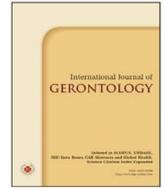




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Original Article

The Association between Sarcopenia and Pulmonary Function in Koreans: A Cross-Sectional Study

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SUMMARY

Objectives: This study examined the association between sarcopenia and spirometry patterns in the restrictive and obstructive patterns and investigated whether there were sex-specific differences.

Methods: This study obtained data from the Korea National Health and Nutrition Examination Survey (KNHANES, 2008–2011), a cross-sectional and nationally representative survey conducted by the Korean Centers for Diseases Control and Prevention.

Results: Of the 11,671 participants included in this study, the prevalence rate of pulmonary function by sarcopenia was classified according to sex. Crude, which did not adjust any variables, showed a 2.770 (2.065–3.715) obstructive of 2.439 (1.824–3.262) compared to normal. Model 3, which adjusted all variables that could affect sarcopenia and pulmonary function, showed significant association only with restrictive pattern (OR 1.736, 95% CI 1.230–2.449). However, when the sex was analyzed separately, only the odds ratio of restrictive patterns increased significantly for men (OR 1.753, 95% CI 1.005–3.059), there was no significant difference in women.

Conclusion: The association between sarcopenia and pulmonary function in the restrictive pattern, not obstructive pattern, was significant in South Korean. The results of this study show that sarcopenia is more associated with a restrictive pattern rather than obstructive, especially in males.

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1. Introduction

Sarcopenia is defined as a decrease in muscle strength and muscle mass due to changes in body components.¹ The mechanism of sarcopenia has not yet been clarified, but it is related to various factors such as lack of exercise, aging, and changes in hormone levels.² Moreover, these factors contribute to the gradual loss of skeletal muscle mass, which is reported not only in the elderly but also in the general population, including the young.^{3,4} Furthermore, it has been known that sarcopenia causes various problems such as diabetes, cardiovascular disease, metabolic disorder, physical disability, and mortality.^{5,6}

There are restrictive and obstructive patterns in the spirometry pattern.⁷ In the case of restrictive patterns, it is caused by a defect in thoracic compatibility, and both forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) are reduced.⁸ On the other hand, an obstructive pattern is mainly caused by airway obstruction associated with smoking, and FEV1 is significantly reduced.⁹

A decrease in skeletal muscle mass associated with aging results in loss of mass of respiratory muscle, thus leading to a decrease in lung capacity.^{4,10} Several prior studies have reported that the decrease in skeletal muscle mass is associated with decreased lung capacity, especially in male chronic obstructive pulmonary disease (COPD) patients.^{11–13} On the contrary, studies have shown that it is

associated with restrictive lung disease rather than COPD.¹⁴

The association between sarcopenia and spirometry pattern is not consistently explained, and there is a lack of research on whether sex-specific differences exist. Therefore, based on the cross-sectional data of a large number of Korean subjects, this study examined the association between sarcopenia and spirometry patterns in the restrictive and obstructive patterns and investigated whether there were sex-specific differences.

2. Methods

2.1. Data source and sampling

This study used the National Health and Nutrition Survey data (2008–2011) conducted by the Korean Centers for Diseases Control and Prevention (KCDC). The subjects were determined to be those who responded to both the examination survey and the health survey among adults aged 19 or older who were subject to the measurement of pulmonary function test (PFT). Among 37,753 subjects that participated in KNHANES, 20,969 who did not measure their PFT, 4,174 who did not measure sarcopenia, and 539 non-participants in the health survey were excluded. Finally, 11,671 people were selected (Figure 1).

2.1.1. Covariates

Body mass index (BMI) was calculated by dividing [weight (kg)/

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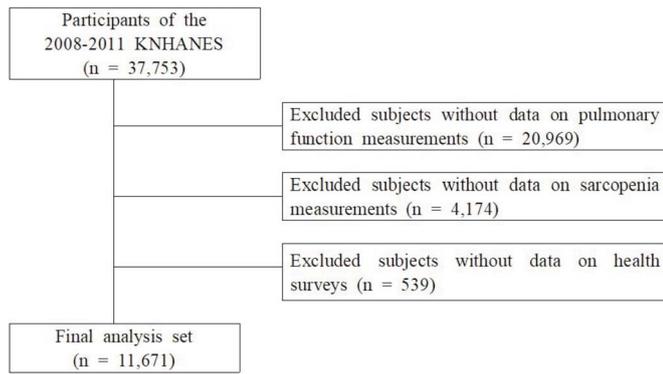


Figure 1. Subject selection from the Korea National Health and Nutrition Examination Survey 2008–2011.

height (m²)). Waist circumference (WC) was measured at the mid-point between the bottom of the rib cage and the top of the lateral border of the iliac crest with full expiration. Blood samples were collected from subjects in the morning after overnight fasting and analyzed at a national central laboratory. Blood pressure was measured using a mercury sphygmomanometer in a seated position after a 10-minute rest period. Two measurements were made for all subjects at 5-minute intervals. An average of two measurements was used for the data analyses. Cigarette smoking condition was categorized as never smokers, ex-smokers and current smokers, and drinking condition was dichotomized as current users and non-users. Physical examinations included weight, fasting glucose, total cholesterol, triglyceride, diastolic and systolic blood pressure, and waist circumference measurement variables.

2.1.2. Measurement of pulmonary function

Pulmonary function was measured using a spirometer (model 2130; SensorMedics, Yorba Linda, California). Participants were classified according to spirometry patterns into a normal group (FEV₁/FVC ≥ .0.70, FVC ≥ .80% predicted), a restrictive pattern group (FVC < 80% predicted, FEV₁/FVC ≥ .0.70), an obstructive pattern group (FEV₁/FVC < 0.70).¹⁵

2.1.3. Sarcopenia

Appendicular skeletal muscle mass (ASM) was measured by dual X-ray absorptiometry (QDR4500A; Hologic, Inc., Bedford, MA). The skeletal muscle mass index (SMI) was calculated as ASM (kg)/BMI (kg/m²), and sarcopenia was defined as an SMI of < 0.789 in males and < 0.521 in females based on the criteria of the Sarcopenia Project.¹⁶

2.2. Data analysis

Since this study use a complex samples data, the weight given by the KNHANES has been applied. General characteristics were compared according to sarcopenia and spirometry patterns through the Chi-square test. A logistic regression analysis was used to analyze the association between sarcopenia and spirometry patterns, and p-values < 0.05 were considered statistically significant. Data analysis uses the SPSS 22.0 window version.

2.3. Ethics statement

KNHANES has been conducting without approval by the research ethics review committee because it is considered the research for public welfare which is conducted by the Korean government.

3. Results

3.1. Characteristics of subjects according to sex and sarcopenia

In both men and women, the prevalence of restrictive pattern was significantly higher than that of an obstructive pattern (restrictive/obstructive: 24.7/27.3 in males, 17.4/9.0 in females). Significance was shown in all variables except weight in women compared to sarcopenia and normal. In men, on the other hand, differences were found in all variables except for total cholesterol, triglyceride, and diastolic blood pressure (Table 1).

Table 1
Characteristics of subjects according to sex and sarcopenia.

| | Males | | | Females | | |
|--|----------------------|--------------------|----------|----------------------|--------------------|----------|
| | Sarcopenia (n = 237) | Normal (n = 4,140) | p | Sarcopenia (n = 361) | Normal (n = 4,924) | p |
| Age (years) | 62.36 ± 1.15 | 46.65 ± 0.37 | < 0.0001 | 63.37 ± 1.14 | 48.46 ± 0.40 | < 0.0001 |
| Restrictive/obstructive (%) | 24.7/27.3 | 10.0/12.5 | < 0.0001 | 17.4/9.0 | 9.1/5.0 | < 0.0001 |
| Weight (kg) | 67.09 ± 0.89 | 71.06 ± 0.21 | < 0.0001 | 58.82 ± 0.71 | 58.74 ± 0.19 | 0.912 |
| BMI (kg/m ²) | 26.19 ± 0.29 | 24.42 ± 0.06 | < 0.0001 | 26.96 ± 0.24 | 23.76 ± 0.07 | < 0.0001 |
| < 18.5 (underweight) | 3 (3.4) | 61 (96.6) | | 2 (1.3) | 110 (98.7) | |
| < 25 (normal) | 87 (2.9) | 2454 (97.1) | | 110 (3.4) | 3217 (96.6) | |
| ≥ 25 (overweight) | 147 (7.1) | 1625 (92.9) | | 249 (13.1) | 1597 (86.9) | |
| Smoking status (%) (current-/ex-/non-smoker) | 54.5/28.4/17.1 | 69.6/14.2/16.3 | 0.009 | 6.6/0.1/93.3 | 11.5/1.5/87.0 | 0.003 |
| Drinking status (%) (current-/non-drinking) | 72.6/27.4 | 87.0/13.0 | < 0.0001 | 45.3/54.7 | 66.8/33.2 | < 0.0001 |
| Fasting glucose (mg/dL) | 108.56 ± 2.29 | 99.75 ± 0.43 | < 0.0001 | 106.19 ± 2.41 | 96.17 ± 0.39 | < 0.0001 |
| Total cholesterol | 188.27 ± 2.89 | 189.22 ± 0.72 | 0.754 | 205.69 ± 2.51 | 189.74 ± 0.68 | < 0.0001 |
| Triglyceride | 187.89 ± 18.48 | 172.45 ± 3.17 | 0.415 | 155.06 ± 5.91 | 120.05 ± 1.84 | < 0.0001 |
| Skeletal muscle index | 0.74 ± 0.00 | 0.99 ± 0.00 | < 0.0001 | 0.49 ± 0.00 | 0.67 ± 0.00 | < 0.0001 |
| SBP (mmHg) | 128.91 ± 1.34 | 121.44 ± 0.37 | < 0.0001 | 129.54 ± 1.30 | 117.55 ± 0.41 | < 0.0001 |
| DBP (mmHg) | 79.66 ± 0.80 | 80.65 ± 0.26 | 0.232 | 78.16 ± 0.71 | 75.13 ± 0.24 | < 0.0001 |
| Waist circumference (cm) | 90.14 ± 0.71 | 85.42 ± 0.18 | < 0.0001 | 87.77 ± 0.85 | 79.64 ± 0.21 | < 0.0001 |
| FVC (% predicted) | 3.37 ± 0.05 | 4.42 ± 0.02 | < 0.0001 | 2.46 ± 0.03 | 3.09 ± 0.01 | < 0.0001 |
| FEV ₁ (L) | 2.53 ± 0.05 | 3.48 ± 0.02 | < 0.0001 | 1.94 ± 0.03 | 2.52 ± 0.01 | < 0.0001 |
| FEV ₁ /FVC | 0.75 ± 0.01 | 0.78 ± 0.01 | < 0.0001 | 0.79 ± 0.01 | 0.81 ± 0.00 | < 0.0001 |

Data were presented as means ± SD or number (%).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 second.

* p < .05 by ANOVA or chi-square test.

3.2. Characteristics of subjects according to sex and pulmonary function test

The average age of the subjects of this study differed significantly depending on whether they had pulmonary dysfunction (restrictive/obstructive/normal: 53.24/62.99/43.85 in males, 52.23/63.75/48.37 in females). In men, smoking status, total cholesterol, and triglyceride did not show significance in each group of pulmonary dysfunctions, BMI, triglyceride, diastolic blood pressure, and WC did not show significance in women. The prevalence of sarcopenia was high in a restrictive pattern, with the highest level of fasting glucose in both men and women (Table 2).

3.3. Odds ratios for pulmonary function according to the sarcopenia

The prevalence of pulmonary function by sarcopenia was classified according to sex. Crude, which did not adjust any variables,

showed a 2.770 (2.065–3.715) obstructive of 2.439 (1.824–3.262) compared to normal. Crude, which did not correct any variables, showed that the probability of restrictive pattern was 2.770 (2.065–3.715), and an obstructive pattern was 2.439 (1.824–3.262) compared to the normal. On the other hand, Model 3, which adjusted all variables that could affect sarcopenia and pulmonary function, showed significant association only with restrictive pattern (OR 1.736, 95% CI 1.230–2.449). However, when the sex was analyzed separately, only the odds ratio of restrictive pattern for sarcopenia in men showed a significant increase (OR 1.753, 95% CI 1.005–3.059) (Table 3).

4. Discussion

In this study of Korean subjects, the main findings are that sarcopenia is independently related to restrictive spirometry pattern, not to obstructive pattern, after adjusted with various confounding variables such as age, gender, various metabolic factors,

Table 2
Characteristics of subjects according to sex and pulmonary function test.

| Pattern on spirometry | Males | | | | Females | | | |
|---------------------------|----------------------------|----------------------------|----------------------------|----------|----------------------------|----------------------------|----------------------------|----------|
| | Restrictive (n = 504) | Obstructive (n = 743) | Normal (n = 3,130) | p | Restrictive (n = 502) | Obstructive (n=284) | Normal (n = 4,499) | p |
| Age (years) | 53.24 ± 0.92 ^a | 62.99 ± 0.65 ^b | 43.85 ± 0.37 ^c | < 0.0001 | 52.23 ± 1.43 ^a | 63.75 ± 1.31 ^b | 48.37 ± 0.38 ^c | < 0.0001 |
| Sarcopenia (%) | 24.7 ^a | 27.3 ^b | 48.0 ^c | < 0.0001 | 17.4 ^a | 9.0 ^b | 73.7 ^c | < 0.0001 |
| Weight (kg) | 72.45 ± 0.717 ^a | 65.96 ± 0.54 ^b | 71.51 ± 0.23 ^a | < 0.0001 | 58.12 ± 0.59 ^a | 55.19 ± 1.06 ^b | 59.04 ± 0.24 ^a | 0.001 |
| BMI (kg/m ²) | 25.45 ± 0.22 ^a | 23.52 ± 0.16 ^b | 24.55 ± 0.06 ^c | < 0.0001 | 24.09 ± 0.26 | 23.47 ± 0.35 | 23.98 ± 0.08 | 0.302 |
| < 18.5 (underweight) | 6 (11.5) | 23 (34.1) | 35 (54.4) | | 25 (32.8) | 15 (10.0) | 72 (57.2) | |
| < 25 (normal) | 218 (7.9) | 510 (15.9) | 1813 (76.1) | | 242 (7.9) | 189 (5.6) | 2896 (86.6) | |
| ≥ 25 (overweight) | 280 (14.3) | 210 (8.8) | 1282 (76.9) | | 235 (10.9) | 80 (4.3) | 1531 (84.7) | |
| Smoking status (%) | 67.1/15.1/17.8 | 65.8/26.2/8.0 | 69.7/12.8/17.5 | 0.191 | 20.7/1.1/85.9 ^a | 20.7/3.1/76.2 ^a | 10.4/1.3/88.3 ^b | 0.001 |
| (current-/ex-/non-smoker) | | | | | | | | |
| Drinking status (%) | 80.9/19.1 ^a | 73.6/26.4 ^b | 89.4/10.6 ^c | < 0.0001 | 54.3/45.7 ^a | 45.9/54.1 ^a | 67.8/32.2 ^b | < 0.0001 |
| (current-/non-drinking) | | | | | | | | |
| Fasting glucose (mg/dL) | 105.43 ± 1.25 ^a | 103.70 ± 0.99 ^b | 98.81 ± 0.49 ^c | < 0.0001 | 102.20 ± 1.78 ^a | 99.95 ± 1.84 ^b | 96.02 ± 0.39 ^b | 0.001 |
| Total cholesterol | 191.12 ± 2.07 | 185.24 ± 1.82 | 189.58 ± 0.81 | 0.059 | 188.58 ± 2.10 ^a | 197.17 ± 2.75 ^b | 190.64 ± 0.72 ^a | 0.039 |
| Triglyceride | 191.03 ± 10.96 | 166.71 ± 7.87 | 171.79 ± 0.01 | 0.196 | 136.93 ± 8.70 | 139.88 ± 12.19 | 119.61 ± 1.75 | 0.106 |
| Skeletal muscle index | 0.94 ± 0.01 ^a | 0.93 ± 0.01 ^b | 0.99 ± 0.00 ^c | < 0.0001 | 0.64 ± 0.01 ^a | 0.62 ± 0.01 ^b | 0.66 ± 0.00 ^c | < 0.0001 |
| Systolic BP (mmHg) | 126.67 ± 1.02 ^a | 127.01 ± 0.85 ^b | 120.20 ± 0.39 ^c | < 0.0001 | 121.85 ± 1.35 ^a | 126.21 ± 1.67 ^b | 117.45 ± 0.41 ^c | < 0.0001 |
| Diastolic BP (mmHg) | 82.31 ± 0.59 ^a | 78.76 ± 0.55 ^b | 80.68 ± 0.29 ^c | 0.002 | 76.07 ± 0.70 | 75.33 ± 0.83 | 75.24 ± 0.24 | 0.495 |
| Waist circumference (cm) | 88.72 ± 0.58 ^a | 85.49 ± 0.44 ^b | 85.23 ± 0.20 ^b | < 0.0001 | 80.99 ± 0.74 | 81.02 ± 0.97 | 80.03 ± 0.21 | 0.399 |
| FVC (% predicted) | 3.41 ± 0.03 ^a | 3.94 ± 0.04 ^b | 4.58 ± 0.02 ^c | < 0.0001 | 2.34 ± 0.02 ^a | 2.63 ± 0.05 ^b | 3.16 ± 0.01 ^c | < 0.0001 |
| FEV ₁ (L) | 2.78 ± 0.03 ^a | 2.48 ± 0.03 ^b | 3.69 ± 0.02 ^c | < 0.0001 | 1.95 ± 0.03 ^a | 1.67 ± 0.03 ^b | 2.59 ± 0.01 ^c | < 0.0001 |
| FEV ₁ /FVC | 0.81 ± 0.01 ^a | 0.63 ± 0.00 ^b | 0.80 ± 0.00 ^a | < 0.0001 | 0.83 ± 0.01 ^a | 0.63 ± 0.01 ^b | 0.82 ± 0.00 ^a | < 0.0001 |

Data were presented as means ± SD or number (%). a, b, c, the same letters indicate non-significant difference between groups based on bonferroni multiple comparison test.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 second.

* $p < .05$ by ANOVA or chi-square test.

Table 3
Odds ratios for pulmonary function according to the sarcopenia.

| | Crude | p | Model 1 | p | Model 2 | p | Model 3 | p |
|----------------|---------------------|----------|---------------------|----------|---------------------|-------|---------------------|-------|
| Males | | | | | | | | |
| Restrictive | 3.989 (2.620–6.074) | < 0.0001 | 2.001 (1.297–3.087) | 0.002 | 1.790 (1.153–2.778) | 0.009 | 1.753 (1.005–3.059) | 0.048 |
| Obstructive | 3.520 (2.482–4.993) | < 0.0001 | 0.972 (0.664–1.424) | 0.885 | 0.993 (0.660–1.493) | 0.973 | 1.167 (0.694–1.962) | 0.559 |
| Females | | | | | | | | |
| Restrictive | 2.229 (1.545–3.217) | < 0.0001 | 1.517 (1.021–2.254) | 0.039 | 1.279 (0.855–1.911) | 0.231 | 1.562 (0.997–2.448) | 0.052 |
| Obstructive | 2.085 (1.301–3.342) | 0.002 | 0.807 (0.500–1.303) | 0.381 | 0.772 (0.471–1.265) | 0.304 | 0.853 (0.457–1.590) | 0.616 |
| Total | | | | | | | | |
| Restrictive | 2.770 (2.065–3.715) | < 0.0001 | 1.723 (1.270–2.338) | < 0.0001 | 1.500 (1.103–2.038) | 0.010 | 1.736 (1.230–2.449) | 0.002 |
| Obstructive | 2.439 (1.824–3.262) | < 0.0001 | 0.909 (1.065–1.223) | 0.528 | 0.925 (0.678–1.262) | 0.623 | 1.116 (0.749–1.664) | 0.589 |

Model 1: adjusted for age. Model 2: Model 1 + BMI, smoking status, drinking status. Model 3: Model 2 + SBP, DBP, weight, waist circumference, fasting glucose, total cholesterol, triglyceride.

Reference category: pulmonary function normal.

* $p < 0.01$, * $p < 0.001$.

smoking, and drinking. This association was prominent in men.

Among the PFT measurement variables, the analysis of PFT according to sarcopenia showed that both men and women had very low variables in subjects with sarcopenia (Table 1). This means that subjects with reduced SMI have weakened their ability to dilate and contract the lungs. Prior studies have shown that FVC and FEV1 are independently associated with SMI even after adjustment to possible confounding variables,¹⁷ especially with upper extremity forces being associated with maximum inspiratory and expiratory pressure.¹⁸ This is consistent with the results in this study that both FVC and FEV1 of restrictive and obstructive pattern are significantly lower than normal. These findings indicate that SMI is associated with respiratory muscle mass.

Another explanation for sarcopenia and spirometry patterns is that the loss of SMI is associated with inflammation, which can reduce lung scalability and elasticity.¹⁹ Reduced SMI may indicate decreased lung volume and increased restriction,⁴ which can be demonstrated in this study to show that FVC is the lowest in the restrictive pattern.

In the association analysis of sarcopenia and spirometry patterns by sex, it is shown that the association between sarcopenia and the restrictive pattern is high in model 3, which adjusted both the relevant confounding variables. Interestingly, however, in sex-based stratified analyses, this association was significant in males, but not in females. These findings suggest that male subjects' lung function was more affected by SMI reduction than female subjects. This sex-specific difference is because oxidative stress is more pronounced in men, and the reduced SMI may have affected lung function.^{20,21}

Another possible explanation is that abdominal obesity may lead to poor pulmonary function. This is because abdominal obesity reduces the movement of the diaphragm, and the accumulation of fat in the abdominal cavity causes restricted lung volume.²² The results of this study showed significantly higher waist circumference in men's restrictive pattern, and no significant differences in women (Table 2). Due to these differences in waist circumferences, we can see that there were significant differences in men in the analysis of the association between sarcopenia and restrictive pattern in model 3, while there were no differences in women (Table 3). The chemical mechanism associated with these results is thought to have caused systemic inflammatory reactions, as abdominal visceral fat affects blood cytokine concentrations such as tumor necrosis factor- α , leptin, adiponectin, and interleukin-6.²³ Many studies have already shown that inflammatory reactions and pulmonary dysfunction are highly linked.^{24,25} These results can be important as a basis for sex-specific therapeutic approaches in clinical practice. However, how much the causal relationship between sex and SMI changes affects spirometry patterns, and further research is needed to explain these mechanisms.

This study was conducted to investigate whether there is an independent association between sarcopenia and spirometry patterns by sex. It is important to consider these confounding factors because SMI, a variable that determines whether sarcopenia, can be influenced by various physical factors such as age, multiple metabolic factors, smoking, and drinking. The results of this study show that sarcopenia is more associated with a restrictive pattern rather than obstructive, especially in males.

Restrictive pulmonary disease is generally known to have a high mortality rate,^{26,27} but most patients do not feel any symptoms.²⁷ Therefore, it is difficult to detect restrictive pattern without performing a PFT. Furthermore, in a restrictive pattern defined as low FVC, subjects with sarcopenia have a significantly lower survival rate

than those without. This suggests that, even for seemingly healthy subjects in clinical settings, subjects with low SMI may need to apply additional PFT, especially in men.

Despite several meaningful findings of this study, there are several limitations to this study. First, KNHANES failed to rule out drugs that could affect lung diseases and sarcopenia because there is no specific data on drug use and type. Second, only cross-sectional areas of SMI were evaluated via dual x-ray, rather than muscle strength, to determine whether sarcopenia is present. Third, only common spirometry parameters were used in this study. Because there were no parameters for pulmonary function such as maximal inspiratory and expiratory pressure, accurate analysis of the respiratory SMI was not possible. Finally, because this study is a cross-sectional design, the temporal relationship could not be explained. As a result, it was impossible to pinpoint the sequence of fundamental causes between sarcopenia and spirometry patterns. Therefore, it would be valuable to conduct future longitudinal studies to reveal the mechanism between the two.

5. Conclusion

In conclusion, after adjusting for covariates, the association between sarcopenia and pulmonary function in restrictive pattern was significant in South Korean. Moreover, after stratifying by sex, the significant association between sarcopenia and restrictive spirometry pattern remained in men.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The author declares that there is no conflict of interests.

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