Relationship between physical fitness and arterial stiffness in Korean older adults

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Abstract
Pulse-wave velocity (PWV) is a widely used clinical marker of arterial stiffness. Associations between several physical fitness measures and arterial stiffness have been examined. However, these results were inconsistent. Therefore, we conducted a cross-sectional study to assess the relationship between various physical fitness parameters and arterial stiffness in older adults. From January 2014 to December 2015, 1500 participants (men, n = 587; mean age, 71.78 ± 5.10 years) in South Korea were enrolled in the study. Koreans aged >65 years who agreed to participate in the study were enrolled. Individuals who were unable to exercise because of underlying conditions were excluded. VO2 max (mL/kg/min), handgrip strength (kg), handgrip strength (kg)/body weight (kg) ratio, one-leg standing time (s), and 10-meter walking speed (m/s) were measured. The brachial-ankle pulse wave velocity (baPWV) was measured using a VP-1000 instrument. VO2 max (mL/kg/min), handgrip (kg)/body weight (kg) ratio, one-leg standing time (s), and 10-meter walking speed (m/s) were significantly inversely associated with baPWV. This association was consistent even after adjusting for confounding factors. Our study revealed a significant association between various aspects of physical fitness and arterial stiffness. This study suggests that physical fitness is a useful predictor of arterial stiffness in older adults.

Keywords: arterial stiffness, brachial-ankle pulse wave velocity, physical fitness

1. Introduction
Brachial-ankle pulse wave velocity (baPWV) is a simple and well-standardized clinical marker of systemic arterial stiffness measured using brachial and tibial arterial wave analyses.[1,2] Increased baPWV, which reflects increased arterial stiffness, has been reported to be a significant predictor of cardiovascular events in various clinical settings and in the absence of conventional cardiovascular risk factors.[3–4]

Even among healthy individuals, arterial stiffness gradually increases with advancing age, especially after the age of 65 but aerobic physical activity may mitigate this pathological process.[5,6] In older adults, observational studies have found that cardiovascular fitness and physical activity are associated with decreased systemic arterial stiffness.[11] Furthermore, experimental studies have shown that exercise programs can reduce arterial stiffness.[12–14] These findings suggest that maintaining physical fitness is crucial to prevent and improve arterial stiffness in older adults.

In light of this importance, the associations of several physical fitness surrogate measures, such as grip strength, walking speed, and balance tests with arterial stiffness, have been examined.[15–17] However, these studies were limited by the small number of participants.[15–17] In addition, some studies have reported inconsistent results.[11,15,16,19] Therefore, this study aimed to investigate the relationship between various physical fitness parameters and systemic arterial stiffness in older adults. We assessed VO2 max, grip strength, one-leg standing time, and walking speed as markers for cardiorespiratory fitness, muscle strength, static balance, and overall functional status, respectively.[20–23] We hypothesized that low VO2 max, weak grip strength, slow walking speed, and poor standing balance would reflect higher arterial stiffness among older adults (>65 years).

Abbreviations: baPWV = brachial-ankle pulse wave velocity, BMI = body mass index, BP = blood pressure, HR = heart rate, KISS FitS = Korea Institute of Sport Science Fitness Standards, PWV = pulse wave velocity, sBP = systolic blood pressure.

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2. Materials and Methods

2.1. Study design
This cross-sectional observational study aimed to assess the relationship between various physical fitness markers, such as grip strength, walking speed, and standing balance time, and baPWV, a marker of arterial stiffness. Data from the Korea Institute of Sport Science Fitness Standards (KISS FitS) project, in which healthy Koreans aged 19 years or older (≥19) participated, were used in this study.[24] From the KISS FitS project data, participants over 65 years of age were included in the analysis. The purpose of the KISS FitS project was to assess the nationwide physical fitness of healthy Koreans, evaluate their health conditions, and recommend appropriate levels of fitness for disease prevention. Informed consent was obtained from each patient before enrollment in the study. This study was approved by the Research Ethics Committee of the Korea Institute of Sport Science (IRB No. KISS-201504-EFS-001-01).

2.2. Study participants
From January 2014 to December 2015, we enrolled participants aged 65 years or older (≥65) who agreed to participate in the physical fitness test and anthropometric data measurement and who could provide medical, social, and family history.[24] The participants were recruited from among the general population living in Korea, and physical fitness tests were conducted at strength certification centers in Korea.

Patients with acute cardiovascular disease, acute or chronic systemic infection and those who could not participate in the test because of acute or chronic musculoskeletal injury were excluded from the test. In addition, people who could not exercise sufficiently due to leg claudication, arthritis, deconditioning pulmonary disease, neuromuscular disorders, including Parkinson disease, or other conditions were excluded. The participants were allowed to participate in a subset of tests depending on their underlying disease/health condition. Finally, participants with missing variables for the analysis were excluded (body mass index [BMI] [n = 1], lean mass [n = 5], systolic blood pressure [sBP] [n = 13], family history of cardiovascular disease [n = 55], smoking [n = 55], active life style [n = 55], 10 m walking speed [n = 107], one leg standing time [n = 51], relative hand grip strength [n = 80], absolute hand grip strength [n = 80], VO2 max [n = 926]) (Fig. 1).

We interviewed each enrolled patient about their family history of cardiovascular disease, smoking, lifestyle using exercise duration per week, and underlying comorbid diseases, including hypertension, dyslipidemia, coronary heart disease, and stroke. Baseline patient characteristics including sex and age were recorded. In addition, anthropometric data including height, weight, BMI (kg/m²), lean body mass (kg), and blood pressure (BP) (mm Hg) were measured. We used a stadiometer (Seca, Seca Corporation, Columbia, MD) and an electronic weight scale (Inbody 720, Biospace, Seoul, Korea) for the height and weight measurements. BMI was calculated as weight in kilograms divided by height in meters squared. Lean body mass was measured using a multifrequency bioelectrical impedance machine (InBody720; Biospace, Seoul, Korea). BP was measured twice consecutively in a sitting position at the brachial artery after 10 minutes of rest using an automated sphygmomanometer (HEM-9000AI, Omron, Japan).[25]

A family history of cardiovascular disease was defined as having first-degree relatives with a stroke or heart disease. Current smokers were defined as those who currently smoked cigarettes and had smoked 100 cigarettes in their lifetime, following the definition of the US Centers for Disease Control and Prevention.[24] An active lifestyle was defined when the participants performed more than 150 minutes of moderate-intensity exercise (4.0 metabolic equivalents) in a week, following the International Physical Activity Questionnaire-Short Form, moderate level of physically active criteria.[27] Hypertension was defined as a sBP > 140 mm Hg or diastolic BP > 90 mm Hg, self-reported history of hypertension, or current antihypertensive medications.

2.3. Pulse-wave velocity (PWV) measurements
BaPWV was recorded in the supine position after the participants had rested for 5 minutes using a VP-1000 (Colin Co, Komak, Japan), which measures bilateral brachial and posterior...
tibial artery pressure waveforms using an oscillometric method with cuffs placed on both arms and ankles. BaPWV was calculated automatically for each arterial segment, as the path length was divided by the corresponding time interval. The coefficients of variation in our sample for the left and right baPWV were 12.3% and 12.6%, respectively. The mean baPWV was adopted as the mean of the right and left measurements and used for the analyses.

2.4. Physical fitness measurement

2.4.1. VO\textsubscript{2} max. We performed a graded exercise test using the modified Bruce protocol on a treadmill to obtain the VO\textsubscript{2} max of the participants.[30] The participants had at least 10 minutes of rest before the resting BP measurement. Subsequently, their resting heart rates (HR) and BPs were measured, their HR reserve ([220-age]-resting HR) was calculated, and their time of exercise on the treadmill (RX9300, Tobeone, Korea) was monitored. BP was measured every 1 minute while dropping an arm to the side, keeping the arm straight using a stress test monitor device (Tango M2, SunTech Medical). The examination was terminated when one of the following criteria was met: study participants requested termination; the participants could not follow the protocol; emergent situations, including chest pain; and when participants showed abnormal signs and symptoms, decreased sBP (>10 mm Hg), acute elevation of BP (sBP > 250 mm Hg and diastolic BP > 115 mm Hg), and a HR of 90% of the HR reserve. We used the total exercise time to calculate VO\textsubscript{2} max using the formula proposed by Bruce et al.[24,29]

2.4.2. Walking speed. Walking speed was evaluated using the 10-m walking test, which has been shown to be the most valid clinical assessment method for walking speed.[31] The participants walked 10 m at their usual pace without assistance, and the time was measured at the intermediate 5 m to allow for acceleration and deceleration. A single examiner recorded the time to complete the intermediate 5-m using a digital stopwatch with a 1/1000 of a second reading. The walking speed test was performed twice, and the higher value was used in the analysis.[31]

2.4.3. Handgrip strength. The handgrip strength of both hands was measured in the standing position with both feet shoulder-width apart, using a hand dynamometer (GRIP-D 5101, Takei, Japan) for 5 seconds, recorded in 0.1-kg increments. The handle of the dynamometer was adjusted to fit the second node of the participant. The arm was fully extended and kept at 15° from the torso. Participants were asked to hold the dynamometer at full force for 5 seconds. Each hand was tested alternately. The highest value from the 2 measurements on each hand (a total of 4 measurements) was used in the analysis. The participants performed the test at 1-minutes intervals, and verbal encouragement was provided between each trial. This hand grip strength measurement was verified in a previous study.[32] We also calculated the body weight divided by handgrip strength using the formula “absolute grip strength [kg/body weight [kg]] x 100.”[33]

2.4.4. One-leg standing time. In the one-leg standing time test, we asked the participants to stand on their preferred leg with eyes open and hands down alongside their trunks. The time interval until the raised leg touched the ground was measured twice for both the legs. The standing time was measured for up to 60 seconds using a stopwatch. The best record of the 4 trials was used in the analysis.[34]

2.5. Statistical analyses

The participants were divided into tertiles (3 groups) for walking speed (10 m), grip strength, VO\textsubscript{2} max, and standing balance time due to the skewed distribution of data. We used baPWV as the outcome variable. The Chi-square test was used to compare categorical variables. Independent sample t test was used to compare means of continuous variables. We used the Spearman correlation test to identify potential confounding factors in the relationship between baPWV and physical fitness. Generalized linear analysis was used to study the association between each exercise capacity (VO\textsubscript{2} max, walking speed, handgrip strength, and one-leg standing time) and baPWV, controlling for the identified confounding factors: sex, age, sBP, lean mass, and BMI, and adjusting for smoking, which is a known risk factor for atherosclerosis.[35–37] In addition, an active lifestyle was adjusted as a confounding factor.[10] A family history of cardiovascular disease was adjusted for as an additional confounding factor.[38]

IBM SPSS Statistics V24 was used for statistical analysis (IBM statistics, IBM Corporation, Chicago, IL). All reported P values were 2-tailed, and a P value of <.05 was considered to indicate statistical significance.

3. Results

3.1. Baseline characteristics of study participants

A total of 1500 participants (587 men and 913 women) underwent physical fitness tests. The mean ages of the men and women participants were 71.64 ± 4.76 and 71.87 ± 5.31 years, respectively. Mean sBP was 130.23 ± 15.45 mm Hg for men and 131.79 ± 17.03 mm Hg for women. 7.7% of men were smokers, while 0.6% of women were smokers. Mean BMI was 23.75 ± 2.52 kg/m\textsuperscript{2} for men and 24.65 ± 3.13 kg/m\textsuperscript{2} for women (Table 1). Among the 1500 participants, 1454 had baPWV data ranging from 895 to 3399 cm/s, with a mean of 1640.39 ± 309.20 cm/s. Mean VO\textsubscript{2} max was 28.23 ± 5.29 mL/kg/min for men, and 24.23 ± 4.83 mL/kg/min for women. Mean hand grip strength was 34.29 ± 5.88 kg for men and 21.72 ± 4.22 kg for women. Mean one leg standing time was 26.47 ± 21.26 s for men and 21.06 ± 20.25 s for women. Mean ten meter walking speed was 1.45 ± 0.25 m/s for men and 1.36 ± 0.26 m/s for women (Table 2).

3.2. Association of each physical fitness measure with baPWV

Table 3 shows the associations between physical fitness and baPWV. The participants were divided into 3 groups (tertiles) to ensure that the number of participants was equal in each group.

3.2.1. VO\textsubscript{2} max (mL/kg/min). A total of 547 participants underwent VO\textsubscript{2} max testing. Compared with the reference group (≥23.86 mL/kg/min), participants with the higher VO\textsubscript{2} max values were shown to have lower baPWV measures (Crude model: VO\textsubscript{2} max ≥ 27.42 mL/kg/min group, P < .01; VO\textsubscript{2} max ≥ 27.42 mL/kg/min group, P < .01). After the adjustment, the association remained statistically significant (Adjusted model: VO\textsubscript{2} max ≥ 27.42 mL/kg/min group, P = .02) (Table 3).

3.2.2. Handgrip strength (kg). A handgrip strength test was performed on 1421 participants. Compared with the reference group (<22.20 kg), the highest handgrip strength group had a significantly lower baPWV (crude model: ≥29.31 kg group, P = .02). However, after adjusting for confounding factors and cardiovascular risk factors, this association was not significant (Adjusted model: 22.21–29.30 kg group, P = .54; ≥29.31 kg group, P = .43).

When we analyzed the handgrip strength adjusted for body weight, there was no significant relationship between the handgrip strength/body weight ratio and baPWV in the crude model (crude model: 38.34–48.70% group, P = .06; ≥48.71% group, P = .06). However, after adjustment, the handgrip strength/body weight ratio showed a significant inverse association with baPWV (Adjusted model: 38.34–48.70% group, P = .01; ≥48.71% group, P = .03) (Table 3).
3.2.3. One-leg standing time (second) A total of 1404 participants completed the one-leg standing test. Compared with the reference group (≤7.89 second), participants with a longer one-leg standing time were shown to have a significantly lower baPWV (crude model: 7.90–26.87 s group, \(P = .02\); ≥26.88 second group, \(P < .01\)). After the adjustment, only the participants with the longest one-leg standing time had significantly lower baPWV than the reference group ≥26.88 second group (\(P = .03\)) (Table 3).
3.2.4. 10-m walking speed (m/s) A total of 1393 participants underwent the 10-m walking speed test. Compared with the reference group (<1.29 m/s), participants with a faster walking speed had a significantly lower baPWV in the unadjusted model (crude model: 1.29–1.49 m/s group, P < .01; ≥1.50 m/s group, P < .01). After adjustment, only participants with the fastest 10-m walking speed demonstrated a significantly lower baPWV (≥1.50 m/s group, P = .02) (Table 3).

4. Discussion
This study aimed to investigate the association between physical fitness measures and arterial stiffness. This study is unique in that, unlike previous studies that focused on a single fitness measure or were conducted in younger populations, we examined several measures in older adults with large sample sizes. In addition, multiple confounding factors were adjusted to validate the study result. Furthermore, as our study participants were recruited among the general population, our result has representativeness for older adults in the community. Our study demonstrated that a higher VO2 max, higher handgrip strength/body weight ratio, longer one-leg standing time, and faster 10-m walking speed were significantly associated with lower systemic arterial stiffness in older Korean adults.

Normal values for baPWV in different age groups vary according to the race and the country of the study was conducted.[10] Our study results showed a mean BaPWV of 1640.39 ± 309.20 cm/s. According to the 2013 National Physical Fitness project in Korea, 283 older adults showed baPWV in the age group 70 to 74 years of 1617.9 ± 244.4. Our study participants showed similar baseline baPWV as in previous reports from the Korean population.[11]

4.1. VO2 max and arterial stiffness
In the previous study using our cohort (KISS FitS) suggested that cut off reference for VO2 max 27.2 ± 5.6 mL/kg/min as normal VO2 max for men and 23.9 ± 4.4 mL/kg/min for women in age 70 to 79.[12] Our study group showed similar VO2 max result. Previous studies have reported conflicting results regarding the relationship between VO2 max and arterial stiffness.[13,14] A study conducted on 87 women aged 42 ± 9 years with central obesity showed that maximal aerobic capacity was inversely associated with arterial stiffness. However, the relationship was not significant after adjusting for cardiovascular disease risk factors (age, BMI, triglycerides, C-reactive protein, homeostasis model assessment-estimated insulin resistance, and pulsatile load).[15] Existing evidence suggests that there are differences in the course of age-related arterial stiffness according to sex, which increases disproportionally after menopause in women.[16] This study included only women, limiting the generalizability of the results to men.

In contrast, a study performed on 146 individuals, aged 21 to 96 years, showed that arterial stiffness was inversely related to VO2 max.[17] Both studies were limited by the small number of participants and the broad range of participants’ ages, which can significantly affect arterial stiffness.[18] Another study conducted in 11,557 subjects showed an inverse relationship between baPWV and VO2 max.[19] A recent study conducted in 405 older adults showed an inverse relationship between cardiovascular fitness, measured as a 400 m walking speed, and aortic stiffness, expressed as cfPWV.[11] This study used cfPWV as a marker for central arterial stiffness, and the study population mainly included Caucasians. Our results are in line with those of previous studies, which suggest that aerobic exercise may be beneficial for systemic arterial stiffness.[10] Our study is unique as we included both men and women. The age group was specified to those over 65, to find out the association specifically in the older adult population. Aerobic exercise can affect systemic arterial resistance through qualitative changes in arterial wall elastin and collagen and a decrease in muscle sympathetic nerve activity.[19] A previous meta-analysis demonstrated that an improvement in VO2 max contributed to a significant reduction in PWV.[20] By showing a significant negative association between higher VO2 max tertile and baPWV, our result is in line with previous findings that a high level of VO2 max is inversely associated with arterial stiffness.

4.2. Handgrip strength and arterial stiffness
According to a previous study that evaluated normal handgrip strength in Korea, 34.7 ± 5.9 and 21.4 ± 4.3 were suggested as normal values for Korean men and women of 70 to 74 years old.[21] The current study population’s hand grip strength value was similar to that of a previous study.[22] Our study did not show a direct association between hand grip strength and baPWV, after adjusting for confounding factors. Similarly, a previous study showed no association between hand grip strength and arterial stiffness during a 2-year follow up and reasoned that handgrip strength was more often used as a marker of frailty in the older age group than as a measure of muscle strength.[23,24] Our study result is meaningful as our study incorporated a larger number of participants, while previous study was limited by relatively small participants.[25] Upper arm resistance training can increase the plasma norepinephrine concentration, which can lead to increased systemic arterial stiffness.[26] Moreover, sympathetic nerve activity increases during handgrip exercise.[27] It is possible that those with high handgrip strength have been chronically exposed to increased sympathetic tone and serum norepinephrine, which eventually leads to increased systemic arterial stiffness.[12,28] Meanwhile, a randomized controlled trial reported that low-intensity resistance training could decrease systemic arterial stiffness.[29] Though there was no statistical significance in our study, we showed a decreasing trend of baPWV as handgrip strength tended to increase. Further studies are needed to validate this relationship.

Previous studies have indicated that body size is a confounding factor in the association between handgrip strength and cardiovascular health.[30] To address the confounding effect of body size, we assessed handgrip strength adjusted for body weight (handgrip strength/body weight ratio), which has been shown to be associated with functional capacity.[31] Additionally, handgrip strength/body weight ratio showed a stronger association with metabolic syndrome[32] which may lead to arterial stiffness.[33] After adjusting for all confounding factors, the handgrip strength/body weight ratio showed a significant relationship with baPWV in this study. Based on previous studies and our study findings, the handgrip strength/body weight ratio, rather than handgrip strength, might be more associated with arterial stiffness.

4.3. One-leg standing time and arterial stiffness
Previous study result for one-leg standing time with eyes open was as follows: In age 70 to 79 group, men (n = 50) 25.9 seconds ± 18.1, women (n = 45) 16.7 ± 15.0, Total (n = 95) 21.5 ± 17.3.[34] Our study results showed similar mean values but a wider standard deviation. The cause of the wider standard deviation in our population might be the wider age range of the study population. The one-leg standing time is a known indicator of static balance.[35] Only a few studies have analyzed the relationship between static balance and baPWV.[36] A study conducted with 2919 participants from the Netherlands assessed the ability to stand with 1 foot for 10 seconds. Although the study failed to show a significant association between physical fitness level and PWV, one-leg standing time was incorporated as a part of physical performance and not as a separate physical fitness entity.[15] Our study assessed one-leg standing time as a
separate physical fitness measure, making the interpretation of the results more straightforward. Furthermore, our study result is novel as our study was conducted in older Asian adults. We showed that one-leg standing time had a statistically significant relationship with PWV, which is in line with the results of a recent study.[10] Arterial stiffness may induce multisystemic failure, which can be attributed to impaired postural control.[11] Another possible explanation for this finding is the association between high baPWV and sarcopenia.[12] Sarcopenia is associated with weak lower extremity strength, which makes a person vulnerable to fall.[63,64] Overall, our results suggested that arterial stiffness is associated with static balance in older adults.

4.4. Walking speed and arterial stiffness

One previous report showed that the mean gait speed for men in their 70s was 133.0 ± 19.6 cm/s, and for women in their 70s, 127.2 ± 21.1 cm/s.[65] Our study participants’ walking speed was faster than that of the study, but this difference can be explained by the different study populations of our study. It is known that walking speed decreases with age.[66] Our study included participants aged >65 years. This could be attributed to the relatively high walking speed of the participants. Previous studies have reported that walking speed has a negative relationship with PWV.[67-69] However, controversies remain, as a study performed by Vandijk et al showed that physical fitness, including walking speed, is not related to PWV.[15] Vandijk study was conducted in different ethnicities and was limited by a relatively small number of participants, which could have masked the potential relationship.[15] Our study was conducted in a larger population and included older Asian adults. We showed a negative relationship between the walking speed and baPWV. This association was statistically significant even after adjusting for confounding factors, suggesting that walking speed is associated with arterial stiffness. According to previous literature, walking speed is related to many factors, including demographic, psychosocial, health, anthropometric, and behavioral factors.[70] Owing to its complexity, the large inequality in walking speed remains unexplained even after simultaneous adjustment for several important determinants of physical functioning in older adults.[70,71] One possible explanation for the findings of our study is the role of microvascular perfusion in the lower extremities and its relationship with arterial stiffness. Increased arterial stiffness has been associated with microvascular and conduit artery dysfunction, which could potentially influence the functional capacity of the lower extremities, causing decreased walking speed.[72-74] Therefore, older adults presenting with slow walking speeds may warrant further evaluation of their arterial conditions or physical interventions to reduce their potential cardiovascular risks.

4.5. Limitations

This study had several limitations. First, VO2 max was deduced using a graded exercise test rather than by measuring actual oxygen consumption. However, estimating VO2 max using the equation proposed by Bruce et al has been validated.[28,29] Second, this study was conducted in the Korean population; therefore, the results may not be generalizable to other populations. Third, even though we adjusted multiple factors that could affect the relationship between baPWV and physical fitness parameters, we could not control factors such as demographic, socioeconomic, and psychological factors, which might have affected the relationship.[75,76] Finally, given the cross-sectional nature of this study, a causal relationship between physical fitness measures and arterial stiffness could not be inferred from our results. Further prospective cohort or interventional studies are needed to confirm whether improving physical fitness measures can improve arterial stiffness.

5. Conclusions

In conclusion, our study showed significant inverse associations between arterial stiffness and VO2 max, handgrip strength/body weight ratio, and one-leg standing time. This study suggests that physical fitness may be a useful predictor of systemic arterial stiffness in the older population.

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