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### Editorial

# Anti-aging medicine needs adequate perspectives including sarcopenia, dynapenia, arteriosclerosis, insulin resistance, and protein intake

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In recent years, anti-aging medicine and diabetes have attracted attention in the medical field worldwide [1]. The authors have traditionally continued medical practice and research in both areas. Among them, nutrition is characterized by the transition from the former calorie restriction (CR) to the current low carbohydrate diet (LCD) [2]. We have continued medical and social movements of developing LCD, associated with three patterns of super LCD, standard LCD, and petit LCD (including 12%, 26%, 40% of carbohydrate, respectively) [3]. Regarding exercise, the importance of muscle training has been emphasized in addition to aerobic exercise [4]. From both perspectives, protein intake in the elderly has been proved to be indispensable [5,6].

As mentioned above, continuing usual medical treatments may lead to actual anti-aging health care and extend the lives of people [7]. The life expectancy up to date has been increasing, with women aged 87.45 and men aged 81.41 (2019) in Japan. Regarding the world aging rate, the results of the United Nations (UN) World population prospects (the 2017 version) are as follows [8]. The aging rate showed Japan 26.6%, Germany 21.1%, Sweden 19.6%, France 18.9%, United Kingdom 18.1%, the United States 14.6%, South Korea 13.0%, Singapore 11.7%, and Thailand 10.6%.

Elderly people are known to be prone to frailty [9]. In general, there are three main influencing factors of frailty syndrome. 1) Physical frailty (sarcopenia, locomotive syndrome), 2) Mental frailty (cognitive dysfunction, depression), 3) Social frailty (living alone, withdrawal, poverty) [10]. In many cases, elderly people cannot move freely and need long-term care. The causes include dementia 24.8%, cerebrovascular disease 18.4%, elderly weakness 12.1%, fracture fall 10.8%, and joint disease 7.0% [11]. From the above, 77% of long-term care has been caused by frailty and arteriosclerosis.

As to the strategy for anti-aging medicine, there are two important factors. They are the prevention of arteriosclerosis and also frailty. The former, arteriosclerosis has been already begun from the early stage of the borderline pre-diabetes stage. There may be involved in four factors as follows: I) endothelial damage due to postprandial hyperglycemia, II) dyslipidemia due to insulin resistance, III) hypertension due to insulin resistance, and IV) weight gain. Hyperglycemia occurs due to this decreased insulin secretion and increased resistance. Furthermore, these processes will be promoted associated with the presence of the aging factor. There was an obvious report concerning the relationship between HbA1c levels and the frequency of dementia [12]. Regarding HbA1c for dementia ratio, they showed 3.7–5.2%

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for 10.7%, 5.3–5.7% for 10.9%, 5.8–6.9% for 11.8%, and 7.0% or more for 49.1%. Consequently, there is a clear correlation between them. Conventionally, the insulin-degrading enzyme (IDE) is known to have a higher substrate affinity for insulin than A $\beta$ . Therefore, the accumulation of amyloid  $\beta$  has been found several decades before the onset of dementia. Characteristic pathological and clinical features include accumulation of amyloid, neurodegeneration due to aggregated hyperphosphorylated protein tau, brain atrophy, memory impairment, and cognitive decline in living function [13].

The latter, the concept of sarcopenia was developed by Irwin Rosenberg [14]. The word was made from muscle (Sarx) and poor (penia). In particular, the muscle mass and strength of the lower limbs are significantly reduced. For usual male adults, muscle mass and strength usually correlate with each other. On the other hand, in the elderly, when they lose weight, they lose muscle mass associated with decreased strength to a larger extent. Even if the elderly gain weight and muscle mass, he may lose strength comparatively. One of these reasons would be the presence of dynapenia [15].

There was the Impact of Diabetes Mellitus on Dynapenia study (iDIAMOND study), which was related to sarcopenia and dynapenia [16]. Sarcopenia has been known for slow gait speed and reduced grip power associated with decreased skeletal muscle mass index. In contrast, dynapenia has been defined as low knee extension and reduced power of grip associated with normal skeletal muscle mass index. The subjects without sarcopenia or dynapenia were evaluated as robust. According to the study, elderly subjects aged  $\geq 65$  years ( $n=1328$ ) showed that sarcopenia vs dynapenia were found as follows: 42.9% vs 11.4% in T1DM, 20.9% vs 13.9% in T2DM, 12.2% vs 0.5% in robust [16]. These results suggested more frequent sarcopenia and dynapenia in diabetes than robust subjects, which might contribute to the impaired QOL and incidental falls. Furthermore, there are some differences between sarcopenia and dynapenia. Sarcopenia is often found in more than 65 years old. In contrast, dynapenia tends to be observed in around 50 years old associated with an increased risk of fall as its characteristic point.

As for dynapenia, another investigation was reported from a Canadian longitudinal study on aging [17]. The subjects were 65-86 years and M/F = 4725/4363. The evaluation was conducted by gait speed, timed up-and-go, chair rise, and balance tests. The results included the estimation method of cut-points of handgrip dynamometry. Their cut-points of men and women were found to be adequate as  $<33.1$ kg and  $<20.4$  kg, which were observed 21.5% and 24.0% in M/F prevalence rates. This study suggested the potential distinct health implications of sarcopenia and dynapenia [17].

From an anti-aging point of view, two indispensable factors include the maintenance and promotion of muscle strength and muscle mass [18]. One is nutrition in which proper protein intake is essential. The other is an adequate continuation of the exercise. The types of exercise that can promote anti-aging conditions include arm curl, push-up, pull-up, squat, leg extension, chair sitting, back kicking, and heel raising [18].

In summary, the important points are as follows: I) Aging affects bodies and minds in various manner, associated with accumulating elements of arteriosclerosis and frailty (sarcopenia, dementia, etc.), and leading to the disability status necessary for long-term care. II) Diabetes develops both arteriosclerosis and frailty. Furthermore, it may easily lead to physical disability by the presence of cerebral infarction, myocardial infarction, dementia, myopathy (sarcopenia, dynapenia), and fragility of bones. III) Insulin resistance and advanced glycation end products (AGEs) are heavily involved in the formation of these pathologies. IV) Eating habits and exercise habits that improve insulin resistance and do not accumulate AGEs are the greatest secrets of anti-aging.

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