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Association between Aging and Changes in the Ankle-Brachial Index after Exercise in Patients with Chest Pain

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Background: The ankle-brachial index is a useful tool to detect lower extremity peripheral artery disease, which is affected by exercise. The aging process causes degenerative vascular changes. The aim of this study was to elucidate the association between aging and changes in the ankle-brachial index after exercise.

Methods: We analyzed data from ninety-nine patients who underwent ankle-brachial index tests and graded maximal aerobic exercise tests because of chest pain. The ankle-brachial index was measured before and after the exercise test. The correlation between age and changes in the ankle-brachial index after exercise was investigated using Pearson's correlation coefficient.

Results: The ankle-brachial index decreased after exercise, compared with that at rest (before vs. after: 1.11±0.06 vs. 1.05±0.08, $P<0.001$, 1.12±0.06, vs. 1.06±0.08, $P<0.001$; right and left, respectively). Upper-extremity systolic blood pressure did not change from baseline, and upper extremity diastolic blood pressure only increased slightly. However, the lower-extremity systolic and diastolic blood pressures decreased significantly. The correlation coefficients of the association between aging and changes in both the right and left ankle-brachial index indices were 0.319 and 0.255 ($P=0.001$ and $P=0.011$), respectively.

Conclusion: A positive correlation was observed between aging and changes in the ankle-brachial index after exercise.

Key Words: Aging, Ankle-brachial index, Exercise

INTRODUCTION

The ankle-brachial index (ABI) is a parameter expressed as the ratio of the systolic blood pressure (SBP) measured at the ankle to that measured at the brachial artery, which is usually an easily used diagnostic test to detect lower extremity peripheral artery disease (PAD) clinically [1-3]. Moreover, the ABI could serve as a marker of cardiovascular disease and an indicator of risk of future cardiovascular events [1,4-7].

During leg exercise, vasoconstriction occurs in nonexercising limbs, which increases the arm SBP [1]. In contrast, vasodilation occurs in exercising muscles, leading to a decrease of ankle SBP [1]. Therefore, there is a mild decrease in the ABI after stopping exercise [8].

There are many vascular changes that develop with aging, for example, arterial distensibility, endothelial nitric oxide release and β-adrenergic vasodilation decreases [9]. Therefore, it could be possible that there is an association between the aging process and the ABI after exercise.

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The purpose of this study was to elucidate the association of aging with the change in the ABI after exercise. We formulated the hypothesis that aging would affect the change in the ABI immediately after exercise. To test our hypothesis, we analyzed the ABI before and after a graded maximal aerobic exercise test (Treadmill test).

MATERIALS AND METHODS

1. Subjects

This study was conducted with a group of ninety-nine serial patients who underwent an ABI study and treadmill test due to chest pain at the Boramae Medical Center between September 2008 and February 2009. The treadmill test was selected as the diagnostic test for coronary artery disease at the discretion of the physician. The patients who could not undergo the treadmill test due to impaired physical performance were excluded. The patients underwent the ABI measurement before and immediately after the treadmill test. Within 10 minutes of stopping the exercise, the measurement of the ABI was performed to elucidate the acute effect of exercise on the ABI. Approval for the study protocol was obtained from the Institutional Review Board of Boramae Medical Center.

Table 1. Baseline characteristics of study group

	Values
Subjects number	99
Male:female	60:39
Age (year)	53.3±13.1
Height (cm)	163.4±8.6
Weight (kg)	65.6±11.3
BMI (kg/m^2)	24.6±3.1
Hypertension (%)	51.5
Diabetes mellitus (%)	14.1
Dyslipidemia (%)	28.3
Smoker (%)	28.3
Stroke (%)	0
Peripheral vascular disease (%)	1.0
Coronary artery diasease (%)	13.1

BMI, body mass index.
Data are expressed as the number, mean±standard deviation, or percentage.

2. Measurement of ABI

The ABI was measured with the VP-2000 machine (Colin Co. Ltd, Komaki, Japan). Using this model, we measured the ABI and blood pressure of four extremities, simultaneously. Blood pressure cuffs were wrapped around both arms and ankles, which were coupled to oscillometric and plethysmographic sensors. The oscillometric sensor determined the blood pressure and the plethysmographic sensor did the pulse volume recording. The machine presented us

Table 3. Ankle-brachial index before and after exercise

	Baseline	Post exercise	Change (%)	P value
Right ABI	1.11±0.06	1.05±0.08	−5.36±5.46	<0.001
Left ABI	1.12±0.06	1.06±0.08	−5.54±5.40	<0.001

ABI, ankle-brachial index.
Data are expressed as the mean±standard deviation. P values were calculated using Pearson's correlation.

Table 2. Arterial blood pressure and heart rate before and after exercise (mmHg)

	Baseline	Post exercise	P value
Right brachial systolic BP (mmHg)	127.9±13.4	126.6±12.2	0.088
Right brachial diastolic BP (mmHg)	77.6±10.0	79.3±9.5	0.004
Left brachial systolic BP (mmHg)	126.7±13.4	126.0±12.4	0.237
Left brachial diastolic BP (mmHg)	77.2±9.7	78.4±8.8	0.008
Right ankle systolic BP (mmHg)	144.0±17/6	134.8±17.6	<0.001
Right ankle diastolic BP (mmHg)	75.0±9.5	71.5±9.6	<0.001
Left ankle systolic BP (mmHg)	144.6±17.4	135.2±17.4	<0.001
Left ankle diastolic BP (mmHg)	76.5±14.0	71.9±9.2	0.001
Heart rate (bpm)	68.3±9.1	81.0±9.9	<0.001

BP, blood pressure.
Data are expressed as the mean±standard deviation. P values were calculated using paired t-test.

with the right and left ABI on the screen, and the results were printed on paper. All the parameters were acquired during regular sinus rhythm automatically.

3. Running exercise

All patients were tested using the standard symptom-limited Bruce's treadmill protocol with a commercially available instrument. All patients were required not to eat, drink caffeinated beverages, or smoke any kind of tobacco for 3 hours before testing. After the baseline 12-lead ECG was recorded, the patient started to exercise on the treadmill. The 12-lead ECG, heart rate and blood pressure were recorded every 3 minutes. If a patient showed abnormal symptoms or signs (moderate to severe angina, a drop in SBP of >10 mmHg from baseline, syncope, severe dyspnea, cyanosis or pallor, sustained ventricular tachycardia, severe ischemic ST depression or ST elevation≥1.0 mm in noninfarct leads without diagnostic Q waves) or the target heart rate was achieved, the recording and treadmill test were stopped. The achieved metabolic equivalents (METs) was recorded for each patient. One MET is equivalent to 3.5 ml of O^2/kg of body weight per min.

4. Statistical analysis

Data were expressed as the mean±standard deviation for continuous variables and percentages for categorical variables. The change in the continuous variables after exercise was performed using paired t-test. Pearson's correlation was used to calculate the association between two continuous variables. In addition, using partial correlation analysis, we adjusted for potential confounders. Statistical analysis was performed with the use of the SPSS/PC software package (SPSS version 12.0). $P<0.05$ was considered to be statistically significant.

RESULTS

The baseline characteristics of the study group are shown in Table 1. The patients were 53.3±13.1 years old, and 61% were men. Their height and weight were 163.4±8.6 cm and 65.6±11.3 kg. In addition, their body mass index (BMI) was 24.6±3.1 kg/m^2. Therefore, relatively obese patients were included in this study.

The duration of the exercise was 9.1±2.1 minutes and the exercise METs was 10.7±2.2. Therefore, the patients were thought to have undergone the graded exercise test adequately.

The brachial SBP did not change significantly after treadmill test. However, the brachial diastolic blood pressures were slightly increased. Furthermore, both the systolic and diastolic ankle blood pressures were decreased. In addition, the heart rate was also increased significantly after the treadmill test (Table 2). The ABI before and after exercise is presented in Table 3. The right ABI was 1.11±0.06 before exercise and 1.05±0.0 after exercise. Likewise, the left ABI was 1.12±0.06 before exercise and 1.06±0.08 after exercise.

There is a positive correlation between age and the change

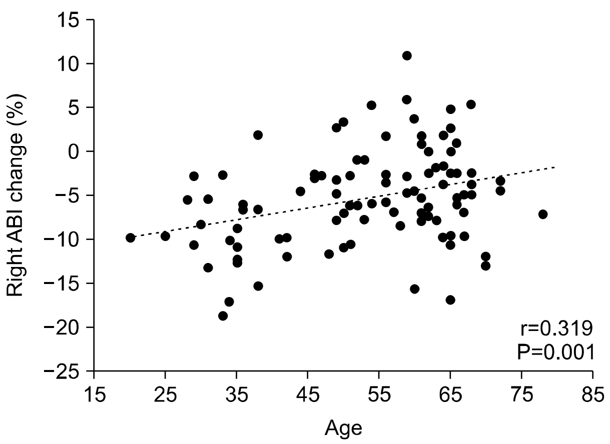

Figure 1. Age and right ankle-brachial index (ABI) change.

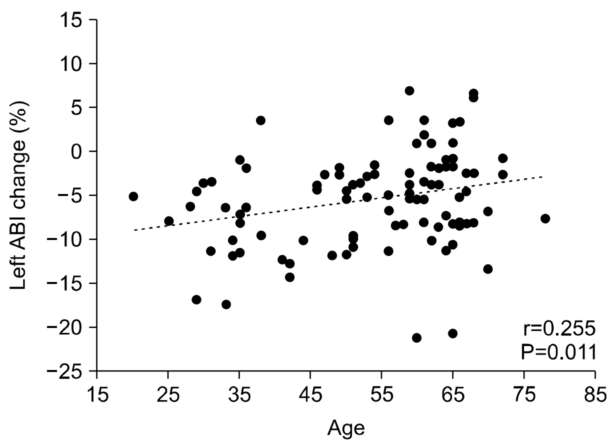

Figure 2. Age and left ankle-brachial index (ABI) change.

in the ABI after exercise. This correlation is shown in Figure 1 and 2. As age increases, the percent change of the ABI is more likely to show a less negative value, even showing a positive value in aged patients. We regarded body mass index, hypertension, diabetes mellitus, dyslipidemia, smoking and coronary artery disease as potential confounders, and partial correlation analysis was done. Because just one patient had a past medical history of PAD, it was not incorporated as a confounder in this analysis. The partial correlation coefficients for the right and left ABI were 0.221 and 0.220, respectively ($P=0.033$, $P=0.034$).

DISCUSSION

In the present study, we found that the ankle blood pressure decreased after the treadmill test but the arm blood pressure did not. Moreover, it was found that the ABI decreased after leg exercise and there was a correlation between aging and the change in the ABI after exercise.

The ABI is a simple ratio of the ankle SBP to the higher brachial pressure of either arm. The ABI is the most commonly used screening test for lower extremity PAD [2]. Besides screening test, in clinical practice, the ABI is used widely as follows. It serves as a marker of PAD progression, a measure of systemic atherosclerosis, and an independent indicator of risk of subsequent atherothrombotic events elsewhere in the vascular system [1]. Therefore, the ABI has an important role in clinical practice when detecting and treating PAD.

As described above, four extremity SBPs are needed to form the ABI. Theoretically, the ABI is calculated from those blood pressures, and it is not affected by the conditions which have influence on four extremity pressures equally. However, several conditions have a differential impact on those pressures. Pollak et al. [10] showed that deviation of the lower extremity from the horizontal position, hip flexion and knee flexion gave rise to a change in the ABI, which is probably due to gravitational effect or arterial kinking. Gornik et al. [11] demonstrated that the ABI of the seated position was 0.35 higher than that of the supine position. Therefore, the patient is required to maintain a flat position on an even plane during the ABI examination. Moreover, Yataco and Gardner [12] investigated the effect of smoking on the ABI in smokers with PAD. They found that the ABI of the nonsmoking day was higher than that of the smoking day and this result came from a lowered ankle blood pressure with no change in the brachial blood pressure.

Aerobic exercise is frequently advised to patients with diabetes, hypertension, dyslipidemia and so on. There are many kinds of aerobic exercise and these lead to a decrease of cardiac parasympathetic tone and an increase of cardiac sympathetic tone, causing an increase of cardiac output [13]. During leg exercise, the brachial SBP goes up following increased left ventricular pressure and vasoconstriction occurs in the nonexercising limbs, whereas vasodilation occurs in the exercising legs [1]. Thereafter, there would be a decrease in the ABI shortly after leg exercise. Our result showing decreased leg blood pressure after the treadmill test agrees with this explanation. However, both brachial artery SBPs did not change after exercise in this study. After exercise, cardiac output declines more rapidly than systemic vascular resistance rises [14]. This results in the so-called post-exercise hypotension. Therefore, the brachial SBP is increased during exercise and decreased after exercise to the level below that at rest. Probably, the brachial SBP of out patients was in the way of declining and expected to be lower after more time passed. In addition, there was different aspect of blood pressure change in this study between the upper and lower extremities, and this is likely due to different exercise load on the upper and lower extremities during the treadmill test which is mainly leg exercise.

Exercise treadmill testing is a kind of physiological testing to detect PAD [15]. The patient with lower extremity PAD may show a normal ABI at rest. However, with exercise, a heightened blood inflow velocity may reveal a hidden stenosis which does not yield an abnormal ABI at rest [16]. In this case, the decreased ABI could be found after exercise. According to the guideline of European society of cardiology, a post-exercise ABI decrease over 20% would be diagnostic of lower extremity PAD [17]. In addition, this guideline suggested that post-exercise ankle SBP decrease over 30 mmHg could be another criteria. Meanwhile, the TASC II

(Inter-Society Consensus for the Management of Peripheral Arterial Disease) guidelines indicated that an ABI decrease of 15%-20% after exercise would be significant for the detection of lower extremity PAD [16]. Considering these criteria for the percent change in the ABI, how do our study results fit these criteria? There were no patients showing ABI decrease over 20%, and several patients showing ABI between 15% and 20%. Moreover, patients showing post-exercise ankle SBP decrease over 30 mmHg were few or none. Therefore, there would be rare patients with hidden PAD in this study.

There was a positive correlation between aging and the change in the ABI after exercise. In other words, older patient showed less decrease in the ABI after exercise, even showing an increase in the ABI in some older patients. Aged persons are more likely to have lower extremity PAD [18]. Therefore, it seems that they have more chances of having a hidden stenosis which is not detected by the ABI at rest and post-exercise ABI may have an important role in detecting PAD. However, the aged patients showed less decrease in the post-exercise ABI in our study which was thought to include rare PAD patients. Godet et al. [19] demonstrated that the decrease in the ABI from resting value was smaller in aged groups than in younger groups after bicycle exercise in asymptomatic adults assumed to be healthy. Our results are in accordance with this result. Taken together, aged adults with no PAD would show less decrease in the ABI after exercise. In other words, there is difference in the change of the ABI after exercise according to age. Therefore, it seems that we are likely to miss lower extremity PAD if judging with the current guidelines for PAD which do not present age-specific cutoff value. We should consider other tests such as transcutaneous oxygen pressure or skin perfusion pressure in patients with suspicious symptoms suggesting lower extremity PAD, showing neither an abnormal ABI nor post-exercise ABI. Eventually, guidelines should be developed that present age-specific cutoff value for post-exercise ABI.

What is the mechanism of the diminished ABI lowering response after exercise even showing an increase in aged subjects? The purpose of this study was just to elucidate whether there is an association between aging and the change in the ABI immediately after aerobic treadmill exercise. Therefore, we could not find the mechanism of that in this study itself. There are many vascular changes as patients get older. The representative changes are as follows; 1) increased arterial wall thickness, 2) deposition of collagen, 3) fracture of elastin fibers, 4) vascular calcification, 5) decreased arterial distensibility, 6) increased endothelin production 7) decreased endothelial nitric oxide release and 8) β-adrenergic-mediated vasodilation [9,20-22]. Probably, these changes are combined to yield a lessened decrease in the post-exercise ABI in aged patients.

Several limitations are present in this study. First, we collected data from a rather limited number of patients from a single hospital. Second, information about medication including antihypertensive drugs was not collected. Third, relatively obese patients were included in this study. Fourth, because we studied patients who complained of chest pain and underwent treadmill test to detect suspected ischemic heart disease, the cohort might include mixed subjects of both healthy and unhealthy vascular function. Considering these limitations, large scale studies that take into account atherosclerotic cardiovascular disease, smoking status, obesity, hypertension, diabetes mellitus, dyslipidemia, medication status and so on are needed in future.

In conclusion, ABI is decreased after aerobic leg exercise, and aging gives rise to a weakened ABI decrease, leading to a positive correlation between aging and the change in the ABI after exercise. In addition, we propose the possibility that this effect could make it more difficult to detect lower extremity PAD in aged patients by exercise ABI test according to current PAD guidelines.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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