The relationship between skeletal muscle mass and arterial stiffness in an elderly Korean population

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The relationship between skeletal muscle mass and arterial stiffness in an elderly Korean population

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ABSTRACT

The relationship between skeletal muscle mass and arterial stiffness in an elderly Korean population

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(Directed by Professor Hyeon Chang Kim, MD, PhD)

Introduction:

Several studies have examined the relationship between skeletal muscle mass and arterial stiffness. The results, mostly, have shown an inverse relationship between skeletal muscle mass and arterial stiffness. But, there were only few studies to examine the

relationship between skeletal muscle mass and arterial stiffness targeting an elderly Korean population. Thus, the aim of this study is to investigate the relationship between skeletal muscle mass and arterial stiffness in an elderly Korean population.

Methods:

This study used data from the Korean Social Life, Health and Aging Project (KSHAP) which started in 2011. A total of 814 people agreed to participate in the KSHAP, and 533 participants completed both questionnaire survey and health examinations. Skeletal muscle mass was measured with bioelectrical impedance analysis method using Inbody370 (Biospace, Seoul, Korea). Augmentation index, an indicator of systemic arterial stiffness, was measured by HEM-9000AI (Omron Healthcare, Kyoto, Japan) and adjusted to heart rate of 75 bpm. In this cross-sectional study, 180 men and 247 women aged 52-95 years were included, after excluding people missing augmentation index measurements (n=91), arm and leg muscle mass (n=15), or laboratory tests (n=17). The relationship between skeletal muscle mass and arterial stiffness was investigated by multiple linear regression analysis.

Results:

Mean age was 71.7 in men and 70.9 in women. In male participants, arm and leg muscle masses were inversely associated with augmentation index when adjusted for age (p=0.0003 and p=0.0007, respectively), and even after additional adjustment for body mass index, brachial systolic blood pressure, total cholesterol, high-density lipoprotein-cholesterol, fasting glucose and insulin, smoking and alcohol intake (p=0.025 and p=0.029, respectively). In women, arm muscle mass was not significantly associated with

augmentation index. Leg muscle mass was associated with augmentation index when adjusted for age (p=0.03) but the association disappeared when fully adjusted (p=0.23). Skeletal muscle mass was not significantly associated with brachial blood pressure in both sexes.

Conclusion:

Decreased skeletal muscle mass was independently associated with arterial stiffness but not with resting brachial blood pressure in an elderly Korean population. Our results suggest that an age-related loss of skeletal muscle mass may affect arterial wall elasticity rather than resting blood pressure.

Keywords: Sarcopenia, arterial stiffness, skeletal muscle mass, elderly, Korea, augmentation index

The relationship between skeletal muscle mass and arterial stiffness in an elderly Korean population

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Ⅰ. Introduction

Sarcopenia, an age-related loss of skeletal muscle mass and strength (Rosenberg, 1997), is a major problem in the global trend toward an aging society (Janssen et al., 2004; Kohara et al., 2012). Sarcopenia, especially in limb muscle mass, leads to

physiological (Abe et al., 2012; Visser et al., 2002), metabolic (Atlantis et al., 2009; Jurca et al., 2005; Londono et al., 2012; Yang et al., 2012), and functional impairments (Amigues et al., 2013; Dutta, 1997) and increased risk of cardiovascular diseases (Chin et al., 2013; Marquis et al., 2002; Sasaki et al., 2007; Stephen and Janssen, 2009). Even though the specific mechanism of sarcopenia has not been fully identified, it is known that is related to aging, malnutrition, sedentary life style, inflammation (Cesari et al., 2005; Jensen, 2008; Roubenoff, 2007), oxidative stress (Semba et al., 2007), insulin resistance (Fielding et al., 2011; Karakelides and Nair, 2005; Yang et al., 2012), decreased testosterone (Ochi et al., 2010).

In an elderly population, as well as a loss of muscle mass, an increase of arterial stiffness is another major concern (Ochi et al., 2010). Arterial stiffness underlies various pathological conditions (Liu et al., 2009) and is well known as an independent predictor of coronary heart disease and stroke (Benetos et al., 1998; Garcia et al., 2001; Laurent et al., 2003). In fact, above mentioned risk factors for sarcopenia, including aging, malnutrition, lack of physical activities and insulin resistance are also related to atherosclerotic cardiovascular disease (Kohara et al., 2012; Ochi et al., 2010; Urbina et al., 2012).

Previous data have shown a relationship between a loss of skeletal muscle mass and arterial stiffness (Abbatecola et al., 2012; Colao, 2008; Loenneke et al., 2013; Ochi et al., 2010). But, only limited data are available on the relationship between skeletal muscle mass and arterial stiffness in elderly Koreans. Thus, the aim of this study was to investigate the relationship between limb muscle mass and arterial stiffness in an elderly Korean population.

Ⅱ. Materials and Methods

Measurements

This study was based on data from the Korean Social Life, Health and Aging Project (KSHAP) which was started in 2011. The KSHAP study which is an ongoing community-based cohort study and recruited an elderly people aged 60 or older and their spouses who have lived in Yangsa-myeon, Ganghwa-gun, Incheon, Korea. A total of 814 people agreed to participate in the KSHAP, and 533 participants completed both questionnaire survey and health examinations including laboratory test and physical examination. Among these 533 participants, after excluding people missing information about augmentation index (n=91), leg muscle mass (n=15), or laboratory tests (n=17), and outliers of leg muscle mass measurement (n=3), 180 men and 247 women with an age range of 52-95 years were included in the current study. The Institutional Review Board of Yonsei University approved the study protocol (YUIRB-2011-012-01) and all participants provided written informed consent.

The information about age, smoking status (never or ever smoker) and alcohol intake (non-drinker or drinker) were obtained using questionnaire survey. Standing height was measured to the nearest 0.1 cm using a stadiometer and body weight was measured to the nearest 0.1 kg on a digital scale up to 0.1 kg according to the predetermined manual. Body mass index (BMI) was calculated as an individual's body weight in kilograms divided by their height in meters squared.

Limb muscle mass was measured with bioelectrical impedance analysis method by Inbody370 (Biospace, Seoul, Korea), according to the instructions provided by the manufacturer. The participants stood up straight and comfortably with barefoot, legs apart

and keep arms out of reach of the body on the analyzer's footplate. This analyzer measures segmental impedances at the right arm, left arm, right leg, left leg and trunk using a multi-frequency of 5 kHz, 50 kHz, and 250 kHz. In this study, we used the estimated muscle masses of arm and leg by this analyzer in order to assess skeletal limb muscle mass. Arm muscle mass was determined as sum of both arms, and leg muscle mass was determined as sum of both legs. Total limb muscle mass was determined as sum of both arms and both legs.

Physical function was assessed by 3-m timed up and go (TUG) test. The TUG, which measures the consuming time that the participants rise from a chair, walk 3 m to the end of a line (Pre-arranged) and then return to the chair and sit down.

Arterial stiffness was assessed by augmentation index, which was calculated with radial pulse waveform analyzer HEM-9000AI (Omron Healthcare, Kyoto, Japan) and adjusted to heart rate of 75 bpm. Augmentation index, which is a noninvasive measure of arterial stiffness, was well known a strong marker for coronary artery disease (Weber et al., 2004) and associated with cardiovascular risk (Nurnberger et al., 2002; Wilkinson et al., 2002). Wilkinson et al. reported that augmentation index was related to hypercholesterolemia in the middle and old ages (age range; 25 to 77 years, mean age; 51 ± 10 years) (Wilkinson et al., 2002). Nurnberger et al. reported that augmentation index was related to estimated risk scores of cardiovascular disease and cardiovascular risk in 144 people with free from coronary or other atherosclerotic disease (46 ± 14 years) and 72 people had atherosclerotic disease (53 ± 12 years) (Nurnberger et al., 2002). Duprez et al. also reported that, augmentation index was associated with Framing Risk Score (206 male and 92 female healthy subjects with a mean age of 50 ± 12 years) when unadjusted model (Duprez et al., 2004).

Augmentation index can be explained the augmented pressure divided by pulse pressure and expressed as a percentage (Ryall et al., 2008). The central aortic pressure wave consists of a forward moving wave produced by left ventricular ejection and a coming later reflected wave from the periphery to the heart (Nichols and Singh, 2002). With increased aortic and arterial stiffness, transmission velocity of both forward and returned waves increase, which brings about early return of reflected waves back to the aorta for a period of systole and this mechanism can increase aortic systolic blood pressure and pulse pressure (Weber et al., 2004). Therefore, a rise of the central aortic blood pressure can be a manifestation of earlier returned waves from peripheral reflecting sites (Benetos et al., 1998). This reflected pressure can either be described as the augmentation index relative to aortic pulse pressure or expressed in absolute terms as augmented pressure (Nurnberger et al., 2002). In this study, augmentation index is defined as a ratio of the peak point 2, at the height of reflected wave, to the pulse pressure (P1) (Fig 1) (Kelly et al., 1989).

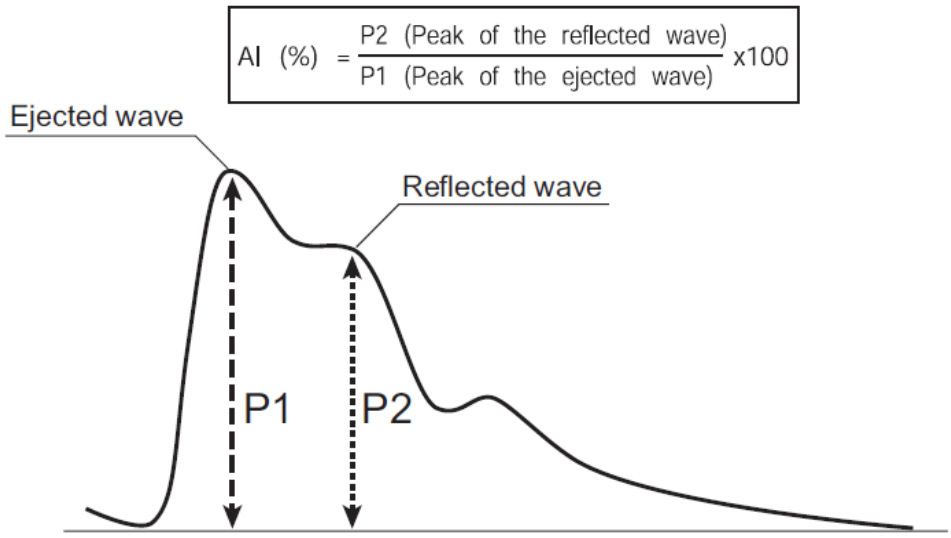


Figure 1. The definition of Augmentation Index

Blood pressure was measured more than twice with oscilloscopic method using automatic sphygmomanometer (Dinamap 1846 SX/P, GE Healthcare, Waukesha, WI, USA). Prior to each measurement, all participants had rested for at least 5 min in a sitting position and cuff size was adapted to their right upper arm circumference. If the first and second measurements differ by ≥10mmHg either SBP or DBP, the additional measurements were performed, and the average of the last two measurements was taken in this analysis.

Blood samples were collected from the antecubital vein of participants, after at least 8 hours of fasting. Total cholesterol, HDL cholesterol, fasting blood glucose and insulin were used in the analysis.

Statistical analyses

All analyses were performed for men and women separately. The data are presented as means ± standard deviation or numbers (percentages). The differences of general characteristics between men and women were analyzed using the independent two sample t-test for continuous variables and the chi-square test for categorical variables. The relationships between skeletal muscle mass and augmentation index was evaluated using Pearson's correlation analysis (Table 2A-D) and their linear relationships are presented with scatter plots (Figure 2, 3). We also evaluated linear trend and presented p for trend according to quartile range of arm and leg muscle mass which was a major interesting variable. In continuous data analysis, a general linear model using contrast coefficients for linear trend analysis was used. In categorical data analysis, Cochran-Armitage test was used (smoking and alcohol intake).

The association between limb muscle mass and augmentation index was investigated by multiple linear regression analysis. We adjusted analyses for variables known or presumed to be associated with augmentation index and skeletal muscle mass including age, BMI, total cholesterol, HDL cholesterol, fasting glucose level, fasting insulin level, 3-m TUG test, smoking and alcohol intake. As skewed, Fasting insulin was log-transformed in statistical analyses. All analyses were performed using SAS statistical software, version 9.2 (SAS Institute Inc., Cary, NC, USA). All statistical tests were two-sided and a *p* value less than 0.05 was considered significant.

Ⅲ. Results

The general characteristics of study population are presented in Table 1. The mean age of the study population was similar for men (71.7 years) and women (70.9 years). Height and weight was significantly higher in men than in women. Arm and leg muscle masses were significantly higher and thigh circumference was larger in men than in women. However, augmentation index, central systolic blood pressure, TUG test score were significantly higher in women compared to men.

Log-transformed insulin, total cholesterol, HDL cholesterol were also significantly higher in women than in men, whereas, fasting glucose level, high sensitivity C-reactive protein were significantly lower in women compared with men. For BMI, SBP, fasting insulin, triglyceride, cigarette smoking and alcohol intake, there were no differences between men and women. In the current analysis, log-transformed insulin was used due to the distribution of fasting insulin was skewed.

Table 1. The general characteristics of study population

Variables	Total (n=427)	Men (n=180)	Women (n=247)	*p*-value
Age, years	71.3 ± 7.1	71.7 ± 6.9	70.9 ± 7.2	0.262
Height, cm	155.6 ± 8.8	162.9 ± 6.3	150.3 ± 6.3	<.0001
Weight, kg	58.3 ± 10.4	62.9 ± 10.0	55.0 ± 9.4	<.0001
BMI, kg/m^2	24.0 ± 3.3	23.7 ± 3.4	24.3 ± 3.3	0.080
Arm muscle mass, kg	4.2 ± 1.1	5.0 ± 0.9	3.7 ± 0.7	<.0001
Leg muscle mass, kg	11.9 ± 2.9	14.4 ± 2.2	10.2 ± 1.8	<.0001
Total limb muscle mass, kg	16.2 ± 3.8	19.4 ± 3.0	13.8 ± 2.4	<.0001
Thigh circumference, cm	47.6 ± 3.8	48.9 ± 3.7	46.8 ± 3.6	<.0001
SBP, mmHg	132.0 ± 18.9	130.5 ± 19.4	133.1 ± 18.6	0.154
DBP, mmHg	71.5 ± 9.8	72.6 ± 10.2	70.6 ± 9.4	0.038
cSBP, mmHg	152.0 ± 20.9	148.0 ± 21.7	155.0 ± 19.8	0.001
Augmentation index, %	88.6 ± 10.2	84.1 ± 10.4	91.9 ± 8.6	<.0001
TUG, sec	12.9 ± 3.6	12.4 ± 3.8	13.3 ± 3.4	0.014
Fasting glucose, mg/dL	92.6 ± 17.6	96.2 ± 22.4	89.9 ± 12.4	0.001
Insulin (log-transformed)	2.0 ± 0.4	1.9 ± 0.5	2.0 ± 0.4	0.010
Total cholesterol, mg/dL	184.1 ± 34.6	173.3 ± 33.2	191.9 ± 33.6	<.0001
HDL cholesterol, mg/dL	52.1 ± 12.2	50.5 ± 12.1	53.3 ± 12.2	0.017
Triglyceride, mg/dL	153.5 ± 78.0	153.2 ± 81.6	153.8 ± 75.4	0.936
CRP, mg/L	2.3 ± 5.4	3.2 ± 6.9	1.6 ± 3.9	0.007
Smoking	62 (14.7)	27 (15.1)	35 (14.4)	0.955
Alcohol intake	130 (30.8)	60 (33.5)	70 (28.8)	0.353

DATA was expressed as mean ± standard deviation or number (percent).
Abbreviations: BMI, body mass index; SBP, brachial systolic blood pressure; DBP, brachial diastolic blood pressure; cSBP, central systolic blood pressure; TUG, 3-m timed up and go test; HDL, high-density lipoprotein; CRP, high sensitivity C-reactive protein

Table 2 presented the correlations between limb muscle mass and other variables using the Pearson's correlation coefficients. In men, arm and leg muscle mass were significantly correlated augmentation index before and after adjusting for age. Augmentation index was significantly correlated with both arm and leg muscle masses. But the correlation was a bit stronger for arm muscle mass. Also, in men, DBP had significant correlations with arm and leg muscle mass in unadjusted model. In women, leg muscle mass had a significant relationship with augmentation index when adjusted for age.

The linear relationship between limb muscle mass and augmentation index was presented using scatter plot, separately in men and women (Figure 2, 3).

Table 3A and 3B present the characteristics of this study population with regard to the categories of arm and leg muscle mass. Arm and leg muscle mass of participants was divided into quartiles.

Table 3A shows characteristics of study population according to the categories of arm muscle mass. Men with lower level of arm muscle mass had significantly higher level of age, TUG and augmentation index. Men with lower level of arm muscle mass also had significantly lower level of BMI, leg muscle mass, fasting glucose, insulin, triglyceride and DBP. In women, arm muscle mass level of participants had marginally significant associations with the level of augmentation index. Also, women with lower level of arm muscle had significantly older age and higher insulin level.

Table 3B was characteristics of study population according to the categories of leg muscle mass. Table 3B is quite similar to the results of arm muscle mass (Table 3A). There was, however, no significant difference across female groups according to leg muscle mass in augmentation index.

Table 2. Correlation between skeletal muscle mass and other variables

	Arm muscle mass				Leg muscle mass			
	unadjusted		adjusted for age		unadjusted		adjusted for age	
	Pearson coefficients	*p*-value	Pearson coefficients	*p*-value	Pearson coefficients	*p*-value	Pearson coefficients	*p*-value
Men (n=180)								
Age	-0.505	<.0001	NA	NA	-0.417	<.0001	NA	NA
BMI	0.583	<.0001	0.554	<.0001	0.419	<.0001	0.365	<.0001
TUG	-0.229	0.002	0.014	0.852	-0.256	0.001	-0.073	0.332
Fasting glucose	0.296	<.0001	0.278	<.001	0.183	0.014	0.150	0.045
Insulin (log-transformed)	0.394	<.0001	0.368	<.0001	0.294	<.0001	0.253	0.001
Total cholesterol	0.032	0.666	0.029	0.699	-0.002	0.978	-0.009	0.906
HDL cholesterol	-0.138	0.065	-0.130	0.083	-0.105	0.160	-0.092	0.220
Triglyceride	0.258	0.001	0.175	0.019	0.249	0.001	0.178	0.017
CRP	-0.092	0.219	-0.072	0.339	-0.119	0.112	-0.104	0.168
SBP	0.013	0.858	0.061	0.417	-0.056	0.453	-0.026	0.725
DBP	0.253	0.001	0.141	0.060	0.200	0.007	0.101	0.178
Augmentation index	-0.249	0.001	-0.268	<.001	-0.243	0.001	-0.252	0.001
Women (n=247)								
Age	-0.409	<.0001	NA	NA	-0.527	<.0001	NA	NA
BMI	0.695	<.0001	0.676	<.0001	0.488	<.0001	0.442	<.0001
TUG	-0.303	<.0001	-0.121	0.058	-0.349	<.0001	-0.110	0.085
Fasting glucose	0.137	0.032	0.155	0.015	0.095	0.135	0.119	0.062
Insulin (log-transformed)	0.351	<.0001	0.354	<.0001	0.286	<.0001	0.294	<.0001
Total cholesterol	0.017	0.791	0.018	0.780	-0.037	0.563	-0.044	0.497
HDL cholesterol	-0.134	0.035	-0.132	0.039	-0.064	0.314	-0.055	0.388
Triglyceride	0.124	0.052	0.154	0.016	0.054	0.394	0.090	0.162
CRP	-0.031	0.624	-0.009	0.892	-0.062	0.334	-0.037	0.565
SBP	-0.061	0.336	-0.005	0.933	-0.094	0.141	-0.025	0.692
DBP	0.113	0.076	0.049	0.448	0.115	0.071	0.032	0.615
Augmentation index	-0.109	0.088	-0.119	0.062	-0.115	0.071	-0.137	0.032

Abbreviations: BMI, body mass index; TUG, 3-m timed up and go test; HDL, high-density lipoprotein; CRP, high sensitivity C-reactive protein; SBP, brachial systolic blood pressure; DBP, brachial diastolic blood pressure

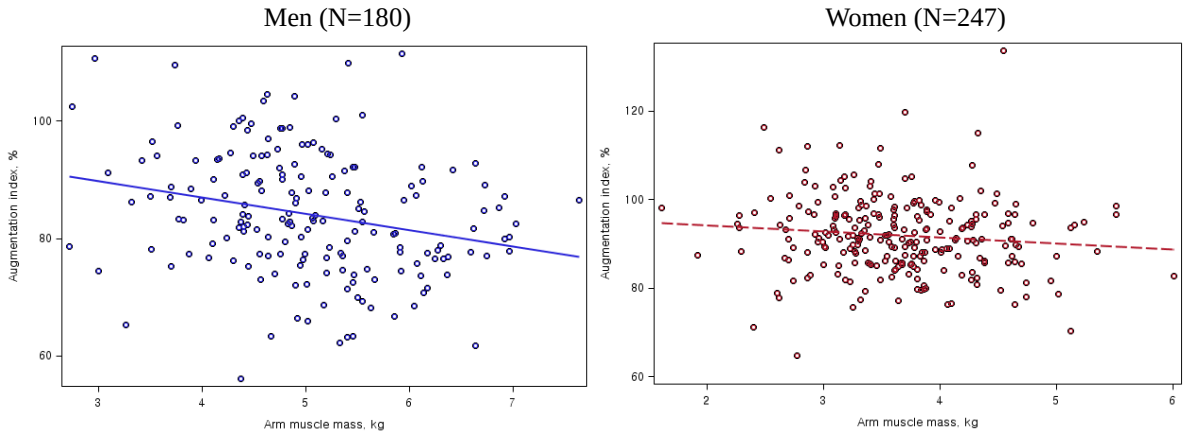


Figure 2. Association between arm muscle mass and augmentation index

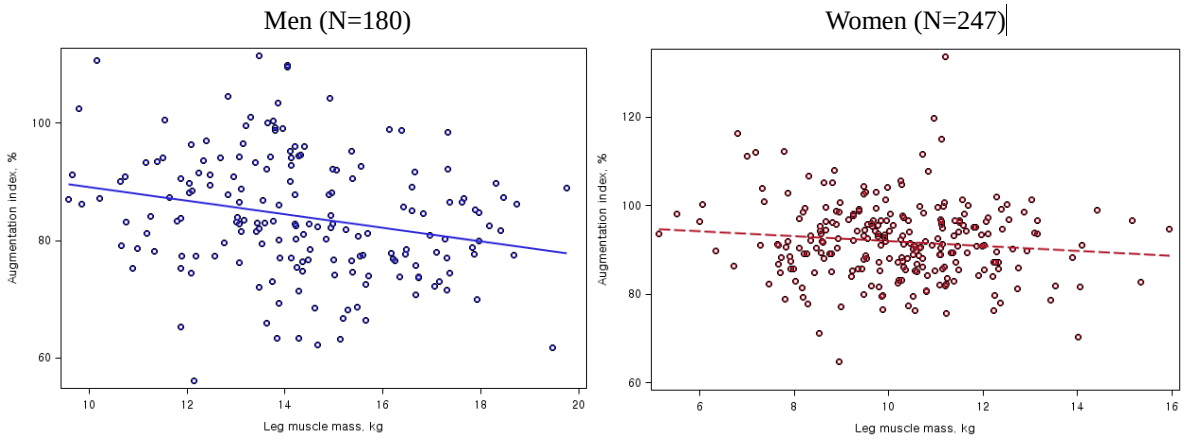
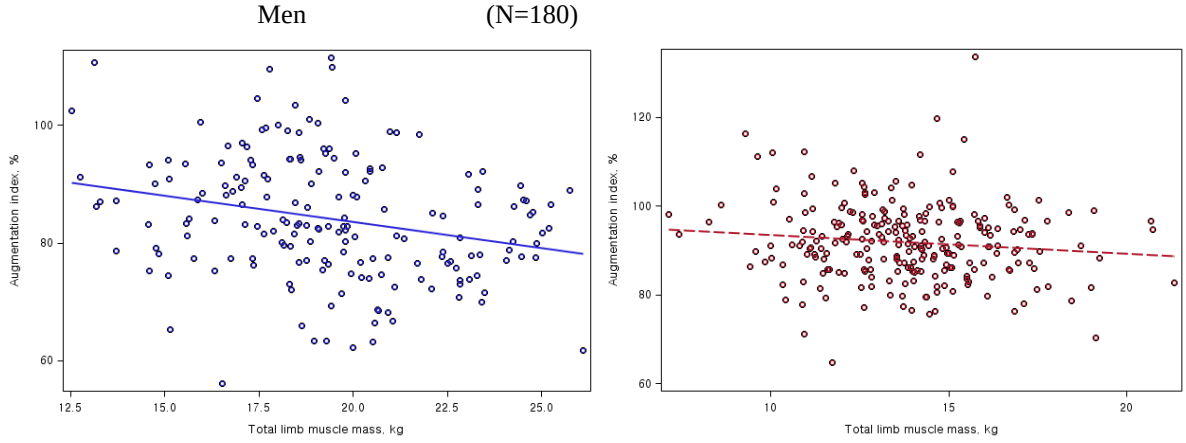


Figure 3. Association between leg muscle mass and augmentation index



Women (N=247)

Figure 4. Association between total limb muscle mass and augmentation index

Table 3A. Characteristics of study participants by arm muscle mass

	Q1	Q2	Q3	Q4	*p*-trend
Men (N=180)	**(n=45)**	**(n=44)**	**(n=44)**	**(n=47)**	
Age, years	76.8 ± 7.5	72.1 ± 5.1	70.7 ± 5.7	67.4 ± 5.7	<.0001
BMI, kg/m^2	21.2 ± 2.5	23.1 ± 3.7	24.1 ± 2.7	26.3 ± 2.5	<.0001
Arm muscle mass, kg	3.9 ± 0.5	4.7 ± 0.2	5.2 ± 0.2	6.2 ± 0.5	<.0001
Leg muscle mass, kg	12.2 ± 1.6	13.9 ± 1.3	14.6 ± 1.4	16.7 ± 1.5	<.0001
Fasting glucose, mg/dL	90.3 ± 11.7	91.4 ± 13.8	98.6 ± 25.1	104.1 ± 30.5	0.001
Insulin (log-transformed)	1.8 ± 0.4	1.7 ± 0.3	1.9 ± 0.4	2.2 ± 0.6	<.0001
Total cholesterol, mg/dL	169.6 ± 33.8	170.1 ± 29.9	177.1 ± 31.7	176.2 ± 37.1	0.227
HDL cholesterol,mg/dL	51.6 ± 11.3	51.9 ± 13.0	50.9 ± 11.8	47.6 ± 12.2	0.109
Triglyceride, mg/dL	133.9 ± 61.1	142.5 ± 76.5	149.1 ± 73.0	185.5 ± 101.7	0.003
CRP, mg/L	3.1 ± 4.8	4.8 ± 11.0	2.8 ± 6.1	2.0 ± 3.7	0.244
TUG, sec	13.9 ± 4.6	12.5 ± 3.6	11.4 ± 2.5	11.9 ± 3.7	0.004
Smoking	6 (13.3)	7 (15.9)	5 (11.6)	9 (19.2)	0.564*
Alcohol intake	15 (33.3)	14 (31.8)	14 (32.6)	17 (36.2)	0.762*
SBP, mmHg	130.5 ± 22.0	133.0 ± 16.3	127.6 ± 14.5	130.8 ± 23.2	0.724
DBP, mmHg	68.8 ± 10.0	73.4 ± 9.9	72.3 ± 10.0	75.7 ± 9.9	0.003
Augmentation index, %	87.1 ± 10.5	86.6 ± 10.1	82.4 ± 10.9	80.5 ± 9.0	0.001
Women (n=247)	**(n=60)**	**(n=60)**	**(n=64)**	**(n=63)**	
Age, years	75.6 ± 7.5	70.0 ± 6.3	70.2 ± 6.2	68.1 ± 6.6	<.0001
BMI, kg/m^2	21.5 ± 2.6	23.7 ± 2.4	24.5 ± 2.6	27.2 ± 2.8	<.0001
Arm muscle mass, kg	2.8 ± 0.3	3.4 ± 0.1	3.8 ± 0.1	4.6 ± 0.4	<.0001
Leg muscle mass, kg	8.4 ± 1.3	9.8 ± 1.0	10.3 ± 1.1	12.1 ± 1.4	<.0001
Fasting glucose, mg/dL	88.8 ± 11.1	89.1 ± 9.8	89.2 ± 9.7	92.5 ± 17.3	0.117
Insulin (log-transformed)	1.9 ± 0.4	1.9 ± 0.4	2.0 ± 0.3	2.2 ± 0.3	<.0001
Total cholesterol, mg/dL	196.5 ± 37.7	186.4 ± 29.5	188.3 ± 30.9	196.6 ± 35.0	0.911
HDL cholesterol,mg/dL	55.7 ± 12.5	52.5 ± 12.6	53.3 ± 11.9	51.8 ± 11.6	0.115
Triglyceride, mg/dL	134.3 ± 61.3	167.1 ± 94.5	144.0 ± 66.6	169.7 ± 71.3	0.051
CRP, mg/L	1.2 ± 2.2	2.1 ± 4.9	1.9 ± 5.4	1.3 ± 1.3	0.987
TUG, sec	15.0 ± 3.9	12.6 ± 2.9	13.6 ± 3.0	12.0 ± 3.0	<.0001
Smoking	11 (18.6)	7 (11.9)	11 (17.2)	6 (9.8)	0.301*
Alcohol intake	20 (33.9)	12 (20.3)	21 (32.8)	17 (27.9)	0.840*
SBP, mmHg	134.4 ± 18.9	133.1 ± 19.4	133.0 ± 19.9	132.1 ± 16.2	0.529
DBP, mmHg	69.0 ± 9.2	71.4 ± 8.9	69.5 ± 9.6	72.5 ± 9.6	0.103
Augmentation index, %	93.5 ± 9.4	92.6 ± 7.4	90.3 ± 7.6	91.1 ± 9.6	0.056

DATA was expressed as mean ± standard deviation or number (percent).

**P*-trend was derived from the Cochran-Armitage trend test

Table 3B. Characteristics of study participants by leg muscle mass

	Q1	Q2	Q3	Q4	*p*-trend
Men (N=180)	**(n=45)**	**(n=45)**	**(n=45)**	**(n=45)**	
Age, years	75.8 ± 7.3	71.6 ± 6.7	71.5 ± 6.2	67.4 ± 5.3	<.0001
BMI, kg/m^2	22.0 ± 2.6	23.3 ± 4.3	23.8 ± 2.8	26.3 ± 2.7	<.0001
Arm muscle mass, kg	4.1 ± 0.7	4.8 ± 0.6	5.1 ± 0.5	6.1 ± 0.7	<.0001
Leg muscle mass, kg	11.6 ± 0.9	13.6 ± 0.4	14.9 ± 0.5	17.3 ± 0.9	<.0001
Fasting glucose, mg/dL	91.8 ± 13.4	96.1 ± 30.0	95.0 ± 22.0	104.1 ± 20.5	0.048
Insulin (log-transformed)	1.8 ± 0.4	1.8 ± 0.4	1.8 ± 0.4	2.2 ± 0.6	<.001
Total cholesterol, mg/dL	168.8 ± 34.8	176.6 ± 31.6	176.7 ± 26.8	176.2 ± 38.8	0.767
HDL cholesterol,mg/dL	50.9 ± 12.2	54.6 ± 13.0	48.4 ± 9.9	47.6 ± 12.2	0.056
Triglyceride, mg/dL	131.2 ± 59.6	132.1 ± 65.8	161.5 ± 73.8	185.5 ± 107.3	<.001
CRP, mg/L	3.5 ± 5.6	3.2 ± 6.4	4.1 ± 10.3	2.0 ± 3.7	0.418
TUG, sec	13.9 ± 4.2	11.9 ± 3.6	12.3 ± 3.3	11.9 ± 3.5	0.006
Smoking	5 (11.1)	5 (11.1)	7 (15.6)	10 (22.7)	0.102*
Alcohol intake	12 (26.7)	13 (28.9)	15 (33.3)	20 (45.5)	0.055*
SBP, mmHg	130.2 ± 21.7	136.5 ± 21.0	126.6 ± 14.0	128.7 ± 18.9	0.259
DBP, mmHg	69.3 ± 11.0	74.1 ± 11.6	72.3 ± 8.1	74.6 ± 9.0	0.035
Augmentation index, %	86.7 ± 9.9	88.5 ± 11.5	80.2 ± 9.8	81.2 ± 8.1	<.001
Women (n=247)	**(n=60)**	**(n=63)**	**(n=62)**	**(n=62)**	
Age, years	77.1 ± 6.7	70.8 ± 6.3	70.2 ± 6.2	68.1 ± 6.0	<.0001
BMI, kg/m^2	22.3 ± 2.9	24.1 ± 2.4	24.5 ± 2.6	27.2 ± 3.2	<.0001
Arm muscle mass, kg	3.0 ± 0.5	3.5 ± 0.4	3.7 ± 0.4	4.4 ± 0.6	<.0001
Leg muscle mass, kg	7.9 ± 0.8	9.6 ± 0.4	10.7 ± 0.3	12.4 ± 1.0	<.0001
Fasting glucose, mg/dL	88.5 ± 9.7	89.7 ± 9.8	89.2 ± 9.7	92.5 ± 16.7	0.173
Insulin (log-transformed)	1.9 ± 0.4	2.0 ± 0.4	2.0 ± 0.3	2.2 ± 0.3	<.001
Total cholesterol, mg/dL	195.4 ± 36.2	190.3 ± 29.5	188.3 ± 30.9	196.6 ± 35.5	0.604
HDL cholesterol,mg/dL	54.9 ± 12.0	53.1 ± 12.6	53.3 ± 11.9	51.8 ± 13.8	0.337
Triglyceride, mg/dL	145.6 ± 67.9	149.9 ± 94.5	144.0 ± 66.6	169.7 ± 72.6	0.309
CRP, mg/L	1.9 ± 5.8	2.0 ± 4.9	1.9 ± 5.4	1.3 ± 1.3	0.238
TUG, sec	15.6 ± 4.1	12.6 ± 2.9	13.6 ± 3.0	12.0 ± 2.8	<.0001
Smoking	11 (18.6)	7 (11.9)	11 (17.2)	6 (9.8)	0.842*
Alcohol intake	21 (33.9)	12 (20.3)	21 (32.8)	17 (27.9)	0.756*
SBP, mmHg	135.1 ± 17.9	133.1 ± 19.4	133.0 ± 19.9	132.1 ± 15.9	0.099
DBP, mmHg	69.3 ± 10.3	71.4 ± 8.9	69.5 ± 9.6	72.5 ± 9.3	0.183
Augmentation index, %	93.1 ± 9.1	92.6 ± 7.4	90.3 ± 7.6	91.1 ± 7.0	0.126

DATA was expressed as mean ± standard deviation or number (percent).

**P*-trend was derived from the Cochran-Armitage trend test

Table 4 shows the relationship between arm and leg muscle mass or masses and augmentation index in multiple linear regression analysis.

In men, for every 1 kg decrease in muscle mass of both arms, augmentation index increased by 2.8 % when unadjusted (p=0.0008), and by 2.3 % after adjustment for BMI, SBP, total cholesterol, HDL cholesterol, fasting glucose, insulin, smoking and alcohol intake (p=0.025). But, in women, there was no significant relationship between arm muscle mass and augmentation index.

For leg muscle mass, in men, the results were similar to the arm muscle mass. For every 1 kg decrease in muscle mass of both legs, augmentation index increased by 1.2 % when unadjusted (p=0.001), and by 0.8 % when adjusted for age, BMI, SBP, total cholesterol, HDL cholesterol, fasting glucose, insulin, smoking and alcohol intake (p=0.029). In women, lower leg muscle mass was significantly associated with increased augmentation index when adjusted for age (β=-1.54, p=0.033) but the association disappeared with additional adjustment.

Table 4. Multiple linear regression coefficients of arm and leg muscle mass with augmentation index in an elderly population

	Arm muscle mass			Leg muscle mass			Total limb muscle mass		
	β	adj R^2	*p*-value	β	adj R^2	*p*-value	β	adj R^2	*p*-value
Men (n=180)									
Unadjusted	-2.76	0.06	0.001	-1.16	0.06	0.001	-0.89	0.07	0.001
Model 1	-3.44	0.06	<.001	-1.32	0.05	0.001	-1.07	0.06	<.001
Model 2	-2.70	0.21	0.010	-0.89	0.20	0.020	-0.76	0.20	0.011
Model 3	-2.34	0.24	0.025	-0.83	0.24	0.029	-0.69	0.24	0.019
Women (n=247)									
Unadjusted	-1.36	0.01	0.088	-0.56	0.01	0.071	-0.43	0.01	0.063
Model 1	-1.63	0.01	0.061	-0.77	0.01	0.033	-0.59	0.01	0.030
Model 2	-0.80	0.05	0.488	-0.52	0.06	0.187	-0.39	0.06	0.216
Model 3	-0.32	0.08	0.784	-0.47	0.09	0.230	-0.32	0.09	0.304

Model 1: adjusted for age
Model 2: adjusted for age, BMI, SBP
Model 3: adjusted for age, BMI, SBP, total cholesterol, HDL cholesterol, fasting glucose, log-transformed insulin, smoking and alcohol intake
Abbreviations: adj, adjusted; BMI, body mass index; SBP, brachial systolic blood pressure; HDL, high-density lipoprotein

Ⅳ. Discussion

We examined the relationship between skeletal muscle mass and arterial stiffness in an elderly Korean population. There was a significant inverse relationship between limb muscle mass and augmentation index particularly in men. But there was no significant relationship between limb muscle mass and brachial blood pressure in the present study.

Skeletal muscle mass in relation to arterial stiffening and brachial blood pressure

Our findings are in keeping with previous studies have reported the inverse relationship between skeletal muscle mass and arterial stiffness in men. Ochi et al. reported thigh muscle volume is related to arterial stiffness in healthy and middle aged men. They presumed sarcopenia, a loss of muscle mass with aging, and atherosclerosis may share a similar pathway and facilitate mutual malfunction (Ochi et al., 2010). Another cross-sectional study reported leg lean mass was associated with central arterial stiffness in the men and women aged 60-86 years (Snijder et al., 2004). This study reported that larger leg lean mass was strongly related to less femoral and brachial arterial stiffness as well as lower central arterial stiffness. In healthy young adults (mean age and standard deviation; 23 and 3), muscle mass is related to brachial systolic blood pressure and inversely associated with augmentation index (Loenneke et al., 2013). In the previous Korean study, which was performed in 526 (men, 191; female 319) healthy adults aged 20-80 years (mean age, 53.6 yeas) to examine association of skeletal muscle mass to visceral fat ratio with pulse wave velocity. This study also reported positive

relationships between skeletal muscle mass and systolic and diastolic blood pressure (Kim et al., 2011). But, in our study, skeletal muscle mass was inversely associated with arterial stiffness in men but not with brachial blood pressure both in men and women.

Sex difference in relationship between skeletal muscle mass and arterial stiffness

We observed sex difference in relationship between skeletal muscle mass and arterial stiffness. The previous studies also have reported sex and race differences of the associations between skeletal muscle mass and arterial stiffness. (Abbatecola et al., 2012; Din-Dzietham et al., 2004; Loenneke et al., 2013; Ochi et al., 2010). With regard to this issue, as reported in the previous studies, involvement of testosterone may account for it (Hougaku et al., 2006; Ochi et al., 2010). It has been reported in several studies that testosterone control the muscle mass of human (Bhasin et al., 1996; Ryall et al., 2008) and serum testosterone level is associated with muscle strength (Hougaku et al., 2006). Recently, it has also reported that free testosterone level was positively associated with thigh muscle mass and negatively associated with brachial-ankle pulse wave velocity in middle-aged men. However, in women, testosterone was not associated with thigh muscle mass after adjustment for other potential confounding variables (Ochi et al., 2010). In our study, sex difference in relationship between skeletal muscle mass and arterial stiffness was probably due to the relatively greater variation range of muscle mass in men as compared with women. Further studies are necessary to specify sex difference in relation to skeletal muscle mass and arterial stiffness.

Potential mechanisms

Although, there were several studies examined the relationship between skeletal muscle mass and arterial stiffness, it has not been able to fully elucidate the mechanism. Specific mechanism between skeletal muscle mass and arterial stiffness is beyond the scope of the current study, but the factors leading to sarcopenia seem to play key roles in increased arterial stiffness and atherosclerosis. Previous studies reported that several factors related to the etiology of sarcopenia including inflammation (Kamel, 2003; Roman et al., 2005; Roubenoff, 2007; Zanoli et al., 2012) , oxidative stress (Kals et al., 2006; Kamel, 2003), malnutrition (Benton et al., 2011; van de Laar et al., 2012), decreased physical activity (Seals et al., 2008; Visser et al., 2002), abnormalities in sex hormones (Baumgartner et al., 1999; Srinivas-Shankar and Wu, 2009).

Recent studies also reported that growth hormone and insulin like growth factor system, which play an essential role in myogenesis (Florini et al., 1996), were associated with increased risk of ischemic heart disease, acute myocardial infarction, stroke, coronary and carotid artery atherosclerosis (Colao, 2008). Thyrotropin-releasing hormone receptor gene was associated with a lean body mass in genome-wide association study (Liu et al., 2009) and thyrotropin-releasing hormone receptor gene was also associated with hypertension in the previous study (Garcia et al., 2001; Kokubo et al., 2006). According to these findings, there is a strong possibility that sarcopenia and increased arterial stiffness have potentially a common genetic background and share common pathological processes.

Furthermore, sarcopenia also could lead to increased insulin resistance and physical incapability (Kim et al., 2011; Ryall et al., 2008), which could promote arterial stiffness. On the other way, arterial stiffness can promote sarcopenia

through decline of appendicular basal blood circulation in arms and legs (Abbatecola et al., 2012). All these findings suggest that sarcopenia and increased arterial stiffness probably interact with each other as well as share the common pathological processes.

Strengths and limitations of the current study

This study had several strengths. First, as far as we know, this study was the first study to examine the relationship between skeletal muscle mass and augmentation index in an elderly Korean population. Second, we recruited participants from community-based Korean elderly population, and consist of a single ethnic group aged 52-95 years. Third, we conducted analysis adjusted to potential confounders including age, BMI, SBP, total cholesterol, HDL cholesterol, glucose, log-transformed insulin, TUG, smoking and alcohol intake.

This study also had limitations. First, this study is limited by its cross-sectional design and relatively small number of subjects. It was not possible to explain the causal relationship between limb muscle mass and arterial stiffness. Large longitudinal studies are needed to identify the causal association between limb muscle mass and arterial stiffness. Second, limb muscle mass was measured with bioelectrical impedance analysis method in this study. Although more accurate tool to measure of skeletal muscle mass is dual-energy X-ray absorptiometry, owing to its limited accessibility, bioelectrical impedance analysis method was used as alternative. Third, it may not be appropriate to generalize it to another ethnic or age group because the study was conducted with Korean subjects lived in a certain region and specific age group. Nevertheless, it is a rare and meaningful study conducted in an elderly Korean population performed in a focused age group,

between ages of 52 and 95 years, considering that age is one of the most determining factors for increasing of arterial stiffness and decreasing of muscle mass. Finally, we could not identify specific mechanism between sarcopenia and atherosclerosis. Accordingly, further longitudinal studies are necessary to specify the relationship between age-related sarcopenia and atherosclerosis.

Conclusions

In conclusion, lower skeletal muscle mass was associated with increased arterial stiffness in Korean male elderly. However, resting brachial blood pressure was not associated with skeletal muscle mass. The results of current study suggest that an age-related loss of skeletal muscle mass may affect arterial wall elasticity rather than resting blood pressure.

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ABSTRACT (Korean)

한국 노인 인구에서 사지 근육량과 동맥경직도의 관련성

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연구 배경 및 목적

노화에 따른 사지 근육량과 동맥경직도에 대한 여러 선행 연구가 있었고, 그 연구들 대부분에서 사지 근육량이 적을수록 동맥경직도의 수준은 높다는 연구 결과를 보고하였다. 하지만 지금까지 한국의 노인 인구를 대상으로 사지 근육량과 동맥경직도의 관련성을 조사한 연구는 거의 보고되지 않았다. 그래서 본 연구에서는 한국 지역사회에 거주하는 노인 인구의 사지 근육량과 동맥경직도의 관련성을 조사하였다.

연구 방법

이 연구는 2011년 Korean Social Life, Health and Aging Project (KSHAP, 국문명; 활발한 노년 사회를 위한 통합적 연구: 사회과학과 생의학의 통합)에 참여한 한국 노인 인구(총 814명)를 대상으로 한 단면 연구이다. 참여자들은 인천광역시 강화군 양사면에 거주하는 60세 이상 노인들과 그들

의 배우자였으며, 현 연구에서는 건강검진과 설문조사를 완료한 533명 중에서 근육량 측정 및 혈관경직도 검사 그리고 혈액 검사를 완료하지 못한 사람들을 제외하고 남자 180명, 여자 247명, 총 427명을 최종 연구 참여자로 선정하였다.

사지 근육량은 생체 전기 저항(bioelectrical impedance method)을 이용해 산출하였고, 양팔 근육량의 합, 양다리 근육량의 합, 그리고 사지근육량의 합을 분석에 사용하였다. 동맥경직도는 요골동맥파 분석(radial pulse waveform analysis)을 통해 augmentation index를 산출하였고, 심박수 75 bpm으로 보정하여 분석에 사용하였다.

주요 통계 분석 방법은 선형회귀분석을 사용하였으며, 인슐린은 모수적 검정 실시를 위해 로그변환하였고, 혼란 변수로서 연령과 체질량지수, 상완수축기 혈압, 총 콜레스테롤, HDL 콜레스테롤, 공복 혈당, 공복 인슐린, 흡연 및 음주 여부 등을 보정하여 분석하였다.

연구 결과

남자와 여자의 평균 나이는 각각 72세와 71세로 참여자의 성별에 따른 연령 차이는 없었다. 남자의 팔 근육량과 다리 근육량은 연령을 보정하기 전과 후 모두 통계적으로 유의한 관련성이 있었으며(β=−3.44, p=0.0003; β=−1.32, p=0.0007)에서 동맥경직도와의 관련성이 통계적으로 유의하였고, 추가적으로 체질량지수, 상완 수축기 혈압, 총 콜레스테롤, HDL 콜레스테롤, 공복 혈당, 인슐린, 흡연 여부 및 음주 여부를 보정했을 때(β=−2.34, p=0.025; β=−0.83, p=0.029)에도 독립적인 관련성이 있었다. 여자의 경우, 팔 근육량은 동맥경직도와 유의한 관련성이 없었으며, 다리 근육량은 연령을 보정한 경우(β=−0.77, p=0.033)에서만 동맥경직도와 유의한 관련성이 있었다. 그리고 남자과 여자 모두 사지 근육량은 상완 혈압과 통계적으로 유의한 관련성이 없었다.

고찰

한국의 노인 인구에서 사지 근육량 감소는 동맥경직도와 독립적인 관련성이 있었으며, 여자보다는 남자에서 더 강한 관련성이 있었다. 본 연구 결과에 따르면, 노화에 따른 사지 근육량의 감소는 상완 혈압보다 동맥 혈관벽의 탄력도와 더 관련이 있었다.

핵심단어: 혈관경직도, 근육량, 심혈관, 한국 노인, 지역사회