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Impact of sarcopenic obesity and physical inactivity on mortality in Korean older adults : a population-based longitudinal study

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Abstract

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OBJECTIVES: To investigate the association between the 4 body composition status of sarcopenic obesity (nonsarcopenic nonobesity; S-O-, nonsarcopenic obesity; S-O+, sarcopenic nonobesity; S+O-, sarcopenic obesity; S+O+) and the mortality risks, and to compare the relative mortality risks of Korean elderly who met the *World Health*

Organization 2020 guidelines on physical activity and sedentary behavior with elderly who did not meet the recommendations.

METHODS: 2,781 participants aged over 65 years in the Korean National Health and Nutrition Examination Survey 2008-2011 (KNHANES IV-V) were included in this study. Sarcopenia was defined by the value of appendicular skeletal muscle mass (ASM) divided by square of height (ht^2) <7.0kg/m^2 and <5.4kg/m^2 for women. Obesity was defined as waist circumference of ≥90cm for men and ≥85 for women. Physical activity was categorized by adherence to aerobic and muscle-strengthening physical activity guidelines. For mortality, we merged mortality information from Korea Centers for Disease Control and Prevention with KNHANES IV-V data to conduct this study. Cox proportional hazards models were used to examine the relative mortality risks of Korean elderly aged over 65 years according to groups for sarcopenia and obesity, using data from the 2008-2011 KNHANES and linked mortality

records for deaths occurring in 2007–2015.

RESULTS: There were 629 deaths during follow-up. S+O+ (HR 1.58; 95% CI 1.16-2.17) and S+O- (HR 1.34; 95% CI 1.09-1.63) demonstrated significantly higher risk of mortality compared to S-O- reference group after adjusting for covariates. However, S-O+ group (HR 1.03; 95% CI 0.84-1.27) did not show significant association with mortality. Meeting the recommendations for aerobic and muscle-strengthening physical activity respectively was associated with substantial survival benefits when compared to S-O- reference group, with all values being invalid for hazard ratios among all groups. Not adhering to the guideline was related to increased mortality risk in most of the groups, when compared to S-O- participants meeting the physical activity guideline reference group. All groups for sarcopenic obesity demonstrated significantly increased mortality risk in group for not adhering to guidelines to muscle-strengthening physical activity. In not adhering to aerobic guideline group, S+O- (HR 1.38;

95% CI 1.04-1.84) and S+O+ group(HR 1.53; 95% CI 1.04-2.26) showed increased risk for mortality, while values for nonsarcopenic nonobese and nonsarcopenic obese group not being significant in the analysis.

CONCLUSION: Subjects with S+O+ were associated with a 58% increased risk of mortality, and 34% for S+O- group when compared to S-O- group; S-O+ groups not showing significant association with mortality. Furthermore, not adhering to physical activity guidelines was associated with increased mortality risks among the Korean elderly, after controlling for lifestyle variables and comorbidities. Efforts to promote healthy aging should focus on preventing obesity, maintaining muscle mass, and engaging in aerobic and muscle-strengthening activities for recommended amount.

Keyword : Sarcopenic obesity, Sarcopenia, Obesity, Physical activity guidelines, Mortality

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1. INTRODUCTION

1.1 Background

Sarcopenic obesity is a condition that develops as muscle mass and strength gradually decline with aging and adiposity levels increase concurrently. From a pathogenetic perspective, sarcopenia and obesity appear to be closely related; obesity-related conditions have been reported to be potential risk factors for sarcopenia since increased adiposity can cause chronic inflammation, which can contribute to the onset and progression of sarcopenia (Stenholm et al., 2008). In reverse, sarcopenic status can cause a decrease in the intensity and duration of physical activity, leading to an increase of the risk of being obese (Di Francesco et al., 2004). Sarcopenia and obesity may increase each other's impact on metabolic and functional disorders (Dominguez et al., 2007; Zamboni et al, 2008).

Physical activity is defined as any bodily movement conducted by skeletal muscles that requires energy expenditure (Caspersen et al., 1985). Engaging

in regular physical activity is related to decreased risks of mortality as well as prevalence of cancer, cardiovascular disease, diabetes, hypertension, and depression (McTiernan, 2008; Blair et al., 2001). Individuals with such chronic health conditions would benefit from physical activity, but the conditions are often considered impediments to physical activity (Barber et al., 2001; Adams et al., 2006). Accordingly, World Health Organization (WHO) recommended an ideal amount of physical activity (e.g., 150-300 minutes of moderate intensity aerobic physical activity or 75-150 minutes of vigorous intensity aerobic physical activity or an equivalent combination of moderate and vigorous intensity physical activity; muscle-strengthening activities on 2 or more days) per week for populations worldwide (WHO, 2020). Maintaining the adequate adiposity level and muscle mass, and sustaining or increasing the amount of physical activity in older people is reported to be associated with reduced mortality rates (Atkins & Wannamathee, 2020; Lee & Skerrett, 2001). However, most of the research have not shown a causal relationship between physical activity and

sarcopenic obesity, and it is yet unclear how variations in physical activity over time will affect the prevalence of sarcopenic obesity. Moreover, few studies have examined the impact of sarcopenia, obesity and physical activity on mortality among Korean elderly population. In fact, most of the Korean studies focusing on sarcopenic obesity or physical inactivity across older population were cross-sectional (Kim et al., 2022; Seo & Lee, 2022). Furthermore, whether adhering to the international physical activity guideline influences longevity of Korean older people categorized by the status of sarcopenic obesity has not been identified.

The aim of the current study was to explore the longitudinal association between the status of sarcopenic obesity, physical activity and the risk for all-cause mortality in a large population of Korean elderly, using data from Korean National Health and Nutrition Examination Survey (KNHANES).

1.2 Purpose

The purpose of this study uses 2008-2011 the Korea National Health and Nutrition Examination Study (KNHANES) to examine:

1. the association between Sarcopenic Obesity groups and mortality in Korean elderly
2. the association between Sarcopenic Obesity groups and mortality according to Physical Activity groups in Korean elderly

1.3 Research hypothesis

To provide the scientific evidence throughout the study, three hypotheses was proposed as presented below.

First, Obese, Sarcopenic, and Sarcopenic Obese groups will be associated with increased risk of mortality when compared to Optimal group.

Second, Significant association will not be found in Obese, Sarcopenic, or Sarcopenic Obese with those adhering to physical activity guideline with increased mortality risk when compared to optimal group adhering to physical activity guidelines.

Third, Significant association will be found in all Sarcopenic Obese groups not adhering to physical activity guidelines with increased mortality when compared to “Adhering to physical activity guideline and Optimal” group.

2. LITERATURE REVIEW

2.1 Sarcopenic Obesity and Mortality

Sarcopenia is an age-related degenerative loss of skeletal muscle mass, strength, and function (Atmis et al., 2019). Adverse effects of sarcopenia include physical disability, depression, metabolic syndrome, increased fall risk, and mortality (Janssen et al., 2006; Zhang et al., 2018; Tsekoura et al., 2017; Yeung et al., 2019). Multiple independent organizations define sarcopenia as a decrease in muscle mass and a decrease in muscular strength or function. One of these organizations is the Asian Working Group on Sarcopenia (AWGS); establishing consensus criteria for classifying sarcopenia among Asian population, suggesting a number of cut-off points for dual X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA) techniques (Chen et al., 2014). AWGS additionally recommends measuring handgrip strength (HGS) and walking speed in order to evaluate muscle function and strength. Sarcopenia was diagnosed if both muscle strength and muscle mass are low. The severity of

sarcopenia was assessed through physical performance. However, there is still no universal consensus for categorization of sarcopenia, definition being still under discussion. Obesity is a significant health condition that contributes to an age-related reduction in functionality in older people (Haslam et al., 2008). In fact, people with a high fat mass are especially susceptible to the negative consequences of sarcopenia. Excess weight and obesity in the elderly is associated with a higher prevalence of chronic health disorders and also demonstrates higher risk of death (Must et al., 1999; Blair & Brodney, 1999). Various anthropometric tools are used to determine obesity in general population (Neovius et al., 2005). Obesity is a significant health problem that affects elderly individuals' functioning abilities. According to some studies, among various measurement tools, waist circumference may be more accurate in determining overweight or obese than body mass index (BMI) (Rothman, 2008; Lambert et al., 2012). Furthermore, waist circumference is reported to be a more precise indicator of risk of developing cardiovascular disease and all-cause

mortality than BMI (Bigaard et al., 2005). Sarcopenia and obesity are age-related risk factors in older population, respectively. Sarcopenic obesity is a new class of obesity in older people characterized by the combination of decreased muscular mass and strength with increased adiposity. Nonetheless, the combination of the two conditions may generate a negative synergetic effect, posing a greater health risk; may interact to have a greater impact on mortality (Goisser et al., 2015). Progression of sarcopenic obesity includes increased inflammation response level, insulin resistance, neuromuscular dysfunction, and degenerative decrease in fat oxidation and energy expenditure. (Lee et al., 2016). A 11.3-year prospective study from the British Regional Heart study found that individuals classified as sarcopenic obese by waist circumference and mid-arm muscle circumference demonstrated the highest risk (HR = 1.72; 95% CI = 1.35-2.18) compared with the nonsarcopenic nonobese group, followed by sarcopenic nonobese (HR = 1.41; 95% CI = 1.22-1.63) and nonsarcopenic obese (HR = 1.21; 95% CI = 1.03-1.42) group (Atkins et al.,

2014). Furthermore, in a cohort study using UK Biobank, involving over 45,000 people, significant association had been found between sarcopenic obesity and mortality; sarcopenic obese group had 31% higher risk of death compared with the non-sarcopenic and non-obese group (Farmer et al., 2019).

2.2 Physical Inactivity and Mortality

Relationship between physical inactivity and premature mortality has long been debated over the past 4 decades (Lee & Paffenbarger, 1996; Morris et al., 1953; Paffenbarger et al., 1978); the benefits of physical activity in reducing premature mortality from all-causes are now widely acknowledged (Yang et al., 2022). Aside from extending life expectancy and enhancing quality of life, engaging in moderate amount of physical activity has been demonstrated to reduce all-cause mortality (Paffenbarger et al., 1986; Blair et al., 1989). Regular physical activity is known to be an effective approach for successful aging (Nelson et al., 2007; Katzmarzyk et al., 2019).

Various organizations, such as the World Health Organization (WHO) and the American College of Sports Medicine (ACSM), and many countries have produced PA guidelines that offer guidelines for physical activity based on evidence. Recommendations from physical activity guideline are made for young children, adolescents, adults, older people,

people with chronic diseases, and for the disabled. In order to enable individualization, guidelines are based on several physical activity dimensions such as mode, frequency, duration, and intensity. Domain-specific physical activity such as leisure, occupational, household, and transportation. A minimum of 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous-intensity physical activity per week, or an equivalent combination of moderate and vigorous exercise, is advised for adults. The terminology metabolic equivalent of task (MET) is used to quantify the energy expenditure during a particular physical activity. The expected value for resting energy consumption is 1 MET. Intensity of physical activity is classified as moderate when it is between 3 to 6 metabolic units (METs), and vigorous when it is over 6 METs. Prevalence of physical inactivity, is the percentage of people who do not meet the physical activity guidelines of at least 150 minutes of moderate intensity physical activity or at least 75 minutes of vigorous physical activity per week for adults, which shows an increasing trend worldwide; only 19% of

adolescents and 17% of adults in large sample of participants from 32 different countries met the guidelines for aerobic physical activity and muscle-strengthening exercise (Garcia-Hermoso et al., 2022). Recommended amount of physical activity is about the same for middle-aged adults and older adults over 65. In fact, older people demonstrated higher prevalence of physical inactivity than adults aged 18-64 since the criteria may be too demanding to the elderly. According to a cohort study that used data from the National Health Interview Survey, individuals who met the guidelines for aerobic activity had a lower mortality risk (HR ranging from 0.65 to 0.75, $p < 0.05$) than those who did not adhere to the criteria (Schoenborn & Stommel, 2011). In a large pooled cohort analysis from 6 prospective cohort studies, adhering to aerobic physical activity guidelines of 150 minutes of moderate to vigorous physical activity (MVPA) per week reduced mortality by range of 20 to 30% (Moore et al., 2012).

2.3 Physical Activity and Sarcopenic Obesity

Over the course of a lifetime, a general pattern is evident in physical activity and body composition. Age onset of adulthood is often when physical function and fat-free mass is on peak. Connection between changes in physical activity throughout one's lifecycle and the emergence of sarcopenic obesity is reported in several studies (Westerterp, 2018; Lee et al., 2016). There is growing evidence that sarcopenia and sarcopenic obesity may become managable. A potential intervention to delay the onset of progression of age-dependent muscle loss, sarcopenia, has emerged among various risk factors: physical activity (Marzetti et al., 2017).

Physical inactivity was reported to have connection with sarcopenic status in a variety of cross-sectional and cohort studies (Aggigo et al., 2016; Ko et al., 2021; Brown & Harhay, 2017), and moderate amount of physical activity was shown to be the enhancer of muscular mass and strength in older population according to intervention studies (Haider et al., 2019). Increased fall risk, decline in occupational activity due to retirement,

decreased participation rate in sport activity due to lowered physical functional level are all potential causes of the decline in aerobic and muscle-strengthening physical activity by aging (Barnett et al., 2012). Additionally, degenerative changes in gastrointestinal function may result in poor digestion, which may contribute to loss of muscle mass due to lower levels of muscular protein synthesis, leading to the onset of sarcopenic obesity (Witard et al., 2016). In general, it has been demonstrated that physical activity prevents increase in adiposity level, lowers fat mass in obese individuals, and increases muscle mass and strength in older people with sarcopenia. For the management and prevention of sarcopenia or obesity in older people, regular physical activity including both aerobic and muscle-strengthening excercise is the key factor (Batsis & Villareal, 2018). According to an umbrella review of systematic review evidence, physical activity and exercises of all types have been found to be the potent treatment for the management of loss of muscle mass and strength (Moore et al., 2020). In order to enhance

or preserve physical function level in elderly people, muscle-strengthening and aerobic exercise are the most general exercise types and commonly recommended (Thomas et al., 2019). Muscle-strengthening exercise focuses on enhancing neuromuscular-adaptive responses, also had been proven to reduce the degenerative effects of aging on functional capacity (Andersen et al., 2005; Fragala et al., 2019); whereas aerobic exercise enhances cardiovascular adaptation strategies, cognitive fundcion, and neural plasticity among older people (Hellsten & Nyberg, 2011; Erickson & Kramer, 2009).

3. METHODS

3.1 Study Population

This study utilized the KNHANES-linked Cause of Death data (version 1.1). KNHANES is a comprehensive, representative survey that assesses the nutritional and overall health of Koreans (Kweon et al., 2014). These personalized data include demographic information, health-related details, comorbidities, physical examination results, and laboratory results.

Previously, the Korea Centers for Disease Control and Prevention added mortality information to KNHANES IV-VI data. From 2007 to 2017, data on all-cause mortality were monitored. Participants who objected to be linked between death data and KNHANES data from 2008 to 2011 were excluded from the research. Among these participants, we enrolled 2,781 adults (≥65 years) without missing data for defining the variables, underweight, history of cancer, stroke, and heart disease.

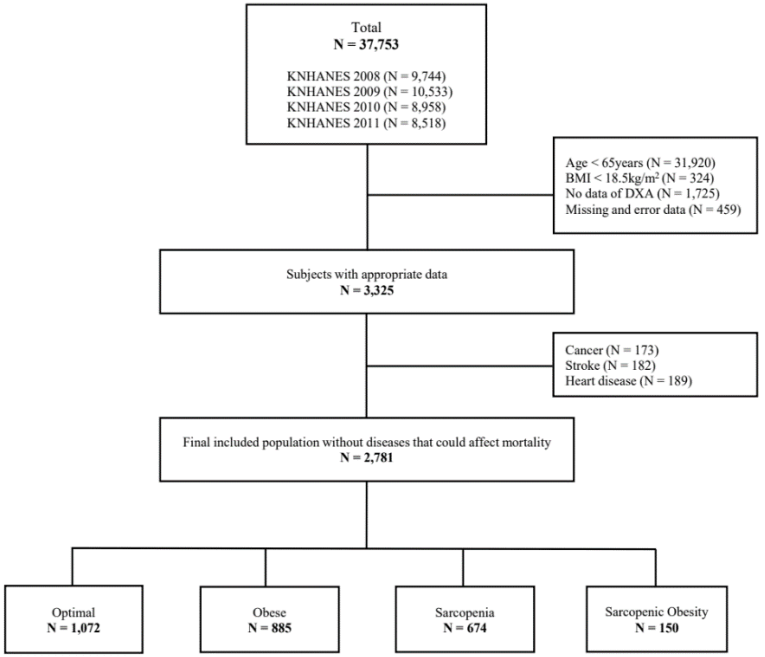

Figure 1. Flow diagram demonstrating participant selection process

3.2 Definition of Variables

3.2.1 Definition of Sarcopenic Obesity

The terms sarcopenia and obesity are combined to define sarcopenic obesity. Dual energy X-ray absorptiometry was used to calculate the total lean mass. Lean soft tissue mass in the arms and legs was added to determine the appendicular skeletal muscle mass (ASM). We evaluated sarcopenia by using the ratio of ASM to height squared (ASM/Ht2 in kg/m2) (Baumgartner et al., 1998). The Asian Working Group for Sarcopenia decided that the cutoff for sarcopenia in 2019 was 7.0 kg/m2 for males and 5.4 kg/m2 for women (AWGS, 2019).

For obesity, waist circumference (WC) was chosen as the indicator of obesity since it could be a more accurate predictor of death in senior individuals than body mass index (BMI). The use of BMI among older people may mislead in classifying obesity since it

cannot distinguish between fat mass and fat-free mass, which have conflicting impacts on the risk of mortality and morbidity. Therefore, it is essential to include both lean mass and fat mass in order to properly comprehend the impact of obesity in the elderly.

The Korean standards for abdominal obesity were used in this study (WC $\geq$ 90 cm in men and $\geq$ 85 cm in women) (Lee et al., 2007). The waist circumference was measured with the arms at the sides relaxed at the midpoint between the top of the iliac crest and the bottom of the last palpable rib. For Sarcopenic Obesity groups, participants without sarcopenia and obesity were classified as “Optimal”, participants without sarcopenia but being obese was “Obese”, participants with sarcopenia but nonobese was “Sarcopenic”, and having both conditions grouped for “Sarcopenic Obesity”.

3.2.2 Definition of Physical Activity

The WHO's International PA Questionnaire (IPAQ) has been used to quantify physical activity by self-report (Armstrong et al., 2006; IPAQ Research Committee, 2005). The IPAQ requires at least 10 minutes of continuous physical activity per week in three different areas; work, transportation, and leisure, and further inquires the intensity of physical activity; moderate or vigorous, frequency; days per week, duration; hours and minutes per week. In order to identify the adherence to physical activity guideline recommendations, total minutes of moderate to vigorous physical activity (MVPA) are calculated as minutes per week. Total MVPA minutes per week were calculated as adding moderate intensity physical activity time to twice the minutes of vigorous intensity physical activity from all physical activity categories. If participants completed at least 150 minutes of MVPA per week, they were considered to be meeting the aerobic physical activity guideline. The recommended frequency of the muscle-strengthening activity was determined to be once per week.

Participants self-reported to the following question about how many days in the last week they had engaged in muscle-strengthening exercises such push-ups, sit-ups, and lifting weights. If a participant engaged in muscle-strengthening activities at least twice a week, they were considered to be following the guidelines (IPAQ Research Committee, 2005).

For the analysis of joint association, participants were divided into eight groups based on combined categories of the adherence to physical activity guideline (adhering to PAG, not adhering to PAG) and the status of sarcopenic obesity (Optimal, Obese, Sarcopenic, Sarcopenic Obese), respectively. "Adhering to PAG" was participants adhering to physical activity guideline, and "Not adhering to PAG" was participants not adhering to physical activity guideline. "Optimal" was without sarcopenia and obesity, "Obese" was obese but not sarcopenic, "Sarcopenic" was sarcopenic but not obese, and "Sarcopenic Obese" was both sarcopenic and obese.

3.2.3 Definition of Mortality

This study used all-cause mortality as the outcome variable, all specified and unknown cause of death were included; using the KNHANES-linked National Death Index public-access files, the mortality status and cause of death were identified. Deaths of participants were monitored from the initial evaluation to 2017. Based on the National Death Index, the underlying causes of death were classified using the Korean Standard Classification of Diseases (KCD) code.

3.3 Statistical Analysis

Clinical characteristics were compared between groups using one-way analysis of variation (ANOVA) for continuous variables. Categorical variables were compared using $\chi 2$ test. Cox proportional hazard regression models were constructed to calculate adjusted hazard ratios (HRs) and their 95% confidence intervals (CIs) for all-cause mortality among Optimal, Obese, Sarcopenic, Sarcopenic Obesity. Three models were constructed. Model 1 included age and sex as covariates. Model 2 lifestyle variables such as education, household income, smoking history, alcohol consumption and all covariates in model 1. Model 3 added history of comorbidities such as hypertension, diabetes mellitus, and dyslipidemia to all covariates in model 2. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using R 4.0.2 software.

4. RESULTS

4.1 General characteristics of the study population

The baseline characteristics of 2,781 participants in this study are shown in Table 1. Participants of Optimal group was 1,072 (38.5%), Obese group 885 (31.8%), Sarcopenic group 674 (24.2%), Sarcopenic Obese 150 (5.39%). Mean age in all participants was 71.5 ± 5 years. The mean of follow-up was 8.7 years among Sarcopenic Obese groups (data not shown). SO group was older than normal group. Proportion of male was the highest in Sarcopenic among four groups. Sarcopenic group had the highest portion in current smoking and heavy drinking, followed by Sarcopenic Obesity, Optimal, and Obese. In the section of physical activity guideline adherence, the number of participants who adhered to aerobic physical activity guideline was highest in the Optimal group (36.5%), sequentially followed by Obese (30.6%), Sarcopenic (28.8%), and Sarcopenic Obese (21.3%). However, adherence rate in muscle-strengthening guideline had an adverse trend; demonstrating lowest percentage in Obese (10.1%) and altogether

similar in Optimal (14.0%), Sarcopenic (14.5%), Sarcopenic Obese (14.7%). In the aspect of history of comorbidities, Sarcopenic obese group had the highest proportion-68.7% in hypertension, 26.7% in diabetes mellitus, and 39.3% in dyslipidemia- and Optimal group being the lowest. The optimal group was generally at the lowest in all anthropometric/metabolic measures, and the sarcopenic obese group was the highest.

Table 1. Baseline Characteristics of Participants According to Sarcopenic Obesity Groups

Denominator	Overall, n = 2,781	Sarcopenic Obesity Groups[a]				*P* -value[b]
		Optimal, n = 1,072 (38.5%)	Obese, n = 885 (31.8%)	Sarcopenic, n = 674 (24.2%)	Sarcopenic Obese, n = 150 (5.39%)	
Age at baseline (mean ± SD)	71 ± 5	71 ± 5	71 ± 4	72 ± 5	73 ± 5	< .001
Male, n (%)	1162 (41.8)	409 (38.2)	265 (30.0)	419 (62.2)	69 (46.0)	< .001
Education, n (%)						.01
≤elementary school	1982 (71.3)	782 (72.9)	657 (74.2)	441 (65.4)	102 (68.0)	
middle school	314 (11.3)	111 (10.4)	92 (10.4)	87 (12.9)	24 (16.0)	
high school	321 (11.5)	116 (10.8)	94 (10.6)	97 (14.4)	14 (9.3)	
≥undergraduate	164 (5.9)	63 (5.9)	42 (4.7)	49 (7.3)	10 (6.7)	
Household income, n (%)						.31
lowest	1485 (53.4)	568 (53.0)	467 (52.8)	378 (56.1)	72 (48.0)	
middle-low	679 (24.4)	268 (25.0)	213 (24.1)	157 (23.3)	41 (27.3)	
middle-high	357 (12.8)	142 (13.2)	110 (12.4)	78 (11.6)	27 (18.0)	
highest	260 (9.3)	94 (8.8)	95 (10.7)	61 (9.1)	10 (6.7)	
Smoking status, n (%)						< .001
non-smoker	1651 (59.4)	661 (61.7)	610 (68.9)	292 (43.3)	88 (58.7)	
past smoker	752 (27.0)	272 (25.4)	196 (22.1)	237 (35.2)	47 (31.3)	
current smoker	378 (13.6)	139 (13.0)	79 (8.9)	145 (21.5)	15 (10.0)	

Alcohol drinking status, n (%)						.08
abstainer	2641 (95.0)	1024 (95.5)	848 (95.8)	628 (93.2)	141 (94.0)	
heavy drinker	140 (5.0)	48 (4.5)	37 (4.2)	46 (6.8)	9 (6.0)	
Physical activity guideline adherence, n (%)						
adherence to aeroguide, n (%)						< .001
no	1893 (68.1)	681 (63.5)	614 (69.4)	480 (71.2)	118 (78.7)	
yes	888 (31.9)	391 (36.5)	271 (30.6)	194 (28.8)	32 (21.3)	
adherence to muscleguide, n (%)						.023
no	2422 (87.1)	922 (86.0)	796 (89.9)	576 (85.5)	128 (85.3)	
yes	359 (12.9)	150 (14.0)	89 (10.1)	98 (14.5)	22 (14.7)	
Comorbidities, n (%)						
Hypertension	1619 (58.2)	562 (52.4)	613 (69.3)	341 (50.6)	103 (68.7)	<.001
Type 2 diabetes mellitus	561 (20.2)	152 (14.2)	237 (26.8)	132 (19.6)	40 (26.7)	<.001
Dyslipidemia	894 (32.1)	293 (27.3)	351 (39.7)	191 (28.3)	59 (39.3)	<.001
Anthropometric/metabolic measures (mean ± SD)						
Systolic blood pressure, mmHG	131.7 ± 17.4	131.1 ± 18.1	133.1 ± 16.2	130.9 ± 18.1	132.0 ± 16.5	<.001
Height, cm	156.8 ± 9.0	155.4 ± 9.2	156.6 ± 8.5	158.9 ± 8.7	158.1 ± 10.0	<.001
Weight, kg	59.0 ± 9.5	56.0 ± 8.3	66.0 ± 8.7	54.1 ± 7.1	61.3 ± 8.2	<.001
BMI, kg/m^2	23.9 ± 3.0	23.1 ± 1.9	26.9 ± 2.5	21.4 ± 1.7	24.5 ± 1.7	<.001
ASM/ht^2, kg/m^2	6.4 ± 0.9	6.6 ± 0.9	6.8 ± 0.9	5.9 ± 0.8	5.8 ± 0.8	<.001
ASM, kg	16.0 ± 3.7	16.1 ± 3.8	16.8 ± 3.8	15.2 ± 3.3	14.7 ± 3.6	<.001

SD = Standard Deviation; BMI = body mass index; ASM = appendicular skeletal muscle mass.
Values are the mean ± SD for continuous variables and the number (%) for categorical variables.
[a]Optimal (men: ASM/ht2 >= 7.0kg/m2, WC < 90cm; women: ASM/ht2 >= 5.4kg/m2, WC < 85cm), Obese (men: ASM/ht2 >= 7.0kg/m2, WC >= 90cm; women: ASM/ht2 >= 5.4kg/m2, WC >= 85cm), Sarcopenic (men: ASM/ht2 < 7.0kg/m2, WC < 90cm; women: ASM/ht2 < 5.4kg/m2, WC < 85cm), Sarcopenic Obese (men: ASM/ht^2 < 7.0kg/m^2, WC >= 90cm; women: ASM/ht2 < 5.4kg/m2, WC >= 85cm).
[b]*P* -value for difference between groups (χ^2 for percentages; analysis of variance for means).

Table 1. Baseline characteristics according to sarcopenic obesity groups

4.2 Association between Sarcopenic Obesity and Mortality

There were 629 deaths among 2,781 participants. 202 death events occurred out of 1,072 Optimal group, 167 out of 885 in Obese, 210 out of 674 in Sarcopenic, 50 out of 150 in Sarcopenic Obese. Unadjusted rates of mortality outcomes were lowest in the optimal reference group and highest in the sarcopenic obese group. Table 2 shows adjusted hazard ratios (HRs) for all-cause mortality by sarcopenic obesity groups. In the age and sex-adjusted model, except for Obese group, Sarcopenic and Sarcopenic Obese group had a significantly greater risk of mortality than the optimal reference group, HR in Sarcopenic Obese group exceeding the HR of Sarcopenia (HR 1.85; 95% CI 1.53-2.25, HR 1.97; 95% CI 1.45-2.69, respectively). This linear trend was consistent even after adjusting for lifestyle variables and for comorbidities, indicating that these covariates only partially account for the association between sarcopenic obesity and mortality. In the analysis of Model 2, Sarcopenic Obesity (HR 1.36; 95% CI 1.11-1.66) demonstrated higher value than Sarcopenia (HR 1.70; 95%

CI 1.24-2.31). In Model 3, Sarcopenic Obesity showed 34% higher mortality, and 58% in Sarcopenia. Sarcopenia and Sarcopenic Obesity were associated with a significantly higher risk of mortality than in the Optimal reference group, and these associations remained significant after adjusting for covariates.

Table 2. Death Events and Mortality According to Sarcopenic Obesity Groups

	Sarcopenic Obesity Groups[a]			
	Optimal HR (95% CI)	**Obese HR (95% CI)**	**Sarcopenic HR (95% CI)**	**Sarcopenic Obese HR (95% CI)**
Total (n = 2,781)	1072	885	674	150
Death events (n = 629)	202	167	210	50
Person-year	10030.16	8230.438	5761.507	1294.068
Incident rate/1000 person-year	20.13925999	20.29053618	36.44879716	38.63784592
Crude	1.00 (reference)	1.01 (0.82-1.24)	1.85 (1.53-2.25)	1.97 (1.45-2.69)
Model 1	1.00 (reference)	1.07 (0.87-1.31)	1.38 (1.13-1.69)	1.59 (1.17-2.17)
Model 2	1.00 (reference)	1.10 (0.89-1.35)	1.36 (1.11-1.66)	1.70 (1.24-2.31)
Model 3	1.00 (reference)	1.03 (0.84-1.27)	1.34 (1.09-1.63)	1.58 (1.16-2.17)

HR = Hazard Ratio; CI = Confidence Interval
Model 1: adjusted for age and sex.
Model 2: Model 1 + education, household income, smoking history, and alcohol consumption.
Model 3: Model 2 + hypertension, diabetes mellitus, and dyslipidemia.
[a]Optimal (men: ASM/ht2 >= 7.0kg/m2, WC < 90cm; women: ASM/ht2 >= 5.4kg/m2, WC < 85cm),
Obese (men: ASM/ht2 >= 7.0kg/m2, WC >= 90cm; women: ASM/ht2 >= 5.4kg/m2, WC >= 85cm),
Sarcopenic (men: ASM/ht2 < 7.0kg/m2, WC < 90cm; women: ASM/ht2 < 5.4kg/m2, WC < 85cm),
Sarcopenic Obese (men: ASM/ht2 < 7.0kg/m2, WC >= 90cm; women: ASM/ht2 < 5.4kg/m2, WC >= 85cm).

Table 2. Death events and mortality according to Sarcopenic Obesity Groups

4.3 Association between Sarcopenic Obesity and Mortality by Physical Activity groups

4.3.1 Muscle-strengthening Physical Activity guideline adherence according to Sarcopenic Groups and mortality

The number of participants (death events) in the "Adhering to PAG and Optimal", "Adhering to PAG and Obese", "Adhering to PAG and Sarcopenic", "Adhering to PAG and Sarcopenic Obese", "Not adhering to PAG and Optimal", "Not adhering to PAG and Obese", "Not adhering to PAG and Sarcopenic", and "Not adhering to PAG and Sarcopenic Obese" groups were 2,781 (629), 150 (16), 89 (9), 98 (20), 22 (2), 922 (186), 796 (158), 576 (190), and 128 (48), respectively. The model was adjusted for sex, age, education, household income, smoking history, alcohol consumption, history of hypertension, diabetes mellitus, and dyslipidemia. Figure 2 shows adjusted HRs for joint associations of muscle-strengthening physical activity guideline adherence and sarcopenic obesity groups with mortality.

Among all participants, those not adhering to muscle-strengthening physical activity guideline demonstrated significantly higher mortality risks regardless of Sarcopenic Obesity groups than in the reference group of "Adhering to PAG and Optimal"; HR in "Not adhering to PAG and Optimal" 1.74 (95% CI 1.04-2.93), "Not adhering to PAG and Obese" 1.78 (95% CI 1.06-3.02), "Not adhering to PAG and Sarcopenic" 2.28 (95% CI 1.36-3.82), and "Not adhering to PAG and Sarcopenic" 2.83 (95% CI 1.59-5.03), showing a linear cumulative trend. In contrast, in all sarcopenic groups adhering to muscle-strengthening physical activity guideline demonstrated no significant associations with mortality risk.

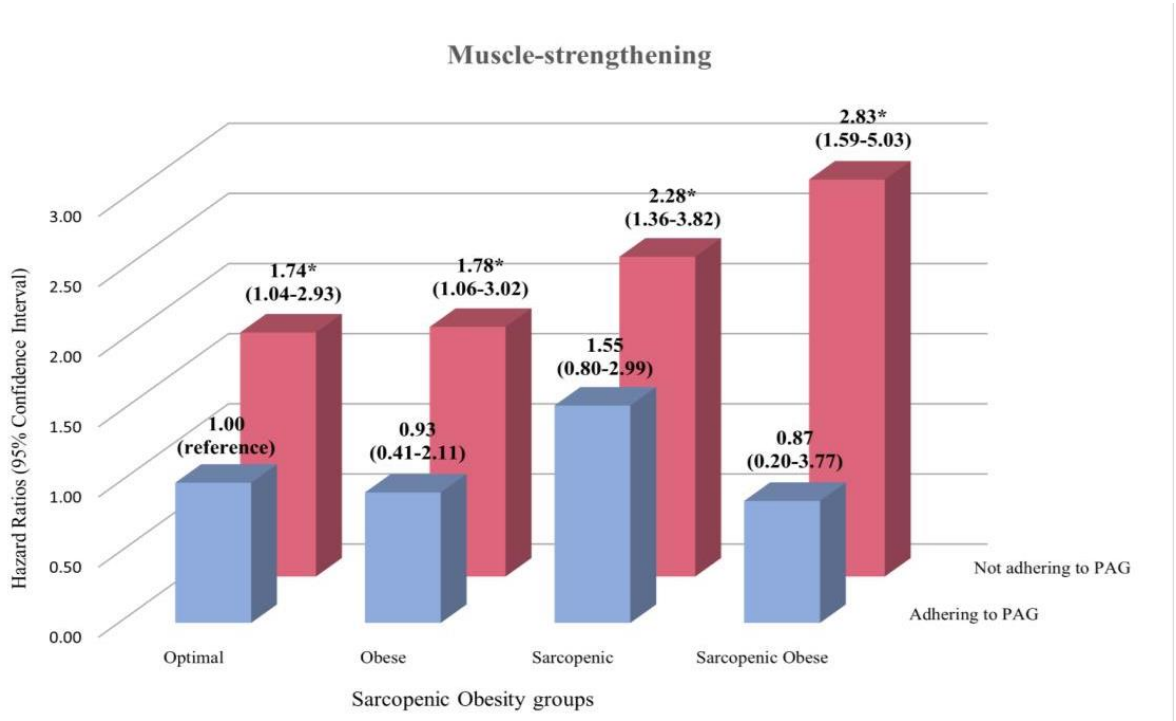

Figure 2. Joint associations of muscle-strengthening physical activity guideline adherence and sarcopenic obesity groups with mortality.

4.3.2 Aerobic Physical Activity guideline adherence according to Sarcopenic Groups and mortality

The number of participants (death events) in the "Adhering to PAG and Optimal", "Adhering to PAG and Obese", "Adhering to PAG and Sarcopenic", "Adhering to PAG and Sarcopenic Obese", "Not adhering to PAG and Optimal", "Not adhering to PAG and Obese", "Not adhering to PAG and Sarcopenic", and "Not adhering to PAG and Sarcopenic Obese" groups were 2,781 (629), 391 (71), 271 (41), 194 (47), 32 (8), 681 (131), 614 (126), 480 (163), and 118 (42), respectively. The model was adjusted for sex, age, education, household income, smoking history, alcohol consumption, history of hypertension, diabetes mellitus, and dyslipidemia. Figure 3 shows adjusted HRs for joint associations of muscle-strengthening physical activity guideline adherence and sarcopenic obesity groups with mortality.

Among participants those not adhering to aerobic physical activity guideline, group of Sarcopenic (HR 1.38; 95% CI 1.04-1.84) and

Sarcopenic Obese (HR 1.53; 95% CI 1.04-2.26) demonstrated significantly higher mortality risks than in the reference group of “Adhering to PAG and Optimal”. “Not adhering to PAG and Optimal” and “Not adhering to PAG and Obese” did not show significant association with mortality. However, in all sarcopenic groups adhering to aerobic physical activity guideline demonstrated no significant associations with mortality risk.

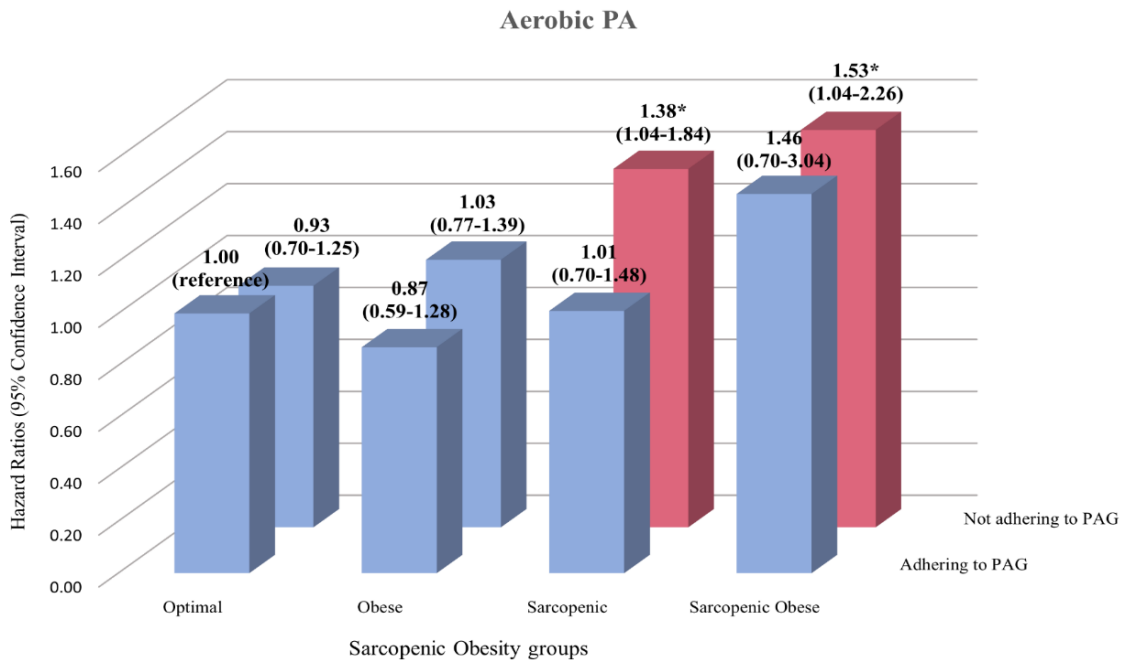

Figure 3. Joint associations of aerobic physical activity guideline adherence and sarcopenic obesity groups with mortality.

5. DISCUSSION

To our knowledge, this is the first study that investigated the impact of sarcopenia, obesity, and sarcopenic obesity, and physical activity on all-cause mortality risk in Korean older population.

The finding of a significant association between sarcopenic and sarcopenic obese with mortality, while obese participants not showing any significant associations, is consistent with a previous prospective study suggesting that muscle mass may have a stronger association with mortality than obesity (Atkins et al., 2014). This phenomenon may be explained by the concept of 'obesity paradox' in older people. Obesity paradox is known as paradoxical benefits of obesity on mortality among older people (Flegal et al., 2013; Veronese et al., 2015). In several studies, obese people with type 2 diabetes or heart disorders also have demonstrated mortality advantages (Carnethon et al., 2012; McAuley et al., 2012). Contentious questions about obesity paradox may have an explanation that is connected

to muscle mass and strength in older people. From a systematic review, those with high BMIs and strong aerobic fitness (nonsarcopenic obese) had lower risks of cardiovascular and all-cause mortality than people with normal BMIs and poor fitness (sarcopenic nonobese) (Fogelholm, 2010). The direction of association between sarcopenic obesity and all-cause mortality was consistent with this study to that of a prior study which found that sarcopenic obese men's mortality risk was approximately 39% higher than nonsarcopenic nonobese men (Rantanen et al., 2000).

Among combined categories of adherence to muscle-strengthening physical activity guideline and the status of sarcopenic obesity, those not adhering to the guideline showed significantly higher mortality risks regardless of sarcopenic obesity groups (HR ranging from 1.74 to 2.83, $p < 0.05$), which supports the study's hypothesis. The result was consistent with limited evidence from a prospective cohort study involving over 479,000 US adults, reporting that those meeting the recommended frequency of muscle-strengthening activity (≥2 times/week) was associated with reduced

risk of cause-specific mortality (cardiovascular disease, cancer, and chronic respiratory tract diseases) (Zhao et al., 2020). Meanwhile, from a systematic review and meta-analysis among 11 studies, it was reported that conducting muscle-strengthening exercise was related to a decreased risk of all-cause mortality, while no significant association was found with cardiovascular disease mortality or cancer mortality (Saeidifard et al., 2019), which was consistent with this study.

Meanwhile, among participants those not adhering to aerobic physical activity guideline, sarcopenic and sarcopenic obese (HR ranging from 1.38 to 1.53, $p < 0.05$) demonstrated increased death risk. When sarcopenia was not present, we discovered a less consistent impact on mortality with obesity alone; which does not confirm the study's hypothesis. The results of the current study may also be explained by the protective effect of obesity for mortality in older population, which is consistent with a prospective study suggesting that obese people without sarcopenia were not associated with increased risk of all-cause mortality (Zheng et al., 2016). In

a cohort study using data from the Aerobics Center Longitudinal Study (ACLS) classifying groups by normal, overweight, and obese, with a total of 25,714 male participants (mean age: 43.8 years), low cardiorespiratory fitness, which is related to aerobic physical activity, was reported to be a strong predictor of mortality, especially in obese men (Wei et al., 1999); which had been inconsistent with this study.

The strength of this study is that it is a large-scale population-based cohort study utilizing data from KNHANES, examining the longitudinal association between sarcopenic obesity and physical activity with all-cause mortality. However, since the data represents the Korean population, findings may not be generalizable to other ethnicity. Moreover, self-reported variables, such as physical activity, may have been misclassified, which was measured subjectively. If objective measurements of physical activity had been available, observed associations between sarcopenic obese groups and mortality may have been different. In order to generalize

the findings of this study, further research focusing on other cohort groups is required.

6. CONCLUSION

In conclusion, sarcopenia and obesity are associated with all-cause mortality, with the highest risk in sarcopenic obese group. Sarcopenia and sarcopenic obesity, but not obesity on its own, were associated with greater all-cause mortality. Furthermore, all sarcopenic obesity groups adhering to physical activity guideline demonstrated an inverse association with the risk of all-cause mortality. Therefore, preserving muscle mass and strength by engaging in recommended amount of physical activity, and preventing obesity should be the priority for healthy aging.

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APPENDIX

Appendix A: Sensitivity Analysis on Death Events and Mortality According to Sarcopenic Obesity Groups

A-1. 1 year Sensitivity Analysis

	Sarcopenic Obesity Groups[a]			
	Optimal HR (95% CI)	**Obese HR (95% CI)**	**Sarcopenic HR (95% CI)**	**Sarcopenic Obese HR (95% CI)**
Total (n = 2,759)	1,069	882	660	148
Death events (n = 607)	199	164	196	48
Person-year	10030.16	8230.438	5761.507	1294.068
Incident rate/1000 person-year	19.84016207	19.92603553	34.01887735	37.09233209
Model 1	1.00 (reference)	1.06 (0.87-1.31)	1.30 (1.06-1.59)	1.55 (1.13-2.13)
Model 2	1.00 (reference)	1.09 (0.89-1.35)	1.28 (1.04-1.57)	1.65 (1.20-2.27)
Model 3	1.00 (reference)	1.03 (0.83-1.27)	1.26 (1.03-1.54)	1.54 (1.12-2.13)

HR = Hazard Ratio; CI = Confidence Interval
Model 1: adjusted for age and sex.
Model 2: Model 1 + education, household income, smoking history, and alcohol consumption.
Model 3: Model 2 + hypertension, diabetes mellitus, and dyslipidemia.
[a]Optimal (men: ASM/ht2 >= 7.0kg/m2, WC < 90cm; women: ASM/ht2 >= 5.4kg/m2, WC < 85cm),
Obese (men: ASM/ht2 >= 7.0kg/m2, WC >= 90cm; women: ASM/ht2 >= 5.4kg/m2, WC >= 85cm),
Sarcopenic (men: ASM/ht2 < 7.0kg/m2, WC < 90cm; women: ASM/ht2 < 5.4kg/m2, WC < 85cm),
Sarcopenic Obese (men: ASM/ht2 < 7.0kg/m2, WC >= 90cm; women: ASM/ht2 < 5.4kg/m2, WC >= 85cm).

A-2. 2 year Sensitivity Analysis

	Sarcopenic Obesity Groups[a]			
	Optimal HR (95% CI)	**Obese HR (95% CI)**	**Sarcopenic HR (95% CI)**	**Sarcopenic Obese HR (95% CI)**
Total (n = 2,722)	1,061	876	641	144
Death events (n = 570)	191	158	177	44
Person-year	10030.16	8230.438	5761.507	1294.068
Incident rate/1000 person-year	19.04256762	19.19703423	30.72112904	34.00130441
Model 1	1.00 (reference)	1.07 (0.87-1.32)	1.22 (0.99-1.51)	1.50 (1.08-2.08)
Model 2	1.00 (reference)	1.10 (0.89-1.36)	1.20 (0.97-1.49)	1.59 (1.14-2.21)
Model 3	1.00 (reference)	1.04 (0.84-1.29)	1.18 (0.96-1.46)	1.49 (1.07-2.08)

HR = Hazard Ratio; CI = Confidence Interval
Model 1: adjusted for age and sex.
Model 2: Model 1 + education, household income, smoking history, and alcohol consumption.
Model 3: Model 2 + hypertension, diabetes mellitus, and dyslipidemia.
[a]Optimal (men: ASM/ht2 >= 7.0kg/m2, WC < 90cm; women: ASM/ht2 >= 5.4kg/m2, WC < 85cm),
Obese (men: ASM/ht2 >= 7.0kg/m2, WC >= 90cm; women: ASM/ht2 >= 5.4kg/m2, WC >= 85cm),
Sarcopenic (men: ASM/ht2 < 7.0kg/m2, WC < 90cm; women: ASM/ht2 < 5.4kg/m2, WC < 85cm),
Sarcopenic Obese (men: ASM/ht2 < 7.0kg/m2, WC >= 90cm; women: ASM/ht2 < 5.4kg/m2, WC >= 85cm).

B. Death Events and Mortality According to Sarcopenic Obesity Groups

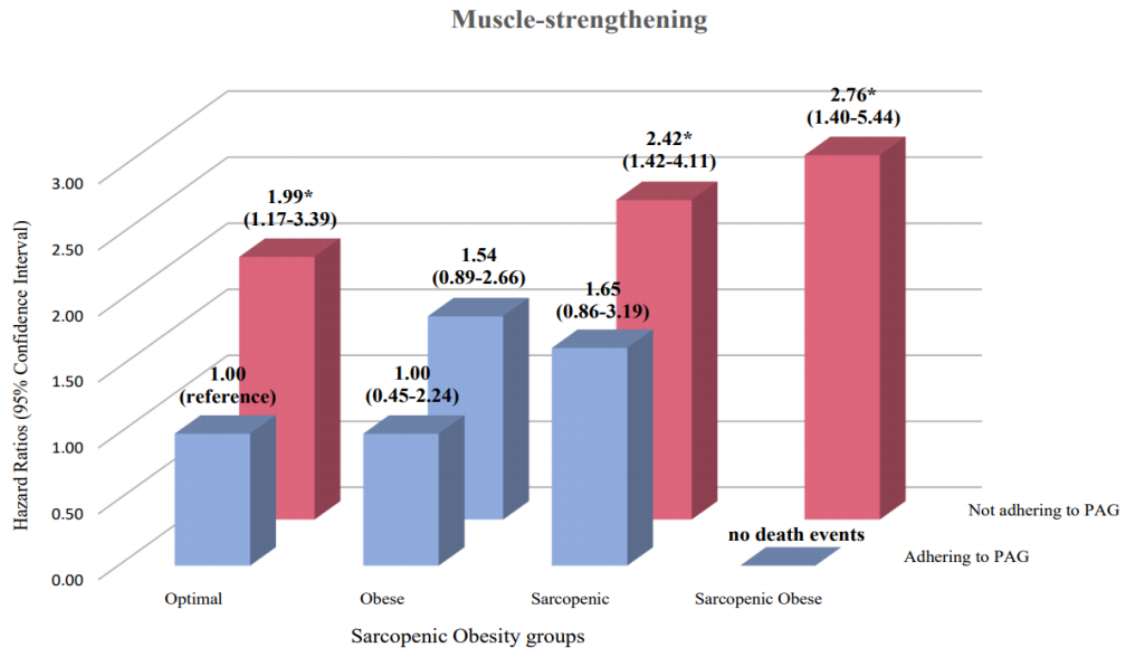
B-1. Defining obesity by BMI

	Sarcopenic Obesity Groups[a]			
	Optimal HR (95% CI)	**Obese HR (95% CI)**	**Sarcopenic HR (95% CI)**	**Sarcopenic Obese HR (95% CI)**
Total (n = 2,781)	1121	836	753	71
Death events (n = 629)	235	134	240	20
Person-year	10414.99	7845.605	6427.008	628.5671
Incident rate/1000 person-year	22.56363184	17.07962611	37.34241501	31.81840093
Crude	1.00 (reference)	0.76 (0.61-0.93)	1.69 (1.41-2.02)	1.44 (0.91-2.28)
Model 1	1.00 (reference)	0.82 (0.66-1.01)	1.28 (1.06-1.54)	1.32 (0.84-2.09)
Model 2	1.00 (reference)	0.85 (0.69-1.05)	1.28 (1.06-1.54)	1.39 (0.88-2.20)
Model 3	1.00 (reference)	0.79 (0.64-0.98)	1.25 (1.04-1.51)	1.24 (0.78-1.96)

HR = Hazard Ratio; CI = Confidence Interval
Model 1: adjusted for age and sex.
Model 2: Model 1 + education, household income, smoking history, and alcohol consumption.
Model 3: Model 2 + hypertension, diabetes mellitus, and dyslipidemia.
[a]Optimal (men: ASM/ht2 >= 7.0kg/m2, BMI < 25.0kg/m2 ; women: ASM/ht2 >= 5.4kg/m2, BMI < 25.0kg/m2),
Obese (men: ASM/ht2 >= 7.0kg/m2, BMI >= 25.0kg/m2; women: ASM/ht2 >= 5.4kg/m2, BMI >= 25.0kg/m2),
Sarcopenic (men: ASM/ht2 < 7.0kg/m2, BMI < 25.0kg/m2; women: ASM/ht2 < 5.4kg/m2, BMI < 25.0kg/m2),
Sarcopenic Obese (men: ASM/ht2 < 7.0kg/m2, BMI >= 25.0kg/m2; women: ASM/ht2 < 5.4kg/m2, BMI >= 25.0kg/m2).

C. Joint Associations of physical activity guideline adherence and sarcopenic obesity groups with mortality

C-1. Muscle-strengthening physical activity guideline adherence



C-2. Aerobic physical activity guideline adherence