ABSTRACT

One of the critical issues that Japan, well known for the world’s highest proportion of older adults, a super-aged society, is currently confronting is how to prevent physical disability in old age. This issue is particularly important not only from a medical perspective such as functional prognoses but also from a socio-economic angle in view of reducing the rapid rise in the cost of medical and long-term care insurance services. Functional decline in old age results not only from acute diseases but also from frailty. Such a common and important syndrome that is increasingly prevalent with advancing age can be the cause. The present article intends to review what is known about frailty, including its definition, epidemiology, and pathophysiology, and to examine potential areas of future research.

Key Words: Frailty, Elderly, Physical disability

INTRODUCTION

Japan is at the forefront of population aging. As of 2010, the number of people age 65 or over was 29.6 million, constituting 23.1 percent of the total population and marking record highs in terms of both number and percentage.1,2) This figure is the highest in the world. The speed of aging among Japan’s population is much faster than that in any of the advanced Western European countries or the U.S.A. Although the elderly population of Japan accounted for only 7.1 percent of the total population in 1970, 24 years later in 1994 it had almost doubled in scale to 14.1 percent. A comparison with other countries clearly highlights the rapid progress of demographic aging in Japan.

During society’s aging process, the proportion of dependent older people and long-term care (LTC) users are increasing in developed countries. In fact, Japan had more than 4,500,000 LTC users in 2008.3) There is a projected trend toward a reduced capacity of institutional care, which in turn will increase the number of severely disabled people living in the community. There is a great deal of public policy and clinical interest in effective and efficient ways to help disabled elderly individuals continue living in community settings.

As the number of elderly people with disabilities or requiring support in their activities of daily
living increases, the demand for LTC services has also increased. Consequently, expenditures for the LTC system are growing steadily, threatening the financial sustainability of the system. To better cope with the accelerated aging of Japanese society and the growing need for nursing care of the elderly, Japan introduced a public LTC insurance (“Kaigo Hoken”) system in 2000.\(^3\)\(^4\) This program enrolled all Japanese nationals aged 65 and older under the coverage of its insurance scheme, creating a radical change from the traditional family-based care toward the socialization of elderly care and the integration of medical care and welfare services. The aims of LTC insurance-based home care programs were not only to reduce the care burden of caregivers but also to maintain and improve functional abilities and well-being of older people, to minimize the use of institutional care services, and to reduce mortality. Under the LTC insurance program, older people who are certified as being either “assistance required” (yo-shien) or “care required” (yo-kaigo) could be provided with any community-based services depending on the certification of care need levels along with a 10% co-payment for services received.

The number of certified older adults has kept increasing, currently reaching more than 4,500,000. According to data from the Ministry of Health, Labour and Welfare, the proportion of disabled older people estimated by the rate of older adults who were judged as requiring support/care at any levels based on the certificates of LTC insurance was 9.9% when LTC insurance system was inaugurated (April, 2000). Nevertheless, certified users of LTC insurance have increased constantly, so that by 2006 the figure had increased to 16.3\(^{\circ}\).\(^5\) Accordingly, the expenditures of LTC insurance had grown in parallel with the constant increase in beneficiaries, threatening the financial sustainability of the system. To maintain that system and to increase the quality of life for older people, it is crucial to prevent disabilities and maintain the status of their daily living activities.

**REASONS FOR LONG-TERM CARE INSURANCE SERVICE USE IN OLDER PEOPLE**

As shown in Fig. 1, among the younger LTC insurance beneficiaries, stroke is a major cause of eligibility for LTC insurance (yo-kaigo) according to the Comprehensive Survey of Living Conditions conducted by the Ministry of Health, Labour and Welfare.\(^6\) However, the percentage of strokes declines as age increases. The percentages of arthropathy, cardiovascular

![Fig. 1](image-url) **Fig. 1** Major causes of long-term care insurance eligibility (yo-kaigo).
and pulmonary diseases, dementia, and fractures as causes of eligibility for LTC insurance are gradually increasing as the applicants become older. In contrast, a rapid increase was observed in the percentage of “weakness due to aging” as age increases, exceeding 50% of total applicants above age 90 or over. According to the survey, “weakness due to aging” accounts for physical dependence in 26.5% of those aged 65 or over, in 30.8% of those aged 75 or over, and 43.9% of those aged 85 or over respectively. As of 2007, it was reported that the total number of older adults certified as requiring care (yo-kaigo) was estimated to be about 4,400,000, which comes to a total of 1,170,000 who were certified as yo-kaigo due to “weakness with aging” in Japan. These data suggest that weakness as a major cause of disability in Japan’s super-aged society has already emerged.

DEFINITION OF FRAILTY

In the field of geriatric medicine, the term “frailty” has long been acknowledged among those who are engaged/involved in the care of older people. In recent years particularly since the definition has been established and become widespread, the concept of frailty has begun to draw growing attention among researchers and clinicians. Frailty may now be regarded as a geriatric syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and leading to adverse health outcomes including physical disability, falls, hospitalization, institutionalization and mortality. This would imply that a common underlying biologic process may be responsible for such a development. Concepts focusing on inflammatory processes, changes in hormonal environment and body composition support this hypothesis. This writer considers that “weakness due to aging” as described above as the major cause of yo-kaigo is equivalent to “frailty due to aging.”

Although there is still a lack of consensus on the definition of frailty, it has been generally accepted that it is distinct from disability and comorbidity, and that it characterizes the weakest and most vulnerable subset of older people due to the declining functions of their multiple organs. As the term “frail” has not yet achieved relevant vernacular meanings given its rather obscure definitions, it covers a wide range of common phenotypes including muscle weakness, bone fragility, very low body mass index, susceptibility to falling, vulnerability to trauma, vulnerability to infection, high risk of delirium, and severely diminished physical capabilities.

There are various proposed phenotypes of frailty among older people. Different definitions of frailty have included a variety of components including weakness, fatigue, weight loss, decreased balance, low levels of physical activity, impaired mobility and performance, and social withdrawal. In 2001, Fried et al. developed screening criteria for frailty as a syndrome requiring the presence of a critical mass (≥3) of the following clinical manifestations: weakness, weight loss, slow walking speed, fatigue, and low levels of activity. That phenotype has been found to predict a variety of poor clinical outcomes, including falls, physical disability, hospitalization, and mortality. Others have also reported that a combination of inactivity and weight loss is a significant predictor of disability and mortality. Based on those observations, a consensus report from a group of Italian and American geriatricians has been published advocating that any criteria used to define physical frailty be based on impairments in physiological domains that include mobility, balance, muscle strength, motor processing, cognition, nutrition status including weight change, endurance (including feelings of fatigue and exhaustion), and physical activity. The validity of those factors as components of frailty is provided by studies showing that in older, non-disabled persons, individual components are associated with geriatric syndromes such as falls, depression, urinary incontinence and functional impairment, which are all strong and
independent risk factors for disability and/or death. The investigation, treatment and care of older people who are both frail and disabled constitute much of the work of geriatric assessment units. However, despite the frequency with which frailty and disability coexist, they are in fact quite separate concepts. Disability indicates a loss of function, and may arise from accidents such as a stroke or hip fracture which therefore require sustained medical care (medical or disease models of disability, see Figs. 2A and 3). Frailty

Fig. 2 Disability models for the elderly. A: Medical (disease) model of disability. B: Frailty model of disability.

Fig. 3 Potential causes of disability and time course of death.
indicates instability and the risk of current or further loss of function, another model of disability for the elderly (frail model, see Figs. 2B and 3). Frailty is the root cause of unstable disability and an appropriate focus for prevention, rehabilitation and public health programs in old age.

FRAILTY AND SARCOPENIA

Aging is associated with significant changes in body composition, with a substantial reduction in both fat-free mass and muscle mass together with an increase in visceral fat. Sarcopenia is a syndrome characterized by a progressive and generalized loss of skeletal muscle mass and strength entailing a risk of adverse outcomes such as physical disability, poor quality of life and eventual death. Although the definition of sarcopenia remains controversial, its prevalence among older adults under the age of 70 is roughly 25% and increases to 40% in adults 80 years or older. Recently, a joint European Working Group on Sarcopenia in Older People (EWGSOP) proposed a working definition. According to EWGSOP, sarcopenia was diagnosed by the presence of low muscle mass plus either low muscle strength or low physical performance. Sarcopenia represents a risk factor for frailty, loss of independence, and physical disability. Impaired mobility resulting from muscle loss is predictive of major physical disability and mortality, and is associated with poor quality of life along with social and health care needs. Several mechanisms may be involved in the onset and progression of sarcopenia. Its possible causes are multi-factorial and can include disuse, changing endocrinal functions, chronic diseases, inflammation, insulin resistance, and nutritional deficiencies. Sarcopenia is thus rightly considered a major component in the pathway leading to frailty (Fig. 4).

CAUSES OF FRAILTY

There is currently no exact universally accepted consensus concerning the causes of frailty, which probably reflects the complexity of multiple interconnected physiological processes which become dysregulated with age. Those physiological processes/pathways include immune/inflammatory processes, neuroendocrine deregulation, mitochondrial dysfunction, hormonal changes, oxidative stress, and metabolic alterations (Fig. 4).

![Fig. 4 Conceptual framework of specific physiological system changes that may contribute to underlying vulnerability and clinical manifestations of frailty.](image)
In particular, evidence has been presented that supports a significant role of inflammation in the process of frailty. It has been suggested that during the aging process, a primary dysregulation of the mechanisms that initiate, modulate and block an inflammatory response often occurs. In fact, it has been demonstrated that among the elderly there are high plasma levels of circulating pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1 (IL-1) in older persons. Such pro-inflammatory mechanisms have also been suggested to be implicated in the development of sarcopenia due to the effects of increased cytokines on reduced muscle protein synthesis and increased protein degradation (Fig. 4).

Several age-related hormonal changes have been linked to the frailty syndrome and to its components (Fig. 4). Among the latter, the hormonal relationship with the decrease in muscle strength has received the most attention. While testosterone, growth hormone (GH) and insulin-like growth factor I (IGF-1) were most intensely studied in this context, open questions still remain with regard to the clinical relevance and the effect of replacement therapy.

While a proposal for the involvement of a molecular and physiological pathway sounds attractive, it requires further substantiation. We also need to continue studying the role of other potential components that contribute to the frailty that comes with aging. It is possible that the biological, psychological, social and environmental factors that interact across the course of life are determinants of the onset of frailty. The components of frailty may include those identified by Fried (decreased physical activity, weakness, diminished endurance, slowness, undernutrition) along with added cognitive, psychological and perhaps social components. The pathway from frailty to its adverse outcomes is also affected by various biological, psychological, social and societal modifiers.

CLINICAL ASPECTS OF FRAILTY

The concept of the presence of a frailty phase during the aging process seems to be quite important, since a considerable number of older people become physically disabled through their frailty status rather than through an abrupt onset of acute medical conditions such as strokes and hip fractures as described above. This process, unique to older individuals, is not observed in younger people. However, the working definition of frailty, based on Fried’s criteria, is only based on physical symptoms and signs. It neglects other potentially important components of the syndromes such as mood, cognitive, sensory impairments and the socioeconomic aspects of older adults’ lives. It is unsatisfactory to define frailty in the physical domain alone, since there are several other phenomena that are yet to be examined but that are commonly observed in the state of frailty.

Gill et al. have demonstrated that frailty is a dynamic process characterized by frequent transitions among frailty states (nonfrail, prefrail, and frail) over time (Fig. 2B). This may illustrate the usefulness of the frailty concept for clinical practice. Some physicians may even regard frailty as an example of the medicalization of old age and be suspicious about its prevention. However, the overall consequences are that the frail elderly are at higher risk of accelerated physical and cognitive decline, disability, and finally death. Needless to say, from a practical point of view, the early identification of a propensity to frailty would prove useful in preventing or delaying its more severe clinical consequences.

From a clinical perspective, two issues are particularly important: first, the identification of the causes of frailty and its association with chronic inflammation and other factors; and second, the development of substantiated strategies for the prevention of frailty. Interventions have been made among older adults that targeted correlates or specific components of frailty. First-line treatments
for primary frailty include an adequate diet with sufficient protein, vitamins and mineral intake, regular physical exercise such as stretching, walking, and lifting weights to preserve and increase muscle mass and strength.

CONCLUSION AND REMARKS

In conclusion there is a growing consensus that frailty is a syndrome that can be identified and measured clinically, and that it is distinct from disability and comorbidity. Frailty is a state of reduced homeostasis leading to increased vulnerability and the risk of adverse outcomes. It results from the impact of multiple system impairment with critical changes in its reserve capacities, especially in its metabolic, cardiovascular, musculoskeletal, immunologic and neurologic systems. It represents a dynamic, complex interaction of biological, psychological, cognitive and social factors as well as a complex interplay of assets and deficits.

Prevention must not only focus on diseases but also on the frailty that is crucial to the well-being of older people in a super-aged society. To establish better strategies for preventing frailty, it is also essential to improve our understanding of the causes and trajectory of frailty in the context of the demography and epidemiology of an older population.

REFERENCES