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Review

Perspectives on Aging and Quality of Life

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Abstract: As the world's population ages and the resulting health problems become more serious, medical and health policies in developed countries are focused on how to prevent and treat the diseases of the aging population and how to maintain their quality of life. Typical age-related diseases include deafness, cataracts, osteoarthritis, chronic obstructive pulmonary disease, diabetes mellitus, and dementia. Although the mechanisms by which these diseases develop differ, they are all caused by the accumulation of molecular and cellular damage over time. In addition, age-related diseases can cause a decline in physical and mental functions and the ability to perform activities of daily living, as well as the loss of roles in society and a sense of fulfillment in life. Therefore, there is a need for treatment and measures to accurately grasp and maintain their quality of life.

Keywords: aging; elderly; lifestyle-related diseases; quality of life

1. Introduction

Population aging has various effects on health, which in turn has a significant impact on medical care and health policy. According to the World Health Organization (WHO) [1], by 2030, one in six people worldwide will be aged 60 years or older. Furthermore, the population aged 60 years and older is expected to increase from 1 billion in 2020 to 1.4 billion in 2030. In addition, by 2050, this population is expected to double (2.1 billion). Similarly, the number of people aged 80 years and older is expected to triple between 2020 and 2050 and reach 426 million. This shift in population distribution toward older adults, known as population aging, began in high-income countries. However, it is most advanced in Japan, where 30% of the population is already aged 60 years or older. Moreover, this aging has further extended to low- and middle-income countries as well. It is estimated that by 2050, two-thirds of the world's population aged 60 and older will live in low- and middle-income countries. The effects of this aging population are causing great concern for human health, and society requires major changes. Of particular importance is the question of how to stay healthy during an extended life expectancy. This is because we desire to live in good health for as long as possible.

According to the Organization for Economic Co-operation and Development (OECD) [2], the average life expectancy after 65 years in member countries was approximately 20 years. Furthermore, it was the longest for Japanese women (25 years). The average life expectancy is increasing every year and has the advantage of providing opportunities to pursue new activities, such as further education, new careers, and long-neglected passions. However, it also leads to the emergence of several complex health conditions, commonly known as geriatric syndromes. How meaningful the remainder of one's life after aging is based on the maintenance of good health. Hence, it is important to avoid falling sick and maintain or improve one's quality of life even after one fall sick. In this paper, we aim to summarize the relationship between diseases that are affected by aging and quality of life.

2. Negative effects of aging on health

At the biological level, aging results from the accumulation of molecular and cellular damage over time. This results in a gradual decline in physical and mental capacities and an increase in the risk of disease. In addition to biological changes, retirement, loss of purpose in life, relocation to more suitable housing, and the death of a friend or partner often also result in psychological damage. In addition to physical and mental decline, social restrictions also result in a diminished quality of life.

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First, with aging, the oxygen supply to all organs and tissues and the partial pressure of oxygen in tissues decrease, resulting in hypoxia, which is thought to contribute to the development of inflammatory diseases, tumors, and cardiovascular diseases [3]. Excessive production of reactive oxygen species also leads to the destruction of nucleic acids and proteins, thereby altering cellular structures and functional outcomes. This oxidative stress causes aging and chronic degenerative diseases such as cardiovascular disease, diabetes mellitus, and chronic kidney disease, Alzheimer's disease (AD), Parkinson's disease and other neurodegenerative diseases [4].

Advanced glycation end-products (AGEs) are a general term for heterogeneous derivatives produced by non-enzymatic reactions of reducing sugars with proteins. It has recently been suggested that AGEs are involved in the pathogenesis of chronic hyperglycemia and age-related diseases. The accumulation of AGEs and their derivatives can modify proteins and could promote aging by activating several inflammatory signaling pathways via AGEs-specific receptors [5].

Shortening of telomeres, specialized nucleoprotein structures at the ends of linear chromosomes, has been linked to aging [6]. When telomeres do not function, chromosomes lose their protective structure, and fusion and breakage phenomena occur, leading to further genomic instability, such as cell arrest and death [7]. Additionally, impairment of the telomere function, coupled with impairment of the senescence/apoptosis response causes chromosomal instability [8].

In addition to the above-mentioned physiological changes, various age-related events negatively impact mental health. Loss of a role or purpose in life after retirement, the independence of children, or the death of a partner or good friend can cause psychological harm. Except for those who can retire with sufficient savings, many elderly people could experience financial hardship due to a decrease in income. It is easily perceived that these factors can negatively impact health.

3. Diseases likely to occur with age

Hearing loss, cataracts, back and neck pain, osteoarthritis, osteoporosis, chronic obstructive pulmonary disease, diabetes, depression, and dementia are common problems in older adults. Older adults are also more susceptible to lifestyle-related diseases, such as stroke, coronary artery disease, and cancer. Furthermore, as people age, they are more likely to experience multiple diseases simultaneously.

Hearing loss is the third most common chronic health condition that affects older adults. Age-related hearing loss affects one in three adults over the age of 65 years. It is caused by exogenous and endogenous factors, such as heredity, aging, and exposure to noise and toxins [9]. Abraham et al. [10] also reported the danger of hiding hearing-impaired in older adults among patients with dementia.

Cataract is the most common cause of blindness worldwide. A report stated that more than 70% of people over the age of 80 years had clinically significant age-related cataracts [11]. Another study reported that cataract patients had an increased risk of dementia if they did not undergo surgical treatment [12].

Osteoarthritis is another common cause of disease in the aging population. The joints of the lower extremities, which generally bear most of the body weight, are most often affected by osteoarthritis. In particular, knee osteoarthritis is a presumed risk factor for several medical conditions, including cardiovascular disease and falls [13]. In contrast, degenerative changes in the joints of the upper extremities are equally common, predisposing to osteoarthritis in shoulder, elbow, and hand joints [14].

Osteoporosis is a bone metabolic disease that women are typically at higher risk of developing than men. A reason for the higher incidence of osteoporosis in women is that production of estrogen by their ovaries becomes variable during perimenopause and ceases post-menopause; noting that estrogen promotes the activity of osteoblast cells that produce bone [15]. Osteoporosis is also a predisposing factor for increased risk of hip, spine, and other skeletal site fractures; the clinical impact and economic burden of such injuries have contributed towards advocacy for periodic physical examinations for older women that prompt appropriate interventions [16].

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide. The greatest risk factors include smoking and aging. COPD develops after the age of 60 years and its

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pathogenesis is characterized by fibrosis and remodeling of the small airways, accompanied by destruction of the lung parenchyma [17]. Furthermore, its pathological mechanisms include multiple aging pathways, including telomere loss, epigenetic changes, altered nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and chronic inflammation [18].

In 2021, 537 million people worldwide were affected by diabetes. Furthermore, this number is expected to increase due to population aging [19]. Diabetes mellitus is a disease associated with end-organ damage, dysfunction, and failure of the retina, kidneys, nervous system, heart, and blood vessels. Furthermore, lifestyle influences the development of diabetes, especially type 2 diabetes. Recently, research has also focused on the relationship between diabetes and age-related cognitive function. According to a large prospective study in the United States, women were more susceptible to diabetes-related cognitive decline with advancing age than men [20].

According to the National Institute on Aging-Alzheimer's Association, Alzheimer's disease assumes that β-amyloid deposition is an etiological factor. Furthermore, its neuropathological diagnosis is based on the coexistence of senile plaques (SP) and neurofibrillary tangles (NFT), designated as neuropathological changes of Alzheimer's disease. NFT are found in approximately 85% and 97% of individuals aged 65 and 80, respectively. Meanwhile, SP occurs in 30% and 50–60% at age 65 and 80, respectively. Alzheimer's disease, a disease of the aging process [21], is the most common form of age-related dementia. It is characterized by progressive memory loss and cognitive impairment. Adult hippocampal neurogenesis (AHN) is known to decline rapidly in patients with Alzheimer's disease [22]. Differences between urban and rural areas have been noted. Patients with dementia in rural areas have higher mortality rates, lower consultation rates, higher doses of antipsychotic medications, and lower use of home care services than those in urban areas [23].

A cohort study of an aging rural Japanese population found that the risk factors for decreased independence included hypertension, diabetes, being overweight, chronic kidney disease, current smoking, and past history of stroke, heart disease, and cancer [24]. In particular, stroke may be the greatest risk factor for decreased activities of daily living and quality of life, as it often results in hemiplegia. Chronic kidney and heart disease also reduce activity and inevitably worsen quality of life. Hypertension, diabetes, obesity, chronic kidney disease, smoking addiction, stroke, and heart disease are lifestyle-related diseases with causal mechanisms distinct to cellular senescence caused by aging. These diseases typically develop from high-calorie diets, lack of exercise, and excessive alcohol consumption; additionally, as life expectancy increases and such habits are prolonged, the risk of developing these diseases increases exponentially. In summary, the risk of developing lifestyle-related diseases increases with age unless lifestyle habits are changed [25–27].

4. Relationship between aging, disease, and quality of life

Aging reduces mental and physical function and decreases the ability to perform activities of daily living and health-related quality of life. Health-related quality of life is a useful outcome measure for treatment, especially in older patients whose physical and mental functions are difficult to improve once they have declined. In particular, the health state utility value is a centralized health-related quality of life score, with 0 indicating death and 1 indicating perfect health, such that scores can be compared between different diseases and across countries. Preference-based measures (PBMs) are usually used to measure the health state utility value. Of the many PBMs, the Euro QOL five-dimensional questionnaire (EQ-5D) is the most widely used PBM worldwide, because it has been translated into various languages and for which country-specific scoring algorithms are available. Several studies using the EQ-5D to study population norms in different countries have been published, as listed in Table 1. Although direct comparisons cannot be made because the country-specific algorithms used to calculate their respective QOL scores are not identical, it is noticeable that the QOL scores decline with age, regardless of country or race. Specifically, although the age ranges were not aligned because of the stated algorithmic differences between the studies, QOL scores clearly declined from age 75 in Poland [28], 71 in Norway [29], 70 in Iran [32], 75 in Bulgaria [33], and over 75 in Japan [34]. This trend was consistent across regions and races.

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Table 1. Comparison of the effects of aging in different countries using the EQ-5D.

First author (date)	Country	Study participants	Mean quality of life (QOL) scores per age category	Measurement
Golicki (2015) [28]	Poland	3,978	45–54: 0.898 55-64: 0.856 65-74: 0.813 75 +: 0.723	EQ-5D-5L
McCaffrey (2016) [29]	Australia	2,908	55–64: 0.89 65–74: 0.87 75+: 0.83	EQ-5D-5L
Stavem (2018) [30]	Norway	1,131	51–60: 0.830 61-70: 0.825 ≥ 71: 0.785	EQ-5D-3L
Yang (2018) [31]	China	650	50–59: 0.954 60-69: 0.957 70 +: 0.912	EQ-5D-5L
Emrani (2020) [32]	Iran	3,060	50–59: 0.75 60-69: 0.74 70 +: 0.67	EQ-5D-5L
Encheva (2020)[33]	Bulgaria	1,005	55-64: 0.914 65-74: 0.876 75 +: 0.789	EQ-5D-5L
Shiroiwa (2021) [34]	Japan	10,185	50–59: 0.850 60-69: 0.859 70-79: 0.826 80-89: 0.758	EQ-5D-5L
Marten (2021) [35]	Germany	290	65–69: 0.92 70-74: 0.85 75-79: 0.82 80 +: 0.68	EQ-5D-5L
Janssen (2021) [36]	European economies	21,425	45–54: 0.927 55-64: 0.885 65-74: 0.865 75 +: 0.785	EQ-5D-3L

Health data from Japan [34], which has the world's oldest population, show a clear decline in health-related QOL after the age of 80. Subjective symptoms, such as back pain, stiff shoulders, and arthritic pain, decreased their health-related QOL. Interestingly, Yang et al. [31] found that in China three aspects of the EQ-5D-5L were affected by aging: mobility, daily life, and anxiety/depression. In contrast, in a study of elderly subjects in European countries using the EQ-5D-3L [37], the scores decreased with age, but problems with pain and discomfort were the most frequent (36%-73%, any problems), and those with self-care were the least frequent (3%-31%, any problems). Next we will review the association between typical age-related diseases and health-related QOL.

Sensory organs play an important role in human life. This role does not change as we age, but unfortunately sensory function does decline.

The first of these is hearing loss. The impact of age-related hearing loss on quality of life has been reported to cause decreased communication and social and emotional interactions [38]. Communication is an important function and means of connecting people. Even if the speech function is unaffected, smooth communication will be difficult if sound recognition is impaired. For hearing loss in older adults, hearing aids were reported to improve quality of life [39]. However, hearing aids are more expensive than eyeglasses; therefore, their cost should be considered.

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Like hearing, vision is one of the most important senses in human life; used in communication, but more so for the enrichment and safety of one's life. However, this function declines with age. In most cases, farsightedness can be compensated for by wearing graduated glasses. However, the impact of cataracts and glaucoma on QOL is more severe because these conditions cannot be improved by purchasing devices such as glasses. Tan et al. [40] reported that vision-related quality of life was significantly impaired in patients with cataract with high myopia. Furthermore, it was significantly improved after cataract surgery. Surgery for cataracts has also been reported to improve vision-related quality of life in both the first and second surgeries [41].

As people age, bone and joint deformities are more likely to occur owing to bone loss and wear-and-tear of cartilage and other tissues.Osteoarthritis of the knee joint is one such condition. A large Korean study reported higher odds ratios for depressed mood, psychological distress, and suicidal ideation, in addition to mobility impairment and pain in those with osteoarthritis [42]. The EQ-5D, a utility value scale, has also been shown to be effective in assessing the impact of changes in chronic pain related to osteoarthritis on quality of life, even though it does not have excellent sensitivity or responsiveness for all diseases [43]. This study demonstrated that knee osteoarthritis sufficiently reduces health-related QOL. In summary, osteoarthritis impairs mobility, increases pain, and causes psychological stress.

The relationship between COPD and quality of life was reported to be determined by specific factors, such as gender, severity index, pulmonary function parameters, body mass index, smoking, symptoms, complications, depression, anxiety, and exacerbations [44]. Lung function declines with age and this can facilitate the onset of COPD. Persistently poor lifestyle habits, such as obesity and smoking, can also contribute to the development of COPD. COPD decreases lung capacity, which consequently reduces the extent of activities in daily life, further diminishing QOL. A study that examined the effect of lung volume reduction surgery for COPD on quality of life indices showed improvement in quality of life as measured by the 36-item Short Form Survey (SF-36) and EQ-5D [45].

Type 2 diabetes mellitus develops when a relative deficiency of insulin ensues from a genetic predisposition to insufficient insulin production, compounded by insulin resistance arising from an environmental predisposition to a poor lifestyle. In particular, an accumulation of fat in the liver and muscles due to lifestyle disorders, such as a high-fat diet, overeating, and a lack of exercise, reduces insulin function. A large European study demonstrated that frailty is more common in elderly diabetics, who tend to be depressed in addition to having low self-health ratings [46]. A study of a cohort of diabetic patients in China reported a correlation between cognitive decline and quality of life [47]. Thus, elderly patients with diabetes not only require insulin injections, but also experience a variety of adverse effects that persist throughout their lives and do not improve their QOL.

One of the most worrisome health conditions associated with aging is dementia, typified by Alzheimer's disease. Dementia is primarily characterized by negative symptoms such as memory and attention impairment. As the disease progresses, positive mental symptoms, such as delusions and personality disorders, gradually become dominant. A systematic review on the relationship between dementia and quality of life found that self-assessment by patients themselves was higher than that by caregivers or other proxies [48]. This is because as dementia progresses, the patient's self-insight declines and they lack a sense of awareness of the disease. It is also important to assess the decline in caregivers' quality of life. Furthermore, it has been found that caregivers' quality of life declines as the patient’s severity of dementia worsens [49]. When discussing the decline in health-related QOL due to dementia, it is as important to pay attention to and possibly measure the QOL of caregivers, such as spouses and children, because caring for dementia patients can be physically and emotionally demanding.

Heart disease and stroke are representative diseases caused by aging and lifestyle-related deteriorations. Both are caused by arteriosclerosis and hypertension, in which blood vessels narrow, owing to deposits of cholesterol and other substances, resulting in poor blood flow. Cerebral infarction is caused by arteriosclerosis; however, in some cases, atrial fibrillation may result in a major cardiogenic cerebral embolism. When older people suffer from heart disease or have a stroke, their

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activity level decreases and their quality of life declines. Golicki et al. [50] showed that the worst poststroke condition, as indicated by the Modified Rankin Scale, has a negative utility value. Although the QOL does not decrease significantly in patients with cardiac disease, it is reported to be lower than that in healthy subjects [51]. Although some improvement can be expected with rehabilitation, these patients do not recover to a state of perfect health as that before their illness. Therefore, a shift is being made in Japan from "medical treatment to cure," which focuses on organ-specific treatment, to "medical treatment to cure and support," which prioritizes treatment to maximize patients' quality of life [52].

5. Discussion

Numerous studies have reported the relationship between aging and various diseases, and the reduced QOL they cause. Particularly clear is the decline in the QOL due to aging in various countries, as measured by the EQ-5D, a globally accepted utility value measure. Since humans are living organisms, aging occurs naturally through cell death and degeneration. These cellular changes lead to muscle weakness and joint damage that impede autonomy in daily life. Additionally, cellular degeneration occurs in nerve cells, leading to a decline in cognitive and mental functions that consequently causes a variety of problems in daily life.

Natural aging not only reduces QOL but also makes people more susceptible to various diseases. Although there are various causes for this, such as heredity, living environment, and lifestyle, this is a reality that occurs for most people.

Therefore, in an aging society, preventive measures are important to delay disease progression as much as possible. In Japan, where the population is aging more than anywhere else in the world, there are measures to prevent long-term care [53]. They aim to maintain and improve physical, oral, and cognitive functions, many of which are implemented at the municipality level. These programs, held approximately once a week, are notable for their definitive effects on improving muscle strength in the upper and lower limbs and maintaining oral function [54].

Furthermore, since poor lifestyle habits, such as unbalanced diets and lack of exercise, are likely to cause diabetes, cardiovascular, and cerebrovascular diseases, efforts have been initiated to alter such habits. To encourage exercise, the number of steps taken were calculated and points awarded using digital devices, such as the Apple Watch. Virtual reality game applications also encourage individuals to improve their exercise habits; for example, Pokémon GO, a location-based augmented reality game for smartphones, has reportedly already improved exercise habits [55].

It is a positive sign that various municipalities and companies are providing services to mitigate the decline in QOL due to aging. The challenge to combat ageing has only just begun, and future developments are expected worldwide.

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