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Association between dietary factors and muscle mass among Koreans

한국인의 근육량과 식생활 요인과의 연관성에 관한 연구

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서울대학교 대학원

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지도교수 정 효 지

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소은진의 박사학위논문을 인준함

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Abstract

Association between dietary factors and muscle mass among Koreans

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Introduction: The progressive loss of muscle mass is a primar criteria used to determine sarcopenia, a syndrome characterized by low muscle mass and strength. Sarcopenia has been associated with an increased risk of falls, fractures, metabolic syndrome, insulin resistance, and reduced cardiopulmonary function. Ultimately, this condition results in disability, hospitalization, and death among older individuals. The etiology of sarcopenia is multifactorial. Although aging is the leading cause of sarcopenia, this condition can be accelerated by modifiable lifestyle and nutritional factors including low physical activity, high alcohol consumption, smoking, and undernutrition. While low protein intake is known to be a major nutritional factor contributing to muscle mass loss, there has been no

Korean cohort study on the long-term effects of dietary protein on muscle mass changes. Furthermore, increasingly accumulating evidence suggests that the current recommended protein daily allowance (RDA) of 0.8 g/kg body weight (BW) might not be adequate to maintain lean mass and prevent functional decline among the elderly. In addition, little is known about the potential interacting effects of sarcopenia-related factors such as obesity, alcohol consumption, and protein intake on sarcopenia. Sarcopenia is common among older adults but can also occur in younger individuals. The Writing Group for the European Working Group on Sarcopenia in Older people 2 (EWGSOP 2) calls for healthcare professionals who treat patients at risk of sarcopenia to take actions that will promote early detection and treatment. Therefore, it is necessary to investigate the association between dietary factors and age-related changes in muscle mass among Korean middle-aged individuals and older adults, whose functional deficits and subsequent risk of falling may substantially increase in the near future.

Objectives: The present study aimed to provide scientific evidence for establishing a policy to prevent muscle mass loss among Korean adults. This study was composed of three sub-studies.

The objective of the first sub-study was to identify the socioeconomic factors associated with inadequate nutrient intake among elderly Koreans using national survey data.

The second sub–study aimed to investigate the effects of protein intake on changes in lean mass according to obesity status in middle–aged individuals using prospective cohort study data.

The objective of the third sub–study was to identify the effects of various recommended protein intake levels on the development of low muscle mass according to levels of alcohol consumption in middle–aged individuals using prospective cohort study data.

Methods: The first sub–study included a total of 1869 elderly people aged 60 years and older who completed a dietary survey from the fifth Korean National Health and Nutrition Examination Survey (2010). The factors that could affect the nutritional status of the elderly such as age, family status, socioeconomic factors (education, family income, livelihood security, employment) and health–related factors (having a chronic disease, functional status, diet therapy, depression, and suicidal thoughts) were examined. Energy and protein intakes were analyzed by using the dietary intake data collected via the 24–h recall method. Based on the dietary reference intakes for Koreans, the relevant factors were analyzed by dividing the participants into a group that consumed more than 75% of the estimated energy requirements (EER) (adequate group) and those who consumed less than 75% of the EER (inadequate group). Subjects were also categorized as below the recommended daily allowance (RDA) for protein (inadequate group; <0.8 g protein/kg) or at or above the RDA (adequate group; ≥0.8 g protein/kg). Multiple logistic regression analysis was performed to estimate the odds ratio (OR) and 95% confidence intervals (CIs) of socioeconomic factors associated with inadequat4e energy and protein intake.

The second sub-study obtained data from the Korea Genome and Epidemiology Study, a population-based prospective cohort study. A total of 4412 middle-aged participants with normal baseline skeletal muscle mass were included. Dietary intake was measured using a validated semi-quantitative food frequency questionnaire. Body composition was measured using bioelectrical impedance analysis at baseline and after a 12-year follow-up. Linear mixed-effects models were used to examine the associations between protein intake at baseline and lean mass at 12-year follow-up.

The third sub-study obtained data from the Korea Genome and Epidemiology Study, a population-based prospective cohort study. A total of 4412 middle-aged participants with normal baseline skeletal muscle mass were included. Dietary intake was measured using a validated semi-quantitative food frequency questionnaire, and baseline alcohol consumption data were collected using a structured questionnaire. The skeletal muscle mass index (SMI), defined as the weight-adjusted skeletal muscle mass, was measured using multi-frequency bioelectrical impedance analyses every 2 years until the study endpoint. Low muscle mass was defined as an SMI <2 standard deviations below the sex-specific normal mean for a young

reference group. Cox proportional hazards regression model was used to calculate the hazard ratios (HRs) and 95% CIs of the association between total protein intake and the development of a low SMI during follow-up according to alcohol consumption.

Results: In the first sub-study, the carbohydrate contribution to the total energy intake in the inadequate energy intake group was significantly higher than that in the adequate intake group ($p<0.05$). In addition, in the groups with insufficient energy and protein intake, the top 5 most consumed foods were vegetables. In both men and women, educational level (OR:1.480 in men, 1.614 in women) and employment status (OR:1.751 in men, 1.464 in women) were associated with inadequate energy intake. Men aged 70 years and older showed 1.475 times higher odds of energy insufficiency compared to those aged 60-69 years, and women living with their families without a spouse showed 1.496 times higher odds of energy insufficiency compared to those living with their partner. Educational level was associated with the inadequate protein intake in both men (OR: 2.092) and women (OR: 2.030). In the family status, men living alone and women living with their families without a spouse showed 2.059 times and 1.728 times higher odds of protein insufficiency compared to those living with their partner, respectively. In addition, unemployment (OR: 1.738) and functional limitation (OR: 1.552) were found to be associated with inadequate protein intake in men.

In the second sub−study, after adjusting for covariates and lean mass at baseline, comparisons between the highest and lowest tertiles revealed that dietary protein intake was positively associated with lean mass in both men (β=0.79, P=0.001) and women (β=0.28, P=0.082) after the 12−year period. However, these differences were attenuated after additional adjustment for fat mass at baseline and were stronger in the normal−weight group (men, β=0.85, P=0.002; women, β=0.97, P<0.001) but were not detected in the obese group. In the obese group, age (men, β=4.08, P<0.001; women, β=2.61, P<0.001) and regular physical activity(men, β=0.88, P=0.054; women, β=0.76, P<0.001) were significantly associated with lean mass after 12 years of follow−up.

Lastly, in the third sub−study, during a 12−year follow−up, 395 subjects developed a low SMI. After multivariate adjustments, high protein intake (≥1.2 g/kg body weight [BW]) was shown to reduce the risk of low SMI development in both men (HR: 0.24; 95% confidence interval [CI]: 0.12, 0.51; p for trend<0.001) and women (HR: 0.29; 95% CI: 0.16, 0.53; p for trend<0.001) compared with low protein intake (<0.8 g/kg BW). An inverse association between high protein intake and risk of a low SMI was limited to women who did not drink alcohol (HR: 0.23; 95% CI: 0.11, 0.45 for comparing ≥1.2 g/kg BW *vs.* <0.8 g/kg BW; p for trend <0.001).

Conclusions: This study found that high dietary protein intake was

associated with improved muscle mass in older adults. Given the increasing prevalence of sarcopenia with aging, dietary protein requirements in older adults may need to be higher than currently recommended intake. In addition, in the groups with insufficient energy and protein intake, the top 5 most consumed foods were vegetables. Therefore, it is important to increase protein intake to prevent sarcopenia. The findings from this study showed that muscle loss could be affected by various factors including diet, lifestyle, and socioeconomic factors, in addition to physiological changes caused by aging. We observed that muscle loss is related to lifestyle factors such as alcohol consumption, exercise, and obesity status in addition to protein intake. Further socioeconomic factors such as family status and employment were also identified as factors related to inadequate energy and protein intake. Therefore, raising public awareness of the importance of protein intake on the status of muscle mass in middle-aged and older adults is critical in the prevention and management of sarcopenia. The study results suggest that comprehensive nutrition programs, including lifestyle improvements, should be implemented to prevent sarcopenia.

Keywords: protein, energy, muscle mass, socioeconomic factors, obesity, alcohol consumption, Korean adults

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Abbreviations

aMED, alternate Mediterranean Diet

ASM, Appendicular Skeletal Muscle Mass

AWGS, Asian Working Group for sarcopenia

BDHQ, Brief-type self-administered Diet History Questionnaire

BIA, Bioimpedance Analysis

BMC, Bone Mineral Content

BMI, Body Bass Bndex

BW, Body Weight

CI, Confidence Interval

CT, Computed Tomography

DASH, Dietary Approaches to Stop Hypertension

DXA, Dual X-ray Absorptiometry

EER, Estimated Energy Requirements (EER)

EWGSOP, European Working Group on Sarcopenia in Older People

FFQ, Food Frequency Questionnaire

HEI, Healthy Eating Index

HR, Hazard Ratio

IWGS, International Working Group on Sarcopenia

KHEI, Korean Healthy Eating Index

KNHNES, Korean National Health and Nutrition Examination Survey

KoGES, Korean Genome and Epidemiology Study

KRW, Korean won

MRI, Magnetic Resonance Imaging

SD, Standard Deviations

SMI, Skeletal Muscle Index

SMM, Skeletal Muscle Mass

SPPB, Short Physical Performance Battery

OR, Odds Ratio

PAGs, Physical Activity Guidelines

PEF, Peak Expiratory Flow

RDA, Recommended Daily Allowance

RFS, Recommended Food Score

UAMA, Upper Arm Muscle Assessment

Chapter 1. Introduction

1–1. Sarcopenia in an aging society

According to the World Health Organization (WHO), the number of individuals aged 60 years or older is expected to increase from 900 million to 2 billion between 2015 and 2050 (1). In other words, the population of elderly individuals who will be exposed to the risks of deteriorating strength and mobility associated with muscle loss is expected to increase enormously. According to recent estimates, the prevalence of sarcopenia ranges from 5% to 13% among individuals aged 60–70 years and from 11% to 50% among those aged ≥80 years (2). Sarcopenia is common among adults of older age but can also occur earlier in life. The Writing Group for the European Working Group on Sarcopenia in Older people 2 (EWGSOP2) emphasizes that early detection and treatment of risk groups are effective for the prevention of sarcopenia in clinical practice (3). Table 1–1 summarizes the sarcopenia prevalence in a study of Asians.

Among older adults, sarcopenia is known to be associated with increased risk of falls, fractures, reduced cardiopulmonary function, metabolic syndrome, insulin resistance, and eventually leads to the disability, hospitalization, and death of older individuals (4). Furthermore, age–related sarcopenia is a common condition associated with high personal and financial costs. One prospective study estimated that sarcopenia increased hospitalization costs by 58.5% and 34% for patients aged <65 and ≥65 years, respectively

(5). A large European study estimated the prevalence of frailty related to sarcopenia at age 50 to 64 years to be 4.1%, increasing to 17% in those aged 65 years and older (6). These results are consistent with estimates from Japan and Korea, where the prevalence of frailty has been estimated to be around 10% (7, 8). Therefore, it is important to provide nutritional guidelines for the prevention of sarcopenia in an aging society to increase the physical independence and quality of life for the elderly, and further reduce the social medical cost.

Table 1-1. Characteristic of studies included in the sarcopenia prevalence in Asia

Author, Country, year	Subjects, Age (years)	Study design	Diagnostic criteria	Cut-off points: Muscle mass (kg/m2)	Cut-off points: Handgrip strength (kg)	Cut-off points: Gait speed (m/s)	Prevalence rate (%)
Tanimoto, Japan, 2012(9)	716, ≥ 65	2 years	EWGSOP	BIA ASM/ht^2 7.0 (m); 5.8 (w)	28 (m);18(w)	Gait speed (5m); 0.8	7.8 (m); 10.2 (w)
Woo, China, 2015(10)	4000, ≥ 65	4~10 years	EWGSOP	DXA ASM/ht^2 6.52 (m); 5.44 (w)	28 (m);18(w)	Gait speed (5m); 0.8	9.50 (m); 8.55 (w)
Kim, Korean, 2014(11)	556, ≥ 65	6 years	EWGSOP	DXA ASM/ht^2 7.09 (m); 5.27 (w) ASM/wt 29.9% (m); 25.1% (w)	Isokinetic device at an angular velocity of 60 °/s (Nm/kg) 0.75 (m); 0.79 (w)	Gait speed (5m); 0.8	ASM/ht^2 8.8 (m); 8.8 (w) ASM/wt 11.6 (m); 41.2 (w)
Han, China, 2015(12)	1076, ≥ 60	Cross-sectional study	AWGS	BIA ASM/ht^2 7.0 (m);	26 (m); 18(w)	Gait speed (4m); 0.8	6.4 (m); 11.5 (w)

				5.7 (w)			
Yu, Hong Kong, 2014(13)	4000, ≥ 65	4 years	EWGSOP	DXA ASM/ht^2 6.52 (m); 5.44 (w)	28 (m); 18(w)	Gait speed (5m); 0.8	9.0
Yuki, Japan, 2015(14)	949, ≥ 65	Cross-sectional	AWGS	DXA 7.0 (m); 5.4 (w) BIA 7.0 (m); 5.7 (w)	26 (m); 18(w)	Gait speed (5m); 0.8	9.6 (m); 7.7 (w)
Yamada, Japan, 2013(15)	1882, 65-89	Cross-sectional	EWGSOP	BIA 6.75 (m); 5.07 (w)	30 (m); 20(w)	Gait speed (10 or 15m); 0.8	21.8 (m); 22.1 (w)
Ishii, Japan 2014(16)	1971, ≥ 65	Cross-sectional	EWGSOP	BIA 7.0 (m); 5.8 (w)	30 (m); 20(w)	Gait speed (5m); 0.8	14.2 (m); 22.1 (w)
Hsu, Taiwan, 2014(17)	353 (m), ≥ 65	Cross-sectional	EWGSOP	BIA 8.87 (m)	22.5 (m)	Gait speed (6m); 0.8	30.9 (m)
Jung,	382,	5 years	AWGS	BIA	26 (m);	Gait speed	28.10 (m);

Korea, 2016(18)	≥ 65			7.0 (m); 5.7 (w)	18(w)	(5m); 0.8	27.44 (w)
Yoshida, Japan, 2014(19)	4811, ≥ 65	Cross-sectional	EWGSOP	BIA 7.09 (m); 5.91 (w)	28.8 (m); 18.2 (w)	Gait speed (6.4m); 0.8	8.2 (m); 6.8 (w)
Kim, Korea, 2009(20)	526, 22-88	Cross-sectional	-	DXA ASM/ht^2 7.40 (m); 5.14 (w) AMS/wt 35.71 (m); 30.70 (w)	-	-	[≥ 60] ASM/ht^2 6.3 (m); 4.1 (w) ASM/wt 5.1 (m); 14.2 (w)
Kim, Korea, 2012(21)	10485, ≥ 20	Cross-sectional	-	DXA ASM/ht^2 8.42(m); 6.18 (w) ASM/wt 35.4 (m); 28.1 (w) Class II ASM/ht^2			Class I ASM/ht^2 30.8 (m); 10.2 (w) ASM/wt 29.5 (m); 30.3 (w) Class II ASM/ht^2

	6.58(m); 4.59 (w) ASM/wt 29.1 (m); 23.0 (w)	12.4 (m); 0.1 (w) ASM/wt 9.7 (m); 11.8 (w)

ASM, appendicular skeletal muscle mass; BIA, bioimpedance analysis; DXA, dual x-ray absorptiometry; EWGSOP, European Working Group on Sarcopenia in Older People; m, men; w, women.

1–2. Definition of sarcopenia

Sarcopenia has been described as an age–related decline in skeletal muscle mass as well as muscle function (defined by muscle strength or physical performance). In 1989, Irwin Rosenberg proposed the term 'sarcopenia' (Greek 'sarx' or flesh + 'penia' or loss) to describe this age–related decrease of muscle mass and strength (22). Subsequently, Baumgartner and colleagues have defined sarcopenia more specifically as a subgroup of older persons with muscle mass depletion, usually defined as being 2 standard deviations below the mean muscle mass of younger persons (usually age 35 years) (23). After that, the rate of publications per year in this field has risen exponentially. As shown in the Figure 1–1, since 1994 when 4 articles on sarcopenia were published, there has been an exponential increase in the number of publications, reaching 140 in 2006 (4). The growing recognition of the significance of sarcopenia has led to standardization in operational definition. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) introduced the first and most widely used definitions, which recommended cut–offs of muscle mass, muscle strength, and physical performance for diagnosing and assessing sarcopenia (24). The EWGSOP paper has been greatly contributed to the sarcopenia, and their paper has been cited more than 1000 times. However, due to differences in ethnicity, genetic background, and body size, the

EWGSOP might not apply to Asians (2). Therefore, sarcopenia experts and researchers from Taiwan, Japan, Hong Kong, South Korea, China, Malaysia, and Thailand established the Asian Working Group for sarcopenia (AWGS), and published guidelines for diagnosing sarcopenia in 2014. The criteria for the diagnosis of sarcopenia proposed by EWGSOP, AWGS, and the International Working Group on Sarcopenia (IWGS) are detailed below.

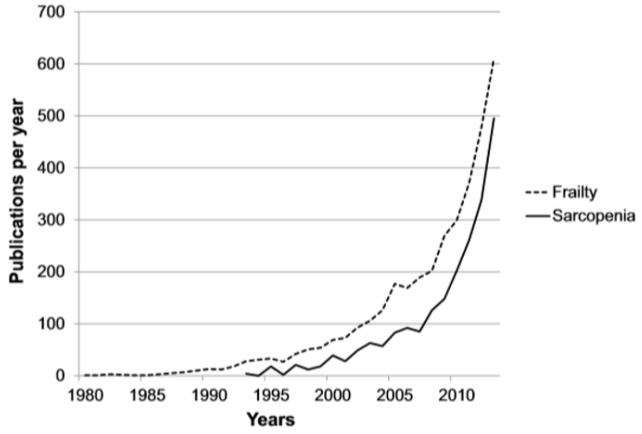


Fig 1−1. Publications per year on frailty and sarcopenia

Source: Cruz−Jentoft et al., 2017 (25)

The EWGSOP suggested different categories to reflect the severity of sarcopenia (Table 1−2). ‘Pre sarcopenia’ was defined as low muscle mass without impact on muscle strength or physical performance. ‘Sarcopenia’ was defined as low muscle mass plus low muscle strength or low physical performance. ‘Severe sarcopenia’ was defined as low muscle mass plus low muscle strength and low physical performance (24).

Table 1-2. EWGSOP conceptual stages of sarcopenia

Stage	Muscle mass	Muscle strength		Performance
Pre sarcopenia	↓			
Sarcopenia	↓	↓	Or	↓
Severe sarcopenia	↓	↓		↓

Source: Cruz-Jentoft et al., 2017 (24)

EWGSOP recommends use of healthy young adults as reference populations, with cut-off points at two standard deviations below the mean reference value: ASM/ht^2 of <6.52 kg/m^2 for men and <5.44 kg/m^2 for women and decreased physical performance (by either handgrip strength <28.0 kg for men and <18.0 kg for women, or gait speed of <0.8m/s). The EWGSOP has developed a suggested algorithm based on gait speed measurement as the easiest and most reliable way to begin sarcopenia case finding or screening in practice.

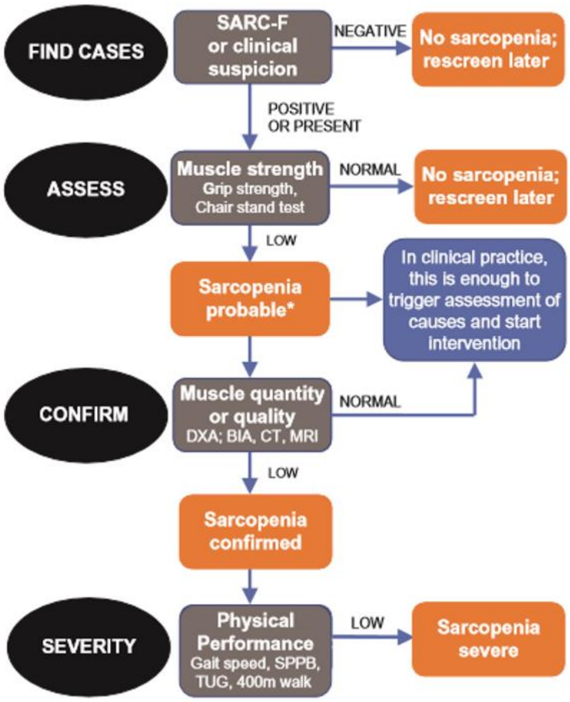


Fig 1–2. EWGSOP2 algorithm for case–finding, making a diagnosis and quantifying severity in practice (2019)

Source: Cruz–Jentoft et al., 2017 (3)

In early 2018, the Working Group met again (EWGSOP2) to update the original definition in order to reflect scientific and clinical evidence accumulated over the last decade (Fig 1–2).

The diagnostic criteria for sarcopenia defined by AWGS are as follows; 2 standard deviations below the mean value of a young reference group, or the lower quintile of the study population as the cut–off points for low muscle mass: ASM/ht^2 <7.0 kg/m^2 for men and 5.4 kg/m^2 for women and decreased physical performance (by either handgrip strength <26.0 kg for men and 18.0 kg for women, or gait speed of <0.8 m/s).

The IWGS recommended that sarcopenia should specifically be considered in patents who are bedridden, cannot independently rise from a chair, or who have a measured gait speed less than 1 m/s^{-1}. Patients who meet these criteria should further undergo body composition assessment using dual energy x-ray absorptiometry with sarcopenia being defined using currently validated definitions. A diagnosis of sarcopenia is consistent with a gait speed of <1 m/s^{-1} and an objectively measured low muscle mass (e.g., appendicular mass relative to ht^2 that is ≤7.23 kg/m^2 in men and ≤5.67 kg/m^2 in women)(27).

Assessment of sarcopenia

A wide range of techniques can be used to assess muscle mass. Cost, availability and ease of use can determine whether the techniques are better suited to clinical practice or are more useful for research.

EWGSOP recommends dual energy X-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI), and bio-impedance analysis (BIA) for sarcopenia research (24). CT and MRI are considered to be very precise imaging systems that can separate fat from other soft tissues of the body, making these methods gold standards for estimating muscle mass in research.

However, high cost, limited access to equipment at some sites and concerns about radiation exposure limit the use of these whole-body imaging methods for routine clinical practice. Thus, DXA is the preferred alternative method for research and clinical use (28).

BIA is a quick noninvasive method for measuring body composition via tissue conductivity. In addition, the test itself is inexpensive, easy to use, readily reproducible and appropriate for both ambulatory and bedridden patients. However, its reliability has been called into question as measurements can vary depending on an individual's hydration status, ethnicity, physical fitness, and age. To overcome these conditions, BIA results under standard conditions have been found to correlate well with MRI predictions (29). Prediction equations have been validated for multiethnic adults and reference values have been established for adult white men and women, including older subjects (30, 31). Thus, EWGSOP suggested BIA as a portable alternative to DXA.

Cut-off points for sarcopenia diagnosis

(1) muscle mass

Muscle mass is correlated with body size, so skeletal muscle mass (SMM) or ASM can be adjusted for body size in different ways, i.e. using height squared (ASM/ht^2), weight (ASM/weight) or body mass index (ASM/BMI). Various options to define sub-normal values for diagnosis of sarcopenia have been suggested. Baumgartner et al. summed the muscle mass of the four limbs from a DXA scan as appendicular skeletal muscle mass (ASM) and defined a skeletal muscle mass index (SMI) as ASM/ht^2 (kg/m^2). An SMI two standard deviations below the mean SMI of young male and female reference groups was defined as the gender−specific cut point for sarcopenia (23). Janssen et al. also used standard deviation to define sarcopenia, measured in terms of skeletal muscle index (SMI), where SMI = (skeletal muscle mass/body mass) x 100. Subjects were considered to have a normal SMI if their SMI was higher than one standard deviation below the gender−specific mean for young adults (aged 18−39 years). Class I sarcopenia was considered present in subjects whose SMI was within one to two standard deviations below mean values for young adults, and Class II sarcopenia was present in subjects whose SMI was below two standard deviations of young adult values (29). Newman et al. classified patients to have sarcopenia using two different approaches to adjust lean mass to body size: appendicular lean mass divided by height squared (aLM/ht^2) and appendicular lean mass adjusted for height and body fat mass (residuals). The gender specific 20th percentile was arbitrarily chosen as the cut−off point for each model (32).

Although the cut−off points for sarcopenia diagnosis depends on the measurement technique chosen and on the availability of reference studies, AWGS recommended 2 standard deviations below the mean value of a young reference group or the lower quintile of the study population as the cut−off points for low muscle mass. It also advocated using a height−adjusted index to estimate skeletal muscle mass in Asians (26). However, several Korean studies preferred using weight−adjusted muscle mass due to the extremely low prevalence of sarcopenia among older Korean women (33, 34). Kwon et al analyzed data from 11,633 Korean women aged 10−97 years and recommended the cut−off for low muscle mass to be 4.4 kg/m^2 for Korean females at any age, which is lower than that recommended by the AWGS or EWGSOP. This difference is probably because Korean women in their thirties and forties were taller than other Asian women of similar ages(35). Other Korean researchers have suggested that height−adjusted muscle index may be more practical for diagnosing sarcopenia in men whereas weight adjustment could be more appropriate for women (31). Table 1−1 shows different cut−off points available from the sarcopenia literature based on normative populations when available or on predictive populations when normative population data were unavailable.

(2) Muscle strength

Although there are fewer well−validated techniques to measure muscle strength, hand−held dynamometers to measure hand grip and quadriceps strength have been commonly used with good reproducibility and validity and are simple to use in the clinical setting (36). Thus, EWGSOP suggested that grip strength is a good simple measure of muscle strength, and it correlates with leg strength (24). According to the EWGSOP guidelines, low muscle strength using the cut-off point for handgrip strength at two standard deviations below the mean reference value is defined as <28.0 kg for men and <18.0 kg for women. Cut-off points of handgrip strength in the AWGS are defined as <26.0 kg for men and < 18.0 kg for women. A recent study in Korea suggested that the cut-off values of handgrip strength for healthy elderly men and women were 28.6 and 16.4 kg, respectively (37). Knee flexion techniques are suitable for research purposes, but their use in clinical practice is limited by the need for special equipment and training. Peak expiratory flow (PEF) measures the strength of respiratory muscle, but it cannot be recommended as an isolated measure due to limited research on the use of PEF as a measure of sarcopenia.

(3) Physical performance

A wide range of tests of physical performance are available, including the Short Physical Performance Battery (SPPB), usual gait speed, 6-min walk test and the stair climb power test (38). The cut-off points of the gait speed for defining low physical performance is <0.8 m/s. It can predict the risk of future disability and may be useful in identifying people in the preclinical stage of sarcopenia who may benefit from intervention. EWGSOP recommended the SPPB as a standard measure both for research and clinical practice (24).

Frailty

Both the concepts of frailty and sarcopenia are evolving, and there is still no full consensus on where to fit each of them in usual clinical practice. Fried et al. developed a phenotypic definition of frailty as the existence of three or more of the following physical characteristics; diagnosis−unintended weight loss, exhaustion, weakness, slow gait speed and low physical activity (39). Sarcopenia includes low physical performance, which means that sarcopenia is an essential component of physical frailty (25). In practice, frailty and sarcopenia significantly overlap (40) (Fig 1−3).

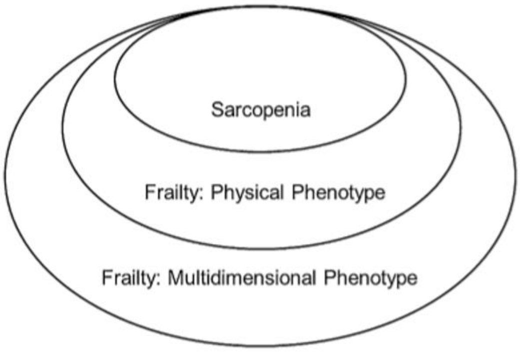


Fig 1−3. Overlap between frailty and sarcopenia

Source: Cruz−Jentoft et al., 2017 (25)

1-3. Etiology of sarcopenia

In some individuals, sarcopenia is largely attributable to ageing, whereas in many others, different causes including genetic affects, chronic diseases, lifestyle factors and socioeconomic status, can be identified. Because a wide range of factors contribute to sarcopenia development, numerous muscle changes seem possible when these multiple factors interact.

Age is well established as a major cause of muscle loss and this may be related to decreases in anabolic hormones such as testosterone, estrogen, growth hormone, and insulin-like growth factor-1 (IGF-1) as well as increases in inflammatory activity and oxidative stress, which contribute to muscle catabolism (41). Muscle mass and strength vary across a lifetime and generally increases during youth and young adulthood stage, being maintained in midlife and then decreasing with ageing. Between the ages of 30 and 50, the average adult is expected to gain approximately 0.45 kg (1 Ib) of fat and lose about 0.23 kg (0.5 Ib) of muscle yearly (42). After the age of 50 years, loss of leg muscle mass (1-2% per year) and loss of strength (1.5-5% per year) have been reported (43). From the age of 60, loss of muscle mass is accelerated and is estimated at 2% annually. The result of these losses is a decrease in total muscle cross-sectional area of about 40% between the ages of 20 and 60 years. Although there are few studies showing an age-specific standard curve for muscle mass loss in Korea, Kim et al. recently published a trend in muscle mass in 28,476 people aged 10 years and older based on data from the 2008–2012 Korean National Health and Nutrition Examination Survey (KNHANES) (44). Figure 1–4 represents the changes in the total muscle mass and ASM by age group. Although there is an evident gender difference, total muscle mass and ASM in both men and women show similar patterns with aging. The total muscle mass and ASM of men increased dramatically until their 30s and then decreased continuously until 90 years of age, with a slight acceleration after 60 years of age. In women, total muscle mass and ASM increased slowly until their 40s, remained constant until their 50s and 60s, and then began to decrease.

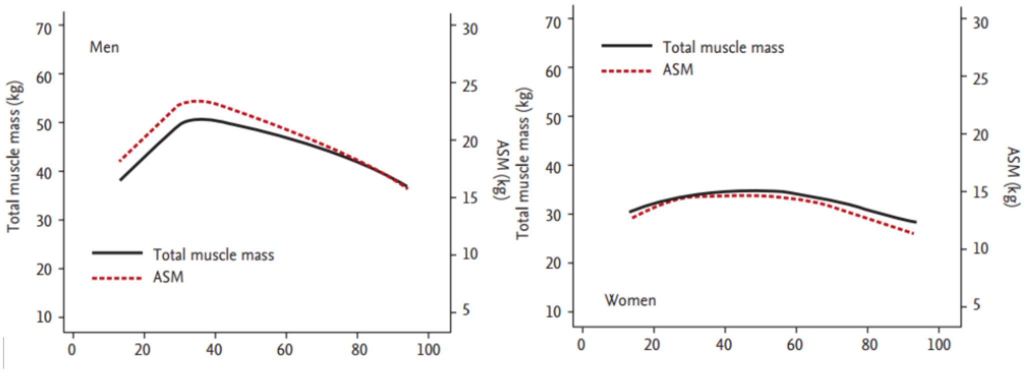


Figure 1–4. Age trend in skeletal muscle mass in men and women

Source: Kim et al., 2016 (44)

In women, the decline in estrogen levels around menopause may play a role, although evidence relating hormonal status and muscle loss is not consistent. Similarly, testosterone status in men may also be related (45, 46). As Figure 1-5 demonstrates, some of the variation in muscle mass and muscle strength with aging can partly be explained by the peak muscle mass attained in early life. Therefore, to prevent or delay sarcopenia, the aim is to maximize muscle mass in youth and young adulthood, maintain muscle mass in middle age and minimize loss in old age. In this regard, studies are needed to provide a basis for the prevention of muscle mass loss in middle-aged and older adults whose functional deficits and subsequent risk of falling may substantially increase in the near future.

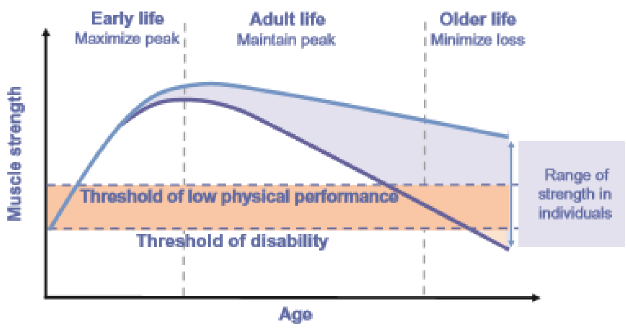


Fig 1-5. Muscle strength and the life course

Source: Cruz-Jentoft et al., 2017 (3)

The genetic component of sarcopenia is complex and driven by many genes. Several genes have been identified that contributable to variation of skeletal muscle mass and strength, including the IGF-1 and vitamin D receptor genes (47). Lifestyle factors including nutrition, physical activity, alcohol consumption, and smoking have a substantial impact on the progression of sarcopenia in old ages.

Since lifestyle habits are more modifiable in comparison to age-related systemic changes and genetic factors, it is of great importance to raise public awareness regarding their influence on the progression of sarcopenia. Most lifestyle habits, including smoking, increased height and weight, and physical inactivity, have been established as factors affecting age-related loss of muscle mass. However, studies on the role of nutrients with the exception of protein are lacking. Alcohol consumption, vitamin D, antioxidants, and dietary fat intake are less established risk factors of sarcopenia (25, 45, 46, 48). Table 1-3 summarizes the biological, nutritional, and lifestyle factors affecting the age-related loss of skeletal muscle mass.

Table 1-3. Summary of the biological, nutritional and lifestyle factors affecting age-related loss of skeletal muscle mass

Criterion	Risk factors
Nutritional factors	Low energy intake
	Low protein intake
	Low diet quality
	Vitamin D deficiency
	Low antioxidant nutrients
Biological and genetic Factors	Increased age
	Women
	Sex hormone deficiency
	Myostatin gene
	Vitamin D receptor gene
Lifestyle factors	Obesity
	Smoking habit
	Alcohol consumption
	Physical inactivity
Comorbidities	Diabetes
	Neuro-degenerative disease
	Use of ACE inhibitors
	Use of steroids
Socio-economic factors	Low income

Therefore, further research on the associations between nutritional factors and muscle mass is needed to develop potential strategies for the prevention and treatment of sarcopenia.

1-4. Dietary factors affecting loss of muscle mass

Nutrition may be involved in exacerbating sarcopenia progression because age is associated with a decrease in dietary nutrient intake and poorer ability to respond to dietary anabolic stimuli, possibly through immunological or hormonal changes (49). Although studies have been conducted on diets related to sarcopenia, most studies focused on protein intake, and there is a lack of studies covering other nutrients, food patterns, or dietary quality (46). In Korea, few studies have examined the dietary factors related to sarcopenia, and most of them have been cross-sectional studies.

(1) Protein

To date, protein intake in terms of the quantity, distribution, and quality has been the main nutritional focus (48, 50-54). Protein quantity and quality in a meal affect muscle mass. However, little is known about the effects of protein distribution in individual meals on adult muscle mass. There is evidence that nitrogen turnover is not only influenced by the amount, but also by the pattern of protein feeding. Several studies have shown that even protein intake has a significant positive effect on muscle mass (51, 55) and strength (56) as well as frailty (57). Diet quality is a relatively new concept that involves the assessment of both quality and variety of the entire diet, thus enabling the examination of the association between whole foods and health status rather than just nutrients (58). This is measured by scoring food patterns in terms of how closely they align with national dietary guidelines and how diverse the variety of healthy choices are within core food groups or equivalent international groupings.

Quantity of protein intake

The adequacy of the current recommended daily allowance (RDA) of protein of 0.8 g/kg body weight (BW), has been questioned. In particular, it has been suggested that this daily allowance might not be adequate to maintain the lean mass as well as prevent functional decline among the elderly (53, 59). Rather, recent reviews and consensus statements have suggested that a protein intake of 1.0–1.5 g/kg BW may confer health benefits beyond those afforded by simply meeting the minimum RDA (60–62). There continues to be debate about the significance of protein intake and requirements in sarcopenia prevention and treatment in older adults, with disagreement in the literature over whether adequate evidence of benefit exists to support an increase in recommended protein intake for older people (63, 64). A summary of the associations between the quantity of protein intake and muscle mass in previous observational studies are presented in Table 1–4.

Proteins from animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt are considered high quality proteins because they contain all nine essential amino acids that can be readily used for protein synthesis. On the other hand, proteins from plant sources such as legumes, grains, nuts, seeds and vegetables are deficient or low in essential amino acids, especially lysine (65, 66). Lean protein-rich foods from animal sources provide a higher protein/energy ratio than plant sources (67). Leucine, an essential amino acid, is also recognized as a potent stimulator of muscle protein synthesis (46, 48, 68). *In vivo* and *in vitro* studies have demonstrated the ability of leucine to attenuate skeletal muscle wasting by interaction with proteolytic pathways (69). Leucine produces its anabolic effects in muscle by stimulating the mammalian target of rapamycin (mTOR) pathway (70). Although protein-rich foods such as red meat are frequently linked with less healthy eating patterns (71, 72), many studies have shown positive effects of animal protein in preventing sarcopenia (54, 73-76).

Distribution of protein intake

Distribution of protein intake is also related to frailty and sarcopenia, although this is less clear (51, 56, 57, 77-79). In one of these studies, the ingestion of 25–30 g of high-quality protein in a single meal enhanced the stimulation of muscle protein synthesis in young and elderly people (79). In the longitudinal study on nutrition and aging, an even distribution of daily protein intake across meals was independently associated with greater muscle strength in older adults

(76–84 years) (56). Another study also suggested that a more uneven distribution, but not quantity of protein intake, was observed in frail compared with that in non-frail community-dwelling elderly persons (≥75 years) (57). A summary of the associations between the distribution of protein intake and muscle mass in previous observational studies is presented in Table 1-5.

Quality of protein intake

Measures of diet quality have evolved with several scoring indices currently in use.

There is some evidence relating handgrip strength to overall dietary quality indicators, such as the Healthy Eating Index (HEI) (80), diet patterns (81, 82), Dietary Approaches to Stop Hypertension (83), Korean Healthy Eating Index (KHEI) (84), and recommended food score (RFS) (85). Dietary patterns associated with sarcopenia have been suggested for Mediterranean diet. One study examined the association between adherence to Mediterranean diet and decline in walking speed over 8 years in elderly people aged 70 years and older in the United States, whereas another study evaluated the relationship between Mediterranean diet and mobility decline among elderly people aged 65 years and older in Italy (82, 86). In both studies, walking speed and Short Physical Performance Battery (SPPB) were significantly higher in the group with the Mediterranean diet. In a recent cohort study in Japan, dietary variety score was associated with physical functions such as grip strength and walking speed, but not with muscle mass (87). Moreover, a recent cross-sectional study involving elderly Korean men suggested an association between RFS and muscle mass (88). A summary of the associations between the quality of protein intake and muscle mass in previous observational studies is presented in Table 1-6.

From the available evidence, adequate protein intake is undoubtedly important for the maintenance of muscle mass during ageing, but the role of other nutrients and other dietary factors such as fat composition, antioxidant nutrients, dietary acid-base load, mineral intake and bioactive compounds deserve further research. A study involving elderly people aged 65 years or older reported that vegetable and fruit intake had a significant relationship with sarcopenia (89). Other cross-sectional studies reported associations between fish intake (90) and grip strength as well as dairy consumption and lean body mass and physical function (76).

Table 1-4. Summary of the associations between quantity of protein and muscle mass in previous observational studies

Author, Country, year	Study design	Subjects, Age (years)	Dietary assessment	Exposure	Outcome	Main results
Houston, USA, 2008(50)	3 years cohort	2066 elderly people, 70-79	FFQ	Quintile of energy adjusted total protein intake	Changes in lean mass	1) Highest quintile of protein intake (↓)
Meng, Australia, 2009(91)	5 years cohort	862 women, 70-85	FFQ	Tertile of protein intake < 66 g 66-87 g > 87 g	UAMA Body composition	1) Protein intake (↑) at baseline 2) Highest tertile (> 87g) (↑) after 5 years except BMC
Kobayashi, Japan, 2013(92)	Cross-sectional	2108 adults, ≥ 65	BDHQ	Protein intake (total, animal, plant, eight selected amino acid)	Frailty	1) The third, fourth, and fifth quintiles of total protein intake (> 69.8 g/d) (↓)
Gregorio,	Cross-	387 women,	4-day	< 0.8 g	Physical	1) < 0.8 g

USA, 2014(93)	sectional	60–90	food record	protein/kg (RDA) ≥ 0.8 g protein/kg	performance Physical activity Health-related quality of life	protein/kg (↓) in body fat, fat-to-lean ratio 2) < 0.8 g protein/kg (↑) in upper and lower extremity function
Chan, China, 2014(94)	4 years cohort	1411 men, 1315 women, ≥ 65	FFQ	Quartile of relative total protein Quartile of relative animal protein Quartile of relative vegetable protein	Physical performance measures Appendicular skeletal muscle mass	1) Highest quartile of relative vegetable protein (↓) less decline skeletal muscle mass over 4-year 2) (-) changes in physical performance measures over 4-year
Isanejad, USA, 2016(95)	3 years intervention study	554 adults, 65.3–71.6	3-day food record	Protein intake ≤ 0.8 g/kg 0.81–1.19 g/kg ≥ 1.2 g/kg	Sarcopenia	1) Higher protein intake (≥1.2g/kg) (↑)

Farsijani, Canada, 2016(51)	2 years cohort	351 men, 361 women, 67-84	3-day 24-h food recalls	Quantile of protein intake Distribution of protein intake	lean mass and appendicular lean mass	1) Evenly distributed protein intake (↑) in both men and women 2) High protein intake (↑) in men
Bradlee, USA, 2017(54)	9 years cohort	5124 adults, ≥ 40	3-day diet record	Protein source (beef/lamb/ port, poultry/ fish, diary, legumes/soy/nuts /seeds, animal protein) servings/day	Preservation of muscle mass and functional performance	1) Protein-source foods (↑) 2) Animal sources (↑) regardless of activity 3) Plant sources (↑) only in physically active adults

(↑) positive association; (↓) negative association; (−) non-significant association; FFQ, food frequency questionnaire; UAMA, upper arm muscle assessment; BMC, bone mineral content; RDA, recommended daily allowance; BDHQ, brief-type self-administered diet history questionnaire.

Table 1-5. Summary of the associations between distribution of protein and muscle mass in previous observational studies

Author, Country, year	Study design	Subjects, Age (years)	Dietary assessment	Exposure	Outcome	Main results
Bollwein, Germany, 2013(57)	Cross-sectional	194 seniors, ≥ 75	FFQ	Protein intake CV (SD/mean)	Non-frail Pre-frail Frail	1) Protein intake (−) 2) The median CV of protein distribution (↑)
Loenneke, USA, 2016(96)	Cross-sectional	1081 adults, 50–85	1-day 24-h dietary recalls	The number of meals Individuals consumed ≥ 30 g of protein per meal (0 times/ 1time/ 2times)	Leg lean mass Knee extensor strength	1) The number of ≥ 30 g protein meal (↑)
Farsijani, Canada, 2016	2 years cohort	351 men, 36 women, 67–84	Three 24-h food	Meal protein distribution CV (SD/mean)	Lean mass loss	1) More-evenly distribution protein intake

(51)			recalls			Lean mass (↑) Appendicular lean mass (↑) The lean mass rate of decline (−)
Farsijani, Canada, 2017(56)	3 years cohort	827 men, 914 women, 67–84	6−day 24−h dietary recalls	Meal protein distribution CV (SD/mean)	Muscle strength (handgrip, arm, leg) Mobility (timed up and go, chair stand, walking speed)	1) More−evenly distribution protein intake Muscle strength (↑) Mobility score (−)

(↑) positive association; (↓) negative association; (−) non−significant association; FFQ, food frequency questionnaire.

Table 1-6. Summary of the associations between quality of protein and muscle mass in previous observational studies

Author, Country, year	Study design	Subjects, Age (years)	Dietary assessment	Exposure	Outcome	Main results
Robinson, UK, 2008(90)	Cross-sectional	2983 adults, 59–73	FFQ	'Prudent' diet score Food consumption (portion per week); fruit, nuts, vegetables, eggs & egg dishes, offal, other meats, white fish & shellfish, fatty fish, breakfast cereals	Handgrip strength	1) Each additional portion of fatty fish consumed per week (↑)
Milaneschi, Italy, 2011(86)	9 years cohort	935 total, ≥ 65	-	Adherence to the Mediterranean diet	SPPB	1) Mediterranean (↑)
Shahar, USA,	8 years cohort	2225 total, ≥ 70	-	Adherence to the Mediterranean diet	20-m walking	1) Mediterranean (↑)

2012(82)					speed	
Hashemi, Iran, 2015(97)	Cross-sectional	300 adults, ≥ 55	FFQ	Tertile of dietary pattern Mediterranean Western Mixed	Sarcopenia	1) Mediterranean (↓) 2) Western (−) 3) Mixed (−)
Yokoyama, Japan, 2017(87)	4 years cohort	935 total, ≥ 65	−	Dietary variety	Lean mass Appendicular lean mass Grip strength Usual gait speed	1) Lean mass (−) 2) Appendicular lean mass (−) 3) Grip strength (↑) 4) Usual gait speed (↑)
Kuczmarski, USA, 2018(83)	Cross-sectional	2486 total, 33-71	2-d 24 h recalls	Adherence to the DASH eating plan and Healthy Eating Index-2010	Handgrip strength	1) The DASH adherence or Health Eating Index-2010 (↑)
Barrea, Italy, 2019 (81)	Cross-sectional	84 women, 65-85	7-d food records	Adherence to the Mediterranean diet	Handgrip strength	1) Mediterranean diet adherence(↑)
Kim,	Cross-	3675 total,	24-h	Adherence to the	Handgrip	1) Three diet

Korea, 2019(85)	sectional	≥ 65	recall	KHEI, aMED, DASH	strength	quality indices- HKEI, aMED, and DASH (↑)
Jung, Korea, 2019(88)	Cross-sectional	263 men, 258women, > 65	-	RFS	ASM Handgrip strength	[men] 1) ASM (↑) 2) Grip strength (↑)
Jeong, Korea, 2019(84)	Cross-sectional	294 men, 328 women, ≥ 65	-	RFS	Handgrip strength	1) RFS (↑)

(↑) positive association; (↓) negative association; (-) non-significant association; FFQ, food frequency questionnaire; SPPB, the short physical performance battery; DASH, dietary approaches to stop hypertension; KHEI, the Korean healthy eating index; aMED, the alternate Mediterranean diet; RFS, the recommended food score; ASM, appendicular skeletal muscle mass.

(2) Energy

Consumed food is metabolized to provide energy for organ function and muscle activity. If intake is insufficient to meet needs, body fat and muscle are catabolized to provide energy. Aging is associated with reduced appetite and low food intake, which was previously termed the "anorexia of ageing" (49). Altered taste and smell, social changes, and economic limitations may also lead to decreased food intake (98). Therefore, in order to maintain muscle mass and physical function, the amount of food and energy consumed is of primary importance.

(3) Vitamin D

Vitamin D levels decline with age and cutaneous vitamin D levels are up to four times lower in older than in younger individuals (99). It is known that vitamin D plays an important role in bone and muscle metabolism. The mechanisms that explain the relationship between vitamin D and muscle mass and strength may be direct or indirect either through calcium handling and signaling and accumulation in the sarcoplasmic reticulum or through the activation of vitamin D receptors found in muscle (100). Recent findings have demonstrated that vitamin D plays an important role in skeletal muscle tissue by maintaining the function of type II fibers, thus preserving muscle strength and preventing falls (101). Korean researchers also found an additive association of vitamin D insufficiency and sarcopenia with low femoral bone mineral density (102). Adequate supplementation of active vitamin D could increase muscle mass, especially among patients with osteoporosis (103). Although vitamin D is highly likely to influence muscle mass, further research is needed to establish the extent to which vitamin D can positively influence muscle mass (104).

(4) Antioxidant nutrients

Oxidative stress and the accumulation of ROS potentially contribute to age-related muscle loss. Thus, consumption of nutrients with antioxidant effects may reduce oxidation in muscle (105). Of the nutrients considered to have antioxidant effects (vitamin C, E, and carotenoids and the trace elements: Cu, Mn, Se, and Zn), few interventional and observational studies have investigated their relationships with vitamin C and E (89, 106, 107). Thus, further research investigating the role of antioxidant nutrients in the prevention of muscle loss will be necessary.

1-5. Lifestyle factors affecting loss of muscle mass

(1) Obesity

Obesity has become an epidemic in the elderly (108) and obese older adults face high risks of age-related muscle wasting such as sarcopenia (109, 110). Obesity may co-exist with sarcopenia with the two conditions acting synergistically in older adults to limit functional capacity and increase the risk of disability, comorbidities, and mortality (109, 111–113). Obese older adults have been shown to have higher muscle mass than non–obese people. However, it has been suggested that muscle quality in obese individuals is poor due to increased intramuscular adipose tissue, leading to muscle weakness, frailty, and disability (98). A combination of excess body fat and reduced muscle mass and/or strength with aging is defined as sarcopenic obesity. Although the molecular mechanisms that underlie obesity–associated dysfunctions in lipid and glucose metabolism have been studied (114), the effects of obesity on the processes that regulate muscle protein metabolism remain largely unknown (115). Intramuscular lipids act as chemoattractants for macrophages that produce pro–inflammatory cytokines (116). These cytokines not only directly contribute to the breakdown of muscle proteins (117) but also interfere with the accretion of contractile material caused by chronic low–intensity muscle overloading (118). Previously, Erskine and colleagues described the paradox that circulating pro–inflammatory cytokines play different roles in neuromuscular remodeling according to the age and adiposity of the individual (119).

Korea is a rapidly aging society, thus, sarcopenia and sarcopenic obesity are important issues in this country. According to the Korean Sarcopenic Obesity Study which included 526 healthy volunteers aged 20–88 years, the prevalence of sarcopenic obesity in older

(≥60 years) men and women was 5.1% and 12.5%, respectively, in 2008. Therefore, research regarding the impact of obesity on muscle mass is essential for the development of public health programs for the increasingly elderly Korean population.

(2) Smoking

Cigarette smoking is associated with poor lifestyle habits, such as levels of physical activity and impaired nutrition (120). However, smoking itself is another lifestyle habit that has been found to be associated with sarcopenia in previous studies (120). Several studies attempted to explain the mechanism by which cigarette smoking promotes muscle catabolism and accelerates the progression of sarcopenia (121−123). As a result, degradation of skeletal muscle is increased and the progression of sarcopenia in elderly smokers may be accelerated, although further studies are needed to present as an established factor (124).

(3) Alcohol consumption

Alcohol consumption has been considered as risk factors for sarcopenia, although the potentially important role of alcohol consumption in the prevention of age−related muscle loss has not been fully investigated (4, 24, 46, 48). Some experimental animal studies have demonstrated a relationship between alcohol consumption and sarcopenia (125−127). Specifically, alcohol consumption inhibited skeletal muscle protein synthesis in rats. In human studies demonstrating the adverse effects of alcohol on skeletal muscle, chronic alcohol consumption may promote loss of muscle mass and strength in old age, although this relationship remains controversial (128–130).

For Korean adults, alcohol drinking is a very common component of the social culture, and according to a nationwide database, 81.6% of adult men and 52.4% of women were reported to be alcohol drinkers (131). Although the percentage of high-risk drinkers among Korean women is still lower than in other countries, this rate is steadily increasing (71). Therefore, reducing alcohol consumption may serve as a strategy for the prevention of sarcopenia.

(4) Physical inactivity

An inactive and sedentary lifestyle is a key factor in the loss of muscle mass and strength of old age (4, 24, 48, 132). In 2010, the WHO released Physical Activity Guidelines (PAGs) for adults aged 65 years and older. It recommended that older adults should do (a total of) at least 150 min of moderate-intensity aerobic physical activity per week or ≥75 minutes of vigorous-intensity aerobic physical activity and/or equivalent combination of moderate- and vigorous-intensity activity (133, 134).

Recent meta-analyses have reported that exercise interventions appear to have a role in increasing muscle strength and improving physical performance (27, 132, 135). In a recent study of the association of protein intake and physical activity with sarcopenia, a higher intake of animal-protein foods alone and especially in combination with a physically active lifestyle was associated with the preservation of muscle mass and functional performance in older adults (54). A randomized controlled trial in elderly Japanese women with sarcopenia confirmed that exercise and amino acid supplementation had significant effects on enhancing not only muscle strength but also the combined variables of muscle mass plus walking speed and muscle mass plus strength (136).

Based on a literature review, the etiology of sarcopenia is considered to be multifactorial (Figure 1-6). Although aging is the leading cause of sarcopenia, this condition can be accelerated by modifiable lifestyle and nutritional factors including physical inactivity, alcohol consumption, smoking, and undernutrition (48). While protein intake is known to be a major nutritional factor contributing to muscle mass loss, there has been no Korean cohort study on the long-term effects of dietary protein on muscle mass changes. Furthermore, little is known about the potential interacting effects of sarcopenia-related factors and protein intake on sarcopenia.

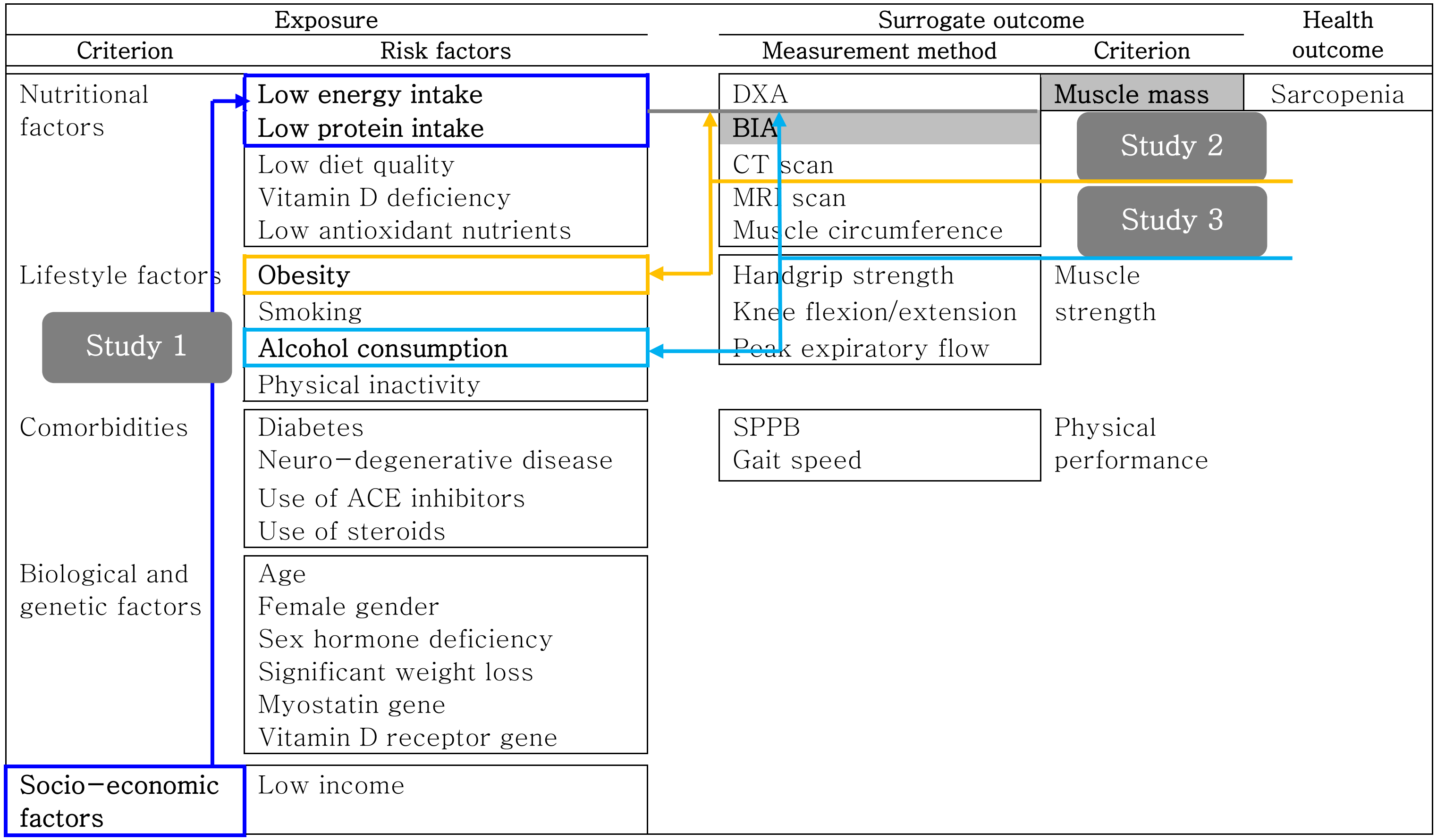


Fig 1−6. Summary of literature review

A reduction in lean body mass and an increase in fat mass is one of the most striking and consistent changes associated with advancing age. These changes in body composition appear to occur throughout life and have important functional and metabolic consequences. Additionally, in older adults with sarcopenic obesity, sarcopenia and obesity may have synergistic effects on physical disability, metabolic disorders, cardiovascular disease, and mortality. However, few studies have been conducted on how obesity affects the muscle preservation effects of dietary protein.

For Korean adults, alcohol consumption is a very common component of the social culture in Korea. While studies have shown that alcohol consumption is a factor affecting muscle mass loss, the relationship between alcohol consumption and muscle mass remains controversial. Moreover, little is known about the potential interacting effects of alcohol consumption and protein intake on muscle mass loss.

The importance of mid-life influences is becoming increasingly apparent regarding the development of sarcopenia (137, 138). WHO recently suggested a life course approach to health that provides a holistic view of people's health and wellbeing at all ages and interlinkages with human capital and sustainable development (139). In other words, risk exposures in early life can affect health, wellbeing and socioeconomic participation decades later. A recent review of sarcopenia reported that the life course approach is important to prevent sarcopenia and provide opportunities for intervention at a younger age (mid-life and before) (137). A previous study using data from the British National Survey of Health and Development (the 1946 birth cohort) showed that those in the top third of lifetime physical activity score across the four time points (at ages 36, 43, 53 and 60-64) had a mean grip strength 2.11 kg (95% CI: 0.88-3.35) stronger than those in the lower third after adjustments (140). Therefore, the findings from studies involving middle-aged individuals could provide a basis for establishing a useful framework for the prevention and management of sarcopenia.

Owing to the worldwide increase in life expectancy, the prevalence and cost of sarcopenia are likely to rise. Developing strategies to prevent and treat sarcopenia is of great importance. Therefore, the present study will be conducted for the following purposes, and the results will contribute to the prevention of muscle mass loss in middle-aged and older adults in Korea.

1-6. Objectives

The present study aimed to provide scientific evidence for establishing policy to prevent muscle mass loss among Korean adults. This study composed of three sub-studies (Figure 1-7).

The objective of the first sub-study was to evaluate the socioeconomic factors associated with inadequate energy and protein intakes intake among the Korean elderly using national survey data.

The second sub−study aimed to investigate the effects of protein intake on changes in lean mass according to obesity status in middle−aged individuals using prospective cohort study data.

Finally, the objective of the third sub−study was to identify the effects of various recommended protein intake levels on the development of low muscle mass according to alcohol consumption in middle−aged individuals using prospective cohort study data.

Title	**Study 1.** Socioeconomic status is associated with the risk of in adequate energy and protein intake among Korean elderly.	**Study 2.** Impact of dietary protein intake and obesity on lean mass in middle-aged individuals after a 12-year follow-up: the Korean Genome and Epidemiology Study (KoGES)	**Study 3.** The effect of protein intake on muscle mass according to the alcohol consumption in middle-aged Korean adults: A 12-year community-based prospective cohort study.
Objective	To evaluate the socio-economic determinant factors influencing the inadequate nutrient intake	To investigate the effects of protein intake on changes in lean mass according to obesity status	To identify the effect of various recommended protein intake levels on the development of the low muscle mass according to alcohol consumption
Design	Cross-sectional study	Cohort study	Cohort study
Subject	Data from the fifth KNHANES (2010)	Data form a large community-based cohort study of the KoGES	Data form a large community-based cohort study of the KoGES

Fig 1−7. Construction of the present study

Chapter 2. Socioeconomic Status is Associated with the Inadequate Energy and Protein Intake Among Korean Elderly[1]

[1] This study was published in the Journal of Nutrition and Health vol.48, no. 4, pages 371-379 in 2015.

Abstract

This study was conducted to evaluate the factors influencing inadequate energy intake among the Korean elderly. Our study included 1869 elderly people (aged 60 years and older) who completed a dietary survey as part of the fifth Korean NHANES (2010). The factors that could affect the nutritional status of the elderly such as age, family status, socioeconomic factors (education, family income, livelihood security, employment) and health-related factors (having a chronic disease, functional status, diet therapy, depression, and suicidal thoughts) were examined. Energy and protein intake were assessed using the dietary intake data via the 24-h recall method. The percentage of people who consumed energy less than 75% of EEA was 23.7% and 31.1% in men and women, respectively. The carbohydrate contribution to the total energy and protein intake in the inadequate energy intake group was significantly higher than that in the adequate intake group($p<0.05$). In addition, in the groups with insufficient energy and protein intake, the top 5 most consumed foods were vegetables. In both men and women, educational level (OR:1.480 in men, 1.614 in women) and employment status (OR:1.751 in men, 1.464 in women) were factors associated with inadequate energy intake. Men aged 70 years and older showed 1.475 times higher odds of energy insufficiency and women living with their families without a spouse showed 1.496 times

higher odds of energy insufficiency. Educational level was a factor associated with inadequate protein intake in both men (OR: 2.092) and women (OR: 2.030). In the family status, men living alone and women living with their families without a spouse showed 2.059 times and 1.728 times higher odds of protein insufficiency, respectively. Unemployed men and those with functional limitation showed 1.738 times and 1.552 times higher odds of protein insufficiency, respectively. In summary, the results suggest that energy and protein intake of the elderly is affected by socio-environmental status, thus, aging and nutrition-related policies for Korean elderly need to be based on the social status as well as health-related conditions.

2-1. Introduction

The Korean population is ageing rapidly. According to the statistics by the National Statistical Office, in 2000, the proportion of the population aged 60 years and older exceeded 7%. In 2026, it is expected that more than 21% of the Korean population will be aged 60 years and older. Due to this aging population, the prevalence of sarcopenia is growing, and it is currently estimated that the prevalence of sarcopenia ranges from 5% to 13% among individuals aged 60–70 years and from 11% to 50% among those aged ≥80 years (2).

Aging is associated with reduced appetite and low food intake, which was previously termed the "anorexia of ageing" (49).

Altered taste and smell, social changes, and economic limitations may also lead to decreased food intake (24). In addition to physical and physiological factors, the nutritional status of the elderly is influenced by socioeconomic factors such as poverty, social isolation, depression, and death of a spouse. A noteworthy example is Bird and Rieker's 'constrained choices' (141) multi-level model which contextualizes women and men's personal health 'choices' and outcomes as influenced and shaped by the communities in which they live and the range of social policies that directly impact their lives. However, most of the nutritional studies of the elderly in Korea have focused on the relationship between specific dietary patterns and diseases. Furthermore, large-scale studies are lacking because most studies were conducted on the elderly in one area or institution. Therefore, to develop an effective nutrition policy for the elderly, studies to identify major social and environmental factors related to malnutrition are needed.

Consumed food is metabolized to provide energy for organ function and muscle activity. If intake is insufficient to meet needs, body fat and muscle are catabolized to produce energy. Furthermore, low nutrient intake can lead to malnutrition (142) which can increase mortality, morbidity, infection rate, and hospitalization costs (143). Malnutrition in the elderly may also be a factor that doubles the physical and mental burden due to physiological aging by affecting depression (144), sarcopenia (48), frailty (145), osteoporosis (146), and would recovery (147). According to data from the 2013 KNHANES, the elderly group aged ≥65 years or older showed an overall insufficiency ratio exceeding 30% of all nutrients except phosphorus, iron, and thiamin. The proportion of malnourished elderly who consume less than 75% of the estimated energy requirements as well as consume less than estimated average calcium, iron, vitamin A, and riboflavin requirements has been reported as 7.8%. In terms of protein intake, 18.8% of adults aged ≥60 years and 34.9% of adults aged ≥70 years consumed less protein then the estimated average requirements for Koreans, indicating that many older Korean adults may have insufficient protein intake.

Therefore, in this study, we evaluated the levels of major nutrient intake and analyzed the socioeconomic factors associated with inadequate energy and protein intake using national data from the KNHANES.

2-2. Subjects and Methods

Study design and participants

This study used data from the fifth (2010) KNHNES, and an ongoing cross-sectional nationwide survey conducted by the Korea Centers for Disease Control and Prevention. A total of 2028 eligible participants aged 60 years or older participated in anthropometric and biochemical measurements. We excluded participants who did not have a 1−day 24−h dietary recall (n=134) and those who did not provide information on family status (n=25). A total of 1869 (826 men and 1043 women) were included in the final analysis. Based on the dietary reference intakes for Koreans, the relevant factors were analyzed by dividing the participants into a group that consumed more than 75% of the estimated energy requirements (EER) (adequate group) and those who consumed less than 75% of the EER (inadequate group). Overall, 319 elderly people (17.1%) who consumed more than 125% of the EER were included in the inadequate group. Subjects were also categorized as below the recommended daily allowance (RDA) for protein (inadequate group; <0.8 g protein/kg) or at or above the RDA (adequate group; ≥0.8 g protein/kg). The KNHANES was approved by the Institute Review Board of the Korea Centers for Disease Control and Prevention and written informed consent was obtained from all participants.

Assessment of dietary intake

Dietary intake was assessed via a 1−day 24−h dietary recall method administered by a trained interviewer at each participant's place of residence. Energy and macronutrient intakes were estimated based on the recall data, which included information on all food and beverages that were consumed by a participant within the 24−h period. Macronutrient intake was calculated as a percentage of energy using standard conversion factors (4 kcal/g for carbohydrate and protein and 9 kcal/g for fat). The energy contribution of carbohydrate, fat, and protein was calculated as the ratio of energy consumed from the nutrients to the total energy. To find the major food sources of energy and protein intake, the sum of energy and protein intake of each food divided by the number of subjects in each group was ordered in descending order. Since then, the list of foods ranked in the first 20 places were suggested based on men, and additional food items that deviated from the standard food list were presented.

Measurement of environmental factors associated with nutrient intake

Based on literature review (148, 149), age, family status, socioeconomic factors (education, household income, livelihood security, employment), and health-related factors (chronic disease, functional status, diet therapy, depression, suicidal ideation) were analyzed as environmental factors associated with nutrient intake. Data on these factors were obtained from the health survey performed by trained interviewers in mobile examination centers. Family status was divided into three categories: partner (living with others, including spouse), others, and living alone. Educational level was divided into two categories: ≤middle school and ≥high school. Household income was divided into two categories: low income (first quartile) and ≥middle-low income (≥second quartile). Chronic disease was measured by participants' self-report of the presence or absence of 18 chronic conditions (circulatory disease, musculoskeletal disease, respiratory disease, metabolic disease, digestive disease, and cancer). Functional status was determined in relation to the question of whether activity limitations existed, "yes" or "no." Suicidal ideation was determined as the question of whether thoughts of suicide existed, "yes" or "no." Other variables examined were diet therapy (yes/no), having livelihood security (yes/no), and having depression (yes/no).

Statistical Analysis

All statistical analyses were stratified by sex and conducted using the IBM SPSS Statistics for Windows, version 24.0 (IBM, Corp., Armonk, NY, USA). A two-sided p-value <0.05 was considered statistically significant. All continuous variables including age and macronutrient intake, were presented as means ± standard error (SE), and all categorical variables such as sociodemographic and lifestyle variables, were presented as percentages (%). Differences in general characteristics and macronutrient intake between groups were assessed using the t-test for continuous variables and a chi-squared test for categorical variables. Multiple logistic regression analysis was performed to estimate the odds ratio (OR) and 95% confidence intervals (CIs) of environmental factors associated with inadequate energy and protein intake.

2−3. Results

The sociodemographic and health−related characteristics of each energy and protein intake group are presented in Tables 2−1 and 2−2. The mean age was higher among women compared to men (69.3 years for men and 71.2 years for women), but the mean age of groups with inadequate energy intake was higher for men compared to women (71.6 years for men and 70.9 years for women). In the protein analysis, the mean age of groups with inadequate protein intake was higher for men than women (71.2 years for men and 70.4 years for women). Men and women who consumed less than 75% of the EER were more likely to be older, have lower employment, and higher activity limitations. Men who lived with their families without a spouse, had low education and household income, and women who had suicidal ideations consumed less than 75% of the EER. Men and women who consumed less than the RDA for protein were more likely to be older, had lower educational levels and family income, and employment, and higher activity limitations. Men who lived with their families without a spouse and had a chronic disease, and women who lived alone and had livelihood security and suicidal ideations consumed less than the RDA for protein.

Table 2-1. Profile of inadequate energy intake among Korean elderly by sex

Variables		Men (n=826)					Women (n=1043)					p (by sex)
		Adequate[1)] (n=630)		Inadequate (n=196)		p	Adequate (n=719)		Inadequate (n=324)		p	
		n	%	n	%		n	%	n	%		
Age (Mean±SD)		68.83±6.1		71.6±7.3		<0.001[2)]	69.66±6.7		70.9±7.9		0.013	0.080
Age	60-69years	366	58.1	78	39.8	<0.001[3)]	394	54.8	149	46.0	0.008	<0.001
	≥70years	264	41.9	118	60.2		325	45.2	175	54.0		0.113
Family status	Partner[4)]	585	92.9	169	86.2	0.008	415	57.7	155	47.8	0.093	0.026
	Others	21	3.3	13	6.6		173	24.1	114	35.2		0.511
	Living alone	24	3.8	14	7.1		131	18.2	55	17.0		0.242
Education	≥High	392	62.2	104	53.1	0.022	194	27.0	74	22.8	0.157	0.024
	≤Middle	238	37.8	92	46.9		525	73.0	250	77.2		0.085
Family income[5)]	≥Middle-low	381	60.5	101	51.5	0.027	358	49.8	171	52.8	0.372	<0.001
	low	249	39.5	95	48.5		361	50.2	153	47.2		0.273
Livelihood security	No	623	99.0	190	97.4	0.087	684	95.3	300	92.9	0.118	<0.001
	Yes	6	1.0	5	2.6		34	4.7	23	7.1		0.502
Employment	Employed	336	56.1	69	38.1	<0.001	223	33.1	69	23.7	0.003	0.020
	Unemployed	263	43.9	112	61.9		450	66.9	222	76.3		0.162

Chronic disease[6)]	No	221	35.1	67	34.2	0.818	171	23.8	80	24.7	0.751	0.016
	Yes	409	64.9	129	65.8		548	76.2	244	75.3		0.004
Functional status[7)]	Independent	497	83.0	136	75.1	0.018	498	74.0	200	67.8	0.048	0.002
	Dependent	102	17.0	45	24.9		175	26.0	95	32.2		0.202
Diet therapy	No	494	78.8	146	74.5	0.207	536	75.0	234	72.4	0.391	0.001
	Yes	133	21.2	50	25.5		179	25.0	89	27.6		0.110
Depression	No	541	90.3	161	89.0	0.591	545	80.9	224	77.0	0.169	0.004
	Yes	58	9.7	20	11.0		129	19.1	67	23.0		0.109
Suicidal ideation[8)]	No	519	86.6	152	84.0	0.365	508	75.5	199	68.6	0.027	0.011
	Yes	80	13.4	29	16.0		165	24.5	91	31.4		0.060

1) Unsatisfactory group : under 75% of EER, satisfactory group : more than 75% of EER 2) p value for t−test by each variables in same sex 3) p value for chi−square tests by each variables in same sex 4) With partner : include with partner, with others 5) Family income, low : Q1 of income quartile(Q) 6) Chronic disease : 18 diseases including circulatory disease, musculoskeletal disease, respiratory disease, metabolic disease, digestive disease, cancer 7) Functional status : Whether activity limitations, "Yes" or "No" 8) Suicidal ideation : Thoughts of suicide

Table 2-2. Profile of inadequate protein intake among Korean elderly by sex

Variables		Men (n=826)					Women (n=1043)					p (by sex)
		Adequate[1)] (n=543)		Inadequate (n=249)		p	Adequate (n=493)		Inadequate (n=497)		p	
		n	%	n	%		n	%	n	%		
Age (Mean±SD)		68.69±6.1		71.2±6.8		0.003[2)]	69.16±6.7		70.4±6.7		0.002	0.080
Age	60-69years	318	58.6	105	42.2	<0.001[3)]	285	5708	238	47.9	0.002	<0.001
	≥70years	225	41.4	144	57.8		208	42.2	259	52.1		<0.001
Family status	Partner[4)]	505	93.0	217	87.1	0.002	301	61.1	239	48.1	0.002	<0.001
	Others	21	3.9	11	4.4		106	21.5	158	31.8		0.006
	Living alone	17	3.1	21	8.4		86	17.4	100	20.1		0.866
Education	≥High	351	64.6	111	44.6	<0.001	140	28.4	75	15.1	<0.001	0.003
	≤Middle	192	35.4	138	55.4		353	71.6	422	84.9		<0.001
Family income[5)]	≥Middle-low	341	62.8	124	49.8	0.001	263	53.3	231	46.5	0.031	<0.001
	low	202	37.2	125	50.2		230	46.7	266	53.5		<0.001
Livelihood security	No	537	98.9	244	98.0	0.313	474	96.1	459	92.4	0.010	<0.001
	Yes	6	1.1	5	2.0		19	3.9	38	7.6		0.182
Employment	Employed	300	56.7	101	40.9	<0.001	162	33.9	129	26.6	0.014	<0.001
	Unemployed	229	43.3	146	59.1		316	66.1	356	73.4		<0.001
Chronic	No	200	36.8	58	23.3	<0.001	107	21.7	91	18.3	0.182	<0.001

disease[6)]	Yes	343	63.2	191	76.7		386	78.3	406	81.7		<0.001
Functional status[7)]	Independent	446	84.3	183	74.1	0.001	365	76.2	332	34.3	0.005	<0.001
	Dependent	83	15.7	64	25.9		114	23.8	156	32.0		0.005
Diet therapy	No	422	78.1	188	75.5	0.409	360	73.5	361	72.9	0.848	<0.001
	Yes	118	21.9	61	24.5		130	26.5	134	27.1		0.001
Depression	No	479	90.4	219	89.0	0.560	386	80.2	382	79.1	0.654	<0.001
	Yes	51	9.6	27	11.0		95	19.8	101	20.9		0.011
Suicidal ideation[8)]	No	463	87.4	204	82.9	0.098	367	76.5	339	70.3	0.032	<0.001
	Yes	67	12.6	42	17.1		113	23.5	143	29.7		0.002

1) Unsatisfactory group : under the RDA for protein, satisfactory group : more than the RDA for protein 2) p value for t−test by each variables in same sex 3) p value for chi−square tests by each variables in same sex 4) With partner : include with partner, with others 5) Family income, low : Q1 of income quartile(Q) 6) Chronic disease : 18 diseases including circulatory disease, musculoskeletal disease, respiratory disease, metabolic disease, digestive disease, cancer 7) Functional status : Whether activity limitations, “Yes” or “No” 8) Suicidal ideation : Thoughts of suicide

Table 2-3 shows the intakes and distribution of macronutrient contribution of energy and protein intakes. The average energy, fat, and protein intake was 2032.2 kcal, 31.4 g, and 70.6 g in men, respectively, and 1522.6 kcal, 20.3 g, 49.1 g in women, respectively. As a result of evaluating the proportion of energy from macronutrients, carbohydrates in the energy intake were significantly higher in the men and women who consumed less than 75% of the EER. The proportion of energy from fat and protein was significantly higher in men, and the carbohydrate was significantly higher in women. The percentage difference between these groups was similarly analyzed in the group that consumed less than RDA protein.

The major food sources of energy intake were white rice, soju (Korean distilled spirits), pork, coffee, and barley in men, and white rice, rice cake, barley, and soybean in women (Table 2-4). For men, energy intake was high from soju or makgeolli (raw rice wine), and for women, fruit and sweet potatoes, and coffee was analyzed as a major source of energy in both men and women. In men, the group with less than 75% of EER did not include pork in the top 10 as the major source of energy intake, and beef ranked 19th. For women who consumed more than 75% of EER, pork and beef were included in the top 10, but those who consumed less than 75% of EER ranked 11th for pork and 16th for beef. In the group with less than 75% energy intake, men had Kimchi and soy paste as the main source of energy intake in the 20^{th}, and women had similar results. The major food sources of protein intake were white rice, pork, beef, soybean, and tofu in both men and women. Kimchi and soybean paste were analyzed as a major source of protein intake in both men and women. In the group that consumed less than the RDA protein, the top 5 were vegetable protein in both men and women. In men and women, coffee was analyzed as a major source of protein in the group that consumed less than the RDA protein (Table 2-5).

Table 2-3. Intakes and distribution of macronutrients contribution of energy and protein intakes among Korean elderly by sex

	Men (n=826)				
	Total	Energy		Protein	
		Adequate (n=630)	Inadequate (n=196)	Adequate (n=543)	Inadequate (n=249)
Total energy (kcal)	2036.2±21.1[1)]	2276.2±22.4	1291.5±40.5[1)]	2291.3±25.8	1522.1±38.4
Carbohydrate (g)	347.4±3.7	382.4±0.9	238.6±7.1	379.4±4.6	286.5±6.9
Total fat (g)	31.4±0.7	36.2±17.0	17.0±1.6	38.4±0.9	17.1±1.4
Total protein (g)	70.6±1.0	79.7±1.3	42.7±2.3	84.7±1.2	41.5±1.8
% of EER[2)]	99.3±34.8[7)]	111.2±30.7	61.2±12.4	111.0±32.7	72.8±20.8
% of protein[3)]	117.7±59.1	132.6±58.4	68.0±23.9	141.5±56.3	66.0±17.0
% CHO/energy[4)]	72.1±10.1	70.9±10.2	75.7±9.0	69.2±9.6	78.5±7.6
% FAT/energy[5)]	13.8±7.7	14.6±7.9	11.2±6.6	15.4±7.7	10.2±6.1
% PRO/energy[6)]	14.2±4.0	14.5±4.1	13.1±3.7	15.4±3.8	11.3±2.4

1) p value for t-test by each variables in same sex (all variables $p < 0.05$) 2) EER: Estimated average requirements

3) Recommended intake: 1g by Ideal Body Weight 4) [carbohydrate intake(g) × 4(kcal/g)]/[carbohydrate intake × 4 + protein intake × 4 + fat intake × 9] ×100 5) [fat intake(g) × 9(kcal/g)]/[carbohydrate intake × 4 + protein intake × 4 + fat intake × 9] ×100 6) [protein intake(g) × 4(kcal/g)]/[carbohydrate intake × 4 + protein intake × 4 + fat intake × 9] ×100 7) Mean±SD

Table 2-3. Intakes and distribution of macronutrients contribution of energy and protein intakes among Korean elderly by sex (continued)

	Women (n=1043)				
	Total	Energy		Protein	
		Adequate (n=719)	Inadequate (n=324)	Adequate (n=493)	Inadequate (n=497)
Total energy (kcal)	1522.6±18.7[1)]	1760.2±13.8	979.3±20.6	1837.0±18.6	1204.4±18.6
Carbohydrate (g)	289.3±3.3	332.7±2.9	190.8±4.3	337.4±4.0	242.6±4.0
Total fat (g)	20.3±0.6	24.1±0.5	11.5±0.8	27.8±0.6	12.5±0.6
Total protein (g)	49.1±0.9	57.0±0.7	30.7±1.1	65.1±0.7	33.1±0.7
% of EER[2)]	91.9±31.6[7)]	106.9±25.6	58.7±12.9	111.2±29.0	73.1±21.0
% of protein[3)]	101.6±48.1	118.5±46.5	63.7±24.3	135.9±43.8	67.6±19.9
% CHO/energy[4)]	76.0±8.9	75.2±9.2	77.6±8.1	72.3±8.9	79.8±6.9
% FAT/energy[5)]	11.4±6.6	12.0±6.8	10.2±5.9	13.5±6.6	9.2±5.6
% PRO/energy[6)]	12.6±3.5	12.8±3.5	12.8±3.4	14.3±3.7	11.0±2.3

1) p value for t-test by each variables in same sex (all variables p <0.05) 2) EER: Estimated average requirements

3) Recommended intake: 1g by Ideal Body Weight 4) [carbohydrate intake(g) × 4(kcal/g)]/[carbohydrate intake × 4 + protein intake × 4 + fat intake × 9] ×100 5) [fat intake(g) × 9(kcal/g)]/[carbohydrate intake × 4 + protein intake × 4 + fat intake × 9] ×100 6) [protein intake(g) × 4(kcal/g)]/[carbohydrate intake × 4 + protein intake × 4 + fat intake × 9] ×100 7) Mean±SD

Table 2-4. Major food sources of energy intakes among Korean elderly by sex

Food	Men (n=826)				Women (n=1043)			
	total		Adequate (n=630)	Inadequate (n=196)	total		Adequate (n=719)	Inadequate (n=324)
	rank	Intake (Kcal)[1)]			rank	Intake (Kcal)		
White rice	1	902.0	1	1	1	747.6	1	1
Soju	2	77.1	2	8	37	4.7	40	31
Pork	3	59.8	3	11	8	24.0	7	11
Coffee	4	43.9	4	2	7	24.2	11	5
Barley	5	39.4	7	3	3	38.4	3	2
Rice cake	6	39.2	5	6	2	45.2	2	4
Glutenous rice	7	37.7	9	5	4	33.0	4	3
Noodles	8	36.0	6	7	6	24.5	6	10
Soybean	9	35.5	11	4	5	25.0	8	7
Breads	10	34.4	10	10	13	18.6	13	13
Beef	11	34.3	8	19	12	20.9	10	16
Makgeolli	12	24.4	12	25	106	1.2	96	163
Apple	13	24.2	14	18	11	21.5	12	9
Ramen	14	23.5	13	22	16	14.7	16	18

Milk	15	22.8	15	12	9	23.4	9	8
Sugar	16	21.9	16	15	20	11.6	20	14
Tofu	17	18.7	18	13	17	13.5	17	17
Brown rice	18	18.4	20	9	14	17.7	15	6
Egg	19	18.2	19	16	18	12.4	18	20
Soybean oil	20	17.0	17	27	22	9.7	22	25
Kimchi, cabbage				14				15
Sweet potato				20	10	22.8	5	
Soybean paste				17	19	12.3	19	12
Mandarin								19
Persimmon					15	16.7	14	

1) Sum of energy intake divided by number of the object

Table 2-5. Major food sources of protein intakes among Korean elderly by sex

Food	Men (n=826)				Women (n=1043)			
	total		Adequate (n=543)	Inadequate (n=249)	total		Adequate (n=493)	Inadequate (n=497)
	rank	Intake (g)[1)]			rank	Intake (g)		
White rice	1	15.6	1	1	1	14.2	1	1
Pork	2	4.4	2	8	4	3.1	4	10
Beef	3	3.7	3	6	2	3.6	2	6
Soybean	4	3.2	4	2	3	3.3	3	2
Tofu	5	2.0	5	5	5	2.3	5	7
Kimchi, cabbage	6	1.9	9	3	8	1.3	9	4
Pollack	7	1.7	7	12	14	1.1	13	14
Egg	8	1.7	8	9	7	1.7	7	11
Chicken	9	1.5	6		13	1.4	8	
Soybean paste	10	1.4	11	4	10	1.2	10	5
Anchovy	11	1.3	12	10	12	1.0	14	13
Mackerel	12	1.2	10		18	0.7	17	
Milk	13	1.2	14	11	6	1.8	6	9
Barley	14	1.1	17	7	9	1.2	11	3

Croaker	15	1.1	13			0.7	18	
Noodles	16	1.0	15	17	15	1.0	15	15
Makgeolli	17	0.9	16					
Breads	18	0.8	18	18	17			
Rice cake	19	0.8	19	14	11	1.2	12	8
Glutinous rice	20	0.8		13	16	0.5	16	12
Squid			20		19	0.7	19	
Ramen				15				
Coffee				16				19
Bean sprouts				19				18
Turnip				20				16
Corn					20	0.6	20	
Brown rice								17
Seaweed								20

1) Sum of energy intake divided by number of the object

The results of the logistic regression analysis consisting of variables affecting energy intake are shown in Table 2−6. In both men and women, educational level and employment were identified as factors associated with inadequate energy intake. In the group with low educational levels, the odds of energy insufficiency was 1.480 (95% CI: 1.028–2.131) for men and 1.614 (95% CI: 1.074–2.425) for women. In the group with unemployment, the odds of energy insufficiency was 1.751 (95% CI: 1.202–2.551) for men and 1.464 (95% CI: 1.053–2.037) for women. Men aged 70 years and older showed a 1.475 (95% CI: 1.009–2.156) times higher odds of energy insufficiency and women living with their families without a spouse showed a 1.496 (95% CI: 1.062–2.098) times higher odds of energy insufficiency. The results of the logistic regression analysis consisting of variables affecting protein intake are shown in Table 2−7. Educational level was identified as a factor associated with inadequate protein intake in both men (OR: 2.092; 95% CI: 1.494–2.929) and women (OR: 2.030; 95% CI: 1.417–2.909). As per family status, men living alone and women living with their families without a spouse showed a 2.059 (95% CI: 1.021–4.152) times and a 1.728 (95% CI: 1.245–2.397) times higher odds of protein insufficiency, respectively. Men with unemployment and functional limitation had 1.738 (95% CI: 1.021–4.152) times and 1.552 (95% CI: 1.042–2.311) times higher odds of protein insufficiency, respectively.

Table 2-6. Socioeconomic factors associated with inadequate energy intake by sex using logistic regression analysis

Variables		Men (n=826)		Women (n=1043)	
		OR	95% CI	OR	95% CI
Age	60-69years	1		1	
	≥70years	1.475	1.009-2.156	1.205	0.893-1.626
	Partner	1		1	
Family status	Others	1.923	0.853-4.332	1.493	1.062-2.098
	Living alone	1.529	0.746-3.134	1.019	0.680-1.527
Education	≥High school	1		1	
	≤Middle school	1.480	1.028-2.131	1.614	1.074-2.425
Family income	≥Middle-low	1		1	
	low	1.000	0.688-1.454	0.834	0.610-1.139
Employment	Employed	1		1	
	Unemployed	1.751	1.202-2.551	1.464	1.053-2.037
Functional status	Independent	1		1	
	Dependent	1.439	0.939-2.203	1.212	0.881-1.667
Suicidal ideation	No	1		1	
	Yes	0.952	0.577-1.570	1.249	0.906-1.722

1) Logistic regression analysis comparing unsatisfactory group (under 75% of EER) with satisfactory group (more than 75% of EER)
2) CI, confidence interval; OR, odds ratio

Table 2-7. Socioeconomic factors associated with inadequate protein intake by sex using logistic regression analysis

Variables		Men (n=826)		Women (n=1043)	
		OR	95% CI	OR	95% CI
Age	60-69years	1		1	
	≥70years	1.374	0.970-1.946	1.160	0.879-1.531
	Partner	1		1	
Family status	Others	1.208	0.534-2.730	1.728	1.245-2.397
	Living alone	2.059	1.021-4.152	1.153	0.800-1.661
Education	≥High school	1		1	
	≤Middle school	2.092	1.494-2.929	2.030	1.417-2.909
Family income	≥Middle-low	1		1	
	low	1.081	0.766-1.526	1.167	0.875-1.557
Employment	Employed	1		1	
	Unemployed	1.738	1.230-2.456	1337	0.997-1.794
Functional status	Independent	1		1	
	Dependent	1.552	1.042-2.311	1.296	0.958-1.755
Suicidal ideation	No	1		1	
	Yes	1.009	0.638-1.596	1.104	0.813-1.497

1) Logistic regression analysis comparing unsatisfactory group (under the RDA for protein) with satisfactory group (more than the RDA for protein)

2) CI, confidence interval; OR, odds ratio

2-4. Discussion

The nutritional status of individuals is influenced by various factors including economic and educational levels, employment, family structure, and residential environment, along with demographic factors such as gender and age (141, 150). The elderly constitutes the population that undergo rapid environmental changes including a drop in socioeconomic status, and bereavement, which may eventually affect nutritional status. In this study, we investigated how environmental factors affect the nutrient intake of the elderly. Educational level and employment status were found to be factors affecting inadequate energy intake in both men and women. Moreover, older men (over 70 years old) and women living with their family without a spouse were significantly more likely to experience inadequate energy intake. Educational levels also affect protein insufficiency in both men and women. Family status was associated with protein insufficiency when women lived alone, and among men who lived with their families without spouses. In addition, unemployed men and those with functional limitation were more likely to have protein insufficiency.

In the 2011 Korea Institute for Health and Social Affairs, those with low educational levels or were unemployed were at high risk of malnutrition. In recent years, attention has been focused on obesity among low-educated and low-income families, but in the elderly, educational background has been suggested as a major variable related to the lack of nutrition (151−153). Our study showed similar results. Educational level can be a cause of poverty, and since poverty is directly related to food purchasing ability, it is closely related to nutritional status (152). In the present study, we found that being unemployed was a factor associated with decreased nutritional intake of both men and women. This may be due to economic effects such as income and self−efficacy obtained from employment. However, as the economy rises and the welfare of the poor improves, employment can be related to the quality of life. Although studies on the relationship between employment and nutrition are scarce, having an adequate income is likely necessary to ensure a more varied and balanced diet for healthy older people, as suggested by Drewnowski et al. (154). In a recent qualitative study, an employment−related economic change was found to negatively impact women's diets through for example limiting the number of daily meals (155). In a Korean study on the relationship between economic characteristics and life satisfaction by income levels among single elderly households, employment was identified as a variable related to increased life satisfaction in high−income households (156). Therefore, it can be inferred that employment, in addition to economic impacts, can affect intake as well as psychological wellbeing.

The odds of energy insufficiency was higher among men aged 70 years and older, and in women who lived with their families without a spouse. This may be due to the difference in life expectancy between men and women (157). Because we stratified the age at 70, the proportion of unhealthy populations may be high in men who have a relatively short life expectancy, and that women are more likely to experience a spouse' s death (158). In women, the influence of spouses requires consideration of social support in addition to physiological factors. Especially, women living with their families had a significantly higher odds of undernourishment than women living alone. This finding was not consistent with previous studies that were the basis of this study's assumption. In a New Zealand study to identify the nutrition risk factors of community-living older people, social factors (losing a spouse and loneliness) were key underlying factors associated nutrition risk (149). Other studies have also shown that widows or elderly people living alone may be undernourished (159). However, in a study in Israel, the family type (married, widowed, and other) was not related to nutrition (153). Woods et al. also suggested that living alone has an inverse relationship with frailty (160). This may result in short-term depressive status, but it does not seem to have a direct effect on nutrition intake by multiple factors, such as the adaptation mechanism of life and emancipation from family caregivers. In a case-control study comparing widowed persons over 60 years of age and married subjects of similar age focusing on changes in eating behaviors, social environment but not economic status was a major factor in reducing the nutritional intake of widows (161). Furthermore, according to the 2011 Korea Institute for Health and Social Affairs, the percentage of cohabitation with children increased significantly to 45.5% in people aged 85 years and older, and 18.5% of the elderly who have activity limitations lived with their family for the caregiving, compared to 4.0% of the elderly who had no activity limitations. The high risk of energy insufficiency among older people living with their families without a spouse appears to be attributable to the risk of malnutrition in elderly people who need family caregiving. In an Italian study comparing the risk of malnutrition between the elderly living in the community and those in nursing homes, the incidence of malnutrition was significantly higher in elderly nursing homes with high demands of caregiving (152). In this regard, there are attempts to identify and improve the problems of the eating environment of the elderly in nursing homes. Therefore, it is necessary to improve diet quality and quality of life rather than just the problem of inadequate intake when establishing a nutrition policy for the elderly supported by family caregivers or those within the nursing home.

The proportion of energy from macronutrients and the major sources of energy intake were analyzed to assess the diet quality. Carbohydrates highly contributed to energy intake in the group with energy insufficiency, and meat as a major source of energy intake was low, and Kimchi and soybean paste were in the top 20. This suggests that the lower the energy intake, the simpler the pattern of carbohydrate-based meals consisting of rice and Kimchi or rice and soup. In Korea, the average proportion of energy from carbohydrates is high around 70% (157). The present study showed that the average proportion of energy from carbohydrates was high at 75.7% for men and 77% for women in the group with energy insufficiency. Diet with high carbohydrate energy ratio could affect abdominal obesity, skeletal muscle mass (162), cognitive function and depression (163), and metabolic syndrome (164) in the elderly. Thus, the problems of the composition of the diet cannot be overlooked. In the group that consumed less than the RDA protein, the top 5 were vegetable protein in both men and women. The influence of dietary protein sources (animal or plant) on the prevention of sarcopenia has not been thoroughly explained (92). Several studies have shown that the Mediterranean diet and vegetable protein intake have a preventive effect on sarcopenia (82, 87, 89), although our study showed that those with protein insufficiency consume vegetable protein-based diets. This may be because protein sources are comparable when the quantity of protein is satisfied. A recent study also found that the consumption of seafood and dairy products, or protein-rich foods may help older Japanese adults to maintain their independence (165). Other studies have also focused on animal protein foods such as beef (74) and fish (90). In our study, eating based on vegetable protein in the group that consumed less than the RDA protein can lead to a lack of essential amino acids. A mixture of essential amino acids appears to consistently enhance muscle protein synthesis and improve physical function. Branched−chain amino acids, including leucine, isoleucine, and valine, are reported to exert beneficial effects on body weight. In particular, leucine plays an important role in muscle protein synthesis (92). Therefore, a better understanding of the association between not only protein but also with individual amino acids to muscle mass would be essential in sarcopenia prevention.

Although in a study of Chinese community−dwelling older people, higher protein intake from the vegetable source was associated with reduced muscle mass (94), most studies emphasize the intake of animal protein as a source of essential amino acids to prevent sarcopenia.

This study had some limitations. First, the cross−sectional design of the KNHANES data made it difficult to identify the causal relationship between socioeconomic factors and inadequate diet intake. Second, data on dietary intake obtained from the 1−day 24−h recall might not present the usual intake of participants. However, a single 24−h recall may be adequate if the sample size is sufficiently large.

2-5 Conclusions

These findings suggest that the nutritional status of older adults is affected by the social environment and social structural changes to which they belong, in addition to the physiological changes caused by aging. Therefore, the results of this study may help to establish nutrition management programs for the elderly, although future epidemiological nutrition studies are needed to more fully elucidate the associated risk factors affecting energy insufficiency in Korea.

Chapter 3. Impact of Dietary Protein Intake and Obesity on Lean Mass in Middle-Aged Individuals After a 12-year Follow-up : the Korean Genome and Epidemiology Study (KoGES)[2]

[2] This study was published in the British Journal of Nutrition vol.122, pages 322-330 in 2019.

Abstract

The present study investigated the association between protein intake and lean mass according to obesity status over a 12-year period. Data on 4412 participants aged 40–69 years were obtained from the Korean Genome and Epidemiology Study. The usual dietary protein intake of these participants was assessed at baseline using a semi-quantitative food frequency questionnaire. Body composition was measured using a bioelectrical impedance analysis at baseline and after a 12-year follow-up. Linear mixed effects models were used to examine the associations between lean mass after a 12-year follow-up and protein intake at baseline. After adjusting for covariates and lean mass at baseline, comparisons between the highest and lowest tertiles revealed that dietary protein intake was positively associated with lean mass in both men (β=0.79, p=0.001) and women (β=0.28, p=0.082) after the 12-year period; however, those differences were attenuated after additional adjustment for fat mass at baseline and were stronger in the normal-weight group (men, β=0.85, p=0.002; women, β=0.97, p<0.001) but were not detected in the obese group. In the obese group, age (men, β=4.08, p<0.001; women, β=2.61, p<0.001) and regular physical activity (men, β=0.88, p=0.054; women, β=0.76, p<0.001) were significantly associated with lean mass after 12 years of follow-up. The results of the present study showed that high protein intake was associated

with the prevention of ageing-related lean mass loss; however, the association between dietary protein intake and lean mass may vary depending on obesity status. Therefore, the maintenance of a healthy body weight during ageing through enhanced protein intake is likely to confer health benefits.

3-1. Introduction

The number of individuals over 60 years of age worldwide is expected to increase from 900 million to 2 billion between 2015 and 2050 (1), with a subsequent increase in the number of people at risk of deteriorating strength and mobility related to muscle loss. Recent estimates indicate that the prevalence of sarcopenia is 5%–13% in individuals 60–70 years of age and 11%–50% in those 80 years of age and older (2). Sarcopenia is a syndrome characterized by the progressive and generalized loss of skeletal muscle mass and strength and is associated with an increased risk of falls and fractures, reduced cardiopulmonary function, metabolic syndrome, and insulin resistance; accordingly, this condition eventually results in disability, hospitalization, and death among older individuals (4). Although there are few estimates of the financial burden of sarcopenia in older adults, the healthcare costs of this condition are likely to be high (166). One prospective study estimated that sarcopenia would increase hospitalization costs by 58.5% and 34% for patients <65 and ≥65 years of age, respectively (167).

Ageing is probably the most important factor contributing to the loss of muscle mass, although this decline can also be accelerated by modifiable lifestyle factors such as physical inactivity, smoking, alcohol consumption, and undernutrition (24). While protein intake has been the main nutritional focus (48, 168), many older adults do not consume adequate amounts of dietary protein due to reduced energy needs, increased physical dependency, anorexia, changes in food preference, anabolic resistance, and increased inflammatory and catabolic conditions (53, 169).

Additionally, obesity has become an epidemic in the elderly (108) and obese older adults face high risks of age-related muscle wasting such as sarcopenia (109, 110). In older adults with sarcopenic obesity, sarcopenia and obesity may synergistically increase their effects on physical disability, metabolic disorders, cardiovascular disease, and mortality (109, 111–113). Although the molecular mechanisms that underlie obesity-associated dysfunctions in lipid and glucose metabolism have been studied extensively (114), the effects of obesity on the processes that regulate muscle protein metabolism are poorly understood(115). Intramuscular lipids act as chemoattractants for macrophages that produce pro-inflammatory cytokines (116). These cytokines not only directly contribute to the breakdown of muscle proteins (117) but also interfere with the accretion of contractile material caused by chronic low-intensity muscle overloading (118). Previously, Erskine and colleagues described the paradox that circulating pro-inflammatory cytokines play different roles in neuromuscular remodeling according to the age and adiposity of the individual (119).

According to the Korea National Statistical Office, the percentage of the Korean population age 65 and older is expected to rise to 24.5% by 2030 and to 38.1% by 2050 (170). Along with the rapid growth in the number of elderly individuals in Korea, sarcopenia and sarcopenic obesity have become important issues in this country. In the Korean Sarcopenic Obesity Study which included 526 healthy volunteers 20–88 years of age, the prevalence of sarcopenic obesity in older (≥60 years) men and women was 5.1% and 12.5%, respectively, as of 2008. However, there have been no Korean cohort studies on the long-term effects of dietary protein on changes in muscle mass according to the obesity status.

In the elderly, the maintenance of muscle mass and strength are critical to the abilities of an individual to survive multiple comorbidities and meet their physical demands. Therefore, we conducted a prospective cohort study of elderly Korean subjects to investigate the effects of protein intake on changes in lean mass according to the obesity status.

3-2. Subjects and Methods

Data source and study population

Data were obtained from the large community-based cohort of the Korean Genome and Epidemiology Study (KoGES). The eligibility criteria for the participants of the KoGES at baseline included residents between the ages of 40 and 69 years who had lived in Ansan (urban) or Ansung (rural), Korea, for at least 6 months before enrolment. Baseline examinations were performed in 2001 and 2002 and follow-up examinations continued every two years until the end of 2014. Detailed information about this study has been provided elsewhere (171). Of the original 10,030 participants, 4412 were included in the final analysis after excluding those who did not complete the baseline food frequency questionnaire (FFQ) or anthropometric data (n=2417), who had abnormally low or high daily energy intakes (<500 or >5,000 kcal/day, n=56), who did not participate in follow-up examinations (n=3042), or who had low skeletal muscle mass (<35.71% in men, <30.70% in women) (20) at baseline (n=103). All participants signed the written informed consent form. This study was approved by the Institutional Review Board (no. KC17ZESI0645) of Catholic Medical Center.

Assessment of usual dietary protein intake

At baseline, the participants' usual dietary protein intake was assessed by trained dietitians using a validated 103-item semi-quantitative FFQ (172). There were nine response options for the frequency of each food (never or almost never, once per month, two or three times per month, one or two times per week, two or three times per week, three or four times per week, five or six times per week, once daily, twice daily, or three times daily) and three response options for the portion size of each food (1/2 serving, 1 serving, and ≥ 2 servings). To enhance the accuracy of recollecting serving size, pictures of each food item were used as a reference. The daily intakes of protein and other nutrients by each individual were estimated from the sum of the intakes of each food item, based on the Food Composition Database (Seoul, Korea: The Rural Development Administration, 2007). Among the 103 food items listed on the FFQ, 79 items classified as the main food sources contributing to protein intake (nine food items from meats including beef, pork, poultry, and meat products, 15 food items from fish and shellfish, three food items from soybean, four food items from milk, one food item from egg, seven food item from rice and other cereals, 27 food items from vegetables, 10 food items from noodles and breads, and three food items from potatoes) were assessed to calculate each subject's protein intake.

Anthropometric measurements

Fat mass and lean mass (fat-free mass) were assessed using a multi−frequency bioelectrical impedance analysis (MF-BIA, InBody 3.0; Biospace, Seoul, Korea) according to standard procedures. The MF-BIA technique assumes that the human body comprises five interconnecting cylinders and measures the direct impedance in these body compartments. Using an eight-polar tactile electrode system, impedance was measured at four specific frequencies (5, 50, 250, and 500 kHz) in five segments (right arm, left arm, trunk, right leg, and left leg) for the estimation of total body water (TBW). The lean mass was estimated from the TBW and anthropometric measurements, using an algorithm for the Asian population. The fat mass was estimated by subtracting the lean mass from the total body weight. The participants fasted overnight prior to the BIA assessment. Before the examination, the researchers confirmed whether the participant had experienced intensive exercise, bathing, or excessive sweating. The body mass index (BMI) was calculated as the weight (kg) divided by the height (m) squared, with participants then classified using Asian criteria in the normal−weight (<23 kg/m^2), overweight (23 to 24.9 kg/m^2), and obesity (≥25 kg/m^2) (173). Due to the small number of participants in the underweight group (n=54; 1.2%), these individuals were included in the normal weight group in the BMI−stratified analyses. Although there is no standardized definition of obesity according to fat mass, the participants were categorized into two groups by percent body fat (%BF) with reference to Asian epidemiologic studies of the %BF (normal group, %BF <25 for men and %BF <30 for women; obese group, %BF ≥25 for men and %BF ≥30 for women) (174, 175).

Covariates

All lifestyle-related information was gathered by the interviewer-administered questionnaire. The questionnaire included questions on sex, age, marital status, education, income, smoking, alcohol consumption, regular physical activity, and self-perceived dental health status. To evaluate the influence of protein intake on age-related muscle loss in younger versus older adults, age was dichotomized as younger or older than 60 years. Smoking status was used to classify participants into 'smokers' (current smoker) and 'non-smokers' (former smokers and non-smokers). Alcohol consumption was used to classify participants into 'alcohol drinkers' (current drinker) and 'non-drinkers' (former and never drinkers). Regular physical activity was defined as 'yes' if the participant performed more than 2.5 hours of exercise per week according to the global WHO recommendation (176, 177). To obtain the MET, participants reported the number of hours spent sleeping and the frequency of five types of activities (sedentary, very light, light, moderate, and heavy activities). Total METs-hours per day was calculated by multiplying the reported hours spent by the MET values determined based on each type of activity(178). Physical activity was categorized as per the METs tertiles into low (T1=9.6 and 9.2 h/day in men and women, respectively), moderate (T2=19.1 g/day in both men and women), and high (T3=39.0 and 39.3 h/day in men and women, respectively). The self-perceived dental health status was categorized as poor or others (good and fair). Chronic diseases were measured by participants' self-report of the presence or absence of 10 chronic conditions (myocardial infarction, congestive heart failure, coronary artery disease, peripheral arterial disease, cerebrovascular disease, asthma, chronic obstructive pulmonary disease, cancer, dementia, and arthritis).

Statistical analysis

Because of the well-established sex differences in the age-related changes in lean mass and muscle strength (179), all analyses were performed separately for men and women. Protein intake was examined by the protein density method, in which nutrient intake was divided by total energy intake (in grams per 1,000 kcal) (180). The protein intake per 1,000 kcal at baseline was categorized into tertiles. The baseline characteristics of the study participants were compared with respect to the tertiles of protein intake per 1,000 kcal, using Mantel-Haenszel χ^2 tests for categorical variables and linear regression analyses for continuous variables. A one-way analysis of variance was used to test for between-group differences in the percent change in body composition after a 12-year follow-up, using the lowest tertile as the reference group. Independent Student's t-tests were used to examine the differences between older ($\geq$50 years) and younger participants (<50 years) in terms of the percent change in body composition after a 12-year follow-up. Multiple linear regression analyses were performed to determine the relative contributions of the evaluated characteristics to the lean mass at baseline. Fat mass (kg), age (<60/$\geq$60 years), protein intake (T1/T2/T3), marital status (married/others), education ($\geq$college/others), income ($\geq$3,000,000 KRW per month/others), smoking (yes/no), alcohol consumption (yes/no), regular physical activity (yes/no), self-perceived dental health status (poor/others), and chronic disease (yes/no) were included as covariates in the model. Variables with p values <0.05 were selected during stepwise regression procedures. The subjects were categorized into the normal and obese groups as %BF for linear mixed effects models to examine the independent effect of protein intake on lean mass after 12 years of follow-up. Potential confounding variables were selected using stepwise regression procedures and entered into the models. Model 1 was adjusted for age, income, alcohol consumption, smoking, regular physical activity, and chronic disease and Model 2 was adjusted for the variables in Model 1 plus fat mass. The effects of the interaction between protein intake and physical activity (METshour per day) on lean mass at baseline using general linear model was significant in both men ($p=0.050$) and women ($p=0.049$). The Interaction between protein intake and BMI and between protein intake and % BF was significant in women ($p=0.021$ and $p=0.006$, respectively). Further analyses were conducted after stratifying by physical activity and BMI and % BF. IBM SPSS Statistics for Windows, version 24.0 (IBM, Corp., Armonk, NY, USA) was used for all statistical analyses. A two-sided p-value < 0.05 was considered statistically significant.

3-3. Results

Table 3-1 shows the characteristics of the study participants according to protein intake at baseline. The protein intakes (g/kg body weight) by tertiles 1, 2, and 3 were 0.8, 1.0, and 1.3 g in men and 0.9, 1.1, and 1.4 g in women, respectively. Both men and women with high protein intakes were significantly younger ($p<0.001$); were more likely to live in a city ($p<0.001$), have a higher educational level ($p<0.001$), have a higher income ($p<0.001$), and have a lower Mets-hours/day ($p<0.001$); tended to be married ($p=0.019$ for men, $p<0.001$ for women); and tended to consume alcohol currently ($p<0.001$ for men, $p=0.001$ for women) and to be physically active ($p<0.001$). Smoking status was not significantly associated with protein intake. Additionally, men and women with higher protein intakes had higher intakes of energy ($p<0.001$) and energy from fat ($p<0.001$) and a lower intake of energy from carbohydrates ($p<0.001$). Regarding body composition, men with a high protein intake had a higher weight ($p<0.001$), BMI ($p<0.001$), fat mass ($p<0.001$), %BF ($p<0.001$), and lean mass ($p<0.001$) at baseline, whereas among women, only lean mass differed significantly in relation to protein intake ($p=0.005$).

Table 3-1. Characteristics of study participants by the levels of protein intake

Protein intake (tertiles)	Men (n=2096)						
	T1[a]		T2		T3		p for trend[b] or p
	Mean	SD	Mean	SD	Mean	SD	
Demographics and lifestyles at baseline							
Age (years)	51.8	8.5	49.6	7.6	49.3	7.6	<0.001
Residential area (city, %)	48.1		75.2		78.0		<0.001
Education (≥college, %)	16.6		26.9		31.4		<0.001
Household income (≥3,000,000 KRW, %)	15.7		28.1		36.6		<0.001
Marital status (married, %)	95.8		97.0		98.0		0.019
Smoking (yes, %)	46.8		42.2		45.2		0.623
Chronic diseases (yes, %)	1.9		1.1		1.3		0.381
Dental health status (poor, %)	39.7		40.4		36.0		0.144
Alcohol drinking (yes, %)	66.7		73.4		80.1		<0.001
Regular physical activity (yes, %)	11.7		18.0		23.3		<0.001
METs-hours/day	25.4	15.8	21.8	13.4	21.6	13.2	<0.001
Nutrient intake at baseline							
Energy (kcal/d)	1,904.3	608.5	1,969.7	483.8	2,138.3	560.1	<0.001
Carbohydrate (% of energy)	75.4	3.9	69.9	3.5	63.7	5.2	<0.001

Fat (% of energy)	11.8	3.7	15.5	3.5	19.3	4.3	<0.001
Protein (% of energy)	11.3	0.9	13.5	0.5	16.0	1.6	<0.001
Protein (g/d)	54.1	17.7	66.3	16.9	85.8	25.2	<0.001
Protein (g/kg body weight)	0.8	0.3	1.0	0.3	1.3	0.4	<0.001
Fat (% of energy)	11.8	3.7	15.5	3.5	19.3	4.3	<0.001
Body composition at baseline							
Weight (kg)	66.9	9.4	68.2	9.0	69.8	9.2	<0.001
Body Mass Index (kg/m^2)	24.1	2.8	24.3	2.7	24.7	2.7	<0.001
Fat mass (kg)	14.4	4.5	14.9	4.5	15.6	4.5	<0.001
Body fat (%)	21.1	4.8	21.5	4.8	22.0	4.5	<0.001
Lean mass (kg)	52.5	6.3	53.2	6.0	54.3	6.1	<0.001

[a] Tertiles of protein intake per 1,000 kcal at baseline.

[b] P for trend was calculated from a linear regression analysis for continuous variables and Mantel−Haenszel χ^2 for categorical variables.

Table 3-1. Characteristics of study participants by the levels of protein intake (continued)

Protein intake (tertiles)	Women (n=2316)						
	T1[a]		T2		T3		p for trend[b] or p
	Mean	SD	Mean	SD	Mean	SD	
Demographics and lifestyles at baseline							
Age (years)	53.33	9.0	50.5	8.1	48.7	7.4	<0.001
Residential area (city, %)	40.9		67.9		74.9		<0.001
Education (≥college, %)	4.1		8.7		11.6		<0.001
Household income (≥3,000,000 KRW, %)	8.9		18.9		24.2		<0.001
Marital status (married, %)	83.7		89.6		91.1		<0.001
Smoking (yes, %)	1.9		2.3		2.8		0.245
Chronic diseases (yes, %)	6.3		4.7		2.5		<0.001
Dental health status (poor, %)	47.9		41.5		35.5		<0.001
Alcohol drinking (yes, %)	22.3		27.7		29.7		0.001
Regular physical activity (yes, %)	9.4		18.9		25.1		<0.001
METs-hours/day	24.4	15.5	21.9	13.3	20.5	11.8	<0.001
Nutrient intake at baseline							
Energy (kcal/d)	1,779.2	606.9	1,890.5	546.4	1,970.6	632.3	<0.001
Carbohydrate (% of energy)	77.5	4.0	71.8	3.7	65.2	5.0	<0.001
Fat (% of energy)	9.9	3.6	13.9	3.6	18.2	4.3	<0.001

Protein (% of energy)	11.2	1.0	13.4	0.5	15.9	1.5	<0.001
Protein (g/d)	50.0	17.7	63.3	18.5	78.6	27.8	<0.001
Protein (g/kg body weight)	0.9	0.3	1.1	0.4	1.4	0.5	<0.001
Fat (% of energy)	9.9	3.6	13.9	3.6	18.2	4.3	<0.001
Body composition at baseline							
Weight (kg)	58.3	8.3	59.1	7.5	58.9	7.4	0.111
Body Mass Index (kg/m^2)	24.7	3.1	24.7	2.8	24.4	2.8	0.078
Fat mass (kg)	18.5	4.9	18.8	4.5	18.5	4.5	0.410
Body fat (%)	31.3	5.0	31.5	4.6	31.0	4.8	0.179
Lean mass (kg)	39.8	4.5	40.3	4.1	40.5	4.2	0.005

[a] Tertiles of protein intake per 1,000 kcal at baseline.

[b] P for trend was calculated from a linear regression analysis for continuous variables and Mantel−Haenszel χ^2 for categorical variables.

In men and women with the highest protein intakes, dietary protein was mostly derived from meats (22.9% in men and 18.4% in women), while dietary protein was mostly derived from vegetable proteins with rice and other cereals in men and women with the lowest protein intakes (41.8% in men and 44.1% in women) (Figure 3-1).

Figure 3-2 shows the distribution of lean mass of study participants categorized by age. The mean lean mass decreased continuously after 40 years in men and after 50 years in women. Both men and women showed a slight acceleration after age 60. In addition, lean mass significantly correlated with age (Figure 3-3). Compared with the preceding age group, there were significant differences between the groups except for those aged 45-49 years and 60-64 years in men (Figure 3-4). For women, there were significant differences between the groups except for those aged 55-54 years.

Among men, the percent change in body composition after 12 years of follow-up did not differ significantly according to protein intake, whereas women with a higher protein intake had lower reductions in weight, BMI, and lean mass during the follow-up period ($p<0.001$, $p=0.014$, and $p<0.001$, respectively). Among both men and women, older participants (≥50 years) had a greater reduction in lean mass compared to younger individuals (<50 years) ($p<0.001$; T1, T2, and T3) (Figure 3-5).

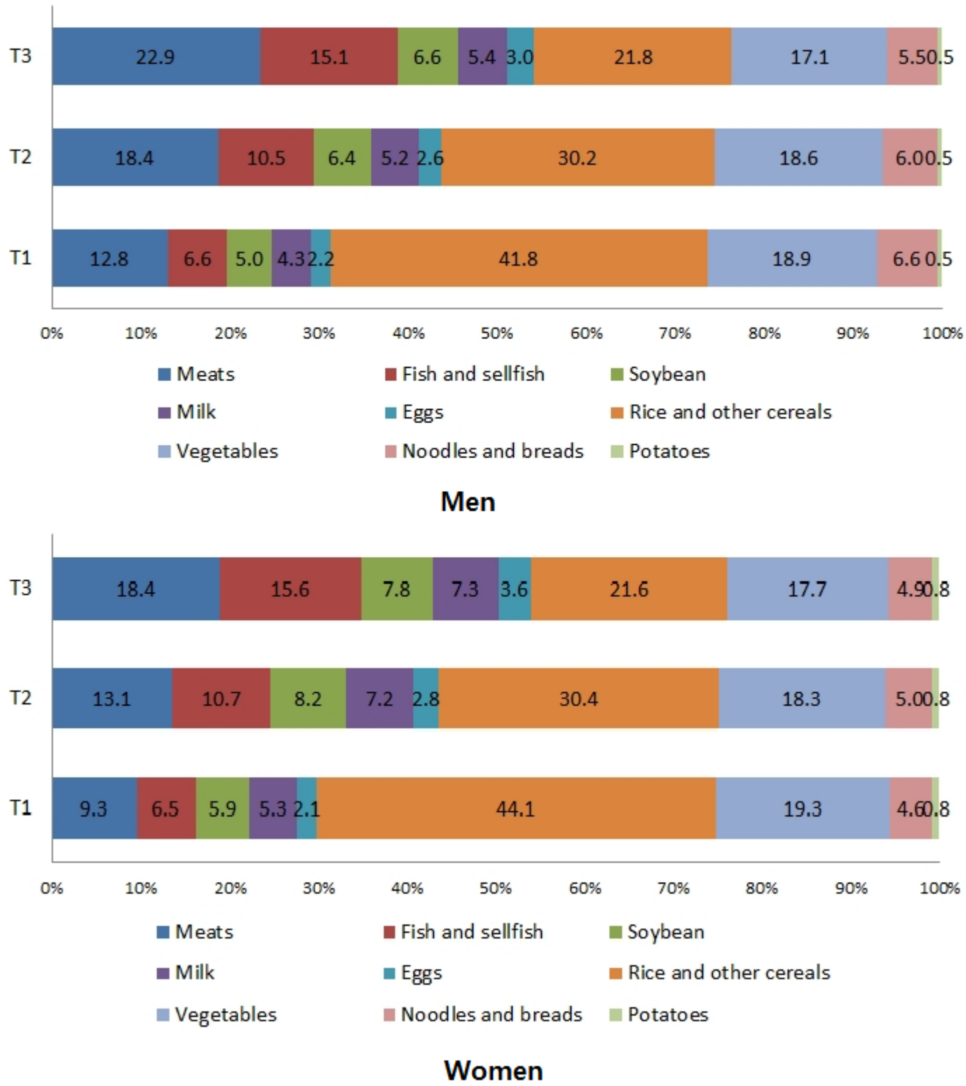


Figure 3-1. Contribution of protein sources foods to total daily protein intake

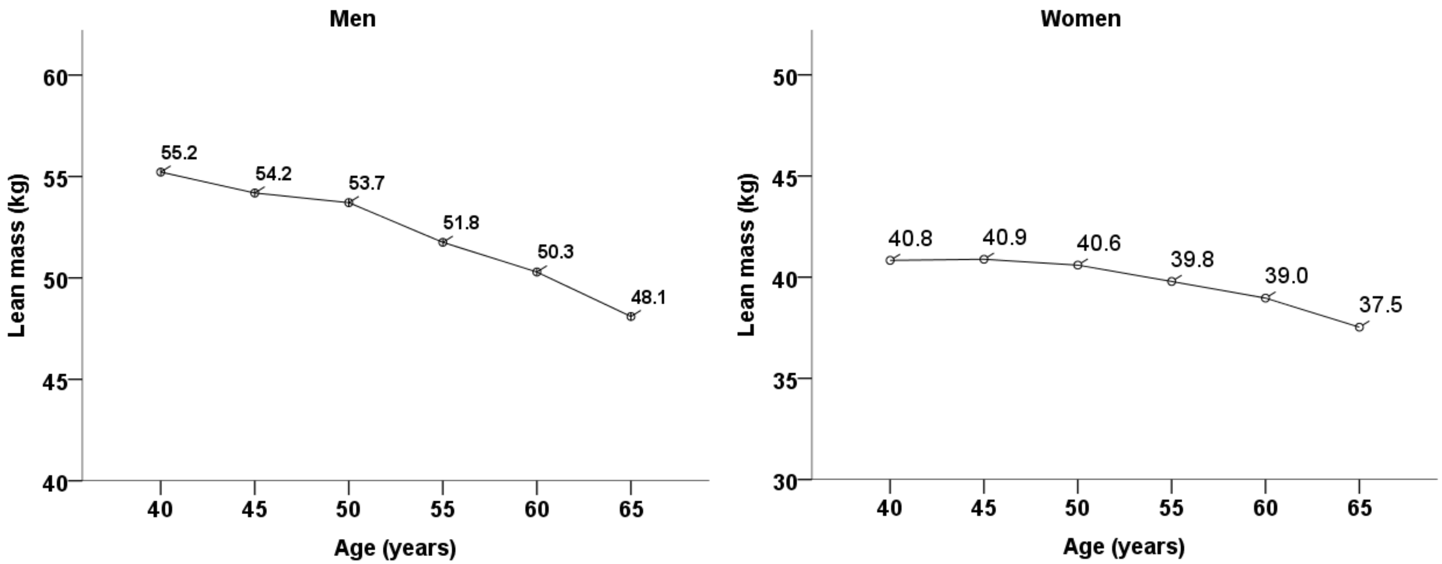


Fig 3−2. Distribution of lean mass (kg) of study participants categorized by age

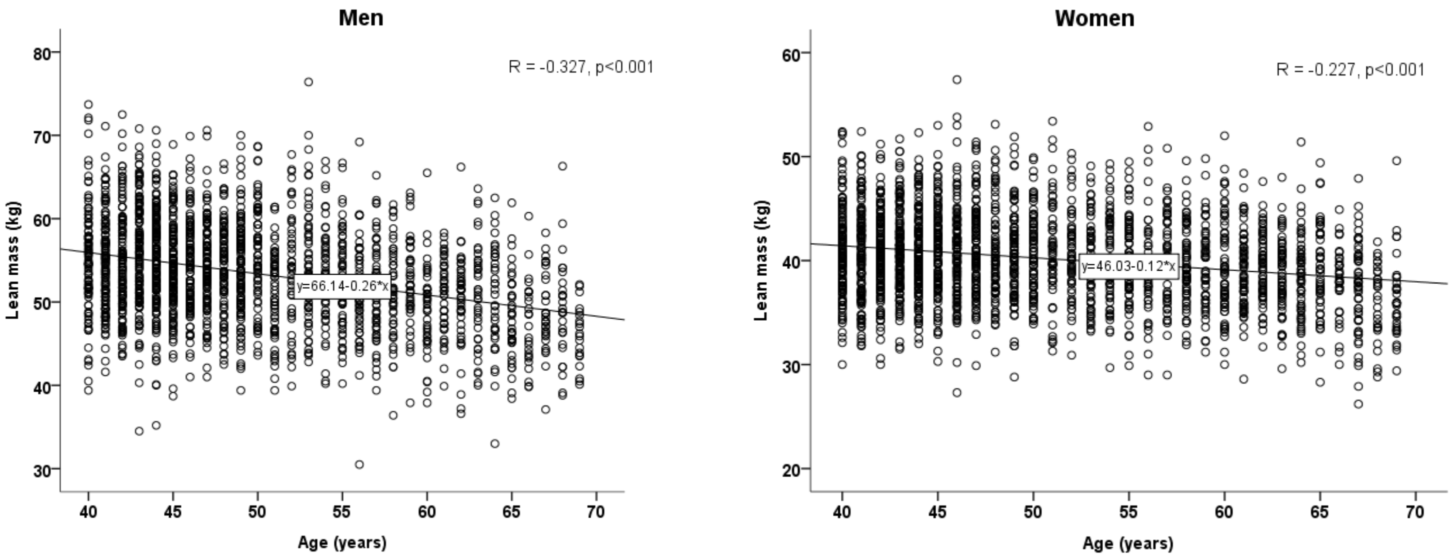
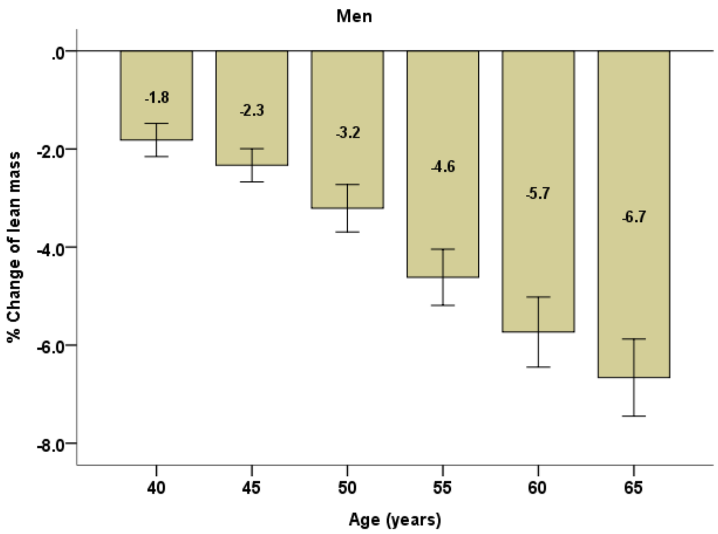


Fig 3-3. Relationship between age and lean mass (kg) by sex



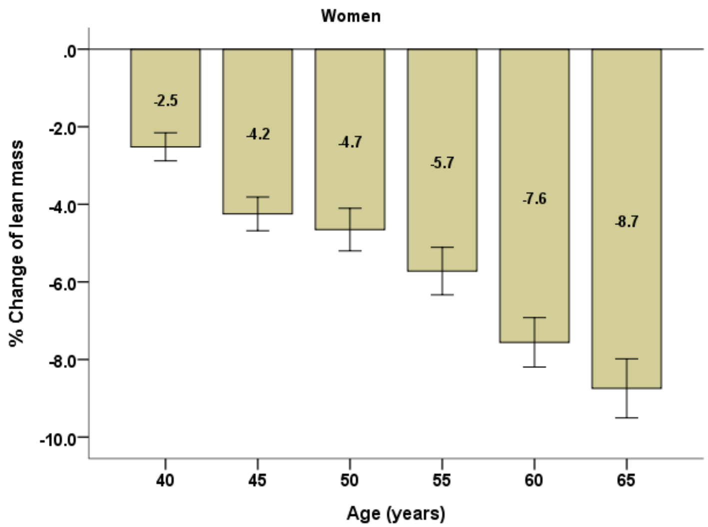


Figure 3-4. % change of lean mass over 12 years of study participants categorized by age

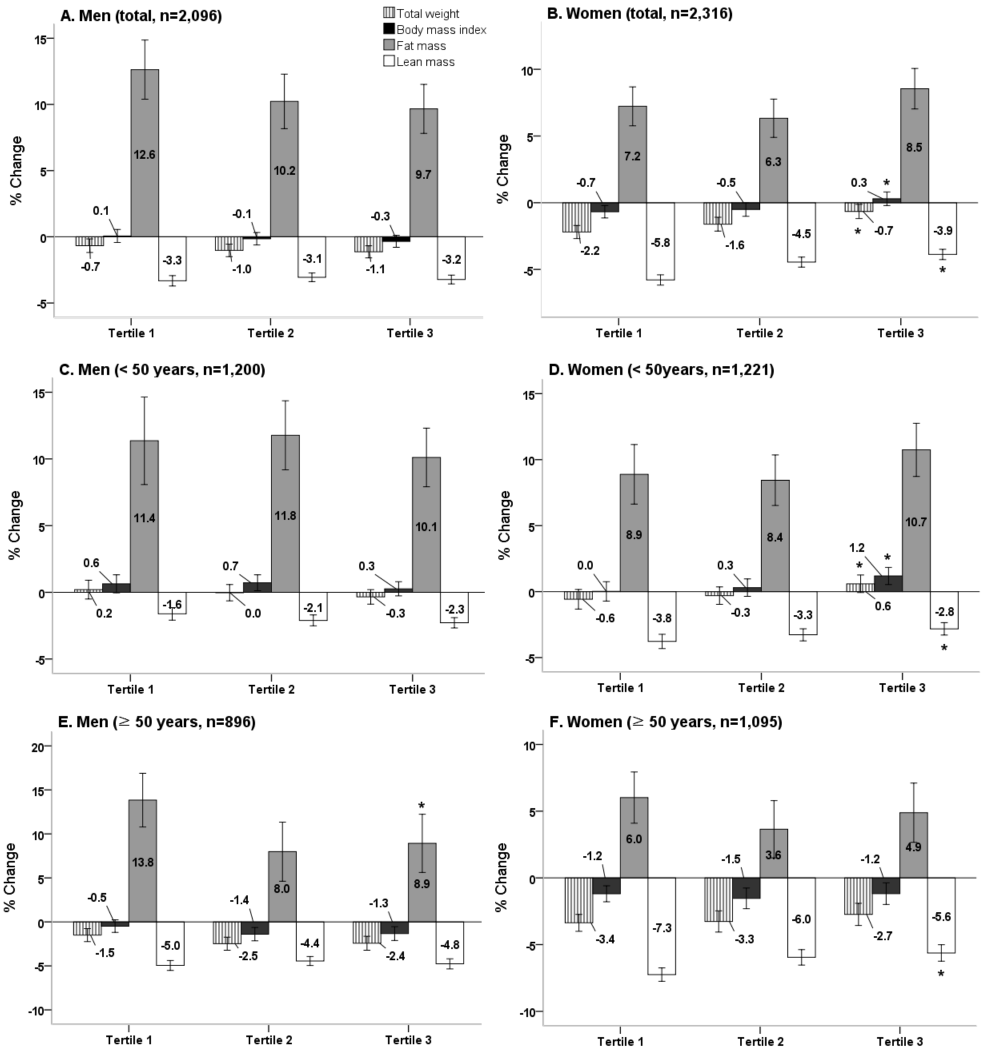


Figure 3-5. % crude change of body composition over 12 years by tertiles of protein intake per 1,000 kcal.

% crude change = ((12-y follow-up value - baseline value)/baseline value x 100). Values are mean.

* Indicates significantly linear trend across tertiles of protein intakes: P for trend<0.05.

Among both men and women, older participants (≥50 years) had a greater reduction in lean mass, compared to the younger group (<50 years) (p<0.001; T1, T2, and T3) using the Student' s t-test.

Table 3-2 shows the results of the multiple linear regression models using a stepwise procedure for selecting variables which predicted lean mass at baseline. In men, a higher fat mass (β=0.59, p<0.001), younger age (β=3.75, p<0.001), regular physical activity (β=1.07, p<0.001), higher income (β=0.83, p=0.002), current smoking (β=0.72, p=0.002), protein intake (β=0.50; p=0.039), and the presence of chronic disease (β=-2.25, p=0.019) were associated with a higher lean mass at baseline. In women, a higher fat mass (β=0.46, p<0.001), younger age (β=2.20; p<0.001), regular physical activity (β=0.89; p<0.001), and alcohol consumption (β=0.63, p<0.001) were associated with a higher lean mass at baseline.

In the linear mixed effects models, higher protein intake at baseline was associated with a higher lean mass after 12 years of follow-up in both men (β=0.79, p=0.001; highest *vs.* lowest tertile) and women (β=0.28, p=0.082; highest *vs.* lowest tertile) after adjusting for covariates (Table 3-3). These associations were attenuated after additional adjustment for fat mass at baseline. In further evaluation according to obesity status, the associations were stronger in the normal-weight group (men, β=0.85, p=0.002; highest *vs.* lowest tertile; women, β=0.97, p<0.001; highest *vs.*

lowest tertile) but were not detected in the obese group. These results were in the same direction when applying the continuous age variable (Table A-1). Age (men, β=4.08, $p<0.001$; women, β=2.61, $p<0.001$) and regular physical activity (men, β=0.88, $p=0.054$; women, β=0.76, $p<0.001$) were significantly associated with lean mass after 12 years of follow-up, regardless of obesity status. Higher income (men, β=1.36, $p=0.001$; women, β=0.43, $p=0.046$) and alcohol consumption (men, β=1.16, $p=0.005$; women, β=0.56, $p=0.002$) in both obese men and women and smoking (β=1.82, $p<0.001$) and chronic disease (β=-2.42, $p=0.071$) in obese men were significantly associated with lean mass after 12 years of follow-up.

Table 3−2. Predictors of lean mass at baseline

Predictor[a]	Men (n=2096)				Women (n=2316)			
	β	SE	P	R^2 (adjusted R^2)	β	SE	P	R^2 (adjusted R^2)
Fat mass, kg	0.59	0.03	<0.001	0.30 (0.30)	0.46	0.16	<0.001	0.31 (0.31)
Age (< 60 years)	3.75	0.32	<0.001		2.20	0.19	<0.001	
Regular physical activity (yes)	1.07	0.30	<0.001		0.89	0.20	<0.001	
Income (≥3,000,000 KRW)	0.83	0.27	0.002		−			
Smoking (yes)	0.72	0.23	0.002		−			
Alcohol consumption (yes)	−				0.63	0.17	<0.001	
Protein intake[b] (Tertile)	0.50	0.24	0.039		−			
Chronic disease (yes)	−2.25	0.96	0.019		−			

[a] Predictors were selected by a regression model with stepwise procedure. [b] Protein intake per 1,000 kcal. Variables initially included in the model were fat mass (kg), age (< 60 years/ ≥ 60 years), protein intake (Tertile), marital status (married/others), education (≥ college/others), income (≥ 3,000,000 KRW per month/others), smoking (yes/no), alcohol consumption (yes/no), regular physical activity (yes/no), self−perceived dental health status (poor/others), chronic diseases (myocardial infarction, congestive heart failure, coronary artery disease, peripheral arterial disease, cerebrovascular disease, asthma, chronic obstructive pulmonary disease, cancer, dementia, and arthritis).

− indicates that the variable was not selected during stepwise procedure due to p>0.05.

Table 3-3. Estimates of lean mass after a 12-year follow-up by protein intake according to % body fat at baseline

Variables	Men			
	Total (n=2096)		Normal[c] (n=1574)	Obese[d] (n=522)
	Model 1	Model 2		
Intercept	45.12	37.76	44.18	48.04
Protein intake at baseline[a]				
Tertile 1	Reference	Reference	Reference	Reference
Tertile 2	−0.01[b]	−0.14	0.13	−0.65
Tertile 3	0.79**	0.35†	0.85**	0.45
Age (<60 years)	5.00**	4.59**	5.29**	4.08**
Income (≥3,000,000 KRW)	1.46**	0.91**	1.49**	1.36**
Alcohol consumption (yes)	0.55**	0.36†	0.33	1.16**
Smoking (yes)	0.20	0.73**	0.23	1.82**
Regular physical activity (yes)	1.44**	1.06**	1.63**	0.88†
Chronic diseases (yes vs. no)	−2.54**	−2.52**	−2.72**	−2.42†
Fat mass (kg)		0.56**	−	−
Goodness-of-fit				
−2Log likelihood	26,374.26	25,537.57	19,908.14	6415.08

*p<0.05, **p<0.01, †p<0.1

[a] Protein intake per 1,000 kcal.

[b] coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

[c] Normal: %BF < 25 for men, and %BF < 30 for women.
[d] Obese: % BF $\geq$ 25 for men, and % BF $\geq$ 30 for women.
Model 1 was adjusted for age, income, alcohol consumption, smoking, regular physical activity, and chronic diseases.
Model 2 was adjusted for variables in Model 1 plus fat mass.

Table 3-3. Estimates of lean mass after a 12-year follow-up by protein intake according to % body fat at baseline (continued)

Variables	Women			
	Total (n=2316)		Normal[c]	Obese[d]
	Model 1	Model 2	(n=809)	(n=1507)
Intercept	36.82	28.95	35.28	37.80
Protein intake at baseline[a]				
Tertile 1	Reference	Reference	Reference	Reference
Tertile 2	0.28†[b]	0.18	0.71**	−0.04
Tertile 3	0.28†	0.28*	0.97**	−0.15
Age (<60 years)	2.74**	2.83**	3.26**	2.61**
Income (≥3,000,000 KRW)	0.25	0.32*	−0.07	0.43*
Alcohol consumption (yes)	0.50**	0.54**	0.31	0.56**
Smoking (yes)	−0.15	0.04	−0.20	0.21
Regular physical activity (yes)	1.22**	0.93**	2.08**	0.76**
Chronic diseases (yes vs. no)	−0.01	0.14	−0.04	0.01
Fat mass (kg)		0.43**	−	−
Goodness-of-fit				
−2Log likelihood	25,576.44	24,465.73	8881.13	16,634.66

*p<0.05, **p<0.01, †p<0.1

[a] Protein intake per 1,000 kcal.

[b] coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

[c] Normal: %BF < 25 for men, and %BF < 30 for women.
[d] Obese: % BF $\geq$ 25 for men, and % BF $\geq$ 30 for women.
Model 1 was adjusted for age, income, alcohol consumption, smoking, regular physical activity, and chronic diseases.
Model 2 was adjusted for variables in Model 1 plus fat mass.

Table 3−4 shows the combined effects of protein intake and BMI on lean mass after 12 years of follow−up in both men and women. The pattern here was similar to that of % BF. In men and women with normal BMI, higher protein intake at baseline was associated with a higher lean mass after 12 years of follow−up after adjusting for covariates (men, β=0.62, p=0.094; highest *vs.* lowest tertile; women, β=0.90, p <0.001; highest *vs.* lowest tertile). However, these associations were not detected in the overweight and obese groups in men and obese group in women. These results were in the same direction when applying the continuous age variable (Table A−2).

Table 3−5 presents the combined effects of protein intake and MET level on lean mass after 12 years of follow−up in both men and women. In men and women with high MET level, higher protein intake at baseline was associated with a higher lean mass after 12 years of follow−up after adjusting for covariates (men, β=0.70, p=0.048; highest *vs.* lowest tertile; women, β=1.19, p<0.001; highest *vs.* lowest tertile). However, these positive associations were not detected in the low and medium MET group in men and women. These results were in the same direction when applying the continuous age variable (Table A-3).

Table 3-4. Estimates of lean mass after a 12-year follow-up by protein intake according to body mass index at baseline[a]

Variables	Men (n=2096)			Women (n=2316)		
	Normal[b] (n=621)	Overweight (n=591)	Obese (n=884)	Normal (n=683)	Overweight (n=601)	Obese (n=1032)
Intercept	42.17	48.27	43.96	33.65	36.85	38.26
Protein intake at baseline[c]						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	0.60[d]†	−0.02	−0.13	0.69**	0.15	−0.07
Tertile 3	0.62†	0.36	0.31	0.90**	0.51†	−0.13
Age (<60 years)	4.16**	3.58**	4.34**	2.77**	2.68**	3.28**
Income (≥3,000,000 KRW)	1.22**	0.89**	0.92**	0.25	0.66*	0.30
Alcohol consumption (yes)	0.33	0.39	0.41	0.50*	0.67**	0.12
Smoking (yes)	0.21	0.74*	0.10**	0.04	−0.14	−0.16
Regular physical activity (yes)	0.43	0.75*	1.09**	1.14**	0.65*	1.35**
Chronic diseases (yes)	−2.39*	−0.90	−3.18**	−0.43	−0.03	0.23
Fat mass (kg)	−	−	−	−	−	−
Goodness-of-fit						
−2Log likelihood	7380.08	7058.09	10,732.51	7090.75	6302.48	11,328.46

*p<0.05, **p<0.01, †p<0.1

[a] Adjusted for age, income, alcohol consumption, smoking, regular physical activity, and chronic diseases.

[b] Normal: BMI<23 kg/m^2; Overweight: 23≤BMI< 25 kg/m^2 ; Obese: BMI≥ 25 kg/m^2.

[c] Protein intake per 1,000 kcal.

[d] Coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

Table 3-5. Estimates of lean mass after a 12-year follow-up by protein intake according to METs level at baseline[a]

Variables	Men (n=2096)			Women (n=2316)		
	Low[b] (n=693)	Medium (n=647)	High (n=701)	Low (n=742)	Medium (n=788)	High (n=737)
Intercept	36.05	32.30	38.52	36.82	35.28	29.70
Protein intake at baseline[c]						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	-0.08[d]	-0.76*	0.41	0.09	0.07	0.66**
Tertile 3	0.55	-0.18	0.70*	-0.01	0.21	1.19**
Age (<60 years)	3.06**	3.79**	5.24**	3.27**	1.82**	3.42**
Income (≥3,000,000 KRW)	0.79*	0.77*	1.97**	0.73	0.52*	0.05
Alcohol consumption (yes)	0.07	0.83*	0.36	0.45*	0.78**	0.44 †
Smoking (yes)	1.05**	0.99*	0.09	-0.13	-0.25	0.46
Physical activity	-	-	-	-	-	-
Chronic diseases (yes)	-4.36**	-1.97	-1.81 †	-0.94*	0.50	0.16
Fat mass (kg)	0.61**	0.61**	0.49**	0.47**	0.43**	0.41**
Goodness-of-fit						
-2Log likelihood	8488.76	7920.27	8548.72	7757.96	8431.83	7860.42

*p<0.05, **p<0.01, † p<0.1

[a] Adjusted for age, income, alcohol consumption, smoking, chronic diseases, and fat mass.

[b] Grouped according to METs tertiles (T1=low, T2=medium, T3=high).
[c] Protein intake per 1,000 kcal.
[d] Coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

3-4. Discussion

To our knowledge, this is the first large community-based prospective cohort study in Korea to investigate the associations between protein intake and changes in lean mass according to obesity status in middle-aged individuals. The results showed that men and women with higher protein intakes had higher lean mass after 12 years of follow-up but that these differences were attenuated after additional adjustment for fat mass at baseline. The associations were stronger in the normal-weight group but were not detected in the obese group.

Women with a higher protein intake had lower reductions in lean mass during the follow-up period. In a meta-analysis of adult men and women with a mean age of 50 years or older, a higher protein intake (≥25% of the daily total energy intake or ≥1.0 g/kg/d) was associated with increased lean mass retention and fat mass loss during intentional weight loss (181). Another cohort study investigated the association between dietary protein and changes in lean mass and appendicular lean mass in older, community-dwelling men and women, and reported that community-dwelling older adults with the highest quintile of protein intake lost ~40% less total lean body mass and appendicular lean mass over three years compared to the loss in the group with the lowest quintile of protein intake (50). Our study showed similar results in women, not in men. In women, high protein intake was associated with smaller reductions in lean mass, weight, and BMI. However, there was no significant association in men between protein intake and changes in body composition. The Quebec longitudinal study on Nutrition as a Determinant of Successful Aging reported a stronger association between protein distribution (SD of grams of protein per meal divided by grams of total protein) and muscle strength in women than that in men (men, $\beta=-0.44$, $p<0.05$; women, $\beta=-0.68$, $p<0.001$) (56). Other studies showed that the associations between diet and grip strength (men, $\beta=0.18$, $p=0.035$; women, $\beta=0.27$, $p<0.001$) (90) or physical performance (men, $\beta=0.995$, $p=0.383$; women, $\beta=0.985$, $p=0.091$) (182) were stronger in women than those in men. Although those studies did not focus on protein intake, the authors noted that women usually had healthier diets with higher micronutrient densities compared to those in men, which may have affected women's health outcomes such as grip strength or physical performance. In another study, however, total protein intake was related to lean mass only in men, while the protein distribution was related to lean mass in both sexes but more so in men (51). Declining muscle mass can be affected by lifestyle factors as well as age-related physiological and systemic changes in the body (48), therefore, the roles played by various lifestyle factors in age-related changes in body function should be further investigated to clarify sex-specific associations between dietary protein intake and lean mass.

Consistent with the results of previous studies, we observed a positive association between protein intake and lean mass retention, after adjusting for covariates and lean mass at baseline in both men and women. Previous cohort studies of older adults have demonstrated that the quantity of dietary protein intake is the main nutritional factor associated with preserving muscle mass and maintaining physical function (91, 94, 95). In one of these studies, compared with those in the lowest tertile of protein intake (<66 g/d), women in the highest tertile (>87 g/d) had 5.4–6.0% higher whole body and appendicular lean mass (91). A Japanese study also reported that the consumption of seafood, dairy products, and protein-rich foods may help older adults to maintain their independence (165). There is growing evidence that protein intake levels exceeding the recommended daily allowance may benefit elderly adults by preventing or mitigating sarcopenia (53, 61). A review study also concluded that a protein intake level meeting the nutritional requirements of all healthy individuals does not provide protection from age-related sarcopenia (45, 60, 62). According to data from the 2008-2012 Korean National Health and Nutrition Examination Survey, 18.8% of adults ≥60 years of age and 34.9% of adults ≥70 years of age consumed less protein than the estimated average requirements for Koreans (40 g/day for men and 35 g/day for women), indicating that many older Korean adults may have insufficient protein intake (183). Therefore, the effects of dietary protein intake in the attenuation of age-related loss of lean mass among older adults require further investigation.

The results of the present study showed that obesity reduced the muscle preservation effects of dietary protein. Dietary protein intake had a significant effect on lean mass after the 12-year follow-up in the normal-weight group but not in the obesity group. Sarcopenia and obesity share several pathophysiological mechanisms (109) that may synergistically increase the risk of negative health outcomes (32). Moreover, the rates of physical disabilities (184, 185), comorbidities (186), and mortality (187, 188) are higher in sarcopenic obesity than those in sarcopenia or obesity alone. A recent cross-sectional study reported that normal weight women had 14% and 10% higher muscle quality values (*i.e.*, leg power [watts] normalized for lower-body mineral-free lean mass [kg]) than those of overweight and obese women, respectively (189). Furthermore, fat mass was associated with functional decline and muscle weakness in elderly individuals (95, 190, 191). In contrast, a recent meta-analysis showed that protein supplementation combined with resistance exercise training effectively prevented age-related muscle mass attenuation and leg strength loss in the elderly, regardless of body weight (135). However, on the basis of protein supplementation alone, individuals with a mean BMI $\geq$30 kg/m^2 did not exhibit a greater change in muscle volume and handgrip strength than that in those with a mean BMI <30 kg/m^2. The authors concluded that protein supplementation may not prevent age–related muscle loss in obese elderly. Although little is known about the mechanisms underlying the impact of obesity on lean mass in the elderly, obesity may be accompanied by a state of chronic oxidative stress, which could promote protein breakdown and direct muscle fibers into a catabolic state that, ultimately, leads to muscle wasting (192). Moreover, in overweight elderly, ineffective autophagic mechanisms may be associated with insulin resistance due to the inhibition of protein synthesis and accumulation of misfolded proteins, thus contributing to age–related skeletal muscle loss (193). In our study, protein intake may have had less impact on the prevention of lean mass loss in elderly obese than that in elderly adults with normal weight. Further research is needed to fully understand the impact of obesity on lean mass.

Similar to the results reported by previous studies, regular physical activity was positively associated with lean mass retention in both men and women, regardless of obesity status. Furthermore, dietary protein intake had a significant effect on lean mass after the 12–year follow–up in the high MET group but not in the low MET group. Recent meta – analyses have reported that exercise interventions may be beneficial in improving muscle strength and physical performance (27, 132, 135). A prospective cohort study concluded that a higher intake of animal protein foods alone, especially in combination with a physically active lifestyle, was associated with the preservation of muscle mass and functional performance in elderly individuals (194). A randomized controlled trial in elderly Japanese women with sarcopenia demonstrated the significant effects of exercise and amino acid supplementation on the enhancement of muscle strength and on the combined variables of muscle mass and walking speed or muscle mass and strength (136). The lifestyles of obese men and women may, therefore, have an important influence on the retention of lean mass.

The strengths of this study included its large cohort and long follow-up period, which enabled the investigation of the associations between protein intake from habitual diets and lean mass in Koreans. However, our study also had several limitations. BIA analysis for assessing muscle mass is a useful non-invasive method in large population-based studies; however, factors such as age, hydration status, food or beverage consumption, and exercise intensity may affect the results. To reduce the possibility of measurement errors, the participants were requested to fast before the BIA assessment and their hydration status was monitored carefully. The European Working Group on Sarcopenia in Older People suggested BIA as a portable alternative to dual-energy X-ray absorptiometry (24). Additionally, we assessed dietary protein intake only at baseline and did not determine whether the protein intake of the participants had changed over the course of the follow-up period.

3–5. Conclusions

In conclusion, our findings support the current evidence that higher protein intakes are beneficial in preserving lean mass. The associations between dietary protein and increased lean mass were more apparent in the normal–weight group but were not detected in the obese group. Our population–based findings may inform the development of improved healthcare programmes for the Korean elderly, with aims to preserve muscle mass and maintain functionality. However, further comprehensive investigations of the factors affecting muscle strength, functional status, and muscle mass are needed to clarify the dose–response effects in older adults of varying weight status.

Chapter 4. The Effect of Protein Intake on Muscle Mass According to the Alcohol Consumption in Middle-aged Korean Adults : A 12-year Community-based Prospective Cohort Study[3]

[3] This study was published in the Nutrients vol.11, pii: E2143 in 2019.

Abstract

The influence of alcohol consumption on the association of protein intake with muscle mass was assessed using data from the Korean Genome and Epidemiology Study. Dietary protein intakes of 4412 middle-aged participants with normal baseline muscle mass were assessed using a semi-quantitative Food Frequency Questionnaire, and baseline alcohol consumption data (e.g., frequency and amount) were collected using a structured questionnaire. The skeletal muscle mass index (SMI), defined as the weight-adjusted skeletal muscle mass, was measured using multi-frequency bioelectrical impedance analyses every 2 years until the study endpoint. Low muscle mass was defined as a SMI <2 standard deviations below the sex-specific normal mean for a young reference group. During a 12-year follow-up, 395 subjects developed a low SMI. After multivariate adjustments, high protein intake (≥1.2 g/kg body weight [BW]) was shown to reduce the risk of low SMI development in both men (hazard ratio [HR]: 0.24; 95% confidence interval [CI]: 0.12, 0.51; *p* for trend <0.001) and women (HR: 0.29; 95% CI: 0.16, 0.53; *p* for trend <0.001), compared with low protein intake (<0.8 g/kg BW). An inverse association between high protein intake and risk of a low SMI was limited to women who did not drink alcohol (HR: 0.23; 95% CI: 0.11, 0.45 for comparing ≥1.2g/kg BW *vs.* <0.8g/kg BW; *p* for trend <0.001). Additional research should clarify the dose-response

effects of alcohol consumption on muscle mass relative to daily protein intake.

4−1. Introduction

The progressive loss of muscle mass is the primary factor used to determine sarcopenia, a syndrome characterized by low muscle mass and strength (3). Sarcopenia has been associated with increased risks of falls and fractures, reduced cardiopulmonary function, metabolic syndrome, and insulin resistance, and eventually leads to the disability, hospitalization, and death of older individuals (4).

According to the World Health Organization, the number of individuals older than 60 years of age is expected to increase from 900 million to 2 billion between 2015 and 2050 (1, 2). In other words, the population of elderly individuals who will be exposed to the risks of deteriorating strength and mobility associated with muscle loss is expected to increase enormously. According to recent estimates, the prevalence of sarcopenia ranges from 5% to 13% among individuals aged 60–70 years and from 11% to 50% among those aged ≥80 years (2). Age−related sarcopenia is a common condition associated with significant personal and financial burdens. One prospective study estimated that sarcopenia would increase hospitalization costs by 58.5% and 34% for patients <65 and ≥65 years of age, respectively (5).

The etiology of sarcopenia is multifactorial. Although aging is the leading cause of sarcopenia, this condition can be accelerated by modifiable lifestyle factors, such as physical inactivity, alcohol consumption, smoking, and undernutrition (24). To date, protein intake, in terms of both the quantity and quality, has been the main nutritional focus (124). However, the evidence increasingly suggests that the current recommended daily allowance (RDA) of protein, 0.8 g/kg body weight (BW), might not be adequate to maintain lean mass and prevent functional declines among the elderly (53, 59). Rather, recent reviews and consensus statements have suggested that a protein intake of 1.0–1.5 g/kg BW may confer health benefits beyond those afforded by simply meeting the minimum RDA (60−62).

The potentially important role of alcohol consumption in the prevention of age−related muscle loss has not been fully investigated. Some experimental animal studies have demonstrated a relationship between alcohol consumption and sarcopenia (125−127). Specifically, alcohol consumption inhibited the synthesis of skeletal muscle proteins in rats. In humans, this relationship remains controversial, although a negative relationship has been reported between alcohol consumption and sarcopenia in the general population (129, 130, 195). Moreover, little is known about the potential interacting effects of alcohol consumption and protein intake on sarcopenia (196).

Therefore, this prospective cohort study investigated the influences of various recommended protein intake levels on the development of low muscle mass according to alcohol consumption in middle-aged individuals.

4-2. Subjects and Methods

Study Population

The data included in this study were obtained from a large community-based cohort based on the Korean Genome and Epidemiology Study (KoGES) (171). For KoGES, the participant eligibility criteria included an age of 40–69 years and residence in Ansan (urban) or Ansung (rural), Korea, for at least 6 months before enrolment. Baseline examinations were performed in 2001 and 2002, and the 6th follow-up examinations were repeated every 2 years through 2014. Out of 10,030 baseline participants, the 6th follow-up was conducted in 5906 participants out of 9397 survivors. Of the original 10,030 participants, 4412 remained in the final analysis after excluding 2417 who did not complete the baseline Food Frequency Questionnaire (FFQ) or who had incomplete anthropometric data, 56 with abnormally low or high daily energy intakes (<500 or >5000 kcal), 3042 who did not participate in the follow-up examinations, and 103 with a low skeletal muscle mass index (SMI) at baseline (Figure 4-1). General characteristics of participants and non-participants in the follow up survey are presented in Table 4-1. There were significant differences in age, household income, smoking, METs, chronic disease, lean mass, and fat mass. Written informed consent was obtained from all participants. All procedures were approved by the Institutional Review Board of the Catholic Medical Center (No. KC17ZESI0645).

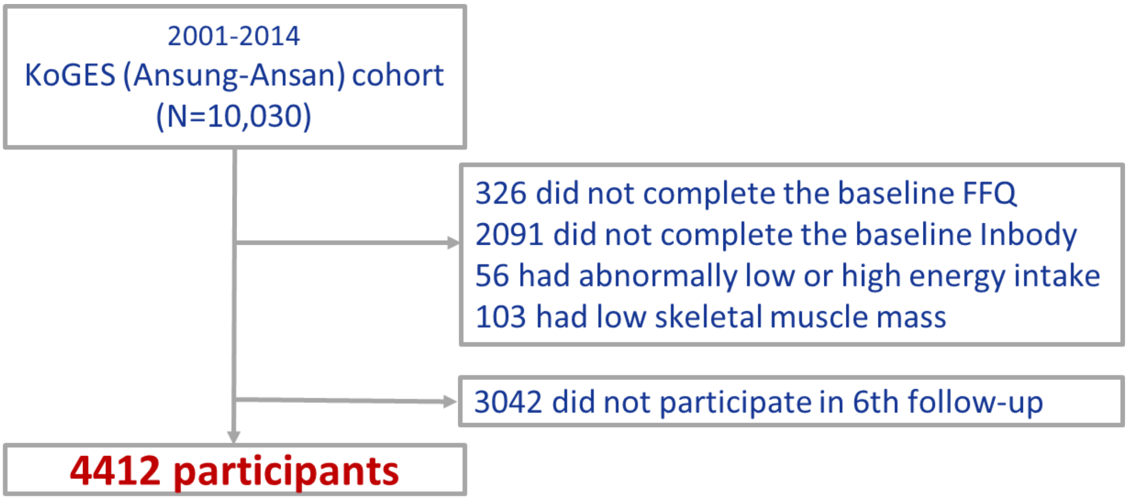


Figure 4-1. Flow chart for the selection of the study population

Table 4-1. Comparison of baseline characteristics of follow-up participants and non-participants in the study

Characteristics	Non-participants[a]	Participants	P-value[d]
N	3042	4412	
Age (years)	52.8 ± 9.4[b]	50.6 ± 8.2	<0.001
Gender, n (%)			
Men	1483 (48.8)	2096 (47.5)	0.291
Women	1559 (51.2)	2316 (52.5)	
Questionnaires			
Household income, n (%)			
≥3,000,000 KRW	536 (17.9)	958 (22.0)	<0.001
< 3,000,000 KRW	2466 (82.1)	3402 (58.0)	
Smoking status, n (%)			
Non-smokers	2153 (71.3)	3393 (77.5)	<0.001
Current smokers	865 (28.7)	987 (22.5)	
Drinking status, n (%)			
Non-drinkers	1602 (52.9)	2247 (51.1)	0.124
Current drinkers	1426 (47.1)	2151 (48.9)	
Mets (h/d)	21.4 ± 14.3	22.5 ± 14.0	0.001
Chronic disease			
Yes	98 (6.3)	136 (3.1)	<0.001
No	1457 (93.7)	4276 (96.9)	
Total energy intake (kcal)	1919.7 ± 603.8	1939.3 ± 585.5	0.161
Total protein intake (g)	65.9 ± 26.5	66.2 ± 24.6	0.539
Anthropometric measurements			
Body mass index (kg/m^2)	24.5±3.2	24.5±2.9	0.779
Lean mass (kg)	45.9 ± 8.5	46.4 ± 8.4	0.003
Fat mass (kg)	27.0 ± 7.4	26.7 ± 6.8	0.024

MET, metabolic equivalent of task.

[a] 'Non-participants' group includes subjects who did not participate in the follow-up examinations.

[b] Means ± standard deviation (SD).

[c] Total energy intake was calculated using food frequency questionnaires.

[d] Statistical significance was evaluated using t-tests or chi-square tests where appropriate.

Assessment of Dietary Intake

At baseline, the participants' usual dietary intakes were assessed by trained dietitians using a validated 103−item semi−quantitative FFQ (172). Nine response options were provided to describe the frequency of consumption of each food (never or almost never, 1 time/month, 2–3 times/month, 1–2 times/week, 2–3 times/week, 3–4 times/week, 5–6 times/week, 1 time/day, 2 times/day, or 3 times/day), and three response options were provided to describe the portion size (1/2 serving, 1 serving, and ≥2 servings). To enhance the accuracy of serving size recall, pictures of each food item were used as references. For each participant, the daily protein and other nutrient intakes were estimated based on the sum of the intake of each food item according to The Food Composition Database (Seoul, Korea: The Rural Development Administration, 2007).

Measurement of Alcohol Consumption

Total alcohol intake was assessed by questioning the participant about his or her alcohol consumption habits during the month before the interview. Participants were asked about the frequency of consumption, amount per serving, and drinking glass size. Six response options were provided to describe the frequency of alcohol consumption (1 time/month, 2–3 times/month, 1 time/week, 2–3 times/week, 4–6 times/week, or >7 per week). The amounts of beer, wine, spirits, Korean distilled spirits, raw rice wine, and refined rice wine were recorded. Total alcohol intake was calculated as the sum of the values converted to the amount of pure alcohol consumed per day for all six beverages. The participants were divided into three groups depending on the amount of alcohol consumed per day: non-drinkers, light-to-moderate drinkers (1-40 g/day for men, 1–20 g/day for women), and heavy drinkers (≥40 g/day for men, ≥20 g/day for women). Binge drinking was defined as the consumption of ≥5 alcoholic drinks for men or ≥4 alcoholic drinks for women on at least one occasion during the previous 30 days, and participants were subcategorized into two groups based on this variable: social drinkers (<1 time/month) and binge drinkers (≥1 time/month) (130).

Measurement of Body Composition

Fat mass and lean mass (i.e., fat-free mass) were assessed using multi-frequency bioelectrical impedance analysis (MF-BIA; InBody 3.0; Biospace, Seoul, Korea) according to standard procedures. The skeletal muscle mass was estimated by dividing the total lean mass by 0.52 (197). In our study, a low muscle mass was defined using the SMI, which was calculated as the total skeletal muscle mass (kg)/weight (kg) × 100.This measure adjusts for stature and the mass of non-skeletal muscle tissues (fat, organs, and bone), as described by Janssen et al. (198). We used SMI cutoff points of 35.71% for men and 30.70% for women to define low muscle mass, based on a threshold of <2 standard deviations below the sex-specific normal means for a young reference group as defined in previous Korean studies (20). The same method was used to determine the incidence of low muscle mass every 2 years until the study endpoint. The permitted range for each follow-up measurement was 24 ± 12 months, while the actual average range was 23.4 ± 0.8 months.

Covariates

The participants' demographic characteristics and medical histories were obtained using an interviewer-administered questionnaire. The questionnaire included items concerning sex, age, marital status, education, smoking habits, regular physical activity, self-perceived dental health status, chronic diseases, and residential area at baseline. To evaluate the influence of protein intake on age-related muscle loss in younger versus older adults, age was dichotomized as younger or older than 60 years. Marital status was categorized as married and unmarried (including divorced, separated, and others). Education level was categorized as high school or lower and college or higher. The smoking status was used to classify participants as smokers (current smokers) and non-smokers (former smokers and non-smokers). Regular physical activity was recorded as " yes " if the participant performed ≥2.5 h of exercise per week according to the global World Health Organization recommendation (133, 134). The self-perceived dental health status was categorized as poor or other (good and fair). The presence or absence of chronic diseases, such as myocardial infarction, congestive heart failure, coronary artery disease, peripheral arterial disease, cerebrovascular disease, asthma, chronic obstructive pulmonary disease, cancer, dementia, and arthritis was recorded.

Statistical Analysis

The weight-adjusted protein intake was categorized according to three different nutritional recommendations: RDA (≤0.8 g/kg BW) (199), International Study Group, to review dietary protein needs with aging (PROT-AGE Study Group) recommendation (0.81-1.19 g/kg BW) (60), and Nordic Nutrition Recommendation 2012 (≥1.2 g/kg BW) (200). For this study, these three recommendations were used to define the low, moderate, and high protein intake groups, respectively, and the low intake group was used as the reference. The baseline characteristics of the study participants are reported as percentages, means, 122and standard deviations and were compared using the Mantel-Haenszel χ^2 test for categorical variables and linear regression analyses for continuous variables. A one-way analysis of variance was used to test any intergroup differences in the baseline measures and percentage changes. Follow-ups for all participants were conducted from June 2001 to December 2014. For each participant, person-time was measured from the date of enrollment in the cohort to date of low SMI diagnosis or the date of end of follow-up survey. A Cox proportional hazards regression model was used to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) of total protein intake associated with the development of a low SMI during follow-up according to alcohol consumption. Age, skeletal muscle mass, energy intake, marital status, education, income, smoking, regular physical activity, self-perceived dental health status, chronic disease, and residential area at baseline were included as covariates in this model. To test for linear trends across the protein intake categories, we created a continuous variable using the median total protein score in each group. IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. A two-sided *p*-value of <0.05 was considered statistically significant.

4-3. Results

During a median follow-up of 141 months (range: 19–152 months), we observed an incidence of newly developed low lean mass of 9.5% (395 cases). The mean development age of low SMI was 63.8 years (62.7 years for men and 64.7 years for women), and men developed low SMI at an earlier age than women. Table 4-2 presents the baseline characteristics of the study participants according to the total protein intake at baseline. Overall, 26.8% of the participants had low protein intake (≤0.8 g/kg BW), 44.2% had a moderate intake (0.81–1.19 g/kg BW), and 28.9% had high protein intake (≥1.2 g/kg BW). Both men and women in the high protein intake group had a higher educational level (p=0.005 and <0.001, respectively), earned a higher income (p=0.024 and <0.001, respectively), and were physically active (p <0.001 and 0.004, respectively). Men with high protein intakes were more likely to be current drinkers (p=0.074), heavy drinkers (p=0.019), and binge drinkers (p=0.033) and to consume alcohol more frequently (p=0.001). Women with high protein intakes were significantly younger (p <0.001). The smoking status was not significantly associated with protein intake. Men and women with high protein intake reported higher intakes of energy (p <0.001) and energy from fat (p <0.001) and a lower intake of energy from carbohydrates (p <0.001), compared to those with a low protein intake. Regarding body composition, both men and women with high protein intake had a lower weight (p <0.001), body mass index (BMI) (p <0.001), fat mass (p <0.001), and lean mass (p <0.001) at baseline than those with a low protein intake. However, high protein intake was associated with a high SMI (p <0.001) in men but a low SMI in women (p <0.

Table 4-2. General characteristics of study participants by the levels of total protein intake at baseline

Protein Intake	Men (n = 2096)			
	≤0.8 g/kg BW	0.81-1.19 g/k BW	≥1.2 g/kg BW	p for trend[1]
	n = 538	n = 980	n = 533	
Demographics and lifestyles (%)				
Age (years, mean ± SD)	50.5 ± 8.0	49.7 ± 7.7	50.5 ± 8.2	0.073
Residential area (city)	61.6	74.4	64.0	0.301
Educational (≥College)	19.9	27.8	27.1	0.005
Household income (≥3,000,000 KRW)	21.7	31.0	27.5	0.024
Marital status (married)	96.9	96.8	97.4	0.673
Smoking (yes)	45.5	42.3	47.8	0.475
Chronic disease (yes)	1.5	1.1	1.9	0.665
Dental health status (poor)	36.3	39.2	40.1	0.189
Regular physical activity (yes)	12.5	19.2	22.0	<0.001
Alcohol drinking (yes)[2]	71.6	73.7	76.3	0.074
Heavy drinking (yes)	13.7	14.6	18.1	0.019
Drinking frequency (≥1 time/week)	49.1	52.8	58.9	0.001
Binge drinker (yes)[3]	42.2	49.4	48.4	0.033
Dietary intake (Mean ± SD)				
Energy (kcal/day)	1528.9 ± 271.5	1961.5 ± 312.4	2628.2 ± 574.4	<0.001
Carbohydrate (% of energy)	74.0 ± 5.0	69.0 ± 5.3	65.0 ± 6.4	<0.001
Fat (% of energy)	12.4 ± 4.1	16.0 ± 4.1	19.0 ± 4.8	<0.001
Protein (% of energy)	12.3 ± 1.7	13.8 ± 1.8	15.3 ± 2.3	<0.001

Protein (g/day)	46.6 ± 9.2	67.3 ± 11.3	99.2 ± 22.7	<0.001
Protein (g/kg body weight)	0.7 ± 0.1	1.0 ± 0.1	1.5 ± 0.3	<0.001
Body composition (Mean ± SD)				
Weight (kg)	71.0 ± 9.5	68.4 ± 9.0	65.4 ± 8.7	<0.001
Body Mass Index (kg/m^2)	25.1 ± 2.8	24.4 ± 2.7	23.5 ± 2.7	<0.001
Fat mass (kg)	16.1 ± 4.7	15.1 ± 4.5	13.6 ± 4.2	<0.001
Lean mass (kg)	54.8 ± 6.2	53.3 ± 6.1	51.8 ± 5.9	<0.001
Skeletal muscle mass index (%)[4]	40.3 ± 2.3	40.7 ± 2.4	41.4 ± 2.5	<0.001

Abbreviations: BW, body weight; SD, standard deviations; KRW, Korean won. [1] P for trend was calculated from a linear regression analysis for continuous variables and Mantel−Haenszel χ^2 for categorical variables; [2] "Yes" was defined as a person who answered, "No" to the question "Do you never drink alcohol or drink from the beginning?"; [3] Binge drinker was defined as a participant who drinks more than once a month of binge drinking; [4] Skeletal muscle mass index (%) = total skeletal muscle mass (kg)/weight (kg) × 10

Table 4-2. General characteristics of study participants by the levels of total protein intake at baseline (continued)

Protein Intake	Women (n = 2316)			
	≤0.8 g/kg BW	0.81-1.19 g/kg BW	≥1.2 g/kg BW	p for trend[1]
	n = 601	n = 972	n = 743	
Demographics and lifestyles (%)				
Age (years, mean ± SD)	52.4 ± 8.6	51.1 ± 8.4	49.6 ± 8.2	<0.001
Residential area (city)	51.4	65.5	60.3	0.003
Educational (≥College)	4.0	7.5	11.5	<0.001
Household income (≥3,000,000 KRW)	11.2	16.2	22.5	<0.001
Marital status (married)	85.2	87.5	90.7	0.002
Smoking (yes)	2.9	2.0	2.3	0.547
Chronic disease (yes)	5.7	4.4	3.9	0.132
Dental health status (poor)	45.5	43.0	37.7	0.004
Regular physical activity (yes)	14.1	17.3	20.1	0.004
Alcohol drinking (yes)[2]	24.7	25.9	28.2	0.142
Heavy drinking (yes)	1.5	1.4	1.2	0.336
Drinking frequency (≥1 time/week)	7.0	7.6	9.2	0.136
Binge drinker (yes)[3]	6.7	7.1	5.7	0.421
Dietary intake (Mean ± SD)				
Energy (kcal/day)	1345.7 ± 291.4	1737.9 ± 296.0	2442.1 ± 617.0	<0.001
Carbohydrate (% of energy)	76.3 ± 5.3	71.9 ± 5.5	68.2 ± 6.7	<0.001
Fat (% of energy)	10.4 ± 4.2	13.7 ± 4.4	16.6 ± 5.0	<0.001

Protein (% of energy)	11.9 ± 1.9	13.3 ± 1.8	14.7 ± 2.2	<0.001
Protein (g/day)	39.4 ± 8.2	58.4 ± 9.4	88.6 ± 24.1	<0.001
Protein (g/kg body weight)	0.7 ± 0.1	1.0 ± 0.1	1.6 ± 0.4	<0.001
Body composition (Mean ± SD)				
Weight (kg)	61.4 ± 8.1	59.1 ± 7.4	56.2 ± 7.2	<0.001
Body Mass Index (kg/m^2)	25.7 ± 3.0	24.8 ± 2.8	23.6 ± 2.7	<0.001
Fat mass (kg)	20.1 ± 4.9	18.8 ± 4.4	17.1 ± 4.3	<0.001
Lean mass (kg)	41.2 ± 4.3	40.3 ± 4.3	39.1 ± 4.1	<0.001
Skeletal muscle mass index (%)[4]	35.2 ± 2.6	35.6 ± 2.4	26.4 ± 2.5	<0.001

Abbreviations: BW, body weight; SD, standard deviations; KRW, Korean won. [1] P for trend was calculated from a linear regression analysis for continuous variables and Mantel−Haenszel χ^2 for categorical variables; [2] "Yes" was defined as a person who answered, "No" to the question "Do you never drink alcohol or drink from the beginning?"; [3] Binge drinker was defined as a participant who drinks more than once a month of binge drinking; [4] Skeletal muscle mass index (%) = total skeletal muscle mass (kg)/weight (kg) × 10

Figure 4−1 shows the percent changes in body composition over the 12−year follow−up period. Both men and women with higher protein intake exhibited lower reductions in weight (*p*=0.003 and <0.001, respectively) and lean mass (*p*=0.001 and <0.001, respectively) during follow−up. By contrast, the mean changes in fat mass (*p*=0.079 for men, 0.009 for women) and BMI (*p*=0.002 for men, <0.001 for women) increased significantly in men and women with a high protein intake.

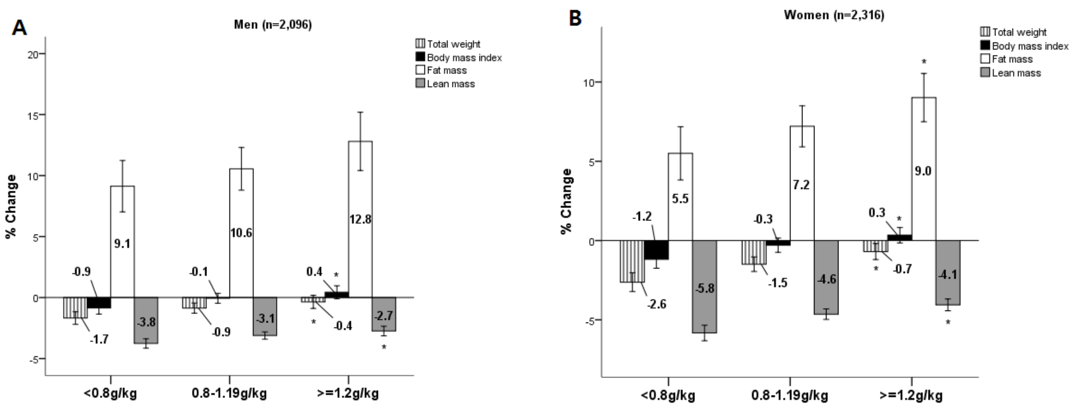


Figure 4−2. % crude change in body composition over 12 years by the levels of dietary protein intake at baselines. (A) men and (B) women. % crude change = ((12−year follow−up value−baseline value)/baseline value × 100). ANOVA = analysis of variance. * Indicates significantly linear trend across the protein intake categories according to different recommendations: *p* for trend < 0.05.

Table 4-2 presents the hazard ratios (HRs) and 95% confidence intervals (95% CIs) of the risk of developing a low SMI for each baseline dietary protein intake level, according to alcohol consumption. After adjusting for covariates, a high total protein intake (≥1.2 g/kg BW) decreased the risk of developing a low SMI in both men (HR: 0.24; 95% CI: 0.12, 0.51; p for trend <0.001) and women (HR: 0.29; 95% CI: 0.16, 0.53; p for trend <0.001) relative to a low protein intake. Women with a moderate total protein intake (0.81–1.19 g/kg BW) had a decreased risk of developing a low SMI relative to those with low protein intake after adjusting for covariates (HR: 0.54; 95% CI: 0.38, 0.76; p for trend <0.001). In covariate-adjusted subgroup analyses, high protein intake was associated with a lower risk of developing a low SMI relative to low protein intake in both men (HR: 0.28; 95% CI: 0.07, 1.09; p for trend=0.064) and women (HR: 0.23; 95% CI: 0.11, 0.45; p for trend <0.001) who did not consume alcohol. However, these associations disappeared in the subgroup of women who consumed alcohol (HR: 0.64; 95% CI: 0.18, 2.25; p for trend=0.478) after adjusting for covariates. Among the total subjects, the associations between protein intake and the development of low muscle mass were significant at ≥0.81 g/kg BW for non-drinkers (HR: 0.55; 95% CI: 0.39, 0.77; p=0.001), those who consumed alcohol <1 time/week (HR: 0.60; 95% CI: 0.44, 0.81; p=0.001), and social drinkers (HR: 0.59; 95% CI: 0.44, 0.78; p <0.001). However, among the total subjects, heavy drinkers with high protein intake were not significantly associated with the development of a low SMI (HR: 0.20; 95% CI: 0.03, 1.50; p=0.117).

Table 4-3. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the risk of developing low SMI by the levels of dietary protein intake at baseline according to alcohol consumption [1]

Alcohol Consumption Status	<0.8 g/kg BW		0.8-1.19 g/kg BW			≥1.2 g/kg BW			p for trend
	Case (n)/ person-Months	Reference	Case (n)/ person-Months	HR	95% CI	Case (n)/ person-Months	HR	95% CI	
Men (n = 2096)	51/81,130	1.00	88/135,815	0.70	(0.47, 1.05)	32/74,611	0.24	(0.12, 0.51)	<0.001
Non-drinkers	13/22,991	1.00	24/35,727	0.85	(0.39, 1.84)	10/17,684	0.28	(0.07, 1.09)	0.064
Drinkers	43/57,861	1.00	64/99,950	0.66	(0.41, 1.07)	22/56,784	0.23	(0.10, 0.54)	0.001
Women (n = 2316)	89/82,518	1.00	87/135,645	0.54	(0.38, 0.76)	42/104,027	0.29	(0.16, 0.53)	<0.001
Non-drinkers	74/61,493	1.00	67/99,664	0.48	(0.32, 0.70)	31/74,485	0.23	(0.11, 0.45)	<0.001
Drinkers	15/20,737	1.00	19/35,141	0.90	(0.40, 2.03)	11/29,260	0.64	(0.18, 2.25)	0.478
Total (n = 4412) Quantity of drinking									
Non-drinkers	87/84,484	1.00	91/135,391	0.55	(0.39, 0.77)	41/92,169	0.24	(0.13, 0.44)	<0.001
Light-to-moderate drinkers	49/64,233	1.00	65/109,753	0.68	(0.44, 1.07)	25/68,138	0.27	(0.12, 0.58)	0.158

Heavy drinkers	7/12,135	1.00	14/20,919	0.68	(0.22, 2.12)	6/14,312	0.20	(0.03, 1.50)	0.024
Frequency of drinking									
<1 time/week	112/117,898	1.00	124/189,519	0.60	(0.44, 0.81)	54/125,281	0.27	(0.16, 0.47)	<0.001
≥1 time/week	34/45,750	1.00	51/81,941	0.71	(0.42, 1.20)	20/53,357	0.28	(0.11, 0.70)	0.007
Presence of binge drinking									
Social drinkers [2]	119/123,801	1.00	128/194,703	0.59	(0.44, 0.78)	63/136,522	0.28	(0.17, 0.47)	<0.001
Binge drinkers [3]	27/39,847	1.00	47/76,757	0.77	(0.41, 1.43)	11/42,116	0.26	(0.08, 0.81)	0.018

Abbreviations: CI, confidence interval; HR, hazards ratio; KRW, Korean won. Estimated using the Cox proportional hazards regression model. [1] Adjusted for age (<60/≥60 years), skeletal muscle mass at baseline, energy intake, marital status (married/others), education (≥college/others), income (≥3,000,000 KRW per month/other), smoking (yes/no), regular physical activity (yes/no), self−perceived dental health status (poor/others), chronic disease (yes/no), residential area (urban/rural). [2] "Social drinker" was defined as a participant who drinks less than once a month of binge drinking. [3] "Binge drinker" was defined as a participant who drinks more than once a month of binge drinking.

4-4. Discussion

To our knowledge, this was the first large community-based prospective cohort study to investigate the association between protein intake and muscle mass according to alcohol consumption in Korean adults. We found that both men and women with a protein intake exceeding 1.2 g/kg BW had a lower risk of developing low SMI, compared to those with a protein intake of <0.8 g/kg BW. However, an inverse association between high protein intake and risk of a low SMI was limited to women who did not drink alcohol.

The average development age for low SMI was 63 years. This result was similar to other studies that reported that muscle mass declined drastically after age 60 (42, 43). We also found that women lose muscle mass at an older age than men. Several studies have shown that relative to men, women have less initial skeletal muscle and exhibit smaller decreases in skeletal muscle due to ageing (201, 202). A study using data from the KNHANES has also shown that the total amount of increment or decline in muscle mass change with aging was smaller in women than in men (44).

Consistent with previous human studies, men and women with higher protein intake had significantly lower decreases in lean mass (50, 91). In an older person, weight loss would be expected to cause losses in both lean mass and fat mass (94, 95). In the 12-year follow-up period of this study, the weight and lean mass decreased, while the fat mass and BMI increased. Recently, however, research has demonstrated that high protein intake could effectively increase the lean mass while maintaining or decreasing the body weight and fat mass. A meta-analysis of randomized controlled trials showed that older men and women who consumed a higher protein diet (vs. a normal protein level) exhibited better lean mass retention even while losing body mass during periods of diet-induced energy restriction (181). In another meta-analysis of randomized controlled trials, Wycherley et al. reported that when compared with an energy-restricted standard protein diet, an isocaloric high protein diet provided modest benefits in terms of reductions in the body weight, fat mass, and triglycerides and mitigated the reductions in lean mass and resting energy expenditure (203). Further community-based large cohort studies or trials are needed to clarify how protein intake affects overall body composition, including fat mass and weight.

In this study, higher protein intake was associated with a decreased risk of developing a low SMI in both men and women, after adjusting for covariates and the SMI at baseline. This finding was consistent with those of previous large prospective studies in which the dietary protein intake was identified as the main nutritional factor associated with the preservation of muscle mass and maintenance of physical function (50, 91, 94, 95). For example, Houston et al. reported that among community-dwelling older adults in the highest protein intake quintile (1.1 g/kg BW), the total losses in lean body mass and appendicular lean mass over 3 years were approximately 40% lower than those of adults in the lowest quintile (0.7 g/kg BW) (50). Another 5-year cohort study found that participants in the highest protein intake tertile (>87 g/day) had whole-body and appendicular lean mass values 5.4–6.0% higher than those of participants in the lowest tertile (91). Moreover, in a meta-analysis of adult men and women with a mean age of ≥50 years, older adults who consumed a higher protein diet (≥1.0 g/kg/day) preserved more lean mass during intentional weight loss, compared to those who consumed a lower protein diet (<1.0 g/kg/day) (181). The current study demonstrated significant associations at protein intake levels of ≥0.81 g/kg BW for women and ≥1.2 g/kg BW for men. These findings seem to support the hypothesis that the current RDA of protein (0.8 g/kg BW) is insufficient to promote optimal health and preserve physical performance in older men (53, 59). Increasing evidence suggests that a protein intake of 1.0–1.2 g/kg BW may benefit older adults by preventing or mitigating sarcopenia (60-62, 204). Further, Suominen et al. suggested that older individuals suffering from illness, physiological stress, or sarcopenia have higher requirements for protein intake (1.2–1.5 g/kg BW) than their healthy counterparts (1–1.2 g/kg BW) (203). Moreover, according to data from the 2008–2012 Korean National Health and Nutrition Examination Survey, 18.8% of adults aged ≥60 years and 34.9% of adults aged ≥70 years consumed less than the estimated average requirements (40 g/day for men and 35 g/d for women); in other words, many older Korean adults consume insufficient amounts of protein (183). Additional evidence from high-quality, multicenter clinical trials is needed to assess the long-term influences of increased protein intake on the preservation of muscle health in older adults.

In the present study, we observed a protective influence of high protein intake against the development of a low SMI in both men and women who did not consume alcohol, whereas this influence disappeared in women who consumed alcohol. Previous studies have attempted to explain the molecular mechanism underlying alcohol-induced muscle damage (205-207). Excessive exposure to alcohol induces defects in muscle tissue, including the formation of aldehyde protein adducts, losses of ribosomes and myofibrillary proteins, a reduction in protein synthesis, and an increase in the level of sarcoplasmic-endoplasmic reticulum Ca^{2+}-ATPase (205). The habitual consumption of extreme amounts of alcohol (>80 g alcohol/day) can lead to chronic alcoholic myopathy and the development of muscle weakness and wasting (207). In animal studies, ethanol impaired skeletal muscle protein synthesis and increased muscle autophagy (125-127). Unfortunately, the few studies that have examined the association between alcohol and muscle mass in humans have not yielded consistent findings (129, 130). A recent meta-analysis of a population of non-cancer patients did not support alcohol consumption as a risk factor for sarcopenia (128). However, that meta-analysis included studies that had been designed to consider the relationship between alcohol consumption and muscle mass as the primary endpoint. In contrast, our study was designed to focus on the interaction of alcohol consumption with the relationship between SMI and protein intake. In the current study, high protein intake did not have a beneficial influence on the prevention of a low SMI among women who consumed alcohol. This finding is consistent with a recent Korean study of postmenopausal women in which participants in the high-risk alcohol consumption group, defined as those with Alcohol Use Disorders Identification Test scores ≥15, had a higher risk of sarcopenia (129). However, another Korean study of men aged 60 years did not observe a difference in the proportion of participants who consumed alcohol between the groups with and without sarcopenia (208). Another study of older men in France did not identify an association between alcohol intake and sarcopenia (122). Furthermore, a recent cross-sectional Korean study found that alcohol consumption was associated with sarcopenia in women, but not in men (130). The authors of that study explained that women experience higher blood alcohol concentrations because their bodies contain smaller volumes of water in which to dilute the alcohol. The bodies of elderly women contain even smaller volumes of water, leading to a decreased tolerance for alcohol and a slower rate of alcohol metabolism (209).

Therefore, our study and previous studies suggest that sex may affect the association between alcohol consumption and muscle mass. Although we could not identify the influences of alcohol consumption on the relationship between protein intake and the development of a low SMI in men, the protective influence of high protein intake against the development of a low SMI disappeared among heavy drinkers in total subjects adjusted for sex. Further studies are needed to examine these sex-specific associations and explore the mechanisms of underlying sex differences in the relationship between alcohol consumption and SMI.

The present study had several strengths, including a large cohort and a long follow-up period, which enabled an investigation of the associations of habitual dietary protein intake and alcohol consumption with the SMI in Korean adults. However, our study also had a few limitations. First, bioelectrical impedance analysis (BIA), a non-invasive method used to assess skeletal muscle mass, is useful in large population-based studies; however, the results may be affected by several factors, including age, hydration status, food or beverage consumption, and exercise intensity. To reduce the possibility of measurement errors, the participants fasted overnight prior to the BIA, and the researchers confirmed any recent history of intensive exercise, bathing, or excessive sweating. In addition, BIA has been validated for the estimation of body composition, using dual energy X-ray absorptiometry (DXA) as a reference standard (210-

212). The European Working Group on Sarcopenia in Older People (EWGSOP) also suggested that the BIA is a portable alternative to DXA (3). Second, we assessed the dietary protein intake and alcohol consumption only at baseline and did not determine whether these variables changed over time. Third, alcohol consumption by women is relatively poorly accepted in Korean culture; accordingly, female participants may have under-reported their alcohol consumption and drinking pattern scores. Fourth, the combination of alcohol abstainers and former alcohol drinkers into a current non-drinkers group might have introduced bias and masked the real effects of alcohol abstention. Fifth, the small sample of heavy drinkers might have led to sampling bias and affected the statistical significance. Finally, our study may have limited generalizability because the subjects were selected to those who participated in the survey up to the sixth round in order to minimize follow-up loss. However, this approach may have increased internal validity. To confirm our findings, future large community-based cohort studies or trials should address alcohol consumption and its relationship with muscle mass.

4-5. Conclusions

In summary, we observed that men and women with high protein intake (≥1.2 g/kg BW) had a lower risk of developing a low SMI, compared to those with low protein intake (<0.8 g/kg BW). However, an inverse association between high protein intake and risk of a low

SMI was limited to women who did not drink alcohol. Our findings suggest that alcohol consumption might reduce the muscle-preserving influences of dietary protein. More comprehensive studies are needed to clarify the dose-response effects of alcohol consumption on the relationship between daily protein intake and declining muscle mass.

Chapter 5. Overall Discussion and Conclusion

5-1. Overall discussion

Main findings of the study

The present study was conducted to provide scientific evidence for establishing a policy to prevent muscle mass loss among Korean adults. The main findings of the study are presented in Table 5-1. First, the socioeconomic factors associated with inadequate energy intake were education level, employment, age, and family status. The factors associated with inadequate protein intake were educational level, family status, employment, and functional limitation. Second, higher protein intakes were beneficial in preserving lean mass. These associations were more apparent in the normal-weight group but were not detected in the obese group. Lastly, high protein intake ($\geq$1.2 g/kg BW) had a lower risk of developing a low SMI, compared to those with low protein intake (<0.8 g/kg BW). However, alcohol consumption attenuated the beneficial influences of a high protein intake against the development of a low SMI in women.

Table 5-1. Summary of the main findings in each sub-study

Study	Study design, data	Subjects	Main exposure	Outcome	Main results	
					Men	Women
1	Cross-sectional, 2010 KNHANES	2010 Korean adults aged ≥ 60 years	Inadequate energy intake Inadequate protein intake	Socioeconomic factors	[Energy intake] Age Education Employment [Protein intake] Living alone Education Employment Functional status	 Living with families without spouse Education Living with families without spouse Education
2	Cohort study, KoGES (Ansan-Ansung cohort)	4412 Korean adults aged 40-69 years	Protein intake Obesity	Changes of lean mass	High protein intake (↑) only in normal weight [Obese group] Age (↓) Regular physical activity (↑)	High protein intake (↑) only in normal weight [Obese group] Age (↓) Regular physical activity (↑)
3	Cohort study, KoGES (Ansan-Ansung cohort)	4412 Korean adults aged 40-69 years	Protein intake Alcohol consumption	Development of low SMI (Skeletal muscle index)	High protein intake (≥1.2g/kg BW) (↓) [Alcohol consumption group] High protein intake (≥1.2g/kg BW) (↓)	High protein intake (≥1.2g/kg BW) (↓) [Alcohol consumption group] High protein intake (≥1.2g/kg BW) (−)

Dietary characteristics of groups with insufficient energy and protein intake

In this study, the proportion of people who consumed less than 75% of EER was 23.7% for men and 31.1% for women. The proportion of people who consumed less than the RDA for protein (0.8 g/kg BW) was 30.0% for men and 47.6% for women. Vegetable protein foods were the main source of the top 5 food in both inadequate energy and protein intake groups. Vegetable protein foods lack essential amino acids, which in turn may have a negative effect on muscle mass. Moreover, carbohydrates highly contributed to energy intake in the group with energy insufficiency, and meat as a major source of energy intake was low, whereas Kimchi and soybean paste were in the top 20. This suggested that the group with energy insufficiency had simple diet patterns of carbohydrate-based meals consisting of rice and Kimchi or rice and soup. Previous studies have reported that most Koreans, especially older adults, still maintain a traditional dietary pattern that is high in carbohydrate (213, 214). Through this study, the lack of quantity in energy and protein intake is related to qualitative deficiencies and may eventually double the negative impact on sarcopenia.

The socioeconomic determinant factors associated with the inadequate energy and protein intake among Korean elderly

According to this study, the factors associated with inadequate energy intake were educational level, employment, age, and family status, and the factors affecting inadequate protein intake were educational level, family status, employment, and functional limitation. Old age is a period of socioeconomic changes such as poverty, social isolation, depression, and bereavement in addition to physiological changes such as altered taste and smell, and the loss of digestive function. Our study showed similar results. In the 2011 Korea Institute for Health and Social Affairs, those with low educational level and unemployment were at high risk of malnutrition. Educational level can be a cause of poverty, and since poverty is directly related to food purchasing ability, it may be closely related to nutritional status (152).

In a recent qualitative study, an employment-related economic change negatively impacted women's diets through, for example, limiting the number of daily meals (155). In a Korean study on the relations between the economic characteristics and life satisfaction by income levels among single elderly households, employment was identified as a variable associated with increased life satisfaction in high-income households (156). Therefore, it can be inferred that employment, in addition to economic impacts can affect intake as well as exert psychological influences.

In the family status, women living with their families without a spouse showed higher odds of energy and protein insufficiency. This finding was not consistent with previous studies that informed our study assumptions. Previous studies have suggested that widows or elderly people living alone are often undernourished (149, 159). However, in other studies, the family type (married, widowed, and other) was not related to nutrition (153, 160). This may result in short-term depressive status, but it does not seem to have a direct effect on nutrition intake by multiple factors, such as the adaptation mechanism of life and emancipation from family caregivers (161). Furthermore, according to the 2011 Korea Institute for Health and Social Affairs, the percentage of cohabitation with children increased significantly in elderly people aged 85 years and older as well as those with activity limitations. The high risk of energy insufficiency among Korean older people living with their families without a spouse appears to be attributable to the risk of malnutrition in elderly people who need family caregiving. In an Italian study comparing the risk of malnutrition between the elderly living in the community and the elderly in nursing homes, the incidence of malnutrition was significantly higher in elderly nursing home residents with high demands of caregiving (152). In this regard, attempts to identify and improve the problems of the eating environment of elderly people who need family caregiving are essential.

These findings indicate that sociodemographic characteristics such as age, education level, family status, employment, and functional limitations should be considered when plaining nutrition education and intervention programs.

The protein intake on muscle mass

This study found that higher protein intakes are beneficial in preserving lean mass. In addition, a second sub-study showed that intakes of protein more than 1.3 g/kg BW for men and 1.4 g/kg BW for women had a positive relationship with muscle mass, while a third sub-study showed that intakes of protein more than 1.2 g/kg BW had positive relationship with muscle mass. Both studies showed that protein intakes needed to preserve muscle mass were higher than the current RDA levels (0.8 g/kg BW). These findings seem to support the hypothesis that the current RDA of protein is insufficient to promote optimal health and preserve physical performance in older men (53, 59).

Moreover, according to data from the 2008-2012 KNHANES, 18.8% of adults aged ≥60 years and 34.9% of adults aged ≥70 years consumed less than the estimated average requirements (40 g/d for men and 35 g/d for women), thus, many older Korean adults consume insufficient amounts of protein (183). Additional evidence from high-quality, multicenter clinical trials are needed to assess the long-term effects of increased protein intake on the preservation of muscle health in older adults. Because methodological limitations of FFQs make it difficult to provide guidelines for protein intake, more studies are also needed to address age-specific protein recommendations particularly for middle-aged, older, and elderly individuals.

Obesity interacts with the effects of protein intake on muscle mass

The second sub-study showed that obesity reduced the muscle preservation effects of dietary protein. Sarcopenia and obesity share several pathophysiological mechanisms (109) that may synergistically increase the risk of negative health outcomes (32). Moreover, the rates of physical disabilities (184, 185), comorbidities (186), and mortality (187, 188) are higher in individuals with both sarcopenia and obesity than those with sarcopenia or obesity alone. Although little is known about the mechanisms underlying the impact of obesity on lean mass in the elderly, obesity may be accompanied by a state of chronic oxidative stress, which could promote protein breakdown and direct muscle fibers into a catabolic state that, ultimately, leads to muscle wasting (192). Moreover, in overweight elderly, ineffective autophagic mechanisms may be associated with insulin resistance due to the inhibition of protein synthesis and accumulation of misfolded proteins, thus contributing to age-related skeletal muscle loss (193). In our study, protein intake may have had less impact on the prevention of lean mass loss in elderly obese than that in elderly adults with normal weight. Further research is needed to fully understand the impact of obesity on lean mass.

Alcohol consumption interacts with the effects of protein intake on muscle mass

The third sub−study showed a protective influence of a high protein intake against the development of a low SMI in both men and women who did not consumed alcohol, whereas this influence disappeared in women who consume alcohol. Previous studies have explained the molecular mechanism underlying alcohol−induced muscle damage (205−207). Unfortunately, the few studies that have examined the association between alcohol and muscle mass in humans have not yielded consistent findings (122, 129, 130, 208). A recent meta−analysis of a population of non−cancer patients did not support alcohol consumption as a risk factor for sarcopenia (128). However, in the current study, a high protein intake did not have a beneficial influence on the prevention of a low SMI among women who consumed alcohol. This finding is consistent with a recent Korean study of postmenopausal women in which participants in the high−risk alcohol consumption group, defined as those with alcohol use disorders identification test scores ≥15, had a higher risk of sarcopenia (129). Furthermore, a recent cross−sectional Korean study found that alcohol consumption was associated with sarcopenia in women, but not in men (130). This can be attributed to the fact that women experience higher blood alcohol concentrations because their bodies contain smaller volumes of water in which to dilute the alcohol. The bodies of elderly women contain even smaller volumes of water, leading to a decreased tolerance for alcohol and a slower rate of alcohol metabolism (209). Therefore, our study as well as previous studies suggest that sex may affect the association between alcohol consumption and muscle mass. Although we did not identify the influence of alcohol consumption on the relationship between protein intake and the development of a low SMI in men, the protective influence of a high protein intake against the development of a low SMI disappeared among heavy drinkers in total subjects after adjusting for sex. Further studies are needed to examine these sex-specific associations and explore the mechanisms of underlying sex differences in the relationship between alcohol consumption and SMI.

Public health implications of the study findings

This study provides several important public health messages. In 2008, Bird and Rieker presented a 'constrained choices multi-level model' which contextualizes women and men's personal health 'choices' and outcomes as influenced and shaped by their communities. In other words, the nutritional status of the elderly is influenced by socioeconomic factors in addition to physiological factors. Our study showed that the socioeconomic factors affecting inadequate energy and protein intake were educational level, employment, and family status. The WHO mentioned that the major noncommunicable chronic diseases could be prevented by individual efforts such as healthy diets and physical activity (215), but when it comes to nutrition management for the elderly, social and systemic support may be needed, as well as encouraging individual efforts.

The present study found that the lower the energy intake, the simpler the pattern of carbohydrate−based meals consisting of rice and Kimchi or rice and soup. In addition, in the groups with insufficient energy and protein intake, the top 5 consumed foods were vegetable protein foods. A recent study suggests that eggs should be encouraged to prevent sarcopenia in elderly people (75). Eggs are easy to cook, which is particularly important for those with limited ability to stand to cook, or with limited cooking skills such as an older man who is widowed or caring for a spouse, and some employed carers. Moreover, eggs are easy to chew and swallow and might be helpful in older people with chewing and swallowing difficulties. Therefore, in future analyses, we plan to conduct research related to suggesting protein foods that the elderly can easily substitute economically and physiologically for the elderly.

Although many older people do meet RDA protein recommendations, various studies suggest that this amount of protein may be insufficient for older people to retain muscle mass and strength (53, 59). This study also showed that protein intakes to preserve muscle mass were higher than current RDA levels (0.8 g/kg BW). Thus, the study findings can facilitate further investigation to set appropriate protein recommendations for the prevention of sarcopenia in Korean older adults.

It is well-known that protein intake has a positive influence on muscle mass. However, muscle mass is affected by a variety of factors. Therefore, in addition to protein intake, research is needed on interaction with various factors that may affect protein intake and muscle mass to develop dietary guidelines for the management of sarcopenia. In particular, this study emphasizes the need for the prevention of obesity, given that the positive effects of protein intake have not been shown in the case of obese participants, and the encouragement of physical activity should be accompanied by the positive effects of muscle mass in the obese group. The present study also showed that alcohol consumption reduces the muscle-preserving effects of dietary protein. Restriction of alcohol consumption should be emphasized in programs to prevent sarcopenia, although more comprehensive studies are needed to clarify the dose-response effects of alcohol consumption on the relationship between daily protein intake and declining muscle mass. Designing effective preventive strategies that people can apply during their lifetime should also be of primary concern. Therefore, an important next step would be a study on life-course factors associated with sarcopenia in later life. Our population-based findings may inform the development of improved nutrition management programs for the Korean elderly to preserve muscle mass and maintain functionality. However, further comprehensive investigations of the factors affecting muscle strength, functional status, and muscle mass are needed to clarify the dose–response effects in older adults.

Considerations for interpreting the study results

To our knowledge, this is the first large community–based prospective cohort study to analyze the associations between protein intake and changes in muscle mass according to obesity status and alcohol consumption among the Korean elderly. However, there are some points to consider when interpreting the results of this study in terms of the study design and dietary assessment methods.

First, data on dietary intake used in the first study was obtained via 1–day 24–h recall. This may not represent the usual intake of participants, but a single 24–h recall may be adequate if the sample size is sufficiently large. In the second and third studies, we used the FFQ data from the KoGES. This is a method that presents limited food items and queries study participants regarding their usual frequency of consumption over the period. The FFQ is relatively inexpensive and convenient to carry out (216). However, food items that are not listed on the questionnaire cannot be investigated to determine exact nutrient and food intakes (217, 218). Despite using validated FFQs (172), some measurement error is inevitable, which in a prospective analysis would most often attenuate the findings toward the null. FFQs are not optimal for measuring an individual's absolute intake, but rather useful in categorizing individuals on the basis of relative intakes and so our finding should be considered as comparisons of the highest versus lowest protein consumption. In addition, in the second and third sub-study, we assessed the dietary protein intake and other related factors only at baseline and did not determine whether these variables changed throughout the follow-up period.

Second, although BIA analysis for assessing muscle mass in the second and third sub-studies is a useful non-invasive method in large population-based studies, factors such as age, hydration status, food or beverage consumption, and exercise intensity may affect the results. To reduce the possibility of measurement errors, the participants were requested to fast before the BIA assessment, and their hydration status was monitored carefully. In addition, BIA has been validated for the estimation of body composition, using DXA as a reference standard (43-45, nutrients). The European Working Group on Sarcopenia in Older People suggested BIA as a portable alternative to dual-energy X-ray absorptiometry (10). Further research is needed to complement these methodological limitations.

Third, this work found decreased muscle mass with higher intakes of dietary protein. Age-related sarcopenia is associated with not only the loss of muscle mass but also an increased risk of adverse outcomes such as physical disability and a poor quality of life. Therefore, we are planning studies related to other outcome such as fracture, frailty, and quality of life, in addition to muscle mass. In addition, we could not assess sarcopenia by using muscle strength and physical performance, which was suggested by EWGSOP (2019 EWGSOP), because they were not evaluated in the KoGES. Future studies should incorporate measures of muscle strength and physical performance when examining the risk of sarcopenia as a function of dietary protein intake.

Finally, our sample size might have been underpowered to sufficiently assess the effects of dietary protein on muscle mass by subgroups. Especially, in the third study, the small sample of heavy drinkers might have led to sampling bias and affected the statistical significance. Further large-scale prospective cohort studies to examine these issues are necessary.

5-2. Conclusions

In conclusion, this study found that higher dietary protein intakes are associated with improved muscle mass in older adults. Given the increasing prevalence of sarcopenia with aging, dietary protein requirements in older adults may need to be higher than currently recommended. In addition, in the groups with insufficient energy and protein intake, the top 5 consumed foods were vegetable protein foods. Therefore, it is important to increase protein intake to prevent sarcopenia. The findings from this study suggest that muscle loss could be affected by various factors, such as diet, lifestyle, and socioeconomic factors, in addition to physiological changes by aging. Therefore, raising public awareness of the importance of protein intake on the status of muscle mass in middle-aged and older adults is of great importance in the management of sarcopenia. The study results suggest that comprehensive nutrition programs including lifestyle improvements are needed to prevent sarcopenia.

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Appendices

Table A-1. Estimates of lean mass after a 12-year follow-up by protein intake according to % body fat at baseline

Variables	Men			
	Total (n=2096)		Normal[c] (n=1574)	Obese[d] (n=522)
	Model 1	Model 2		
Intercept	63.61	54.71	63.81	63.11
Protein intake at baseline[a]				
Tertile 1	Reference	Reference	Reference	Reference
Tertile 2	0.01[b]	−0.11	0.07	−0.47
Tertile 3	0.78**	0.35†	0.89**	0.34
Age (years)	−0.26**	−0.26**	−0.29**	−0.20**
Income (≥3,000,000 KRW)	1.19**	0.68**	1.23**	0.97*
Alcohol consumption (yes)	0.57*	0.32†	0.35	1.23**
Smoking (yes)	−0.03	0.51**	−0.45*	1.56**
Physical activity[e]	−0.02**	0.01*	−0.01†	−0.03*
Chronic diseases (yes vs. no)	−2.04**	−2.07**	−2.34*	−1.71
Fat mass (kg)		0.58**	−	−
Goodness-of-fit				
−2Log likelihood	25,672.57	24,806.49	19,357.31	6277.18

*p<0.05, **p<0.01, †p<0.1

[a] Protein intake per 1,000 kcal.

[b] coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

[c] Normal: %BF < 25 for men, and %BF < 30 for women.
[d] Obese: % BF $\geq$ 25 for men, and % BF $\geq$ 30 for women.
[e] Assesed by METs−hours/day.
Model 1 was adjusted for age, income, alcohol consumption, smoking, regular physical activity, and chronic diseases.
Model 2 was adjusted for variables in Model 1 plus fat mass.

Table A-1. Estimates of lean mass after a 12-year follow-up by protein intake according to % body fat at baseline (continued)

Variables	Women			
	Total (n=2316)		Normal[c]	Obese[d]
	Model 1	Model 2	(n=809)	(n=1507)
Intercept	46.63	39.36	46.99	47.22
Protein intake at baseline[a]				
Tertile 1	Reference	Reference	Reference	Reference
Tertile 2	0.33*[b]	0.19	0.73**	0.10
Tertile 3	0.34*	0.28*	1.12**	−0.13
Age (years)	−0.15**	−0.18**	−0.18**	−0.15**
Income (≥3,000,000 KRW)	0.14	0.14	−0.04	0.27
Alcohol consumption (yes)	0.40**	0.36**	0.29	0.44*
Smoking (yes)	−0.34	−0.09	−0.30	−0.05
Physical activity[e]	0.002	0.02**	0.02†	0.006
Chronic diseases (yes vs. no)	0.07	0.04	0.17	−0.002
Fat mass (kg)		0.46**	−	−
Goodness-of-fit				
−2Log likelihood	25,182.47	23,939.00	8793.61	16,338.88

*p<0.05, **p<0.01, †p<0.1

[a] Protein intake per 1,000 kcal.

[b] coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

[c] Normal: %BF < 25 for men, and %BF < 30 for women.
[d] Obese: % BF ≥ 25 for men, and % BF ≥ 30 for women.
[e] Assesed by METs−hours/day.
Model 1 was adjusted for age, income, alcohol consumption, smoking, regular physical activity, and chronic diseases.
Model 2 was adjusted for variables in Model 1 plus fat mass.

Table A-2. Estimates of lean mass after a 12-year follow-up by protein intake according to body mass index at baseline[a]

Variables	Men (n=2096)			Women (n=2316)		
	Normal[b] (n=621)	Overweight (n=591)	Obese (n=884)	Normal (n=683)	Overweight (n=601)	Obese (n=1032)
Intercept	58.97	62.65	64.66	44.11	46.89	50.94
Protein intake at baseline[c]						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	0.33[d]	0.22	−0.08	0.62*	0.24	−0.05
Tertile 3	0.49	0.48	0.30	0.80**	0.52†	−0.08
Age (years)	−0.24**	−0.22**	−0.23**	−0.17**	−0.17**	−0.19**
Income (≥3,000,000 KRW)	1.04**	0.52	0.67*	0.13	0.34	0.15
Alcohol consumption (yes)	0.45	0.33	0.39	0.32	0.48*	−0.06
Smoking (yes)	0.12	0.51	−0.74**	0.06	−0.57	−0.33
Physical activity[e]	−0.004	0.01	−0.02†	0.01†	0.01†	−0.007
Chronic diseases (yes)	−1.55	−0.42	−2.89*	−0.59	0.19	0.31
Fat mass (kg)	−	−	−	−	−	−
Goodness-of-fit						
−2Log likelihood	7031.09	6881.37	10,559.00	6970.42	6251.52	11,045.67

*p<0.05, **p<0.01, †p<0.1

[a] Adjusted for age, income, alcohol consumption, smoking, regular physical activity, and chronic diseases.

[b] Normal: BMI<23 kg/m^2; Overweight: 23≤BMI< 25 kg/m^2 ; Obese: BMI≥ 25 kg/m^2.

[c] Protein intake per 1,000 kcal.

[d] Coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

[e] Assesed by METs−hours/day.

Table A-3. Estimates of lean mass after a 12-year follow-up by protein intake according to METs level at baseline[a]

Variables	Men (n=2096)			Women (n=2316)		
	Low[b] (n=693)	Medium (n=647)	High (n=701)	Low (n=742)	Medium (n=788)	High (n=737)
Intercept	50.35	52.92	60.15	37.80	38.41	43.63
Protein intake at baseline[c]						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	−0.02[d]	−0.75*	0.13	0.10	0.04	0.36
Tertile 3	0.47	−0.23	0.50	−0.01	0.12	0.73**
Age (years)	−0.21**	−0.21**	−0.33**	−0.17**	−0.13**	−0.23**
Income (≥3,000,000 KRW)	0.57†	0.51	1.26**	0.46†	0.33	−0.58†
Alcohol consumption (yes)	−0.12	0.86*	0.21	0.39†	0.51*	0.17
Smoking (yes)	0.87**	0.81**	−0.06	−0.09	−0.15	0.10
Physical activity	−	−	−	−	−	−
Chronic diseases (yes)	−3.30*	−1.87	−1.55	−0.90*	0.87	0.33
Fat mass (kg)	0.62**	0.61**	0.50**	0.50**	0.45**	0.42**
Goodness-of-fit						
−2Log likelihood	8414.31	7884.85	8466.85	7725.80	8378.42	7775.01

*p<0.05, **p<0.01, †p<0.1

a Adjusted for age, income, alcohol consumption, smoking, chronic diseases, and fat mass.

b Grouped according to METs tertiles (T1=low, T2=medium, T3=high).

c Protein intake per 1,000 kcal.

d Coefficient estimates and SEs are derived from linear mixed effects models adjusted for lean mass at baseline.

Abstract (in Korean)

한국인의 근육량과 식생활 요인과의 연관성에 관한 연구

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서론

근육량의 감소는 근육량과 근육강도의 소실로 정의되는 근감소증의 직접적인 원인이 되며 노화와 밀접한 관련성을 보인다. 근감소증은 신체적 기능의 저하로 이어질 수 있으며, 낙상 및 골절 위험의 증가, 심폐 기능 감소, 대사 증후군 및 인슐린 저항성 증가로 결국 기능장애, 입원 및 사망위험을 증가시킨다고 알려져 있다. 근감소증은 다양한 위험요인과 메커니즘에 의하여 발전된다. 노화가 근감소증의 주요 유발 요인으로 알려져 있지만, 이 상태는 신체활동부족, 알코올섭취, 흡연 및 영양부족 등 중재 가능한 생활양식 및 영양요소에 의해 악화될 수 있다고 보고되고

있다. 최근 들어 근감소증과 관련한 식사요인에 대한 연구가 진행되고 있지만 대부분 단백질 중심으로 이루어졌으며, 우리나라의 경우 대부분 단면연구에 불과하였다. 또한 현재 일일 단백질 섭취 권장량 0.8g/kg BW(body weight)이 노인의 제지방을 유지하고 기능 저하를 예방하기에는 부족할 수 있다는 연구결과가 제시되고 있다. 더욱이 비만 및 알코올 섭취와 같은 근감소증 관련 요인과 단백질 섭취의 근감소증 예방효과와의 잠재적 상호 작요 효과와 관련한 연구는 거의 찾아볼 수 없었다. 근감소증은 노년기의 사회적 문제로 이슈화 되었지만 최근에는 이른 시기에 발생할 수 있다는 점에 관심이 모아지고 있다. 이에 EWGSOP2 개정 내용에서도 근감소증의 빠른 발견과 대응이 중요함을 강조하고 있다. 그러므로 가까운 미래에 근감소증으로 인한 기능저하의 위험성이 커지는 중년 한국인을 대상으로 근육량 저하와 식사요인과의 관련성에 대한 과학적 근거를 마련할 필요가 있다.

목적

본 연구의 목적은 한국인의 근감소증과 관련된 식생활요인을 파악하고, 단백질 섭취상태와 근감소증 발생과의 관련성을 규명함으로써, 한국인의 근감소증 예방 및 관리를 위한 식사지침의 과학적인 근거를 제공하기 위함이다. 본 연구는 세 가지의 세부 연구로 구성되어 있으며, 첫 번째 연구의 목적은 한국 노인의 영양소 섭취 실태를 파악하고, 영양소 섭취 부족의 사회경제적 결정요인을 분석하는 것이다. 두 번째 연구에서는 한국 중년 성인의 비만에 따른 단백질 섭취와 근감소증의 연관성을 분석하고자 하였으며, 세 번째 연구에서는 한국 중년 성인에 있어 다양한 권장

단백질 섭취수준과 근감소증의 연관성을 평가하고, 알코올 섭취와의 상호작용을 확인하고자 하였다.

연구 방법 및 결과

Study 1.

첫 번째 연구는 2010년 제 5기 1차년도(2010) 국민건강영양조사에 참여한 대상자 중 건강설문조사, 검진조사, 영양조사를 완료한 만 60세 이상 노인인구 1869명을 대상으로 하였다. 노인의 영양 상태에 영향을 줄 수 있는 요인으로 알려진 연령, 가족 상태, 사회경제적 요인 (학력, 가구소득, 기초수급, 경제활동), 건강 관련요인 (만성질환, 활동제한, 식사요법, 우울, 자살생각)에 대해 분석하였다. 에너지 및 단백질 섭취량은 국민건강영양조사 내용 중 24시간 회상법으로 수집한 식사섭취조사자료를 이용하였다. 한국인 영양섭취기준 (dietary reference intakes for Korean)을 참고로 에너지 필요 추정량 (estimated energy requirement, EER)의 75% 이상 섭취한 군 (adequate group)과 미만으로 섭취한 군 (inadequate group)으로 구분하여 관련 요인을 분석하였다. 단백질은 하루 섭취 권고량 (recommended daily allowance)을 기준으로 0.8g protein/kg 이상으로 섭취한 군 (adequate group)과 미만으로 섭취한 군 (inadequate group)으로 구분하여 분석하였다. 로지스틱 회귀분석을 통해 에너지와 단백질 섭취 부족에 영향을 주는 사회경제적 요인들의 OR 값을 산출하였다.

에너지 필요 추정량의 75% 미만으로 섭취하는 노인의 비율이 남자는

23.7%, 여자는 31.1%으로 나타났다. 부족한 영양소 섭취 그룹의 총 에너지 섭취량에 대한 탄수화물 기여도는 적절한 섭취 그룹의 경우보다 현저히 높았다 ($p <0.05$). 또한 에너지 및 단백질 섭취가 불충분한 그룹에서 상위 5개의 주요 급원식품이 대부분 식물성 단백질 식품이었다. 남녀 모두 학력(OR; 남자 1.480, 여자 1.614)과 경제활동 여부(OR; 남자 1.751, 여자 1.464)가 에너지 섭취 부족에 영향을 주는 요인으로 분석되었고, 남자는 70세 이상인 경우 에너지 섭취가 부족할 확률이 1.475배, 여자는 배우자 없이 가족과 동거하는 그룹의 경우 1.496배 높았다. 단백질 섭취 부족에 영향을 주는 요인으로는 남녀 모두 학력 (OR; 남자 2.092, 여자 2.030)으로 나타났고, 독거하는 남자와 배우자없이 가족과 동거하는 여자의 경우 단백질 부족할 확률이 각각 2.059배, 1.728배로 높았다. 이 외에도 남자는 경제활동 여부 (OR: 1.738)와 활동제한(OR: 1.552)이 단백질 부족과 관련된 요인으로 분석되었다.

Study 2.

두 번째 연구는 대규모의 전향적 역학조사인 한국인유전체역학조사사업의 지역사회기반 코호트 자료를 이용하여 경기도 안성과 안산에 거주하는 40~69세 성인 10,030명을 대상으로 하였다. 연구 대상자는 2001~2002년에 모집되었으며, 2년 간격으로 추적되었다. 본 연구에서는 제 7기(2013~2014년)까지의 추적조사 자료를 사용하여, 기반조사에서 정상 근육량을 가진 총 4412 명을 분석에 포함하였다. 1일 영양소 섭취량은 타당도가 검증된 반정량적 식품섭취빈도조사지를 이용하여 산출되었다. 신체 조성은 기준 시점 및 12 년 추적 조사 후에 생체 전기 임피던스 분석을 사용하여 측정하였다. 선형 혼합 효과 모델을 사용하여

12 년 추적 조사 후 제지방과 기반조사에서의 단백질 섭취 간의 연관성을 조사하였다.

보정변수 및 기반조사에서의 제지방을 조정한 후, 최고 및 최저 삼분위수를 비교 한 결과 식이 단백질 섭취가 남성 (β=0.79, P=0.001)과 여성 (β=0.28, P=0.082) 모두에서 12년 후의 제지방과 양의 관계를 나타냈다. 그러나, 이러한 차이는 베이스 라인의 체지방을 추가로 보정한 후에 약화되었으며, 정상 체중 그룹에서 관련성이 더 강한 것으로 나타났지만 (남자, β=0.85, P=0.002; 여자, β=0.97, P<0.001), 비만 그룹에서는 관련성을 보이지 않았다. 비만군에서는 연령 (남자, β=4.08, P<0.001; 여자, β=2.61, P<0.001) 및 규칙적인 신체 활동 (남자, β=0.88, P=0.054; 여자, β=0.76, P<0.001)이 12 년의 추적 조사 후 제지방과 유의한 관련이 있었다.

Study 3.

세 번째 연구는 대규모의 전향적 역학조사인 한국인유전체역학조사사업의 지역사회기반 코호트 자료를 이용하여 경기도 안성과 안산에 거주하는 40~69세 성인 10,030명을 대상으로 하였다. 연구 대상자는 2001~2002년에 모집되었으며, 2년 간격으로 추적되었다. 본 연구에서는 제 7기(2013~2014년)까지의 추적조사 자료를 사용하여, 기반조사에서 정상 근육량을 가진 총 4412 명을 분석에 포함하였다. 1일 영양소 섭취량은 타당도가 검증된 반정량적 식품섭취빈도조사지를 이용하여 산출되었다. 체중을 보정한 골격근 질량으로 정의된 골격근 질량 지수를 연구 종료 시점까지 2 년마다 다 생체 전기 임피던스 분석을 사용하여 평가하였다. 낮은 근육량은 젊은 기준 그룹에 대한 성별-특정 정상 평

균 미만의 골격근 질량 지수 <2 SD로 정의하였다. 단백질 섭취 수준에 따른 근감소증의 발생 비교위험도를 산출하기 위하여 콕스비례위험모형을 사용하였다.

12 년의 추적 조사 기간 동안 395 명의 참여자가 낮은 SMI로 진단되었다. 콕스비례위험모형을 사용하여 다변량 보정 후, 고단백 섭취 (≥1.2 g/kg BW)는 낮은 단백질 섭취(<0.8 g/kg BW)와 비교했을 때 남자와 여자 모두에서 낮은 SMI 발생의 위험을 감소시키는 것으로 나타났다 (남자: HR, 0.29; 95% CI, 0.16, 0.53; p for trend <0.001; 여자: HR, 0.29; 95 % CI, 0.16, 0.53; p for trend <0.001). SMI 발생에 대한 단백질 섭취의 보호자 영향은 알코올을 섭취하지 않는 여성에서만 나타났다 (HR: 0.23; 95% CI: 0.11, 0.45 for comparing ≥1.2g/kg BW *vs.* <0.8g/kg BW; p for trend <0.001).

결론

이상의 결과를 종합하여 볼 때, 높은 단백질 섭취는 노인의 근육량 개선과 관련이 있는 것으로 규명되었다. 노화와 함께 근감소증의 유병률이 증가함에 따라 노인의 식이 단백질 요구량이 현재 권장되는 것보다 상향 조정되는 부분을 검토할 필요가 있겠다. 또한 에너지 및 단백질 섭취가 불충분한 그룹에서 상위 5개의 주요 급원식품이 대부분 식물성 식품인 점에서 근감소증 예방을 위한 프로그램 마련에 있어 노인의 단백질 섭취량을 증가시키기 위한 실천적 방법을 모색하는 것이 필요하다. 근감소증은 노화에 의한 생리학적 변화 외에도 식사, 생활습관 및 사회경제적 요인과 같은 다양한 요인에 의해 영향을 받을 수 있음을 확인하였다. 따라

서, 우리나라 중년 및 노인의 근감소증의 예방 및 중재의 전략으로서 단백질 섭취의 중요성에 대한 대중의 인식을 높이는 것이 매우 중요하겠다. 또한 본 연구결과는 근감소증 예방을 위한 영양프로그램 마련에 있어 영양적 요인과 더불어 금주 및 신체활동 증가 등 생활습관의 개선이 필요함을 시사한다.

주요어: 단백질, 에너지, 근육량, 사회경제적요인, 비만, 알코올 섭취, 한국성인

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