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Sarcopenia and Sarcopenic Obesity – A Brief Review

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Abstract

Sarcopenia, as the connotation given in its definition by academic societies "age-related loss of skeletal muscle mass plus loss of muscle strength and/or reduced physical performance", is an emerging clinical disorder that has gained wide appreciation regarding its impact on the general health of aging people. The loss of skeletal muscle mass and strength as well as consequent reduction in physical activities not only can cause disability in the carry-out of independent daily activities in the elderly, but also can induce insulin resistance, which has been widely recognized as a hallmark of pathogenesis in various metabolic disorders including diabetes mellitus, dyslipidemia, and gain of fat in this specific population. The accumulation of excessive adipose tissue with re-distribution to muscular tissue that usually accompanies the loss of skeletal muscle (i.e. sarcopenic obesity) has been observed to frequently co-exist with cardiometabolic syndrome (a clinical phenotype presenting with various combinations of impaired glucose tolerance, diabetes mellitus, dyslipidemia, hypertension, and central adiposity, all risk factors that independently or in cluster closely associated with higher cardiovascular events or mortality), the combination of which could further jeopardize the health condition and cause higher mortality than in sarcopenia or obesity alone in the elderly population. With the increasing life span and rapid rise of elderly populations in modern day, sarcopenic obesity thus deserves high clinical attention as to timely diagnosis and management to bring back health to the seniors. Physical exercises (especially resistance training) and concomitant dietary therapy with adequate protein supply are currently the mainstay of strategies in the management of sarcopenia and sarcopenic obesity. (J Intern Med Taiwan 2022; 33: 332-346)

Key Words: Aging, Cardiometabolic Syndrome, Physical exercise, Sarcopenia, Sarcopenic obesity

Introduction

The quantity and quality of skeletal muscle (SM) have been regarded as important elements in maintaining the general health in human beings. In addition to its primary roles of maintaining posture, breathing and locomotion, SM also functions as important storage for nutrients and regulator of metabolic processes. However, various observational and clinical studies have noted there is impairment in the anabolic (i.e. growth) process of the SM when people are aging, which would then lead to reductions in muscle mass and strength, and these latter factors have been thought to be associated with the mortality rates in the elderly[1]. In age-related sarcopenia, progressive loss of muscle mass and strength

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underlie the decrease in physical performance. Given that muscle tissue plays multiple important biological roles in insulin sensitivity, glucose and lipid metabolism, sarcopenia may also be associated with cardiometabolic syndrome, a disease entity with combination of metabolic dysfunctions mainly characterized by insulin resistance (IR), impaired glucose tolerance, dyslipidemia, hypertension, and central adiposity, that may all lead to diverse adverse health outcomes in the elderly[2-4].

Pathophysiology underlying development of sarcopenia/sarcopenic obesity

Since the first proposal for its definition as a novel clinical entity by Rosenburg in 1997[5], numerous studies have shown that the causes of sarcopenia developing with aging are widely regarded as multifactorial, with decline in neurological function, physical activity, changes in hormonal system, activation in inflammatory pathway, coexistence of chronic illnesses, infiltration of adipose tissue, and poor nutrition, factors that all have been proposed to be contributing[6]. Molecular level changes with aging including apoptosis, mitochondrial decline, and the angiotensin system in SM could all play notable pathologic role in the development of sarcopenia, over which the discussion in detail is beyond the scope of this current review more on the clinical aspects[7].

Inflammation markers

As age takes toll, changes starting to occur in structures and mechanisms at cellular and subcellular levels of the muscular tissues underlie the occurrence of dysfunction in the individual motor unit, and dysfunction of mitochondria in the muscle is believed to play the major role that leads to an increased level of apoptosis and reduced capabilities for muscle regeneration[8,9] With progressive aging, mitochondria homeostasis can no longer maintain due to the build-up of reactive oxygen species (ROS) which could be caused by the reduction in antioxidant enzyme levels in both muscle and neuron cells. This accumulation of ROS results in mtDNA deletion or mutation and dysfunction of mitochondria, as had been demonstrated in both human and animal studies[10-12]. Loss of muscle mass with aging is largely due to the progressive loss of motoneurons (motor neurons), which is associated with reduced number and size of muscle fiber. When motoneuron loss is not adequately compensated for by re-innervation of muscle fibers by the remaining motoneurons, muscle function would progressively decline[13]. Earlier studies had demonstrated that higher concentration of markers of chronic inflammation like plasma tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and C-reactive protein precede a significant decline in muscle strength in elderly people[14-16]. There was also study demonstrating that decrease of TNF-α level mediated by muscle training may help muscle regeneration[17]. Recently, a cross-sectional study carried out in China that had recruited 4,224 adults (M/F:1,514/2,710, mean age 62.3 ± 8.2 years) in the West China Health and Aging Trend (WCHAT) study, 814 (19.3%) among the cohort who were diagnosed as sarcopenia were noted to be older, with higher percentage of smoking and heavier chronic diseases burden (with two or more chronic diseases), as compared to the non-sarcopenic group. Among the inflammatory markers evaluated, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and systemic immune-inflammation index were significantly associated with sarcopenia. Participants having the highest values of the above parameters had significantly higher odds for sarcopenia than those in the lowest value group[18].

Insulin resistance

Insulin is a potent anabolic stimulus for SM. In type 2 diabetes, IR comprising one of the most

prominent mechanisms not only could lead to glucose dys-regulation, but the reduced insulin signaling may also lead to decreased protein synthesis and increased protein degradation, which can ultimately result in reduced muscle mass. Skeletal muscle accounts for up to 40-50% of lean body mass in an adult human and therefore accounting for the majority of whole-body insulin-stimulated glucose disposal. Previous studies have shown that physiological hyperinsulinemia increases SM protein synthesis and anabolism in young healthy subjects, as long as blood flow and amino acid delivery to the muscle are stimulated by insulin, and these have been reported to be impaired in muscles in older subjects, with or without diabetes mellitus as compared to the non-diabetic younger age group[19]. In the elderly, it was also shown that aerobic exercise restores muscle protein anabolism in response to insulin by improving vasodilation in older subjects. Studies in humans have suggested that these effects are most likely mediated through enhanced amino acid availability or delivery through increased perfusion, the impaired function of which have been reported in aged muscle[20,21]. Insulin resistance may also cause aberrant distribution of adipose tissues, including intra-muscular site, which may further impair normal physiological function of SM in terms of carbohydrate and lipid metabolism. Furthermore, in vitro study had shown a link between expansion of visceral adipose tissue (VAT) and an induced muscle atrophy by secretome of obese adipocytes, a phenomenon in which reduced expression of contractile proteins in human myotubes was observed when co-cultured with visceral adipocytes from obese subjects (BMI $\geq$ 40 kg/m^2). The key contributors to these results were found to be cytokines and chemokines with IL-6 and IL-1b that were secreted by these co-cultured cells[22]. These findings may be extrapolated as the pathophysiological changes underlying sarcopenia in aged people, especially when sarcopenia and obesity co-exist (sarcopenic obesity, SO), also a gradually recognized and highly appreciated clinical finding in addition to sarcopenia or obesity alone when people age, due to their association with accelerated functional decline and increased risks of cardiometabolic diseases and mortality[23-28].

Risk factors for development of sarcopenia/sarcopenic obesity

Risk factors predisposing to the development of sarcopenia in the elderly had been studied in a telephone-survey given to 1,068 adults aged $\geq$ 65 years in Taiwan, and the results showed that among health behaviors, an unbalanced food selection, failure to meet physical activity recommendations (< 150 min/week), and a longer time spent on sitting ($\geq$ 7 hour/day) were risk factors for sarcopenia among older adults. The authors concluded that intervention programs for sarcopenia prevention in older adults should focus on the promotion of balanced food selection, sufficient physical activity, and reduced sitting time[29]. Other cross-sectional study has found age, pre-frailty, and low activity as independent factors associated with sarcopenia[30]. Excess energy intake, physical inactivity, low-grade inflammation, and IR have been proposed as predisposing factors to the development of SO[31].

Health outcomes associated with sarcopenia/sacropenic obesity

By using data obtained from the Korea National Health and Nutrition Examination Survey (KNHANES) 2008-2010 (n = 20,812, $\geq$ 20 years old), one of the calculations used to define sarcopenia was to divide appendicular SM mass (ASM) as measured by dual energy X-ray absorptiometry (DEXA) by weight in kilogram (ASM/wt). Sarcopenia was then stratified into class I or class II defined by one or two standard deviations (SDs), respectively, below the sex-specific means of reference values obtained from adults aged 20-29

years. The results showed that the prevalence rates of class I and class II sarcopenia based on ASM/wt index were 25.1% and 4.7% in men, and 23.6% and 5.5% in women, respectively. The rate of metabolic syndrome (MetS) and IR index increased with the severity of sarcopenia[32]. A meta-analysis using data derived from recent studies (published between 2012 and 2015) that had been designed for prospective follow-up (ranging from 3 months to 9.8 years) had found that, in addition to the significant association between sarcopenia and functional performance decline, a higher rate of falls and a higher incidence of hospitalizations, there was also a significantly higher rate of mortality among sarcopenic subjects as compared to the non-sarcopenic counterpart [pooled odds ratio (OR) 3.596; 95% confidence interval (CI), 2.96 - 4.37]. Subgroup analysis revealed that age by itself had played a significant role since there existed a significantly higher association between sarcopenia and mortality in subjects aged 79 years or older (OR 4.42; 95% CI, 3.60 - 5.42) as compared with the figure for the younger subjects (OR 3.09; 95% CI, 2.49 - 3.84; $p = 0.02$)[33].

Lean muscle mass generally contributes up to ~50% of total body weight in young adults but declines with aging to half that amount at 75-80 years of age, and the loss of muscle mass is typically replaced by gains in fat mass. Sarcopenia has also been observed to be frequently associated with higher percentage of body fat, from which derived the term SO[34,35]. One of the morphologic changes in sarcopenia is the infiltration of muscle tissue components by lipids because of the increased frequency of adipocyte or lipid deposition within muscle fibers[36]. As with precursor cells in bone marrow, liver, and kidney, muscle satellite cells that can express an adipocytic phenotype increase with age[37]. In a 2-year follow-up study in 26 healthy, elderly African-American women (age at baseline: 75.5 ± 5.1 year), it was observed that there were age-related body composition changes encompassing progressive loss of SM mass and increases in both visceral abdominal adipose tissue (VAT) and intermuscular adipose tissue (IMAT). This change of body composition with time showed that, by DEXA measurement, there were significant decreases in both total body SM and bone masses, and regional analyses showed a decrease in leg SM; while increases in VAT and IMAT were identified in whole-body magnetic resonance imaging[38]. In a multi-continent observational study conducted in countries across Europe, Asia, South America, and Africa where the prevalence of sarcopenia has been found to range from 12.6% to 17.5%, higher percentage of body fat was found to be associated with lower SM mass in subjects of sarcopenia in all participating countries, and the prevalence of SO ranged from 1.3% to 11.0%. Furthermore, there also existed a dose-dependent association between higher numbers of chronic diseases and SO[39].

Impact from sarcopenia and obesity in combination has been associated with disability and worse outcomes in older adults. Using data obtained from two Swedish population studies (521 women and men aged 75 from the Gothenburg H70 Birth Cohort Studies, and 288 men aged 87 from the Uppsala Longitudinal Study of Adult Men (ULSAM), the risk of mortality associated with SO and its various components was examined[40]. In this prospective observational study, sarcopenia was defined by the updated EWGSOP2 definition[41], and obesity was defined by any of three established definitions as follows: body mass index (BMI) ≥ 30 kg/m^2, fat mass > 30%/ > 42% or waist circumference (WC) ≥ 88 cm/ ≥102 cm for women and men, respectively. The results showed that SO was observed in 4% of the women and 11% of the men in the H70 cohort, and in 10% of the ULSAM male cohort. The 75-year-old women with SO had a higher risk (HR 3.25; 95% CI, 1.2-8.9) of mortality within 10 years compared to those with a normal phenotype. A similar trend of association with mortality among the 75-year-old men

was also noted, although statistically non-significant. However, in the very old men aged 87 years, obesity was instead associated with increased survival. It was concluded from this study that, in 75-year-old women, SO appeared to be associated with an increased risk of mortality within 10 years. The possible explanation why there was no clear corresponding association between SO or obesity and mortality among the 75-year-old men could be that there was gender difference in the health consequences of obesity. The male pattern of obesity is usually more related to increased risks, e.g., MetS that may explain the fact that men have a shorter life expectancy than women[42]. It is possible, therefore, that some men at increased risk had passed away before the age of 75. Thus, a selection of men with less metabolically active obesity could have been included in this study and a corresponding selection may not yet have occurred in the counterpart comprising 75-year-old women. Other evidences supporting an earlier development of MetS in male population as compared to the females could be found in a cross-sectional study investigating into gender differences in the prevalence and development of MetS in a cohort of Chinese population with abdominal obesity that was defined as WC ≥ 90 cm in male or ≥ 80 cm in female subjects according to the International Diabetes Federation criteria[43] (n = 19,046, M/F:6,261/12,785). The results showed that there were significantly higher prevalence of MetS (73.7% vs 36.9%, $p < 0.001$) and a significantly higher proportions of combinations of three or four MetS components than females (36.4% vs 30.2% and 18.4% vs 5%, respectively). Males developed MetS significantly faster than females in the group aged < 50 years [relative risk (RR): 1.533; 95% CI, 1.178-1.993)], whereas no such difference in rate of development time existed between males and females aged 50 years and older (RR: 0.974; 95% CI, 0.837-1.134). The authors concluded that, compared with females, Chinese males with abdominal obesity should be paid more clinical attention not only because of their higher prevalence of MetS and its components, but also a faster development in age of this metabolic disorder[44]. Risks that may lead to higher mortality in this group of elderly subjects might be multifactorial. In overweight and obese elderly adults, self-reported mobility capacity is markedly diminished as compared with lean counterpart, and disability per se, regardless of underlying disorders has been noted to be associated with higher mortality in the elderly[44]. A general belief is that measured BMI is inversely associated with physical performance assessed in the elderly population, be the conclusions drawn from results from cross-sectional or longitudinal follow-up studies[46-48], although these observations have been challenged by findings from one recent study carried out in the very old populations (> 80 of age) indicating a higher BMI, but not underweight, may instead be protective in daily activities performance[49]. From these studies specifically designed for and conducted in individuals with sarcopenia or obesity, it would be intuitive to consider that having both low muscle mass and high fat mass levels in the same individual (an SO phenotype) may lead to more functional limitations, as well as to more metabolic disorders due to the underlying pathophysiological mechanisms that could be added up[50,51]. Studies have indicated that individuals with SO are associated with increased WC, elevated fasting blood glucose, IR, higher blood pressure, and dyslipidemia as compared to sarcopenia or obesity alone[52,53]. A meta-analysis including 606 articles has demonstrated that SO increases the risk of type 2 diabetes by almost 38% compared to individuals with excess weight or obesity alone[54]. The cluster of abdominal obesity, hyperglycemia, hyperinsulinemia, dyslipidemia, and hypertension progressively leads to diabetes and CVD. Metabolic disorders including cardiometabolic syndrome (CMS), diabetes, and CVD have been noted to be common comorbidities of SO, as compared to non-

sarcopenic or non-obese counterpart[55,56]. All these findings indicate there are higher risks for and worse outcomes in cardiometabolic events in subjects having both sarcopenia and obesity, a clinical entity that should gain higher attention for timely recognition and optimal management in order to reduce the associated morbidities and mortality.

Diagnosis of sarcopenia/sarcopenic obesity

The term of Sarcopenia (in Greek *sarx* for flesh and *penia* for loss) was first described by Irwin Rosenberg in 1988 in a conference convened to look at various measurements related to the assessment of age-related decrease in SM mass and function[57]. After a decade or so, Baumgartner and colleagues proposed an equation (ASM mass in kg/ square of height in meter = kg/m^2) to define sarcopenia as being less than two SDs below the mean of a young reference group[58]. After more robust data have been accrued from serial and systemic researches, currently the diagnosis of sarcopenia is clearly delineated by academic societies for the formation of guidelines or consensus, though criteria may differ due to differences caused by geographical, cultural, and ethnic reasons. According to the consensus reached by experts from different countries in Asia, the Asian Working Group for Sarcopenia (AWGS) had recommended the requirement in assessing both quality and quantity of the SM system. A summary of diagnostic criteria is given below: low muscle strength as handgrip strength (GS) < 28 kg for men and < 18 kg for women; low physical performance includes 6-meter walk < 1.0 m/s, Short Physical Performance Battery score ≤ 9, or 5-time chair stand test ≥ 12 seconds. Cutoffs for height-adjusted muscle mass are: < 7.0 kg/m^2 in men and < 5.4 kg/m^2 in women when measured by DEXA; and < 7.0 kg/m^2 in men and < 5.7 kg/m^2 in women when bioimpedance method is used. For screening purpose, either calf circumference (< 34 cm in men, < 33 cm in women), SARC-F (sluggishness, assistance in walking, rise from a chair, climb stairs, falls) questionnaire ≥ 4, or SARC-CalF (including calf circumference as an additional item) ≥ 11, is recommended to facilitate earlier identification of people at risk for sarcopenia[59] (Table 1). For diagnosis of SO, there is currently no consistent criteria available. Nevertheless, an adequate one should include the individual diagnosis given for obesity and sarcopenia. For Asian population, a BMI ≥ 27.5 kg/m^2 or WC ≥ 90 cm in men and ≥ 80 cm in women is considered obese[43,60]. Subsequent validation based on homogeneous study designs and databases is required to reach a consensus for diagnosis of SO, which would help the setting of the most effective prevention and treatment strategies [61].

Management of sarcopenia/sarcopenic obesity in the elderly

Physical exercise

Physical exercise has been found to be effective in preventing deterioration or even reversal of SO in the elderly people. Recommendations on several kinds of physical exercise with aims to “grow stronger” and at the same time “keep safe” in senior population have been available[62,63]. A combination of resistance training and aerobic training seems to be the most practical way to improve physical performance [64,65].

Among different kinds of exercise programs recommended, the progressive elastic band resistance training (ERT) as resistance exercise is regarded pragmatic to promote similar strength gains equal to those achieved by conventional resistance training programs, especially for its being a relatively easy and safe task to adopt by the seniors[66]. A pilot randomized controlled trial aiming to assess the effect of progressive ERT was conducted in a group of elderly women with SO in Taiwan. A total of 35 women aged > 60 years old were recruited and the resistance training given to 18 women lasted

for 12 weeks (3 times per week), while the other 17 women received only exercise concept lessons. The results showed that, in the exercise group, various parameters of body compositions as measured by the DEXA method had found significant decrease in proportion of fat in the right upper extremity ($p = 0.03$), left upper extremity ($p = 0.04$), total fat ($p = 0.035$), and fat percentage ($p = 0.012$), as compared to the baseline measurement. Increase in bone mineral density (BMD) ($p = 0.026$), T-score ($p = 0.028$), and Z-score ($p = 0.021$) in the exercise group were noted, while no such findings were observed in the control group. The authors concluded that progressive ERT over 12 weeks can significantly reduce fat mass and increase BMD in elderly women with SO[67].

In another clinical study aiming to assess the effect of ERT on muscle mass and physical function in older women with sarcopenic obesity, 56 Taiwanese women (mean ± SD age 67.3 ± 5.1 years) were recruited and randomly assigned to the experimental group receiving 12 weeks of ERT and to the control group without exercise intervention. All patients in the active exercise group were trained and supervised by a licensed senior physical therapist who was unware of the study assignment. The training protocol was designed based on the Ameri-

Table 1. Diagnosis for sarcopenia/sarcopenic obesity in Asian population and treatment strategies

Clinical entity	Diagnostic criteria (AWGS)*	Treatment
Sarcopenia	Screening purpose: ■ Calf circumference- < 34 cm (men), < 33 cm (women). ■ SARC-F questionnaire ≥ 4, or ■ SARC-CalF ≥ 11	Physical exercise: ■ Combination of resistance and aerobic training, ■ Progressive elastic band resistance training (recommended)
	Quality assessment: ■ Low muscle strength- GS < 28 kg (men), < 18 kg (women); ■ Low physical performance- 6-meter walk < 1.0 m/s, Short Physical Performance Battery score ≤ 9, or 5-time chair stand test ≥ 12 seconds.	Nutritional intervention: ■ Protein intake- > 1 g/kg adjusted body weight/day ■ β-hydroxyl β-methylbutyrate** ■ Nutritional intervention plus physical exercise: helps gain more
	Quantity assessment: Height-adjusted muscle mass: ■ DEXA method: < 7.0 kg/m^2 (men), < 5.4 kg/m^2 (women) ■ Bioimpedance method: < 7.0 kg/m^2 (men), < 5.7 kg/m^2 (women)	Pharmacologic therapy*** ■ For patients with more severe frailty or at bedridden status
Sarcopenic obesity	As for sarcopenia, plus ■ BMI ≥ 27.5 kg/m^2 ■ WC ≥ 90 cm (men), ≥ 80 (women)	As for sarcopenia

Abbreviations: AWGS: the Asian Working Group for Sarcopenia (*ref. 59); BMI: body mass index (kg/m2); DEXA: dual energy X-ray absorptiometry; GS: handgrip strength; SARC-F: sluggishness, assistance in walking, rise from a chair, climb stairs, falls; SARC-CalF: including calf circumference as an additional item; WC: waste circumference.

** a metabolite of the essential amino acid leucine.

***Medicines designed to promote mitochondria biogenesis, restore mitochondrial functions, reduce inflammation reactions, promote muscle tissue regeneration, and muscle strength restoration could all be of therapeutic potential, but more clinical evidences are required (ref. 93-95).

can College of Sports Medicine guidelines for resistance training for older subjects[68]. Assessment included lean muscle mass (by DEXA) and physical capacity by the global physical capacity score. The results showed that, at 3- and 9-month follow-up assessment, there were significant mean differences with greater increase in total SM of 0.70 kg (95% CI, 0.12-1.28; $p < 0.05$) and 0.72 kg (95% CI, 0.21-1.23; $p < 0.01$), respectively, as compared to the baseline measurement than figures observed in the control group. Similar results were found for results in muscle quality, physical capacity, and physical function. The authors concluded that ERT showed significant benefit in SM mass, muscle quality, as well as physical function in older women having sarcopenic obesity[69].

In a systemic review on data derived from 5 randomized, controlled trials (RCT) that all had tested the efficacy of isolated exercise programs to improve sarcopenia components in the elderly as compared to without physical intervention (only health education given), it was found that resistance training was the main intervention applied in all the trials. Muscle strength, muscle quality, and muscle function were improved after physical training applying the resistance training protocols in the elderly[70]. A more recent meta-analysis out of a total of 25 eligible studies (n = 2,267 participants) had also revealed that resistance training programs lasting for at least 8 weeks had resulted in significantly favorable changes presented as effect sizes (ES, calculated as the standardized mean differences between the resistance training group and the control group). Significant differences between the two groups existed as handgrip (ES = 0.51, $p = 0.001$), lower-limb strength (ES = 0.93, $p < 0.001$), agility (ES = 0.78, $p = 0.003$), gait speed (ES = 0.75, $p < 0.001$), postural stability (ES = 0.68, $p = 0.007$), functional performance (ES = 0.76, $p < 0.001$), fat mass (ES = 0.41, $p = 0.001$), and muscle mass (ES = 0.29, $p = 0.002$). Based on these findings, the authors concluded that resistance training interventions are particularly beneficial to delay and reduce the causes (e.g., loss of muscle mass) and consequences (e.g., loss of muscular strength or functionality) of sarcopenia and physical frailty in the elderly[71]. Supervised exercise has also been advocated to be adopted as an effective strategy to treat sarcopenia and physical frailty, which may consequently prevent severe functional decline and strength loss in institutionalized older adults[72].

Osteoporosis in the elderly often coexists with reduced muscle mass and muscle strength, as well as an increase in adiposity, from which derived the term osteosarcopenic obesity (OSO) given by investigators who have noted the clinical significance regarding its association with decreased physical performance[73-75]. Loads on skeletal system are dominated by muscle action. Both bone and muscle share environmental, endocrine and paracrine influences. One of the physiological factors considered to contribute to this relationship is that muscles may also behave as an endocrine system that produces bioactive molecules, regulating homeostasis of masses of both muscle and bone[76]. In a cross-sectional study to find relationship between BMD and body composition (obesity, sarcopenia, and SO) as measured by DEXA, 128 very-old subjects aged between 80 and 95 years were recruited for assessment. The results showed that subjects with sarcopenia had lower BMD compared to the obesity group, with higher risk for presence of osteopenia/osteoporosis in the spine (OR: 2.81; 95% CI, 1.11-7.11) and femur (OR: 2.75; 95% CI, 1.02-7.44). Obesity, instead, was shown to be a protective factor for osteopenia/osteoporosis in the spine. The authors concluded from this study which was carried out in this very-old population that lean muscle mass is more directly related to BMD (of total, femur, and spine), and sarcopenia is associated with the presence of osteopenia/osteoporosis[77]. Physical trainings to enhance BMD, hence the strength gained by the skeletal system, may in

a reciprocal way help build muscle mass due to the close connection of structures and coordination of functions between these two systems.

Nutritional intervention

Low protein intake has been linked to reduced muscle strength and physical performance in older adults. In a longitudinal 5-year follow-up study that was conducted among a cohort of very old community-dwelling individuals (n = 722, ≥ 85 year of age, % M/F:60/40), the effects of low protein intake [defined as intake of < 1 g protein/ adjusted (ideal) BW/day (< 1 g/kg aBW/d)] on muscle strength and physical performance were periodically assessed for changes in GS and timed up-and-go (TUG) tests over the 5-year study period at baseline, 18, 36, and 60 months, respectively. Protein intake was estimated with a validated 24-hr multiple-pass dietary recall. In those 390 (54%) participants who had reported low protein intake, as opposed to those with good intake (> 1 g/kg aBW/d), there was a 1.62 kg lower GS (p = 0.008) in all participants. It was concluded that intake of < 1 g protein/kg aBW/d may negatively affect muscle strength and physical performance in late life, independently of other important covariates adjusted, examples of which included factors from anthropometry, multi-morbidity, cognitive impairment, or protein intake distribution as diet-related factors[78]. Among a very-old population (people aged 85.0 years old (± 0.5)), a longitudinal study has found that higher protein intake was more likely to have fewer disabilities at baseline assessment and shallower disability trajectories over the subsequent 5 years of follow-up[79].

Since amino acids (AA) and energy are required for muscle synthesis, studies on the effect of nutritional therapy on sarcopenia have included evaluation of whole protein, essential AA and β-hydroxyl β-methylbutyrate (HMB). Whole-protein supplementation failed to show a consistent effect on muscle mass, strength or function. Essential AA supplements also failed to show consistent effect. Variations in study design, composition of the protein supplement and the failure to monitor voluntary food intake, adherence and baseline nutritional status could all contribute to the inconsistent findings. As a metabolite of the essential AA leucine and one of the dietary supplements promoted to enhance gains in strength and lean body mass, some studies on HMB supplement have shown beneficial effect for young or older adults[80,81]. However, with limited clinical trials available thus far and the different methodologies that have been applied, more studies are still needed to confirm the role of HMB as a promising agent to treat sarcopenia[82]. Regarding the effect of timing and distribution of dietary proteins consumption on protein absorption, different proposals have been raised from various studies. One of those is there existing a ceiling effect on the amount of protein used for synthesis at a given meal and an optimum protein intake of 20-30 g per meal would be optimal[83]. Protein that is fed evenly spread throughout meals gives greater fractional synthesis rate compared with a skewed distribution has been advocated by some investigators[84]. However, others had argued against this view and instead proposed that a large bolus of protein should be as useful as providing the same amount spread over the day[85]. There are also evidences showing that pulse feeding of protein (72-80 % provided at lunch) could increase whole-body protein retention, lean muscle index (lean soft-tissue mass/height m^2) and ASM mass index (sum of lean soft-tissue in the four limbs/height m^2) compared with evenly spread protein consumption[86]. The acquirement of nutrition by the periphery tissues after food digestion may also play another critical role in build-up of muscles. An increased splanchnic AA sequestration with age has been observed in human studies comparing splanchnic extraction of dietary leucine in different age groups (68.2 ± 0.8 vs 22.7 ± 0.4 years). Study results showed that in elderly men

there is higher leucine extraction by the gut, liver, or both during feeding (two-fold as high in elderly men (50 ± 11% compared with 23 ± 2%, $p < 0.05$), which could lead to a lower peripheral availability of dietary leucine, and this could potentially complicate the supplementation of essential AA to stimulate muscle protein synthesis and distribution[87,88].

Nutritional intervention plus physical exercise helps gain more

The clinical effects of healthy diet (e.g. good intake of protein > 1 g/kg aBW/day) on the prevention and treatment of sarcopenia in the elderly has been recognized as having positive effect on sarcopenia management; however, concomitant physical exercise programs designed to improve muscle mass and its function should be key to reduce consequences associated with sarcopenia[89,90]. To evaluate the effects of types and levels of physical activity (PA) in conjunction with protein intake and vitamin D on sarcopenia and obesity status in an elderly population, a survey among a large cohort of participants > 60 year of age (n = 4,452, M/F = 1,928/2,523) who had completed a body composition analysis by DEXA method and provided health and dietary data had been conducted in Korea. Body composition revealed higher appendicular SM mass/weight in the non-obese (BMI < 25 kg/m^2) group. Sarcopenic participants had a significantly higher index of homeostasis model assessment of insulin resistance than those without sarcopenia in both the obese and non-obese groups, after adjusting for age, sex, and exercise. A diet deficient of protein intake and vitamin D was associated with relatively increased prevalence of obesity, sarcopenia, and sarcopenic obesity. The rate of all types of exercise (vigorous PA: ≥ 3 d of vigorous activity for ≥ 20 min/day; moderate PA or walking PA: ≥ 5 d of moderate-intense activity or walking for ≥ 30 min/day; flexibility or strength exercise: ≥ 2 day/week) was much higher in participants without sarcopenia compared with those with sarcopenia, in both obese groups. It is suggested from this cross-sectional study that enhanced protein intake and vitamin D and resistance exercise may help maintain healthy body weight and, hence offset sarcopenia in people of this age group[91].

Pharmacological therapy

Despite its obvious effect on subjects with sarcopenia, physical exercise intervention may be only feasible for those who are actively mobile, and may not be practically applicable to patients with more severe frailty or at bedridden status, who in fact are also in need for an effective therapy to reduce further loss or even restore muscle mass to achieve better QoL. There had been clinical trials performed on testing the effects of hormonal replacement (testosterone, dehydroepiandrosterone and growth hormone) in an attempt to reverse age-related loss of muscle mass and strength, however, with inconsistent results obtained[92]. With today's advent of regenerative medicine owing to their ability to regrow, repair or replace damaged or diseased cells, organs or tissues, novel pharmacological therapeutics that are designed to promote mitochondria biogenesis or restore mitochondrial functions, reduce inflammation reactions in aging muscle, and promote muscle tissue regeneration and concomitantly muscle strength restoration could all be potential therapeutics for subjects with sarcopenia/sarcopenic obesity. Taking stem cell therapy as an example, such transplantation could potentially be a novel intervention for sarcopenia alleviation owing to its regenerative capabilities and its ability to produce anti-inflammatory cytokines that in turn change the microenvironment into one that promotes re-innervation and regeneration. Further studies in this advanced field are required before definite conclusion could be drawn[93-95].

Conclusion

Thanks to the progressive understanding of

the physiological basis of ageing and more hygienic conditions of modern life (at least observed in high-income countries), fewer sources of physical stress, earlier interventions to maintain health and medical approaches to counteract disease in later life, people worldwidely are now living longer and for the first time in history, most people can expect to live into their sixties and beyond[96,97]. However, along with longer life span comes with more critical prospects with hope of extending the period free of age-related disability and disease, with sarcopenia/sarcopenic obesity becoming such common clinical scenario in the elderly population living in this era. Having sarcopenia or sarcopenic obesity renders the elderly not only to suffer from reduced abilities in free performance of daily activities as when young, but also the underlying pathophysiology that cause reduced muscle mass, muscle strength, as well as the accumulation of adipose tissue distributed to ectopic sites may accrue with time more risk factors for metabolic and CV disorders, and even a higher mortality than those without sarcopenia. Early recognition and diagnosis of the reductions in muscle mass and strength in the elderly is fundamental to the initiation of optimal management comprising physical exercise therapy and nutritional intervention by providing adequate amount of dietary proteins, the combination of which is regarded most effective strategy in bring back muscle mass and strength, and hence healthier status for the seniors in current clinical practice.

References

1. McLeod M, Breen L, Hamilton DL, et al. Live strong and prosper: The importance of skeletal muscle strength for healthy ageing. Biogerontology 2016; 17:497-510. doi: 10.1007/s10522-015-9631-7.
2. Kim TN, Park MS, Lim KI, et al. Relationships between sarcopenic obesity and insulin resistance, inflammation, and vitamin D status: The Korean Sarcopenic Obesity Study. Clin Endocrinol (Oxf) 2013;78:525-32.
3. de Campos GC, Lourenço RA, CS. Prevalence of sarcopenic obesity and its association with functionality, lifestyle, biomarkers and morbidities in older adults: The FIBRA-RJ Study of frailty in older Brazilian adults. Clinics (Sao Paulo) 2020; 75: e1814. doi: 10.6061/clinics/2020/e1814.
4. Sinclair AJ and Abdelhafiz AH. Cardiometabolic disease in the older person: Prediction and prevention for the generalist physician. Cardiovascular Endocrinology & Metabolism 2020;9: 90-5. doi: 10.1097/XCE.0000000000000193.
5. Rosenberg I. Symposium: sarcopenia: Diagnosis and mechanisms. J Nutr 1997; 127:990S-991S.
6. Ogawa S, Yakabe M, Akishita M. Age-related sarcopenia and its pathophysiological bases. Inflam Regen 2016; 36:17. doi 10.1186/s41232-016-0022-5.
7. Wiedmer P, Jung T, Castro JP, et al. Sarcopenia - molecular mechanisms and open questions. Ageing Res Rev 2021; 65: 101200. https://doi.org/10.1016/j.arr.2020.101200.
8. Marzetti E and Leeuwenburgh C. Skeletal muscle apoptosis, sarcopenia and frailty at old age. Exp Gerontol 2006; 41: 1234-8.
9. Ryan MJ, Jackson JR, Hao Y, et al. Inhibition of xanthine oxidase reduces oxidative stress and improves skeletal muscle function in response to electrically stimulated isometric contractions in aged mice. Free Radic Biol Med 2011; 51:38-52.
10. Peterson CM, Johannsen DL, Ravussin E. Skeletal muscle mitochondria and aging: a review. J Aging Res 2012; Volume 2012, Article ID 194821. doi:10.1155/2012/194821.
11. Carter HN, Chen CC, Hood DA. Mitochondria, muscle health, and exercise with advancing age. Physiology 2015; 30:208-23.
12. Seo DY, Lee SR, Kima N, et al. Age-related changes in skeletal muscle mitochondria: The role of exercise. Integr Med Res 2016;5: 182-6.
13. Larsson L, Degens H, Li M, et al. Sarcopenia: aging-related loss of muscle mass and function. Physiol Rev 2019; 99: 427-511.
14. Visser M, Pahor M, Taaffe DR, et al. Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: The Health ABC Study. J Gerontol: Series A 2002;57: M326-32. doi: 10.1093/gerona/57.5.m326.
15. Taekema DG, Westendorp RG, Frölich M, et al. High innate production capacity of tumor necrosis factor-alpha and decline of handgrip strength in old age. Mech Ageing Dev 2007;128: 517-21.
16. Schaap LA, Pluijm SM, Deeg DJ, et al. for the Health ABC Study. Higher inflammatory marker levels in older persons: Associations with 5-year change in muscle mass and muscle strength. J Gerontol: Series A 2009; 64:1183-9.
17. Greiwe JS, Cheng B, Rubin DC, et al. Resistance exercise decreases skeletal muscle tumor necrosis factor alpha in frail elderly humans. FASEB J 2001;15: 475-82.
18. Zhao WY, Zhang Y, Hou LS, et al. The association between systemic inflammatory markers and sarcopenia: results from the West China Health and Aging Trend Study (WCHAT). Arch Gerontol Geriatr 2021;92:104262. doi: 10.1016/j.archger.2020.104262.
19. Fujita S, Glynn EL, Timmerman KL, et al. Supraphysiological hyperinsulinaemia is necessary to stimulate skeletal

muscle protein anabolism in older adults: evidence of a true age-related insulin resistance of muscle protein metabolism. Diabetologia 2009; 52:1889-98.
20. Timmerman KL, Lee JL, Fujita S, et al. Pharmacological vasodilation improves insulin-stimulated muscle protein anabolism but not glucose utilization in older adults. Diabetes 2010; 59: 2764-71.
21. Groen BB, Hamer HM, Snijders T, et al. Skeletal muscle capillary density and microvascular function are compromised with aging and type 2 diabetes. J Appl Physiol 2014; 116: 998-1005.
22. Pellegrinelli V, Rouault C, Rodriguez-Cuenca S, et al. Human adipocytes induce inflammation and atrophy in muscle cells during obesity. Diabetes 2015; 64:3121-34.
23. Atkins JL, Whincup PH, Morris RW, et al. Sarcopenic obesity and risk of cardiovascular disease and mortality: A population-based cohort study of older men. J Am Geriatr Soc 2014; 62:253-60. doi: 10.1111/jgs.12652.
24. Batsis J, Mackenzie T, Barre L, et al. Sarcopenia, sarcopenic obesity and mortality in older adults: Results from the national health and nutrition examination survey III. Eur J Clin Nutr 2014; 68:1001-7. doi: 10.1038/ejcn.2014.117.
25. Yang M, Jiang J, Hao Q, et al. Dynapenic obesity and lower extremity function in elderly adults. J Am Med Dir Assoc 2015; 16:31-6. doi: 10.1016/j.jamda.2014.06.019.
26. Jung S, Yabushita N, Kim M, et al. Obesity and muscle weakness as risk factors for mobility limitation in community-dwelling older Japanese women: A two-year follow-up investigation. J Nutr Health Aging 2016; 20:28-34. doi: 10.1007/s12603-016-0672-7.
27. Barazzoni R, Bischoff S, Boirie Y, et al. Sarcopenic obesity: Time to meet the challenge. Obes Facts 2018; 11:294-305. doi: 10.1159/000490361.
28. Roh E and Choi KM. Health consequences of sarcopenic obesity: A narrative review. Front Endocrinol 2020; 11:332. doi: 10.3389/fendo.2020.00332.
29. Tzeng PL, Lin CY, Lai TF, et al. Daily lifestyle behaviors and risks of sarcopenia among older adults. Arch Public Health 2020; 78:113. https://doi.org/10.1186/s13690-020-00498-9.
30. Therakomen V, Petchlorlian A, Lakananurak N. Prevalence and risk factors of primary sarcopenia in community-dwelling outpatient elderly: A cross-sectional study. Sci Rep 2020; 10:19551. https://doi.org/10.1038/s41598-020-75250-y.
31. Choi KM. Sarcopenia and sarcopenic obesity. Korean J Intern Med 2016; 31:1054-60. https://doi.org/10.3904/kjim.2016.193.
32. Kima KM, Lima S, Choi SH, et al. Cardiometabolic implication of sarcopenia: the Korea National Health and Nutrition Examination Study (KNHANES) 2008-2010. IJC Metab Endocr 2014; 4: 63-9.
33. Beaudart C, Zaaria M, Pasleau F, et al. Health outcomes of sarcopenia: A systematic review and meta-analysis. PLoS ONE 2017; 12(1): e0169548. doi:10.1371/journal.pone.0169548.
34. Baumgartner RN. Body composition in healthy aging. Ann N Y Acad Sci 2000; 904:437-48. doi: 10.1111/j.1749-6632.2000.tb06498.x.
35. Sakuma K and Yamaguchi A. Sarcopenic obesity and endocrinal adaptation with age. Int J Endocrinol 2013; 2013:204164. doi: 10.1155/2013/204164.
36. Dubé J and Goodpaster BH. Assessment of intramuscular triglycerides: contribution to metabolic abnormalities. Curr Opin Clin Nutr Metab Care 2006; 9: 553-9.
37. Shefer G, Wleklinski-Lee M, and Yablonka-Reuveni Z. Skeletal muscle satellite cells can spontaneously enter an alternative mesenchymal pathway. J Cell Sci 2004; 117: 5393-404.
38. Song MY, Ruts E, Kim J, et al. Sarcopenia and increased adipose tissue infiltration of muscle in elderly African American women. Am J Clin Nutr 2004;79: 874-80. doi: 10.1093/ajcn/79.5.874.
39. Tyrovolas S, Koyanagi A, Olaya B, et al. Factors associated with skeletal muscle mass, sarcopenia, and sarcopenic obesity in older adults: a multi-continent study. J Cachexia Sarcopenia Muscle 2016; 7: 312-21.
40. von Berens Å, Obling SR, Nydahl M, et al. Sarcopenic obesity and associations with mortality in older women and men - a prospective observational study. BMC Geriatrics 2020; 20: 199. https://doi.org/10.1186/s12877-020-01578-9.
41. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. for the European Working Group on Sarcopenia in older people 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019; 48: 16-31. doi: 10.1093/ageing/afy169.
42. Mauvais-Jarvis F. Epidemiology of gender differences in diabetes and obesity. Adv Exp Med Biol 2017;1043:3-8.
43. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome-a new world-wide definition. A consensus statement from the International Diabetes Federation. Diabet Med 2006; 23: 469-80. doi:10.1007/BF02706751.
44. Xu S, Gao B, Xing Y, et al. on behalf of the China National Diabetes and Metabolic Disorders Study Group. Gender differences in the prevalence and development of metabolic syndrome in Chinese population with abdominal obesity. PLoS ONE 2013; 18(10): e78270. doi:10.1371/journal.pone.0078270.
45. Grande G, Vetrano DL, Fratiglioni L, et al. Disability trajectories and mortality in older adults with different cognitive and physical profiles. Aging Clin Exp Res 2020; 32:1007-16. https://doi.org/10.1007/s40520-019-01297-1.
46. Koyanagi A, Moneta MV, Garin N, et al. The association between obesity and severe disability among adults aged 50 or over in nine high-income, middle-income and low-income countries: A cross-sectional study. BMJ Open 2015; 5:e007313. doi:10.1136/bmjopen-2014-007313.
47. Corona LP, da Silva Alexandre T, de Oliveira Duarte YA, et al. Abdominal obesity as a risk factor for disability in Brazilian older adults. Public Health Nutr 2017; 20: 1046-53. doi:10.1017/S1368980016003505.
48. de Souza Barbosa JF, dos Santos Gomes C, Costa JV, et al. Abdominal obesity and mobility disability in older adults: A 4-year follow-up of the International Mobility in Aging Study. J Nutr Health Aging 2018; 22: 1228-37.
49. Lv YB, Yuan JQ, Mao C, et al. Association of body mass index with disability in activities of daily living among Chinese adults 80 years of age or older. JAMA Network Open 2018;1:

e181915. doi:10.1001/jamanetworkopen.2018.1915.
50. Tian S and Xu Y. Association of sarcopenic obesity with the risk of all-cause mortality: A meta-analysis of prospective cohort studies. Geriatr Gerontol Int 2016; 16:155-66. doi: 10.1111/ggi.12579.
51. Sanada K, Chen R, Willcox B, et al. Association of sarcopenic obesity predicted by anthropometric measurements and twenty-four year all-cause mortality in elderly men: the kuakini honolulu heart program. Nutrition 2017; 46:97. doi: 10.1016/j.nut.2017.09.003.
52. Kim TN, Park MS, Lim KI, et al. Relationships between sarcopenic obesity and insulin resistance, inflammation, and vitamin D status: The Korean sarcopenic obesity study. Clin Endocrinol 2013; 78:525-32. doi: 10.1111/j.1365-2265.2012.04433.x.
53. Baek SJ, Nam GE, Han KD, et al. Sarcopenia and sarcopenic obesity and their association with dyslipidemia in Korean elderly men: the 2008-2010 Korea National health and nutrition examination survey. J Endocrinol Invest 2014; 37:247-60. doi: 10.1007/s40618-013-0011-3.
54. Khan RMM, Chua ZJY, Tan JC, et al. From pre-diabetes to diabetes: Diagnosis, treatments and translational research. Medicina (Kaunas) 2019; 55:546. doi: 10.3390/medicina55090546.
55. Kim JH, Cho JJ, Park YS. Relationship between sarcopenic obesity and cardiovascular disease risk as estimated by the Framingham risk score. J Korean Med Sci 2015; 30:264. doi: 10.3346/jkms.2015.30.3.264.
56. Hong SH and Choi KM. Sarcopenic obesity, insulin resistance, and their implications in cardiovascular and metabolic consequences. Int J Mol Sci 2020; 21:E494. doi: 10.3390/ijms21020494.
57. Rosenberg IH. Sarcopenia: Origins and clinical relevance. J Nutr 1997, 127: 990S-991S.
58. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol 1998; 147:755-63.
59. Chen LK, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. J Am Med Dir Assoc 2020; 21:300-7. e2. doi: 10.1016/j.jamda.2019.12.012.
60. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004 363(9403):157-63. doi: 10.1016/S0140-6736(03)15268-3.
61. Donini LM, Busetto L, Bauer JM, et al. Critical appraisal of definitions and diagnostic criteria for sarcopenic obesity based on a systematic review. Clin Nutr 2020;39:2368-88. doi: 10.1016/j.clnu.2019.11.024.
62. Elsawys B and Higgins KE. Physical activity guidelines for older adults. Am Fam Physician 2010;81:55-9.
63. Lee PG, Jackson EA, Richardson CR. Exercise prescriptions in older adults. Am Fam Physician 2017; 95:425-32.
64. Batsis JA and Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. Nat Rev Endocrinol 2018; 14:513-37. doi: 10.1038/s41574-018-0062-9.
65. Wang M, Tan Y, Shi Y, et al. Diabetes and sarcopenic obesity: pathogenesis, diagnosis, and treatments. Front Endocrinol 2020; 11:568. doi: 10.3389/fendo.2020.00568.
66. Lopes JSS, Machado AF, Micheletti JK, et al. Effects of training with elastic resistance versus conventional resistance on muscular strength: A systematic review and meta-analysis. SAGE open medicine 2019; 7:2050312119831116. doi:10.1177/2050312119831116.
67. Huang SW, Ku JW, Lin LF, et al. Body composition influenced by progressive elastic band resistance exercise of sarcopenic obesity elderly women: A pilot randomized controlled trial. Eur J Phys Rehabil Med 2017; 53:556-63. doi: 10.23736/S1973-9087.17.04443-4.
68. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Circulation 2007; 116:1094-105. https://doi.org/10.1161/circulationaha.107.185650.
69. Liao CD, Tsauo JY, Huang SW, et al. Effects of elastic band exercise on lean mass and physical capacity in older women with sarcopenic obesity: A randomized controlled trial. Sci Rep 2018; 8:2317. doi:10.1038/s41598-018-20677-7.
70. de Mello RGB, Corte RRD, Gioscia J, et al. Effects of physical exercise programs on sarcopenia management, dynapenia, and physical performance in the elderly: A systematic review of randomized clinical trials. J Aging Res 2019; Article ID 1959486. https://doi.org/10.1155/2019/1959486.
71. Talar K, Hernández-Belmonte A, Vetrovsky T, et al. Benefits of resistance training in early and late stages of frailty and sarcopenia: A systematic review and meta-analysis of randomized controlled studies. J Clin Med 2021; 10: 1630. https://doi.org/10.3390/jcm10081630.
72. Courel-Ibáñez J, Pallarés JG, García-Conesa S, et al. Supervised exercise (Vivifrail) protects institutionalized older adults against severe functional decline after 14 weeks of COVID confinement. J Am Med Dir Assoc 2021; 22: 217-9. e2.
73. Ilich JZ, Inglis JE, Kelly OJ, et al. Osteosarcopenic obesity is associated with reduced handgrip strength, walking abilities, and balance in postmenopausal women. Osteoporos Int 2015; 26: 2587-95. https://doi.org/10.1007/s00198-015-3186-y.
74. Bauer JM, Cruz-Jentoft AJ, Fielding RA, et al. Is there enough evidence for osteosarcopenic obesity as a distinct entity? a critical literature review. Calcifed Tissue International 2019; 105:109-24. https://doi.org/10.1007/s00223-019-00561-w.
75. Kelly OJ, Gilman JC, Boschiero D, et al. Osteosarcopenic obesity: Current knowledge, revised identification criteria and treatment principles. Nutrients 2019; 11:747. doi:10.3390/nu11040747.
76. Karasik D and Kiel DP. Evidence for pleiotropic factors in genetics of the musculoskeletal system. Bone 2010; 46:1226-37.
77. dos Santosa VR, Christofarob DGD, Gomes IC, et al. Relationship between obesity, sarcopenia, sarcopenic obesity, and bone mineral density in elderly subjects aged 80 years

and over. Rev Bras Ortop 2018;53:300-5.
78. Granic A, Mendonça N, Sayer AA, et al. Low protein intake, muscle strength and physical performance in the very old: The Newcastle 85+ Study. Clin Nutr 2018; 37: 2260-70.
79. Mendonça N, Granic A, Hill TR, et al. Protein intake and disability trajectories in very old adults: The Newcastle 85+ Study. J Am Geriatr Soc 2019; 67:50-6.
80. Stahn AC, Maggioni MA, Gunga HC, et al. Combined protein and calcium β-hydroxy-β-methylbutyrate induced gains in leg fat free mass: A double-blinded, placebo-controlled study. J Int Soc Sports Nutr 2020; 17:16. https://doi.org/10.1186/s12970-020-0336-1.
81. Peng LN, Cheng YC, Yu PC, et al. Oral nutritional supplement with β-hydroxy-β-methylbutyrate (HMB) improves nutrition, physical performance and ameliorates intramuscular adiposity in pre-frail older adults: A randomized controlled trial. J Nutr Health Aging 2021; https://doi.org/10.1007/s12603-021-1621-7.
82. Costa Riela NA, Alvim Guimarães MM, Oliveira de Almeid D, et al. Effects of beta-hydroxy-beta-methylbutyrate supplementation on elderly body composition and muscle strength: A review of clinical trials. Ann Nutr Metab 2021;77:16-22. doi: 10.1159/000514236.
83. Walrand S, Short KR, Bigelow ML, et al. Functional impact of high protein intake on healthy elderly people. Am J Physiol Endocrinol Metab 2008; 295, E921-E928.
84. Mamerow MM, Mettler J, English KL, et al. Dietary protein distribution positively influences 24-h muscle protein synthesis in healthy adults. J Nutr 2014; 144: 876-80.
85. Deutz NEP and Wolfe RR. Is there a maximal anabolic response to protein intake with a meal? Clin Nutr 2013; 32, 309-13.
86. Bouillanne O, Curis E, Hamon-Vilcot B, et al. Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: A randomized controlled trial. Clin Nutr 2013; 32:186-92.
87. Boirie Y, Gachon P, Beaufrere B. Splanchnic and whole-body elderly men13 leucine kinetics in young and elderly men. Am J Clin Nutr 1997; 65:489-95.
88. Hickson M. Nutritional interventions in sarcopenia: A critical review. Proc Nutr Soc 2015; 74: 378-86. doi:10.1017/S0029665115002049.
89. Woo J. Nutritional interventions in sarcopenia: Where do we stand? Curr Opin Clin Nutr Metab Care 2018; 21:19-23. doi:10.1097/MCO.0000000000000432.
90. Robinson SM, Reginster JY, Rizzoli R, et al. for the ESCEO working group. Does nutrition play a role in the prevention and management of sarcopenia? Clin Nutr 2018; 37: 1121-32. http://creativecommons.org/licenses/by-nc-nd/4.0/.
91. Oh C, Jeon BH, Storm SNR, et al. The most effective factors to offset sarcopenia and obesity in the older Korean: Physical activity, vitamin D, and protein intake. Nutrition 2017; 33: 169-73.
92. Borst SE. Interventions for sarcopenia and muscle weakness in older people. Age Ageing 2004;33:548-55. doi: 10.1093/ageing/afh201.
93. Ocampo A, Reddy P, Martinez-Redondo P, et al. In vivo amelioration of age-associated hallmarks by partial reprogramming. Cell 2016; 167:1719-33.
94. Zakrzewski W, Dobrzynski M, Szymonowicz M, et al. Stem cells: Past, present, and future. Stem Cell Res Ther 2019;10:68. doi: 10.1186/s13287-019-1165-5.
95. Lo JHT, U HP, Yiu T, et al. Sarcopenia: current treatments and new regenerative therapeutic approaches. J Orthop Translat 2020;23:38-52.
96. Kirkwood TBL. Why and how are we living longer? Exp Physiol 2017; 102: 1067-74. doi:10.1113/EP086205.
97. Wahl HW. Aging successfully: possible in principle? possible for all? desirable for all? Integr Psych Behav 2020; 54:251-68. https://doi.org/10.1007/s12124-020-09513-8.

肌少症與肌少性肥胖症－小型文獻回顧

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摘　要

隨著年齡增長，肌少症引起骨骼肌在質與量皆減少，活動力因而減弱。骨骼肌的在保持人體健康的角色，除了讓個體能自由與自主性進行各種體能活動，在新陳代謝功能的正常運作也具有極重要的調節角色，例如胰島素在各種新陳代謝功能的調控需依賴足夠量的肌肉組織，才能正常運作，在肌少症常見的胰島素阻抗現象，不僅導致血糖，血脂代謝異常，也與心血管疾病各類風險因子有關聯性。另外常與肌少症同時存在的臨床表象是脂肪組織的異常堆積，兩者同時存在時，心血管疾病的發生機率比單獨存在時明顯增加。因著現代醫學發展，人類的壽命得以明顯延長，但是常伴隨著老化而來的肌少症，甚或肌少症與肥胖症並存的臨床現象，應予以高度重視，適時的診斷與治療對策的擬定應予倡導，希冀改善高齡長者的生活品質。目前眾多的研究結果皆顯示：規律的運動，尤其以阻力性運動為主，加上補充足量蛋白質的食物療法，可以有效的減緩肌肉量的減少，並且同時增強肌力，二者同時進行可以收到最理想的臨床效果。