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Association between pulse pressure and low muscle mass in Korean adults

A nationwide cross-sectional study

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Abstract

Sarcopenia is characterized by a loss of muscle mass and strength and is associated with a high risk of cardiovascular events and increased mortality. Pulse pressure (PP) serves as a marker for changes in heart structure and function, as well as arterial stiffness. A high PP also increases the risk of cardiovascular disease and all-cause mortality. However, the relationship between PP and sarcopenia is poorly understood. We used the data of participants of the Korea National Health and Nutrition Examination Survey (KNHANES) of 2008 to 2011. Participants were divided into a control group (PP < 40 mm Hg) and a high-PP group (PP ≥ 40 mm Hg). PP was calculated by subtracting the diastolic blood pressure (DBP) from the systolic blood pressure (SBP), and the low muscle index was assessed using appendicular skeletal muscle mass (ASM) normalized by body mass index (BMI). Multiple logistic regression analyses were performed to examine the association between PP and the prevalence of low muscle mass, adjusting for potential confounders. The high-PP group had a higher age, SBP, DBP, and prevalence of hypertension, diabetes and hyperlipidemia than the control group. The high-PP group had a higher prevalence of low muscle mass than the control group in all models. A high PP is significantly associated with a higher prevalence of low muscle mass. Therefore, PP monitoring may help identify individuals at risk of sarcopenia and guide interventions to improve health outcomes.

Abbreviations: ASM = appendicular skeletal muscle mass, BMI = body mass index, BP = blood pressure, CI = confidence interval, DBP = diastolic blood pressure, KNHANES = Korea National Health and Nutrition Examination Survey, PP = pulse pressure, SBP = systolic blood pressure.

Keywords: cardiovascular disease, prevalence, pulse pressure, sarcopenia, skeletal muscle mass

1. Introduction

Sarcopenia is a common age-related condition characterized by a loss of skeletal muscle mass and a decline of muscle function (muscular strength or physical function).[1,2] Although the prevalence of sarcopenia varies depending on the classification and cutoff used, it ranges from 8% to 36% in individuals younger than 60 and from 10% to 27% in individuals 60 years old or older.[3] Sarcopenia is closely related to fractures, falls, physical activity, quality of life, and mortality.[4–6] According to a recent meta-analysis, individuals with sarcopenia have a significantly higher risk of fractures and falls than those without.[4] In one study, sarcopenia was associated with physical disability in older men, mediated by low cardiopulmonary fitness.[5] In another study, older English adults with sarcopenia at baseline had a lower quality of life at follow-up than those without.[6] Therefore, the identification of risk factors and markers for sarcopenia is crucial for early detection and targeted interventions to prevent or manage various negative health outcomes in patients with comorbidities as well as healthy individuals.

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The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

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Blood pressure (BP) is defined as the force of circulating blood against the blood vessel walls, and pulse pressure (PP) is defined as the difference between the systolic and diastolic BPs.[7] PP is an indicator of changes in heart structure or function and arterial stiffness because it reflects cardiac output, arterial elasticity, and peripheral vascular resistance.[8,9] An increase in PP increases the risk of cardiovascular disease, kidney disease, and all-cause mortality[10–14] and is associated with endothelial dysfunction and impaired microvascular perfusion.[15,16] However, the association between PP and skeletal muscle mass, a crucial component of sarcopenia, has not been extensively investigated.

In the present study, we aimed to determine the relationship between PP and several clinical characteristics by using Korea National Health and Nutrition Examination Survey (KNHANES) data and to examine changes in PP and the prevalence of low muscle mass according to participant age. Moreover, the association between PP and the prevalence of low muscle mass in the Korean population was determined.

2. Methods

2.1. Participants

For this study, we used the data of participants of the KNHANES of 2008 to 2011. This cross-sectional, population-based survey was carried out annually by the Korea Disease Control and Prevention Agency. The data include health interviews, nutrition surveys, questionnaire-based health data, standardized physical examinations, imaging studies, and blood/urine tests. Since this survey is open to the general public, the data can be downloaded from https://knhanes.kdca.go.kr/knhanes/main.do. Among the 37,753 participants in the database, we excluded the following participants from this study: those younger than 19 years, those diagnosed with, any type of cancer, myocardial infarction, angina pectoris, or stroke at baseline, and those with missing data. This study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital (IRB No. 04-2023-027).

2.2. Study variables

Systolic BP (SBP) and diastolic BP (DBP) were obtained from physical examination data. Other clinical factors collected were smoking status, alcohol intake, physical activity, hypertension, diabetes and hyperlipidemia. Regarding smoking status, patients were divided into smokers (current or previous smokers) and never smokers. Participants were categorized as drinkers if they had consumed alcohol more than once a month in the past year. Physical activity was defined as moderate-intensity physical activity for more than 150 minutes weekly or high-intensity physical activity for more than 60 minutes weekly.

Participants were categorized as having hypertension if their BP exceeded certain thresholds (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg) or if they were taking antihypertensive agents. Participants were classified as having diabetes if their fasting glucose concentration was higher than 126 mg/dL or if they were treated for diabetes. Participants were classified as having hyperlipidemia if their total cholesterol concentration was higher than 240 mg/dL or if they were taking hyperlipidemia medication, according to the KNHANES definition.

2.3. Pulse pressure

PP was calculated by subtracting the DBP from the SBP. Each BP measurement was taken 3 times, and the average of the second and third measurements was used for analyses. In the Disease Control and Prevention headquarters' investigation team, 4 well-trained nurses responsible for BP measurements performed manual measurements. During BP measurement, if the individual arm is not positioned at the standard level, the American Heart Association stated that one must adjust for hydrostatic pressure by adding or subtracting 0.7 mm Hg for each centimeter of vertical height above or below the heart level, respectively.[17] Therefore, the BP measurement was corrected based on the average arm height (83 cm for men and 81 cm for women) to calculate the prevalence of hypertension. The participants were divided into a control group (PP < 40 mm Hg) and a high-PP group (PP ≥ 40 mm Hg).

2.4. Low muscle mass

Appendicular skeletal muscle mass (ASM) derived from dual-energy X-ray absorptiometry (Hologic Discovery; Hologic Inc., Bedford, MA, USA) was calculated as the sum of the skeletal muscle mass (lean body mass—bone mineral content) in the arms and legs. ASM normalized according to BMI (ASM/BMI) is the most prevalent measurement for approximation of muscle mass in studies for sarcopenia.[18] BMI-adjusted ASM may be more effective than unadjusted muscle mass in the prediction of functional outcomes and disability in older adults.[1,19] In addition, BMI-adjusted ASM was more strongly associated with cardiometabolic risk factors than height-adjusted ASM in Korean adults.[20] Thus, based on the recommendation of the Foundation for the National Institutes of Health Sarcopenia Project, low muscle mass was deemed present when the ASM/BMI ratio was <0.789 for men and 0.512 for women, respectively.[21]

2.5. Statistical analyses

A complex sampling design, which included integrated weights, stratification, and clusters, was used to identify representative samples at the national level, according to guidelines for data analysis from the KNHANES.

The baseline characteristics of participants were assessed using the t-test or chi-squared test. Data were presented as means ± standard errors for continuous variables and as frequencies and weighted percentages for categorical variables. We investigated the association between PP and the prevalence of low muscle mass via multiple logistic regression, adjusting for the following potential confounders: age, sex, smoking status, drinking status, physical activity, hypertension, diabetes, and hyperlipidemia. Statistical analyses were conducted using IBM SPSS Statistics for Windows version 21 (IBM Corp., Armonk, NY, USA). A P value < .05 was deemed statistically significant.

3. Results

3.1. Characteristics of the participants

Of the 37,753 screened individuals, 17,397 were included after excluding participants who meet the exclusion criteria. The control (PP < 40 mm Hg) and high-PP (PP ≥ 40 mm Hg) groups consisted of 8431 and 8966 participants, respectively (Fig. 1). Table 1 summarizes the baseline characteristics of the participants. The male and female ratios did not significantly differ between the 2 groups, but the mean age, SBP, and DBP were significantly higher in the high-PP group than those in the control group. Significant differences were also observed in drinking status and marital status between the groups. However, smoking status and physical activity did not significantly differ between the 2 groups. In addition, the percentages of participants with hypertension, diabetes, and hyperlipidemia were significantly higher in the high-PP group than those in the control group. Interestingly, the ASM/BMI in the high-PP group was significantly lower than that in the control group. When analyzing the relationship between skeletal muscle mass and clinical variables, low muscle mass was associated with age, gender, drinking, physical activity, hypertension, diabetes, and hyperlipidemia,

except for smoking status (Table S1, http://links.lww.com/MD/L61).

3.2. ASM/BMI according to PP change

The mean PP and the prevalence of low muscle mass according to age are displayed in Figure 2. SBP tended to be higher in older participants, whereas DBP tended to peak at the age of 50 to 59 (Fig. 2A). The value of PP was approximately 40 mm Hg at the age of 50 and tended to be higher in older participants (Fig. 2A). In addition, the prevalence of participants with low muscle mass was higher in older men and women (Fig. 2B). After confirming those results, the values of ASM/BMI were determined as PP increased in males and females. Compared to men and women with a PP of 20 mm Hg to < 40 mm Hg, those with a higher PP had a lower ASM/BMI for each PP range (Fig. 2C).

3.3. The relationship between PP and the prevalence of low muscle mass

Results of the multiple logistic regression analysis for the relationship between PP and the prevalence of low muscle mass are summarized in Table 2. Compared to the control group, the high-PP group had a significantly higher prevalence of low muscle mass (model 1, odds ratio: 2.953, 95% confidence interval [CI]: 2.554–3.415). Subsequently, as the prevalence of low muscle mass appeared to differ depending on age or sex, model 2 was corrected for both these factors. The resultant odds ratio for the prevalence of low muscle mass was 1.367 (95% CI: 1.156–1.617) for the high-PP group compared to the control group. After adjusting for multiple confounding variables (age, sex, smoking status, drinking status, physical activity, hypertension, diabetes, and hyperlipidemia), a high-PP group was still significantly associated with a higher prevalence of low muscle mass (model 3, odds ratio: 1.233, 95% CI: 1.003–1.476) compared to the control group.

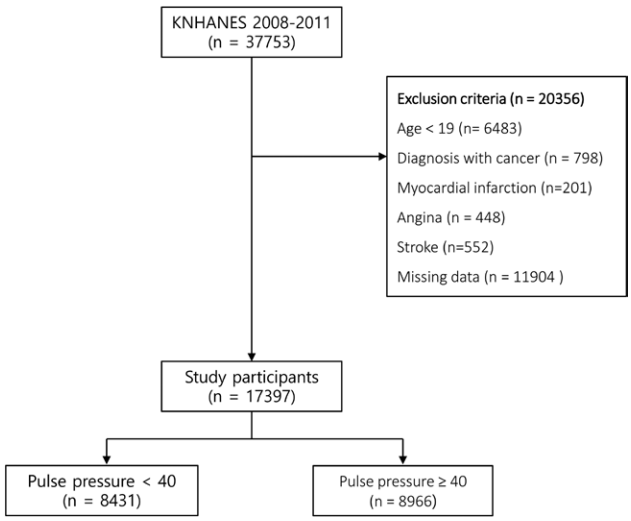

Figure 1. Flow diagram of study participants in KNHANES 2008 to 2011. KNHANES = Korea National Health and Nutrition Examination Survey.

3.4. Association between PP and the prevalence of low muscle mass according to age group

To determine the relationship between PP and the prevalence of low muscle mass according to age group, a subgroup analysis using multiple regression was conducted by dividing the subjects into 19 to 49 and over 50 age groups, because increased age was associated with decreased muscle mass and the slope of PP changed with age at approximately 50 years of age (Table 3). In both age groups, the high-PP group showed a significantly higher prevalence of low muscle mass compared to the control group in all models, except for that in model 3 of the over 50 age group.

4. Discussion

In this study, we examined the relationship between PP and several clinical characteristics and determined the association between PP and the prevalence of low muscle mass in the Korean population by using data from the KNHANES.

In several previous studies, a high PP was associated with hypertension, hypercholesterolemia, diabetes, and metabolic syndrome, reflecting the roles of those parameters in cardiovascular diseases and arterial stiffness.[22–24] A high PP was more commonly observed in patients diagnosed with hypertension and cardiovascular diseases[22] and was independently associated with a higher risk of diabetes in women.[23] In addition, PP and metabolic syndrome were positively related among older Korean men and women.[24] Consistent with those studies, the high-PP group in our study had larger proportions of patients with hypertension, diabetes, and hyperlipidemia than the control group (Table 1). These results indicate a potential relationship between a high PP and the risks of metabolic and cardiovascular diseases.

Table 1

Baseline characteristics of study participants.

	N	PP < 40 (n = 8431)	PP ≥ 40 (n = 8966)	*P* value
Age (yr)	17401	38.73 ± 0.201	49.92 ± 0.346	<.001
Sex (male)	17397	3595 (49.2)	3835 (50.8)	.052
SBP (mm Hg)	17397	108.60 ± 0.194	127.94 ± 0.287	<.001
DBP (mm Hg)	17397	75.56 ± 0.203	78.33 ± 0.211	<.001
Smoking status, n (%)	17339			.358
Smokers	7164	3520 (46.9)	3644 (46.1)	
Never smokers	10175	4889 (53.1)	5286 (53.9)	
Drinking, n (%) (yes)	17317	4987 (20.4)	4517 (22.3)	<.001
Physical Activity, n (%) (regular)	17331	2007 (23.8)	2160 (224.4)	.508
Hypertension, n (%)	17385	1160 (12.9)	4084 (37.3)	<.001
Diabetes, n (%)	16331	363 (4.4)	1077 (12.3)	<.001
Hyperlipidemia, n (%)	16851	654 (6.8)	1339 (13.1)	<.001
ASM/BMI	17397	0.814 ± 0.003	0.768 ± 0.003	<.001

P < .05, Based on t-test or chi-square test. Values are presented as number (weighted percentage) or mean ± standard error.

ALM = appendicular lean mass, ASM = appendicular skeletal muscle mass, BMI = body mass index, DBP = diastolic blood pressure, N = number, PP = pulse pressure, SBP = systolic blood pressure.

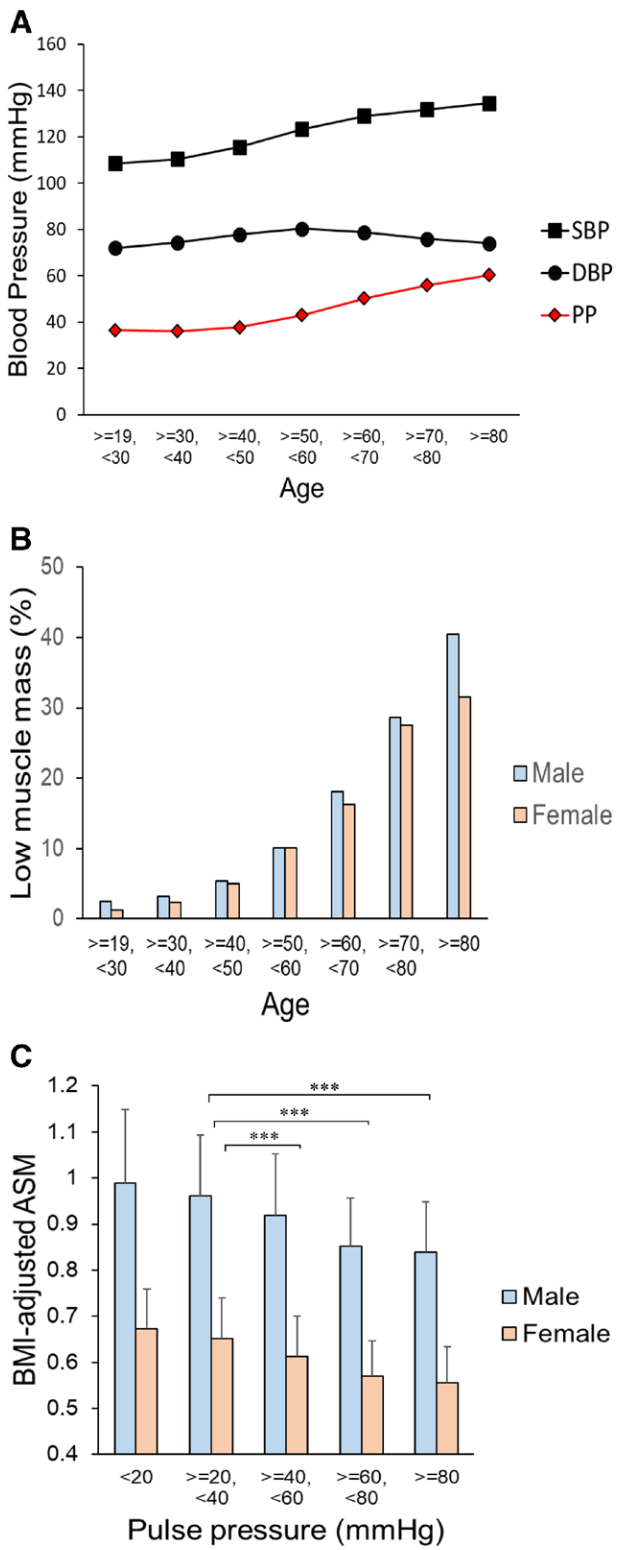

Figure 2. Relationships between blood pressure, age, prevalence of low muscle mass, and ASM/BMI. (A) SBP (square), DBP (circle), and PP (diamond) according to age category. (B) Prevalence of low muscle mass in men and women of different age groups. Male (blue), Female (orange). (C) Mean ASM/BMI of men and women of different age groups. Male (blue), Female (orange). ASM = appendicular skeletal muscle mass, BMI = body mass index, DBP = diastolic blood pressure, PP = pulse pressure, SBP = systolic blood pressure. Two-sample t-test test for intergroup analysis. Statistical significance was set at $P < .05$.

PP and the ASM/BMI ratio tend to rise with age.[25,26] Chou et al revealed that the PP in men increased after the age of 50 years, and that in women increased after the age of 40 years.[25] Kim et al reported that the prevalence of low muscle mass generally follows an upward trend with age.[26] Consistent with previous studies, this study confirmed an age-related positive relationship between PP and the prevalence of low muscle mass in a Korean population-based cohort (Fig. 2). These results indicate the relevance of PP and low muscle mass as important markers of age. Moreover, the positive correlation between PP and BMI-adjusted ASM suggests that a high PP may contribute to sarcopenia in aging populations, reflecting an increased arterial stiffness and reduced arterial compliance.

Table 2

Association between pulse pressure and low muscle mass.

	Model 1	Model 2	Model 3
Pulse pressure			
< 40	Reference	Reference	Reference
≥ 40	2.953 (2.554–3.415)a	1.367 (1.156–1.617)a	1.233 (1.030–1.476)a

Values are presented as odd ratio (95% CI).

BMI = body mass index, CI = confidence intervals.

[a]*P* value < .05, Model 1 was unadjusted; Model 2 was adjusted for age and sex; Model 3 was adjusted for age, sex, smoking status, drinking, physical activity, hypertension, diabetes and hyperlipidemia.

Sarcopenia refers to the age-related loss of muscle mass, strength, and function, which can lead to decreased physical performance and increased vulnerability to adverse health outcomes. Among these parameters, reduced muscle mass is a key component of sarcopenia and is used to identify individuals with inadequate muscle tissue for their age and sex. As with sarcopenia, low muscle mass is known to be closely associated with fractures, quality of life, and cardiovascular diseases.[27–31] In one study, a low skeletal muscle mass was a significant predictor of distal radius fractures.[27] A meta-analysis revealed an association between low skeletal muscle mass and reduced health-related quality of life in patients with cancer,[28] although the interpretation of that correlation is hindered by the diverse classification of low muscle mass among studies. A low skeletal muscle mass before kidney transplantation is reportedly associated with an increased likelihood of mortality and hospital readmission after kidney transplantation.[29] Notably, a low muscle mass was highly correlated with cardiovascular diseases in previous studies. Participants with a low skeletal muscle mass were at greater risk of experiencing cardiovascular events (acute myocardial infarction, unstable angina pectoris, hospitalization for heart failure, coronary revascularization, ischemic stroke, and cardiovascular death).[30] Moreover, low skeletal muscle mass was significantly and independently associated with arteriosclerosis overall and in various age and both sex subgroups.[31] PP serves as an indicator of changes in arterial stiffness.[16,18] A high PP previously exhibited a positive correlation with coronary heart disease[13,14] and increased the risk of nephropathy.[12] In addition, PP has been revealed as a significant predictor for both cardiovascular and total mortality.[10,11] As both PP and sarcopenia are related to cardiovascular diseases, Coelho Júnior et al conducted a study on the correlation between PP and sarcopenia.[32] They discovered that a high PP in older women with sarcopenia was associated with low muscle function and high cardiovascular risk compared to those without sarcopenia. Ohara et al also revealed that a high brachial PP is significantly associated with a low muscle mass.[33] Although the study group, age group, muscle mass measurement method, and definition of low muscle mass were different in this study compared to the reported studies, consistent with those results, a high PP was correlated with a low muscle mass in the Korean population (Tables 2 and 3). Thus, individuals with a high PP may be at an increased risk of sarcopenia.

Table 3

Association between pulse pressure and low muscle mass by age group.

Age		Model 1	Model 2	Model 3
19–49	PP < 40	Reference	Reference	Reference
	PP ≥ 40	1.724 (1.330–2.236)[a]	1.632 (1.257–2.120)[a]	1.547 (1.164–2.055)[a]
≥ 50	PP < 40	Reference	Reference	Reference
	PP ≥ 40	1.614 (1.250–2.084)[a]	1.406 (1.084–1.823)[a]	1.267 (0.975–1.645)

Values are presented as odd ratio (95% CI) [a]p value < 0.05, Model 1 was unadjusted; Model 2 was adjusted for age and sex; Model 3 was adjusted for age, sex, smoking status, drinking, physical activity, hypertension, diabetes and hyperlipidemia.

BMI = body mass index, CI = confidence intervals, PP = pulse pressure.

The association between PP and low muscle mass may provide valuable clinical information for healthcare professionals and patients alike. Monitoring PP levels, a readily accessible and noninvasive measure, may serve as a potential screening tool for the identification of individuals at risk of low muscle mass. Early detection of low skeletal muscle mass can prompt timely interventions, such as targeted exercise programs or nutritional support, to mitigate the progression of muscle loss and improve overall health outcomes.

4.1. Possible mechanism

Sarcopenia is a complex condition. Although the specific mechanisms linking PP changes and sarcopenia have not been extensively studied, several potential pathways can be considered. First, a high PP represents high arterial stiffness and low arterial compliance. This may lead to endothelial dysfunction, reducing blood flow and oxygen delivery to peripheral tissues.[15] Inadequate oxygen supply to the muscles can contribute to muscle wasting and dysfunction, potentially promoting the development of sarcopenia.[34] Second, arterial stiffness is associated with chronic inflammation and oxidative stress.[34,35] These factors can negatively impact muscle tissue and contribute to muscle wasting. Inflammatory cytokines and reactive oxygen species may disrupt muscle protein synthesis and promote protein degradation, exacerbating sarcopenia. However, further research is needed to explore the precise mechanisms by which PP changes may contribute to sarcopenia and identify potential therapeutic targets for intervention and the prevention of sarcopenia related to arterial stiffness.

5. Strengths and limitations

First, as far as we know, this is the first study in which the association between PP and low muscle mass was determined in Korean population. Because changes in the slope of PP at 50 years of age were observed (Fig. 2A), in this study, the multiple logistic regression analysis was also performed in young and old adult groups (Table 3). The inclusion of individuals aged 19 and above in such studies is crucial to understand the continuum of the association with age. Second, this study is representative of the general population of South Korea because the KNHANES contains the data of participants across ages, the sexes, and regions. This enhances the generalizability of the results to the Korean population. However, this study also has several limitations. First, its cross-sectional design prevented us from establishing a causal relationship between PP and decreased muscle mass. Longitudinal studies are warranted to determine the temporal association between PP changes and a decrease in muscle mass. Second, only the SI was used to determine whether PP was associated with the prevalence of sarcopenia. Although low muscle mass is a fundamental element of sarcopenia, future studies are needed to confirm the relationship between PP and muscle function. Third, we did not adjust our models for treatment with antihypertensive drugs, anticoagulants, and inotropic agents known to affect PP[36] because this information was not available. Therefore, our results must be interpreted with caution.

6. Conclusion

In conclusion, This study provides compelling evidence for a significant association between increased PP and a higher prevalence of sarcopenia, defined as low muscle mass. This result underscores the importance of considering high PP as a potential risk factor for sarcopenia. Moreover, PP monitoring may serve as a simple and accessible screening tool to identify individuals at risk of sarcopenia. Ultimately, early detection and intervention strategies targeting arterial stiffness may mitigate the burden of sarcopenia and improve overall health outcomes in the Korean population. Future research should focus on elucidating the underlying mechanisms of the relationship between PP and sarcopenia towards the identification of novel therapeutic targets and interventions for the prevention and management of sarcopenia.

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