Review Article

An Overview of Frailty in Elderly

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Abstract

Frailty is an ageing phenomenon and it becomes essential to understand frailty, its causes and consequences as well as the risk factors that will enable us to plan appropriate interventions to target elderly who are at risk and thus preventing them from developing frailty. Frailty is linked with multiple morbidities and it adds on to the burden of the disease on the elderly making them dependent for their basic activities of daily living further deteriorating their overall quality of life. Limited studies have been done to determine association of frailty with nutritional status in the western countries, but in developing countries like India, where the elderly population is increasing at a faster pace; there is a dearth of information regarding the prevalence rates and the associated risk factors. This article attempts to provide an overview of frailty in elderly which may help create awareness among the older age groups and in focusing the attention of the healthcare providers in preventing this phenomenon to reduce the health care costs in our country.

Keywords: Frailty, elderly, ageing, dependency, disability, sarcopenia, malnutrition

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INTRODUCTION

With ageing, many body functions decline, there is accompanying change in structure and there is a loss of lean mass and relative increase in fat mass. Earlier these were considered to be essentially due to ageing; however, research over the past several decades have attributed them to be due to disuse related to age, inactivity and degenerative diseases that influence the food and nutrient intakes, food preferences and the diet patterns of older persons. The nutritional requirements also undergo considerable change with advancing age. Changes in body composition includes the changes in lean body mass, fat mass, bone health, immune function, neuro and cognitive functions, taste sensitivity, gastro-intestinal changes and difficulty in feeding.

In addition to the age-related physiological decline, there is the burden of chronic degenerative diseases in old age, e.g., hypertension, cardiovascular disorders, diabetes and cancers. In fact, multiple morbidities are very commonly found in this age group. Furthermore, there is "clustering" of multiple diseases towards the end part of life.

Definition of Frailty

Frailty is commonly used to address older persons who are at increased risk for morbidity and mortality[1]. There is a growing consensus among experts accepting frailty as a diverse syndrome that occurs in elderly individuals who are highly susceptible and at increased risk of dependency and hospitalization and decreased life expectancy.[2,3,4] There is a agreement on the fact that frailty should be defined as a composite of multiple factors that are linked to a state of reduced physiological

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reserve resulting in decreased capacity to withstand environmental stress[5].

Frailty is a geriatric syndrome characterized by weakness, weight loss, and low activity that is associated with adverse health outcomes. Frailty is usually seen as age-related, biologically vulnerable to stressors and decreased physiological reserves resulting in a limited capacity to maintain homeostasis.[3] The Fried's Phenotype criteria that are validated and widely used five-item frailty criteria for screening: exhaustion, slowed walking speed, weakness, unintentional weight loss (10 lbs/ ~4.5 Kgs in past year), and low physical activity are composite outcomes of multiple organ systems.[4]

Causes of frailty

Frailty is predisposed by ageing in combination with a number of physiological changes. Frailty is associated with age, however, not all old people turn out to be frail.[4,6,7] It is generally considered that unlike the ageing process, frailty is in some parts reversible and responsive to interventions.[7] Although ageing is mainly an internal process, a person's lifestyle contributes to the ageing process in a positive or negative way. Two physical changes that are associated with ageing may be the main cause of frailty, namely, loss of muscle mass and bone density.[4,8]

Frailty has multiple etiology and genes along with environment and lifestyle all play a pivotal role in the pathway leading to frailty. As a person ages, conditions like anorexia, inactivity/lack of exercise and depression, all can lead to frailty. Anorexia or loss of appetite results in a low body weight or weight loss whereas inactivity and the development of fear of falling lead to sarcopenia (which is interrelated with weight loss) and both of which cause frailty. Chronic morbidities like diabetes, atherosclerosis and heart disease further accelerate the development of frailty in elderly. Depression in elderly along with delirium may lead to cognitive impairment which reduces the processing speed of the brain and leads to the development of frailty. Other social factors like low education, low income (lack of purchasing power), and lack of family also play role in the development of frailty.[9]

Consequences of frailty

There is a deterioration of activities of daily living (ADL) in frail elderly leading to increased dependency causing a higher risk for admission to a nursing home or other residential healthcare facility.[10] Frailty is the precursor of functional deterioration, which leads to recurrent hospitalization, institutionalization, and death.[8,11] Frail persons have a decreased social activity[4,12] which may be due to the fact that frailty is often associated with incontinence which is a major determinant in decreasing social activity and leading to institutionalization.[12,13]

Nutrition, Sarcopenia and Frailty: A Complex Relationship

Sarcopenia is defined as the loss of skeletal muscle mass and function which is associated with age. Sarcopenia strongly influences the muscle strength, gait and balance, while it contributesto the risk of falls and frailty in older persons. The causes of sarcopenia are multifactorial and include disuse (due to physical inactivity), changes in the endocrine function, and presence of chronic diseases, inflammation, insulin resistance, and nutritional deficiencies.

Sarcopenia is also defined as a condition of lowered muscle mass and decreased muscle strength that is often age-associated, but can also be caused by clinical conditions that may be independent of the process of ageing, including chronic disease and under-nutrition.[14] To qualify for the structural definition of sarcopenia, the muscle mass needs to be at least 2SD below mean for young adults. The prevalence of sarcopenia ranges from 13-24 percent in persons aged 65 to 70 years and over 50 percent for those older than 80 years.[15]

An altered endocrine function (decrease of testosterone, estrogens and growth hormones), reduced physical activity, increase in the number of chronic illness (increase of cytokines) and inadequate nutrition play an important role in the reduction of muscle mass with aging. Sarcopenia may be prevented or treated, essentially with lifestyle interventions like exercise and nutritional supplementation or pharmacological treatment like testosterone or growth hormone replacement.[16]

With ageing, there is a decline in energy requirements; this decline results mostly from physical inactivity. In many people over 65 years of age, caloric intake may be reduced beyond the point of lowered needs, thus creating a macronutrient deficit. And in addition, the vitamin and mineral requirements do not decline with aging, so older people are at risk for deficient intake of micronutrients. Studies have shown links between frailty and low protein intake[17] as well as with deficits in vitamins D, E, and other vitamins.[18,19,20] Deficient intake of energy and protein, reduced intake of vitamin D, acute and chronic co-

morbidities and reduced physical activity are some of the extrinsic conditions leading to sarcopenia.[21,22]

Incidence of Frailty

It is mostly seen that prevalence of frailty is higher with age, in women, and in the presence of chronic disease.[4,23,24] There are limited studies that have studied the prevalence in the west and there is a dearth of information in the Indian setting. A multi-country study by WHO Study on global health and AGEing (SAGE) in samples of adults aged 50 years and older collected health and disability data in China, Ghana, India, Mexico, Russian federation and South Africa between 2007 and 2010. A deficit accumulation criterion was used to define frailty in community-dwelling older persons and in India, it was found to be 55.5%.[25] Khandelwal et al (2012) have shown frailty to be 33.2% in a sample of 250 older hospitalized patients.[26] Further studies are needed to define the prevalence of physical frailty in India and its risk factors. A systematic review recently done, investigated the prevalence of frailty in Western countries.[27] The definitions and the criteria that were used for frailty varied between the studies, which explain the considerable variation in the reported frailty prevalence rates among these countries.

Frailty and Nutrition

Malnourished older persons have vitamin deficiencies leading to impairment in cognition.[8] Morley described malnutrition as a strong determinant of frailty.[29] Cognitive dysfunction may also lead to frailty due to decreased food intake [30]. A study by Smit et al showed that serum albumin, carotenoids and Se levels are lower in frail adults as compared to their non-frail counterparts. They also found frailty to be most prevalent in obese people and lowest in underweight people. Interestingly, the energy intake (independent of the Body Mass Index) was lowest in people who were frail while it was found to be the highest in people who were not frail.[31]

Low intake of protein may be a risk factor for frailty.[17,32] A study found that the intakes of protein (both animal and plant) were found to be inversely associated with frailty.[33] Not only the amount of protein intake but its distribution over the day is thought to affect the protein anabolism, though not significant. It was also seen that the participants who were frail consumed significantly less protein in the morning but more at noon than their pre-frail and non-frail counterparts.[34]

The energy intake of ≤ 21 kcal/kg/day was found to be significantly associated with frailty and a low intake of protein; vitamins D, E, C, and folate; and having a low intake of more than three nutrients were seen to be significantly and even independently related to frailty (after adjusting for energy intake)[17], although carbohydrate, fat, protein, and dietary fibre showed no consistent associations with frailty status in another study.[35]

Mortality showed a positive association with frailty in a study, the risk being significantly higher among participants who were frail and had low serum 25(OH) D [36] while lower levels of 25(OH)D were associated with being pre-frail.[37] Wilhelm-Leen et al (2010) reported that vitamin D deficiency can cause a 3.7 time increase in the risk of frailty amongst whites and a fourfold increase in the odds of developing frailty amongst non-whites.[38] Chang et al (2010) showed similar significant results.[39]

Another study by Ensrud et al (2010) reported association between 25(OH) D level and odds of frailty at baseline (though U-shaped) and also found that the lowest risk was in women with levels 20.0-29.9 ng/ml (referent group).[40] Tajar et al (2013) also showed that among the five phenotypic criteria by Fried, only sarcopenia was not associated with the serum 25(OH) D levels against the other four.[37] A number of rural elderly experience physical disabilities and exhibit an increased risk for major health problems. The sedentariness criterion of frailty was found to be the most predominant in a sample of 572 elderly.[41]

Several large epidemiological trials have elucidated potential nutritional risk factors. The Women's Health and Aging Studies I and II (WHAS) used the definition by Fried et al (2001) for identifying frailty in a cohort of 1,002 women in 1992.[17,42] Women with lower serum carotenoids were at a slightly greater risk for frailty than those in the higher quartiles. Frail women also showed lower serum levels of alpha-tocopherol, 25-hydroxyvitamin D, selenium, and zinc. No significant differences were seen in folate or vitamins A, B_6 or B_{12} between frail and non-frail women.[42]

In an analysis of a subset of women from these studies, the strongest association demonstrated between nutrient deficiencies and frailty was for total carotenoids, betacarotene and lutein/zeaxanthin.[17]

Frailty, Muscle Atrophy and Sarcopenia

Functional muscle loss is manifested in frail elderly. This is termed as 'sarcopenia'. It may be

defined by the loss of muscle mass that is age-related and responsible for the decline in muscle strength. It plays a major role in the pathogenesis of frailty.[43] Ageing is often accompanied by anuncoupling phenomenon of the muscle cross-sectional area and the fibre strength of the muscle. With ageing, there is a build-up of fat in the muscle (termed as 'myosteatosis') which leads to a decline in muscle strength causing functional impairment and physical disability that bringschanges in gait and balance.[44] However, a subset of obese personsmay be sarcopenic (termed as 'sarcopenia obese' or "fat frail"). Inadequate physical activity and/or exercise may lead to frailty in this group of sarcopenic obese individuals.[45]

Loss of muscle with ageing is viewed as largely inevitable. After reaching a peak in adult life, skeletal muscle mass begins to decline by ≈0.5–1.0%y^{-1}at about 40 years of age. In the early stages, the loss of lean muscle mass may be gradual and gets masked by a concurrent increase in fat mass along with subtle lifestyle modifications. However, there may be a breakpoint that can occur when an individual previously asymptomatic experiences an injurious event and may get acutely/temporarily disabled.[46] In such cases, there may be accelerated loss of skeletal muscle which may facilitate a greater loss of functional capacity. Sarcopenia is associated with a high risk of disability up to 3- to 4-folds, which in turn is associated with greater socio- economic and health care spending.

A fall is seen in the level of testosterone in advancing age which is associated with a decrease in muscle strength and function. The rate of fall of testosterone with aging is nearly 1% annually.[47] Muscle mass has shown atrophy with androgen deprivation.[48] Testosterone has shown to stimulate protein synthesis and satellite cell production.[49]

The consequences of sarcopenia are continuous sense of fatigue, weakness of muscle, increased susceptibility to metabolic disorders and an increased risk of falls and fractures especially in older adults.[50] Studies suggest that loss of muscle mass can predict functional decline in older adults who are independent and those with disability.[51,52] Interestingly, Reid et al (2008) showed that the lower extremity muscle mass independently predicts functional impairment.[53] Loss of strength with aging follows a similar trajectory with loss of muscle mass in many of the physiological studies although the decline in muscle strength is sharper than the decline in muscle mass.[54]

Frailty and Cardiovascular Health

Studies have shown that frailty and chronic disease frequently co-exist[55] especially cardiovascular disease (CVD).[56,57] A systematic review of studies found that the odds ratios for prevalent frailty associated with CVD.[58] In individuals with no history of CVD, the extent of underlying cardiovascular disease may be related to frailty. A study by Newman et al showed that infarct-like lesions in the brain are also related to frailty.[11] A significant association exists between frailty and risk of incident heart failure in older individuals.[59]

Frailty also predicts mortality in patients with CVD independent of their age, the underlying disease severity, comorbidities and disability. The Cardiovascular Health Study (CHS) found a threefold increase in the presence of frailty in patients with CVD.[11] In another study of 2515 individuals, a 1 point increase (out of 5) in the frailty score was linked with a 35% increase in the risk of having a CVD. CVD and frailty, like any other chronic conditions, develop progressively over a course of time and exhibit a long subclinical phase.[60] Thus prevention and control of risk factors may play a significant role in evading adverse health outcomes. The chief modifiable risk factors include unsuitable eating habits, diabetes, hypertension, sedentary life style, and smoking.[61] Individuals between 45 and 69 years of age and with more of the CVD risk factors were found to have higher odds of developing frailty.[62] Factors that have been found to play a pivotal role in this relationship include inflammation, chronic kidney disease and low alanine transaminase.[63-65] Amore detailed and better insight on the cardiovascular risk profile of frail elderly is needed to permit better clinical management of such patients.

Frailty and Exercise

With age, there is a decline in the muscle mass and strength and it is even more distinct in frailty.[67] Studies show that exercise is favourable in older adults, even in the frailest subset benefit from it. The benefits of exercise in the elderly are numerous and include increased mobility, improved performance of activities of daily living (ADL), better gait, less incidence of falls, increased bone mineral density, and improvements in overall well-being.[68-70]

In a group of nursing home patients, Fiatarone et al (1994) found that an exercise regime comprising of resistance training significantly improved muscle strength, muscle size in the lower

extremities and gait velocity compared to a control group which showed either marginal increases or declines in these areas.[71] There is no ideal recommendation for exercise in frail elderly; however, studies have shown benefit from resistance training on as few as 2 days per week.[72] Miller et al (2000) found that walking about 1 mile per week was linked to gradual development of functional limitations over a follow-up of 6 months.[73]

Health Care of Frail elderly

Khandelwal et al (2012) reported that almost a third of hospitalized older patients are frail, anemic, with higher frequency of CHF, have cognitive impairment, stay longer in the hospital and have higher mortality.[26] Frailty is generally found in community patients with heart failure. Frailty is also a robust and autonomous predictor of emergency department visits and hospitalizations. Since frailty is potentially modifiable, it should be integrated in the clinical assessment of patients with heart failure.[74] Older persons, especially when frail, account for the highest costs in health care in developed countries.[75] This makes it absolutely obligatory that policy-makers clearly state their target population (age group, sex) when applying these rates of frailty especially in a developing country like India.

Conclusion

Frailty is an ageing phenomenon and it becomes critical in understanding the risk factors that lead to frailty in elderly. It is multifactorial and linked to various morbidities. It deteriorates the quality of life of the elderly by making them dependent in their basic activities of daily living. It is a commonly used term among the geriatricians and many studies have been conducted to understand the concept of frailty in terms of deficits as well as its physical manifestations. Recognizing frailty in elderly at an early stage will enable us to plan suitable interventions to prevent at-risk elderly from developing the syndrome. Limited studies have been done in India to comment on the risk factors to which our elderly are exposed to or to identify those risk factors that may be specific to a developing country like ours. Further studies are needed to establish relationships between frailty and nutrition, lifestyle, psychological factors, socio-economic factors etc. in India.

List of Abbreviations

SAGE: Study on global AGEing and adult health

WHO: World Health Organization

25(OH)D: 25 Hydroxy Vitamin D

WHAS: Women's Health and Ageing Studies

CVD: Cardiovascular Disease

ECG: Electrocardiography

CHS: Cardiovascular Health Study

LV: Left Ventricular

DM: Diabetes Mellitus

ALT: Alanine Transaminase

CHF: Congestive Heart Failure

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