

## Age-Dependent Brain Disorders and Frailty Syndrome

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### Abstract

Frailty syndrome is the decline in physical and social capabilities by aging with concomitant health problems of malnutrition, bed-ridden and subsequent dysfunction of vital organs. Although attention tends to focus on declining physical capabilities and deteriorating nutritional status as a vicious circle of frailty, the concomitant decline in brain function should also be noted, which contributes to the reduction of physical and social activity, leads to bed-ridden status and plays a role in relatively early death. Brain disorders such as Alzheimer's and cerebrovascular dementia and Parkinson's disease are becoming more prominent as causes of death in the elderly. In addition to these clearly named diseases, there are more or less age-related declines in brain function, which must play a role in the decline of physical and social activities in frailty syndrome, and the need for interventions from a neurological perspective should be emphasised more strongly. The targets of neurological intervention in frailty syndromes are to implement a radical treatment of the underlying disease, if possible, or to increase quality of life by reducing pain and improving motivation through the appropriate use of psychotropic drugs and other symptomatic treatments, activating physical and social activities and improving appetite and nutritional status, to break out of the negative cycle of frailty. With regard to dementia, aphasia and motor disorders of the central nervous system, the appropriate assessment of their effects on physical and social activities and providing complementary functions to replace them using AI and other means will be a future goal.

**Keywords:** *Circle of Frailty; Quality of Life; Alzheimer's Disease; Parkinson's Disease; Depression*

Although temporarily (we hope) disrupted by Covid-19, in terms of broad trends, the structure of causes of death in Japan and other industrialised countries is changing dramatically with the increase in life expectancy [1,2]. The era of infectious diseases ended in the second half of the 20<sup>th</sup> century and chronic non-communicable diseases, such as hypertension, diabetes, cancer, myocardial infarction and stroke, became the central public health problem in developed countries. Prevention measures began with secondary prevention, aimed at early diagnosis through active general health checks and cancer screening, and subsequent early treatment. At the end of the 20<sup>th</sup> century, Japan began to name these non-communicable chronic diseases as lifestyle-related diseases and the emphasis of measures shifted to primary prevention, which focuses on improving lifestyle habits such as diet, smoking and exercise in the pre-disease phase. As a result, life expectancy now exceeds 80 years for both men and women, and now the inevitable deterioration of the health status of the elderly population is beginning to attract attention as a public health challenge. The main causes of death are now directly related to ageing, such as chronic heart failure, chronic kidney disease, pneumonia including aspiration pneumonia and senility as a form of multi-organ failure. This age-related deterioration of health has been given names such as geriatric syndrome [3], disuse syndrome [4], locomotive syndrome

[5], etc. from various perspectives, but the common outline is that the decline in activity capacity due to muscle weakness makes daily life difficult and results in death due to a decline in vital organ function. Fried., *et al.* [6] proposed a vicious cycle in frailty syndrome in which muscle weakness (sarcopenia) leads to reduced activity, which in turn leads to reduced appetite, which in turn leads to worsened nutritional status, which in turn leads to further sarcopenia. This has been widely accepted, and the government and other authorities have taken preventive measures, mainly by providing guidance on exercise practices and other lifestyle including diet, targeting the elderly.

Metabolic syndrome is considered the main cause of lifestyle-related diseases except for cancer, and frailty syndromes in the elderly. Metabolic syndrome is a condition of central, or visceral, obesity accompanied with two or more of dyslipidaemia, diabetes mellitus and hypertension according to the Japanese official definition, and by peripheral vascular disorders due to arteriosclerosis, leading to cardiovascular diseases such as myocardial infarction and stroke as acute diseases. In frailty syndrome as more aged conditions, chronic kidney disease, congestive cardiac hypertrophy and multiple organ failure due to other disorders of the vital organs are also resulted from long lasting metabolic syndrome.

The concepts of primary, secondary and tertiary prevention were popularised by Mausner and Kramer, who presented them clearly in the “natural history of the disease diagram” in their text [7], but in frailty syndromes, which are disorders of health that progress rather slowly with age, the concept of primary, secondary and tertiary prevention was not clearly applicable [2]. The three phases of onset, latent and clinical disease are not clearly delineated, and the measures must be a mixture of the three preventive phases. It may be appropriate to regard this as tertiary prevention if it is considered similar to rehabilitation after a stroke, expecting recovery, or at least, prevention of the worsening of health condition., or primary prevention if it is considered a type of health promotion, but it is also necessary to consider secondary prevention as it seems obvious that healthcare intervention should be based on an accurate assessment of the medical condition through examination.

With the increase in life expectancy in Japan, Alzheimer disease and other dementia are counted as major cause of death among elderly people [8]. Parkinson disease is also a brain disorder significantly contributing death of elderly people [9]. These brain disorders do not directly cause death by themselves but indirectly cause mal functioning of physical activity by lack of appropriate control, as ICD-10 adopts original causes of death rather than direct causes of death as a basis of cause of death statistics. In addition to these clearly named diseases, there are more or less age-related declines in brain function, which must play a role in the decline of physical and social activities in frailty syndrome. The sharp increase mortality rates with age of unintentional accidental death in the elderly is thought to be one consequence of the frailty syndrome, but it is obvious that, in addition to the decline in muscle strength, deterioration of the brain’s ability to make choices of behaviour and control movements also contributes significantly. Psychosis is also an important brain disorder in relation to quality of life (QoL). Depression and schizophrenia can lead to a significant reduction in QoL and even suicide, and neurosis and panic disorder can cause significant inconvenience in life.

More active interventions from a neurology perspective are, thus, needed in the prevention and treatment of frailty syndromes. There is no dispute that exercise and nutritional guidance are important to break the vicious circle of frailty, and that it is necessary to improve QoL, or at least prevent its decline. Care for dementia and active treatment of psychiatric disorders are naturally important to prevent loss of motivation for life, such as the desire to exercise and appetite, and to maintain social activities.

Extending healthy life expectancy, i.e. living longer while maintaining a high QoL, is the aim of modern healthcare, and QoL, which is essentially a subjective measure of comfort, has a positive correlation with activities of daily living (ADL), an objective measure of daily living ability. However, there are cases where discrepancies can be found between the ADL values and the ADL. When long-term care insurance was introduced in Japan, the assessment of the level of care required was based on ADL, but for patients with psychosis or

dementia, there was a large discrepancy between their objective ADL and the level of care required due to social life problems such as depression and wandering, so the assessment criteria needed to be revised. There have been cases such as that of Dr. Hawking, whose ADL was extremely low due to amyotrophic lateral sclerosis (ALS), but who, thanks to his exceptional intellectual abilities and the support of his environment, continued to engage in ambitious intellectual productive activities until his death, so that his QoL was not necessarily considered low. On the other hand, a not insignificant percentage of ALS patients who retain high intellectual capacity but significantly reduced physical capacity consider their QoL to be rather low and wish to end their lives, and in some countries euthanasia based on patient self-determination is now legally recognised.

Rapid advances in AI are making it possible for computing machines to complement the functions of the human brain. As automated driving of cars has become a reality, it is thought that computers already have enough functions to assist people in locomotion such as walking, supplement memory and provide advice on decision-making, but the problem lies in whether a good mechanism can be created to exchange information between computers and people.

The possibility of regenerating brain function has often been mentioned in recent years. Evidence for existence of undifferentiated, dividable cells remain at the level of the brain of elder people [10]. It is also becoming possible to improve personality changes through pharmacotherapy and direct brain stimulation. In recent years, the effectiveness of transcranial magnetic stimulation for depression and other conditions has been reported [11].

The targets of neurological intervention in frailty syndromes are to implement radical treatment of the underlying disease, if possible, or else, increasing QoL by reducing pain and improving motivation through the appropriate use of psychotropic drugs and other symptomatic treatment, and by activating physical and social activities and improving appetite and nutritional status, to break out of the negative cycle of frailty. For dementia, aphasia and central nervous system motor disorders, the appropriate assessment of the impact of these on physical and social motor dysfunction and the acquisition of complementary functions to replace them using AI and other means will also be a future target.

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