nutrients was associated with an increased mean number of frailty criteria [62]. A recommended intake of 25–30 kcal/kg/day. A daily energy intake of ≤ 21 kcal/kg was significantly associated with frailty. Malnutrition was significantly associated with feelings of exhaustion and muscle weakness. After adjusting for energy intake, the association remained significant for poor muscle strength, but not for feelings of exhaustion [63,64]. In addition, low intakes of protein, vitamins D, E, C and folic acid were independently associated with frailty after adjusting for energy intake [65]. The current recommendation for protein intake for all males and females aged 19 years and older is 0.8g/kg, the elderly are recommended 1–1.2 g/kg/day. Consumption of about 25-30g of protein per meal maximally stimulates muscle protein synthesis in both young and elderly people [66,67]. A diet rich in antioxidants, vegetables, fruits, vitamin D, leucine, creatine supplementation are also beneficial for aging [68].

Conclusions

Frailty syndrome, due to the multitude of factors that influence it, requires a multidisciplinary approach. It plays a key role in quality of life and involves several areas, including physical, social, and psychological domains. Self-reliance, independence, optimal management of chronic diseases, avoidance of polypharmacotherapy are increasingly important for older people. The World Health Organization recommends a holistic approach to elderly care. Focusing on only one aspect, exacerbates deficits from another area. Evidence from clinical trials is often disparate due to the variety of tools for diagnosing frailty syndrome, as well as its prevention and treatment. However, all interventions work toward a single goal of improving function and activity in older adults, preventing disease progression and complications, hospitalization rates and ultimately death.

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