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Sarcopenia: Nutrition and Related Diseases

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ABSTRACT

"Sarcopenia", sarcopenia is an old age syndrome, and used to describe the reduction of skeletal muscle. Initially, it was thought that sarcopenia was only a senile disease characterized by degeneration of muscle tissue. However, its cause is widely regarded as multifactorial, with neurological decline, hormonal changes, inflammatory pathway activation, declines in activity, chronic illness, fatty infiltration, and poor nutrition, all shown to be contributing factors. Skeletal muscle mass can be measured by a variety of methods, currently, the commonly used methods are dual-energy X-ray scanning (DXA), computer tomography (CT), magnetic resonance imaging (MRI), etc. Muscular skeletal disorders can also be assessed by measuring appendicular skeletal muscle (ASM), particularly muscle tissue content. At the same time, sarcopenia refers to skeletal muscle cell denervation, mitochondrial dysfunction, inflammation, hormone synthesis and secretion changes and a series of consequences caused by the above process and is a progressive loss of skeletal muscle syndrome, which can lead to the decrease of muscle strength, physical and functional disorders, and increase the risk of death. Sarcopenia is mainly associated with the aging process, but also related to other causes such as severe malnutrition, neurodegenerative diseases, and disuse and endocrine diseases associated with muscular dystrophy, and it is the comprehensive results of multi-factors, so it is difficult to define that sarcopenia is caused by a specific disease. With the aging problem of the population, the incidence of this disease is increasingly common, and seriously affects the quality of the life of the elderly. This paper reviews the etiology and pathogenesis of myopathy, screening methods and diagnosis, the influence of eating habits, etc, and hopes to provide reference for the diagnosis and treatment of this disease. At present, adequate nutrition and targeted exercise remain the gold standard for the therapy of sarcopenia.

Keywords: sarcopenia, ageing, chronic diseases, nutrients, protein intake

INTRODUCTION

The term "Sarcopenia" was first proposed by professor Irwin Rosenberg of Tufts University in the United States. The term is derived from Greek: "sarco" refers to the muscle (Greek sarX); "penia" means loss or reduction, and then, "sarcopenia" means muscle loss (Santilli, Bernetti, Mangone, & Paoloni, 2014; Oliveira & Vaz, 2015). Sarcopenia appears at the early stage of the aging process, and the mass of skeletal muscle also varies. In 1989, Irwin Rosenberg identified that sarcopenia is a natural aging phenomenon that the muscle mass and muscle strength are diminishing with the growth of age (Woong & Choi, 2012). The concept of sarcopenia is not limited to aging, almost all age levels are likely to occur. Among elderly patients, sarcopenia may be combined with the presence of a variety of causes except for age, for example, skeletal muscle waste, changes in endocrine function, some chronic wasting disease, inflammatory response, insulin resistance and nutritional deficiencies, etc. Considering current research results, in 2010, European Working Group (EwGSOP) on sarcopenia in older people defined sarcopenia as a progressive body-wide reduction in skeletal muscle fiber volume and mass, decreased skeletal muscle strength, and dysfunction (Cruz-Jentoft et al., 2010). This degenerative symptom associates with increased connective tissue and fat, and it leads to the decrease of body function and quality of life, and increases the risk of adverse events, even death (Delmonico et al., 2007). This definition takes the practical needs of clinical work into consideration, emphasizing that muscle mass (including volume and amount), skeletal muscle strength and functional decline are its main feature. Now there are 50 million patients with sarcopenia in the whole world and the number of patients is expected to be above 500 million in 2050. The population of the elderly in Korea has risen sharply. The population of 65

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years old and above is 400,000 (3.1%) in 1979, 11% in 2010, and 14.3% in 2018. The aging problem has become a social problem and has brought great pressure to social economy.

Many studies have shown that a variety of physiological changes in the elderly are increasing with age. For example, osteoporosis, which was found 50 years ago, the researchers found that with the growth of age, when the bone density decreases, the incidence of osteoporosis increases (Bijlsma, Meskers, Westendorp, & Maier, 2012), then the reduction in muscle mass can cause the morbidity of sarcopenia. Therefore, with time going, a large number of researchers around the world began to pay attention to sarcopenia. For example, there were American scholars 'Obesity Sarcopenia and Inflammatory Relations' in 2012 (Batsis et al., 2016), Japanese scholars 'white rice intake frequency, metabolic syndrome and Sarcopenia's relationship' in 2013 (Yoko Watanabe), Korean scholars, 'Relationship between Korean blood pressure and Sarcopenia' in 2014 (Park et al., 2014), Polish scholars 'BMI and Sarcopenia in 2014 (Krzymi et al., 2014) and many other related resear ches. A variety of studies have shown that sarcopenia associates with cardiovascular disease, diabetes, metabolic syndrome, insulin resistance syndrome, and life-threatening disorders. Therefore, in October 2016, the US Centers for Disease Control ranked sarcopenia as a disease. In this paper, it conducts the research from the definition of sarcopenia, diagnostic methods, associated diseases, nutrition and other aspects.

This article summaries and gets conclusion basing on the etiology, pathogenesis, screening methods, diagnosis, eating habits and other aspects of sarcopenia and hopes this thesis can help for the diagnosis and treatment of this disease and provide a reference, more importantly, make the common pay more attention to this universal age-type disease.

BODY COMPOSITION CHANGE WITH AGE

Over 30 years of age, human function begins to decline, meanwhile, muscle atrophy, and the adipose tissue increases. For the group of 35~70 years old, the function of the heart, liver, pancreas and other organs decline by 30%. For example, the muscle mass of man is 30% atrophy, and the amount of fat increases by 50%. Women's waist, hips, and thigh fats also increase. With age, changes in physical function is reflected by three points. 1. The relationship between exercise and muscle tissue. 2. With the decline of important organ function, muscle strength decreases. 3. Abdominal fat increases, heart disease, hypertension, the incidence of diabetes also increases. In addition, as the age increases, protein intake must increase in the process of aging, the formation of IGF-cortisol, testosterone, estrogen is susceptible. These hormones not only assimilate in muscle protein metabolism but also affect alienation. The reduction of IGF-cortisol in the elderly results in the increase of visceral fat and the decrease of muscle mass and bone mineral density (Moller, Copeland, & Nair, 2007). Vitamin D deficiency not only affects bone metabolism, but also associates with cardiovascular disease, diabetes, metabolic syndrome, cancer, autoimmune diseases, multiple sclerosis and other diseases (Salo & Logomarsino, 2011). Studies have shown that vitamin D and muscle are function-related, and vitamin D deficiency can lead to the increase of body shaking and the decrease of muscle strength (Lopes et al., 2012). Among the elderly population, people with high body mass index (BMI) share a very significant relationship with the incidence of muscle (Han, Tajar, & Lean, 2011).

Sarcopenia commonly occurs to the elderly, and with the growth of age, the morbidity increases, for example, the studies of Baumgartner (Lexell, 1993) and other researchers have shown for the group of 65 to 70-year-old, the incidence of sarcopenia is 13% to 24%, while in the 80-year-old population, the incidence of sarcopenia is more than 50%. Meanwhile, studies show that the incidence of sarcopenia for men is higher than women. What is more, epidemiological data shows that in the age of 20 to 80 years of age, the body fat-free weight fat free body (FFM), also known as lean body mass (LBM) in men decreases by about 18% on average, while in women, the average reduction is about 27%, and at any age level, female body LBM is significantly lower than men (Grimby & Saltin, 1983). Older people are more likely to develop sarcopenia, which may associate with abnormalities in protein metabolism, denervation of skeletal muscle, and increased oxidative stress (Di et al., 2006). In the 1990s, Castaneda et al. (1995) found that older women in the low-protein diet can occur the decline in LBM with weight loss and muscle dysfunction.

Campbell et al. (1999) found when people of high-protein

intake participate in strength training, their skeletal muscle growth is significantly higher than people of low-protein intake. The studies of Wilson & Morley (2003) show that loss of appetite and malnutrition causes not only the decrease of muscle mass but also the increase of fat mass. And this is mainly because when the malnutrition, the organism catabolizes, the protein consumption increases relatively, and the synthesis is lack, which leads to the reduction of muscle mass. For the majority of the elderly, the sense of smell and sense of taste will appear dysfunction, delayed gastric emptying or loss of appetite, which results from inadequate intake of nutrients, in addition, many clinical consumptive diseases and most malignant tumor development process competitively consume the protein in the body by different levels. These conditions are the causes of body protein synthesis and catabolism imbalance, and eventually lead to the occurrence of sarcopenia. A variety of hormones in the body can participate in protein synthesis and decomposition of the metabolic process, and the hormones which can promote protein synthesis are insulin, testosterone, growth hormone, insulin-like growth factor 1 and vitamin D, etc. The glucagon, cortisol and inflammatory mediators, etc, are to promote the degradation process of protein (Dreyer & Volpi, 2005). With age and certain disease states, such as diabetes, breast cancer, the body of the hormone levels and their sensitivity change, resulting in protein synthesis and catabolism of the body, to a certain extent, and affect the occurrence and development of the sarcopenia. For example, chronic wasting disease and systemic inflammatory response both lead to the occurrence of sarcopenia. Most of patients with cirrhosis, liver cancer, pancreatic cancer and other diseases, have the sarcopenia in varying degrees, and many researchers have found that the assessment of sarcopenia can be used as an independent prognostic factor for the disease to assess the prognosis of patients (Iritani et al., 2014).

In addition, there is a chronic, low-grade systemic inflammatory response in the mammalian body with the growth of age (Carlson et al., 2009). Systemic inflammatory response is an important factor in the aging of skeletal muscle, mainly due to the increasing levels of some proinflammatory cytokines, such as TNF-α, IL-6, C-reactive protein, etc. (Bartlett et al., 2012). There is an amount of studies about the effects of proinflammatory cytokines in the development and progression of muscular dystrophy.

Studies show that after 30 years, the human skeletal muscle volume decreases 6% every 10 years, and for the age of 40 to 60 years, skeletal muscle mass decreases by about 40%. While muscle fiber also decreases, I (slow muscle), II (fast muscle) type muscle fiber volume and muscle cell volume both decrease, especially type II muscle fiber is more pronounced (Lexell, 1993). Although skeletal muscle atrophy, decreased quality, muscle mass continue to decrease, muscle reduction in patients with adipose tissue and other non-muscle tissue decrease inconspicuously and even increased, so compared with normal people, muscle changes in patients with little weight change, and even increase, and the muscles of patients are still with characteristics of fat muscle, which is commonly named as obesity-type sarcopenia (Grimby & Saltin, 1983). And eventually it leads to the decrease of muscle power and explosive decline of the elderly.

DIAGNOSIS METHODS FOR SARCOPENIA

Skeletal muscle mass can be measured by a variety of methods, at present, the commonly used methods are dual energy X-ray scanning (DXA), computed tomography (CT), magnetic resonance imaging (MRI), etc. At the same time, it can apply to Bioelectrical Impedance Analysis (BIA) to assess the incidence of muscular dystrophy, particularly LBM (Kim & Choi, 2013).

DXA

DXA is mainly used for the measurement of bone mineral density, with the development of technology in recent years, it also begins to measure the body's soft tissue. DXA is divided into lean body and adipose tissue by the optical density of non-bone tissue, which is used in the assessment of lean tissue quality. DXA is superior to local measurement in accuracy and body measurement of human skeletal muscle mass, and is more accurate in local measurement than in other parts of the body. However, for the DXA method, there are complex operation, high cost and other shortcomings (Lu & Chen, 2014).

Sarcopenia has been lack of publicly recognized diagnostic criteria all the time, in 1998, Baumgartner et al. (1998) published a method to diagnose sarcopenia by using the height-related

muscle mass. The skeletal muscle mass (ASM) is measured with DXA. The square ratio of skeletal muscle mass (kg) to height (m) is skeletal muscle index (SMI). Sarcopenia is most likely to occur if the SMI is lower than 2 SD for healthy young people of the same sex. Recently, SMI adjusted for men <8.50 kg/m^2, women <5.75 kg/m^2 for the diagnosis (Janssen et al., 2004). The standard takes lean body mass into account, but muscle assessment only involves muscle mass, fat factors are not considered, and muscle strength and muscle function are not evaluated. The diagnostic criteria proposed by EwGsOP is consist of muscle mass, muscle strength and muscle function these three facets. Evaluation of these three elements can be divided into three stages of muscle reduction: pre-sarcopenia, only muscle mass (volume and quantity) reduction; sarcopenia, skeletal muscle mass reduction, accompanying with skeletal muscle strength or skeletal muscle dysfunction; severe sarcopenia, the presence of skeletal muscle mass reduction, muscle strength and reduced function. International Sarcopenia Consensus Conference Working Group (ISCCWG) also proposed a similar diagnostic criteria (2011): the application of DXA for muscle measurement, if the male ASM ≤7.23 kg/m^2, ASM ≤5.67 kg/m^2 women, while the pace of <1m/s, can be diagnosed for the disease of sarcopenia (Fielding et al., 2011).

CT or MRI

CT means computer tomography method, the principle of CT is that the X-ray beam through the body tissue can decline, then depend on the degree of attenuation, at last, produce the image of the corresponding parts. In fact, CT, as an effective method of measuring body composition, is the theoretical basis of different degrees of attenuation of bone, muscle and adipose tissue. Therefore, it can easily scan any part of the body of the three different tissue cross-sectional images by CT, and then measure different components of the human body. The method of MRI is similar to the CT. These two methods of measurement of human body components have a high accuracy.

Currently, CT or MRI is used to determine the quality of human skeletal muscle, including measuring the level of L3 muscle cross-sectional area (CSA) (Mitsiopoulos et al., 1998) and the mid-thigh muscle cross-sectional area (Visser et al., 2002). It is generally believed that the measurement results are lower than the reference average of more than 2 standard, it can be identified as sarcopenia. According to the relevant literature, the method to determine the reference value for muscular hypothyroidism is women ≤38.5 to 41.0, men≤ 43.75 to 52.4 (Roberts, Lowry, & Sayer, 2014).

BIA

BIA is a method of measuring water by electrical tech nology, and is a non-invasive, safe and simple measurement method. And the water content of non-fatty substances is relatively fixed. By total body water (TBW) or extracellular water (ECW), one can estimate non-fatty substances (FFW), which have only recently been extended for analysis and evaluation of human body composition. BIA can effectively measure the body's weight, fat body weight, body fat ratio, muscle morphology and other indicators. BIA is helpful to objectively assess body's physical and nutritional status. At present, there is a variety of applications on the market about the bioelectrical impedance method for the determination of human body components of the analytical instruments, and their accessibility is better, the operation is simple, the cost is also lower, However, there are also studies showing that bioelectrical impedance measurement of the results compared with DXA, etc., its consistency is still controversial. Some researchers think that the bioelectrical impedance method may underestimate adipose tissue content and overestimate muscle tissue content (Newton et al., 2005). Therefore, the accuracy of BIA is questioned.

In addition, the balance test, 4 m timed walking test, and regular sit-up test of the body physical function measurement can increase the diagnosis of muscle hypersensitivity. These tests can predict the risk of disability, and contribute to the pre-judgment of clinical sarcopenia.

SARCOPENIA RELATED DISEASES

Sarcopenia is a disease of muscle loss with age. With the increase of age, patients will have physical disorders, metabolic disorders, casualty rates, increased fat, weight loss and other symptoms. Sarcopenia and obesity can lead to the increase of metabolic dysfunction for the elderly. The important reasons for the incidence of hypertension are the increase of body fat and overweight. Hypertension is an important cause

of cardiovascular morbidity. However, many studies have shown that cardiovascular disease and metabolic syndrome are mutually associated. Most scholars believe that the reduction in muscle is one of the reasons for the obesity and cardiovascular disease. The reduction in muscle strength increases the incidence of obesity in sarcopenia and cardiovascular disease. Sarcopenia can spur the morbidity of visceral fat, inflammation, and chronic disease with the growth of age, and is also related to abdominal fat (Woong & Choi, 2012). Metabolic syndrome is an important factor in cardiovascular disease and diabetes. Kim et al. (2014) presents many negative health- related consequences of sarcopenia, including impaired energy homeostasis, risk of falls and cardiovascular disease, and subsequently higher mortality. It is becoming evident that sarcopenia has a negative impact on the healthy life of the elderly, and there also have been many investigations about sarcopenia in Korea.

The aging problem in Korea is increasing rapidly, so it is necessary to pay attention to the prevention of sarcopenia. In Leenders et al. (2013)'s studies, it was found that diabetes and myopathy are age-related diseases, and with age, diabetes, muscle mass, strength and physical activity were significantly reduced. Skeletal muscle is one of the main sites for sugar intake and storage. As age increases, the ability of muscle mitochondria shifting from catalyzing fatty acid metabolism will decline, and then accelerate obesity-related insulin resistance and glucose metabolism disorders (Park et al., 2009). While mitochondrial dysfunction, ATP synthesis can cause insufficient muscle protein synthesis. Elderly patients with type 2 diabetes mellitus (T2DM), insulin resistance is very common, and it can cause insulin or insulin-like growth factor 1 (IGF-1), so that the functions of phosphatidylinositol 3 kinase (PI3K) protein kinase system will descend and the protein synthesis will decrease, while promote the forehead transcription factor O1 (FOXO1) phosphorylation, and then phosphorylated FOXO1 will promote the expression of ubiquitin E3 ligase muscle degeneration factors (atrogin-1) and muscular ring finger protein 1 (MuRF-1) through activation of the ubiquitin proteasome system (UPS) (Wang, Hu, Du, & Mitch, 2006), eventually lead to the increase of muscle protein degradation. Myostatin (MSN) is a member of the transforming growth factor beta superfamily and a skeletal muscle growth inhibitor, insulin attenuates the up-regulation of MSN gene expression (Dutra et al., 2012). In studies of diabetic mice, the increased levels of MSN mRNA and increased levels of activin type II receptors have been observed in insulin-dependent mice (Brandt et al., 2012). The mechanism of senile type 1 diabetes mellitus and muscle reduction is not clear, and it may associate with insulin deficiency caused by reducing muscle protein synthesis.

The statistics of Kalyani et al. (2015) have shown that hyperglycemia which is measured by glycated hemoglobin (HbA1c) associates with decreased muscle function in the elderly, when the HbA1c $\geq$8%, the risk of muscle loss even the falls of the elderly will increase (Rebecca et al., 2013). Long-term hyperglycemic toxicity can lead to non-enzymatic glycosylation of many structural proteins, functional proteins and nucleic acid proteins in the body, eventually leading to the formation of irreversible advanced glycation end products (AGEs). After the bond of AGEs and endothelial receptors, it can activate and induce a series of pro-inflammatory reaction, and produce a large number of reactive oxygen species (ROS). ROS activates nuclear transcription factor kappa B (NFKB), and promotes the target cells in the injured response gene expression. AGEs accumulate in the skeletal muscle of diabetic patients which can cause the decline in muscle function (Semba et al., 2010).

DIET FOR PREVENTION AND IMPROVEMENT OF SARCOPENIA

Nutritional support, to a certain extent, can improve the quality of life of the elderly and the people who are prone to get the chronic wasting disease. Therefore, poor nutrition intake, inadequate intake of energy protein and muscle loss are highly related to the elderly who are supposed to be provided with high protein and high calorie foods to improve nutrition and functional status. Some scholars believe that the prevention of muscle sarcopenia need to add protein in the diet, daily 1.0~1.2 g/kg of protein intake divided equally into three meals (Iritani et al., 2015). For the elderly, the decrease of food intake may lead to muscle and strength decline. First, if the energy intake is adequate, but the weight reduces, this indicates the loss of muscle quality of the elderly (Nieuwenhuizen, Weenen, Rigby, & Hetherington, 2010). Second, the elderly take a small amount of nutritious food, which may

meet their nutritional needs, especially for micronutrients. The elderly who have the problem of digestion and absorption dysfunction requires a relatively low amount of food intake, but taking nutritional reasons into consideration, the nutritional quality of food intake is particularly important. Although the importance of adequate nutrition has been recognised for a long time, its contribution to muscle mass and strength has not been studied extensively and many of researches in this field are relatively new (Kaiser, Bandinelli, & Lunenfeld, 2010). A number of interventions have been studied, ranging from provision of nutritional support (Ha, Hauge, Spenning, & Iversen, 2010) to supplementation with specific nutrients (Bischoff-Ferrari et al., 2009). The nutrients which have been most consistently linked to sarcopenia and frailty in older adults are vitamin D, protein, and a number of antioxidant nutrients which include carotenoids, selenium, and vitamins E and C (Kaiser, Bandinelli, & Lunenfeld, 2010). However, there are also some evidences showing that variations in long-chain polyunsaturated fatty acid status may have important effects on muscle strength in older people (Calder, 2006). However, a number of studies have shown that nutritional support can not effectively improve muscle mass in patients with reduced muscle function and improve their state (Carlson et al., 2009; Bartlett et al., 2012). Therefore, the nutritional intervention for patients with muscle reduction need further study.

Sports on the maintenance of physiological functions have a positive effect. There are many studies having confirmed that physical exercise can significantly improve muscle mass in patients with muscle dysfunction and its function. Visser et al. (2002) found that various forms of exercise, even housework, can effectively prevent muscle reduction and atrophy. In the cohort study, it was found that the elderly take resistance training, their muscle mass and function can improve significantly, and to a certain degree, it can help to prevent from falls and decreased mobility (Liu & Latham, 2009).

Exercise also shows an effective influence on the increase of muscle strength and improvement of the physical function of the elderly (Liu & Latham, 2009). Thus, diet and exercise are interactive in the process of muscle loss, and play a certain degree of intervention to each other. Therefore, for the prevention of sarcopenia, diet combining with exercise may be more effective than a single nutrient intake. The interactive effects of diet and exercise on the function of the body is most widely studied, for example, supplements for proteins and amino acids. High protein consumption has been shown to increase muscle protein synthesis in older adults by 50%, while bind to high protein with appropriate exercise increases the synthesis of more than 100% (Symons et al., 2010). Therefore, supplementation of Vitamin D and exercise play effective roles in muscle strength and function (Bunouta et al., 2006).

Benefits of Korean Rice-based Meals

According to the National Bureau of Statistics (NSO), annual per capita rice consumption has declined from its highest level in 1972 to 134.5 kg in 1992 to 112.9 kg in 1992 and 69.8 kg in 2012. By analyzing the National Health and Nutrition Examination Survey in 2010, to determine the risk of health traits and the impact of rice consumption on nutrition for the 60-year-old, we are expected to provide health care and disease prevention to the elderly. High-carbohydrate-depleting rice in the elderly can reduce the incidence of chronic diseases, such as stroke, muscle wasting, high blood pressure, and dyslipidemia. Reduction of muscle mass in the elderly is a form of energy expenditure and a cause of visceral obesity, however, these changes are known to associate with insulin resistance and type 2 diabetes, hyperlipidemia, and hypertension in the elderly.

According to South Korean's eating habits, white rice is regarded as the staple food. National Health Nutrition Organization in 2007, 2008, 2009, using 65 years of age or older as the objective to investigate, it was found that in the carbohydrate normal population of meat, eggs, alcohol, milk and dairy products intake ratio is too high. Among them, 81% of the elderly carbohydrate intake is too high (Park, Suh, & Chung, 2014). Carbohydrate energy than the abnormal blood lipid levels can require appropriate intake of carbohydrates which can help the research of the chronic disease of the elderly and obesity. British scholars study showed eating habits and different consumption are the main reasons for the difference of muscle function. For example, if the fish intake is higher, the human intake of vitamin D and n-3 long-chain polyunsaturated fatty acids (LCPUFAs) will increase, at the same time, the muscle function will also improve (Robinson et al., 2009). The cumulative effects of nutrient deficiencies have been

described by Semba et al. (2006), in which he estimated that each additional nutrient deficiency raised the risk of frailty in older women by almost 10%. This reflects the importance of the quality of the diet for the elderly, and thus, it is supposed to ensure that the intake of various nutrients is sufficient. Compared with the evidence that links variations in nutrient intake and status to physical function, much less is known about the influence of dietary patterns and dietary quality in older age. The characteristics of healthy diet are full of sufficient fruits, vegetables, grains and fish, and healthy diet has proved to be of great help to the strength of older adults (Robinson et al., 2009). From the study data, adults are also consistent with this conclusion. For example, among women aged 42～52 years, "unhealthy" diet, characterized by higher saturated fat intakes and lower fruit and vegetable consumption, associates with greater functional limitations over a 4-year follow-up period (Tomey et al., 2008). Benefits of healthy diet and greater fruit and vegetable consumption on physical function in mid-life have also been described in women in the Whitehall study (Stafford et al., 1998), and in men and women in the Atherosclerosis Risk in Communities Study (Houston, Stevens, Cai, & Haines,. 2005). Therefore, nutrient supplementation is more effective in preventing age- related muscle mass loss.

Control of Carbohydrates: Insulin Resistance Perspective

With the increase of age, muscle mass, body fat mass and insulin resistance growth all share the close relationship. In the sarcopenia state, muscle mass, insulin resistance and obesity increase, therefore, the incidence of diabetes and metabolic syndrome also increase. In addition, decreased muscle mass, decreased basal metabolic rate and physical activity can cause dysfunction, metabolic syndrome, and cardiovascular disease, at the same time, the mortality increases (Lee et al., 2012). The known proinflammatory cytokine is associated with the regulation of insulin resistance and obesity, and fat deposition in the muscle of obesity leads to insulin resistance, whereby catabolic fats are promoted by insulin.

Increase-Protein-Intake: Effect of Protein on Muscle

About 40% of body weight is made up of skeletal muscle, and about 50% to 75% of systemic protein is in skeletal muscle, there is 1% to 2% of the muscle protein synthesis and degradation in the whole body. The process of protein renewal is very complex, mainly involving gene transcription, protein translation, protein degradation process, and mTOR is the main signal pathway of the regulation of muscle protein synthesis. Muscle contraction, insulin, essential amino acids or energy and other stimulating factors to promote protein synthesis are mainly through the mTORc 1 signal pathway (Shioi et al., 2003). In addition, the nutrients themselves, as a substrate for protein synthesis, glucose and amino acid , can also stimulate the mTORcl signaling pathway, and promote muscle protein translation, then promote muscle protein synthesis. The activation of mTORcl by hVps34, MAP4K3 and RagGTPases; The activation of mTORcl by the Akt and Tscl/2 complexes by growth factors. The activation of mTORcl by the activation of the insulin pathway. Nutrients can directly or indirectly affect the above three factors, activation of mTORcl pathway, thereby promote muscle protein synthesis. Inflammatory reaction, oxidative stress, impaired mitochondrial function, inadequate intake of energy and nutrients can cause muscle protein decomposition increase. The ubiquitination of protein is the main mechanism of protein reduction in skeletal muscle during muscle wasting. Most of the intracellular proteins are degraded by ubiquitin-proteasome pathway (UPP). Long-term bed rest, chronic heart failure, chronic, kidney disease, chronic obstructive pulmonary diseases have increased proteasome activity, thus, promote the body protein, especially promote the degradation of muscle protein. While some factors, for example, insulin may inhibit protein degradation by lowering the proteasome activity.

In addition, the amino acid or protein balance may affect the proteasome activity and inhibit the degradation of the body protein. Ubiquitin-proteasome system (UPS) is a major system for the degradation of tumor cachexia proteins, and protein degradation occurs before the loss of muscle tissue. Proteins which are ubiquitinated by ubiquitination enzymes are degraded by proteasomes. Atrogin-1 and MuRF-1 are the major ubiquitinating enzymes in skeletal muscle reduction (Bossola et al., 2003; Bossola et al., 2001).

Transforming growth factor (TGF) D and others can stimulate the transcription of Atrogin-1, MuRF-1 mRNA, synthesis of more Atrogin-1 and MuRF-1 ubiqutinase, thereby promote the degradation of protein, especially the degradation of ske-

letal muscle Protein degradation (Morley et al., 2010). Maki et al. (2012) found that branched-chain amino acids (BCAA) induce the ubiquitination of Atrogin-1 and MuRF-1 in hind limb suspension induce the decrease of muscle atrophy (HSIMA), and then inhibit the degradation of muscle protein, and help to prevent muscle loss. The incidence of sarcopenia and protein intake is related, and senile sarcopenia is associated with the elderly who have the problem of insufficient protein intake. Maki et al. (2012) reported that the daily intake of protein of 32% to 41% of women whose age is over 50 years old and 22% to 38% of men is below the recommended amount (0.89/oyster). Essential amino acids (EAA) is the main factor that stimulates muscle protein synthesis. Although early studies suggested that nutrient intake or compound amino acid intake affects the protein synthesis from 30% to 100%, but subsequent studies have shown that intake of EAA is largely responsible for this. Basic acid is the basic unit of protein nutrition and metabolism. BCAA includes leucine, isoleucine and valine, and they are required EAA for human body and are neutral amino acids. The catabolism of BCAA is mainly in skeletal muscle. All the time, BCAA has been shown to have an anti-anorectic and anthelmintic effect. In recent years, BCAA has been shown to stimulate food intake and antagonize the loss of muscle function in anorexia and weight loss, and BCAA promotes muscle synthesis through the mTOR pathway (Kimbau & Jefferson, 2006). HsIMA is a common mouse model of muscle weakness which can simulate reduction in muscle caused by long-term bed rest. Maki et al. (2012) found that BCAA to HsIMA model rats' ubiquitination enzyme Atrogin-1, MuRF-1 expression decreased, protein ubiquitination degradation is inhibited, thereby help to prevent muscle loss. Increasing protein intake is the basis for inhibition of muscle reduction, high EAA, high BCAA, especially leucine intake can promote muscle protein synthesis, and prevent from the protein degradation. The protein therapy of muscle-reduction requires a combination of exercise and other measures to stimulate muscle synthesis.

Vitamin D

Vitamin D is an important factor in regulating the balance of calcium, phosphorus and bone metabolism and is associated with a variety of diseases. At present, vitamin D deficiency has become a global public health problem. Vitamin D deficiency can affect muscle function, and lead to the decrease of muscle strength and balance, and increase the risk of fracture of the elderly. The supplementation of vitamin D can improve muscle function and reduce the occurrence of fall and fracture. The main active form of vitamin D which is after transformation in the body is 1,25-dihydroxyvitamin D,1,25 (OH) 2D. And vitamin D is an important factor in regulating the balance of calcium, phosphorus and bone metabolism. The secondary parathyroid hormone secretion induce by the lack or deficiency of vitamin D is one of the pathophysiological mechanisms of osteoporosis (Kota et al., 2002). Vitamin D deficiency not only affects bone metabolism, but also associates with cardiovascular disease, diabetes, metabolic syndrome, cancer, autoimmune diseases, multiple sclerosis and other related diseases (Ascherio, Munger, & Simon, 2010; Abdulameer et al., 2012; Antico, Tampoia, Tozzoli, & Bizzaro, 2012; Mayer et al., 2012; Lopes et al., 2012). Studies have shown that vitamin D and muscle are function-related, and vitamin D deficiency can lead to the increase of body shaking and the decrease of muscle strength. Muscle weakness, muscle contraction, and muscular diastolic dysfunction occur in a variety of vitamin D-deficient states, such as osteoporosis, malabsorption syndrome, gastrectomy, and chronic kidney disease (Visser, Deeg, & Lips, 2003; Pfeifer, Begerow, & Minne, 2002).

In a prospective cohort study, serum 25 (OH) D levels <25 nmol/L in patients with a previous history of multiple fractures had the highest risk of falling (Snijder et al., 2006). A Dutch study of older people whose age is over 65 years found significant reduction in body function over the 3-year period when serum 25 (OH) D levels were <20 nmol/L (Wicherts et al., 2007).

Recently, Ensrud et al. (2010) performed a large cohort study of osteoporotic fractures in middle-aged and older women. A cross-sectional and 6-year follow-up analysis showed that female indicators who are 25 (OH) D levels <20 nmol/ (OH) D levels between 20～30 nmol/L that the decrease of their body function has no significant change. In a prospective cohort study of older men with osteoporosis, serum 25 (OH) D levels of <20 nmol/L were independently associated with decreasing body function at baseline (Ensrud et al., 2011). In summary, cross-sectional studies and cohort studies have

shown that serum levels of 25 (OH) D <20 nmol/L, which is commonly considered as vitamin D deficiency, are associated with the decrease of body function in the elderly population and may increase the risk of falls. Vitamin D and calcium on the prevention of non-vertebral fracture is not only to increase bone strength, but alao to reduce the incidence of falls and prevent from fractures. An analysis that included 29 studies found that supplementation of calcium and vitamin D is associated with a reduced rate of hip and spine bone loss and a significant reduction in the risk of fracture (24%) in people over 50 years of age, suggesting that vitamin D and calcium (1,200 mg/d) in combination can effectively prevent and treat osteoporosis, and this amount recommended as the minimum (Tang et al., 2007). Pfeifer et al. (2000) studied 242 older women whose age is from 73 to 81 living in the communities with 25 (OH) D levels <78 nmol/L, 1,000 mg of calcium or 1,000 mg of calcium combined with 800 U of vitamin D for 12 months and discontinuation of follow-up for 8 months. The combination of vitamin D and calcium significantly reduces the risk of primary fractures (12 months: −27%; 20 months: −39%), and greatly improves quadriceps strength (+8 %), reduced body swing (+28%), and shortens the time to complete the walking-walking experiment (−11%). Glerup et al. (2000) found that women living in Denmark, muscle strength and its serum 25 (OH) D levels are significantly related.

In women with vitamin D deficiency [serum 25 (OH) levels <20 nmol/L], the maximum self-extension of the knee joint reduces by 34% compared with the Danish control group. Monthly intramuscular injection of 100,000 U ergocalciferol, daily oral administration of 1,200 g of calcium and 400 U ergocalciferol, treatment of 3 months and 6 months after the maximum muscle maximum voluntary contractility increase by 13% and 24%. Myasthenia is a common symptom in patients with vitamin D deficiency [serum 25 (OH) D levels <30 nmol/L]. Evidence suggests that body swing is an early manifestation of vitamin D deficiency-related myopathy, with the increase of serum 25 (OH) D levels <50 nmol/L). As a result, the incidence of non-vertebral fractures and falls reduces in the elderly population using vitamin D prophylaxis. Because vitamin D levels are influenced by many factors, such as age, sex, heredity, culture background, lifestyle, region and season, the standard of vitamin D status is not unified at present. Vitamin D and calcium deficiency in patients currently recommended 800 U vitamin D and 1,200 mg of calcium in combination therapy, but vitamin D levels in patients with normal vitamin D has the significance of the prevention from falls, and maintaining the normal muscle strength required for proper vitamin D levels and the effects of vitamin D and muscle function of the specific mechanism of action still need further study.

CONCLUSION

Sarcopenia is a common clinical syndrome characterized by decreased skeletal muscle mass and diminished function. It is also found in malnutrition, chronic wasting disease, malignancy, and inflammatory diseases, as well as in the elderly. Although the etiology and the pathogenesis, the diagnosis of sarcopenia are obscure, the sequel of sarcopenia, i.e. morbidity and mortality, metabolic complications, are major public health problem. Particularly, aged people in Korea are increasing rapidly more than expected therefore, the interest of sarcopenia is increasing rapidly. Sarcopenia presents many negative health-related consequences, including impaired energy homeostasis, risk of falls and cardiovascular disease, and subsequently higher mortality. It is becoming evident that sarcopenia has a negative impact on the healthy life of the elderly, and there also have been many investigations about sarcopenia in Korea.

From the very beginning of the concept of sarcopenia, international researches on this syndrome have studied more than 20 years. For the definition, pathogenesis, diagnosis, detection methods and interventions of sarcopenia, there is a certain amount of accumulation. The current study of muscle reduction is still in the exploratory stage, and its pathogenesis and treatment are still not very clear. Therefore, in-depth study of sarcopenia has a significant influence on the development of related medical field.

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