

## Post-Exercise Ankle-Brachial Pressure Index Demonstrates Altered Endothelial Function in the Elderly

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### Abstract:

**Background:** The ankle-brachial pressure index (ABI), the ratio of the systolic blood pressure of the ankle to the systolic brachial pressure, is commonly measured at rest, but ABI values post-exercise enhance the sensitivity of the test and can be used to identify atherosclerotic vascular damage. However, it has not been established whether or not enhanced post-exercise ABI is also associated with endothelial dysfunction. We hypothesized that a decrease in post-exercise ABI is related to impaired endothelial function.

**Purpose:** To investigate alterations in post-exercise ABI values and endothelial dysfunction in the elderly.

**Methods:** The study population comprised 35 men and women aged 51–77 years (mean age: 66 years). Patients with peripheral arterial disease or a history of heart failure were excluded. The ABI was estimated at rest and immediately after exercise. The exercise protocol comprised 2.5 min of active pedal flexion exercises at a speed of 60 times/min. Endothelial function was assessed by measuring flow-mediated vasodilation (FMD) in the brachial artery using ultrasound imaging.

**Results:** No correlation was found between FMD and the ABI at rest. However, a weak correlation was found between FMD and post-exercise ABI ( $r = 0.46$ ,  $P = 0.06$ ). A strong correlation was observed between FMD and a decrease in post-exercise ABI compared to baseline readings ( $r = -0.52$ ,  $P = 0.01$ ). Multiple linear regression analysis was used to generate a prediction equation for FMD using the percentage decrease in post-exercise ABI. Significant correlations were observed between the ultrasound imaging-measured FMD and the predicted FMD ( $R^2 = 0.27$ ,  $P = 0.001$ ).

**Conclusions:** Post-exercise ABI appears to be a simple surrogate marker for endothelial function in the elderly, although larger studies are required for validation.

**Keywords:** ABI, endothelial function, elder, FMD, exercise

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## Introduction

The endothelium, the monolayer of endothelial cells lining the lumen of all blood vessels, plays an important role in the regulation of vasomotor tone control with the release of vasoconstrictor mediators.<sup>1</sup> Endothelial function can be assessed by flow-mediated dilatation (FMD) which be carried out noninvasively with ultrasound techniques on the brachial artery. FMD are widely used as modalities for evaluating atherosclerosis and can be used to predict cardiovascular events.<sup>2,3</sup>

The ankle-brachial pressure index (ABI), the ratio of the systolic blood pressure of the ankle to the systolic brachial pressure, is an index of lower extremity arterial obstruction and a test for the screening of patients with peripheral arterial disease (PAD). In healthy subjects, the blood pressure in the ankle artery is higher than that in the brachial, but, when systemic atherosclerosis in an artery of the lower extremities is present, ankle blood flow is barred, resulting in a drop in ankle pressure. The ABI is commonly measured at rest, but ABI values post-exercise enhance the sensitivity of the test and can be used to identify subclinical atherosclerotic vascular damage.<sup>4,5</sup> However, it has not been established whether enhanced post-exercise ABI is also associated with endothelial dysfunction. We hypothesized that a decrease in post-exercise ABI is related to impaired endothelial function. To test this hypothesis, we investigated changes in post-exercise ABI values and FMD in the elderly.

## Material and Methods

The study population comprised 35 men and women aged 51–77 years (5 men, 30 women, mean age:  $66.2 \pm 6.7$  years) who were admitted to the Wellness 2008 Center in Osaka Sangyo University for exercise prescription and health counseling. Of these participants, 1 had angina pectoris, 4 had diabetes, and 3 had a history of smoking. Patients who had PAD or heart failure were excluded because of severe peripheral vascular damage. This study conformed to the ethical and human principles of research, and written informed consent was obtained from all study participants.

Resting ABI was measured by a Doppler flow meter (VaSera, VS-1000, Fukuda denshi, Japan) in

the supine position following a standard protocol. ABI was also measured immediately post-exercise.<sup>6</sup> The exercise protocol consisted of 2.5 minutes of active pedal flexion exercises at a speed of 60 times/min.<sup>6</sup>

Endothelial function was assessed by measuring FMD in the brachial artery using ultrasound imaging (UNEXEF, UNEX, Japan), as previously described.<sup>7</sup>

Data are expressed as mean  $\pm$  standard deviation (SD). Pearson's simple correlation coefficient between ABI and FMD was determined. Multivariate correlation analysis included age, body mass index, systolic blood pressure, and the presence of angina pectoris, as well as diabetes and a history of smoking, irrespective of the significance level in univariate analysis. A value of  $P < 0.05$  was considered statistically significant.

## Results

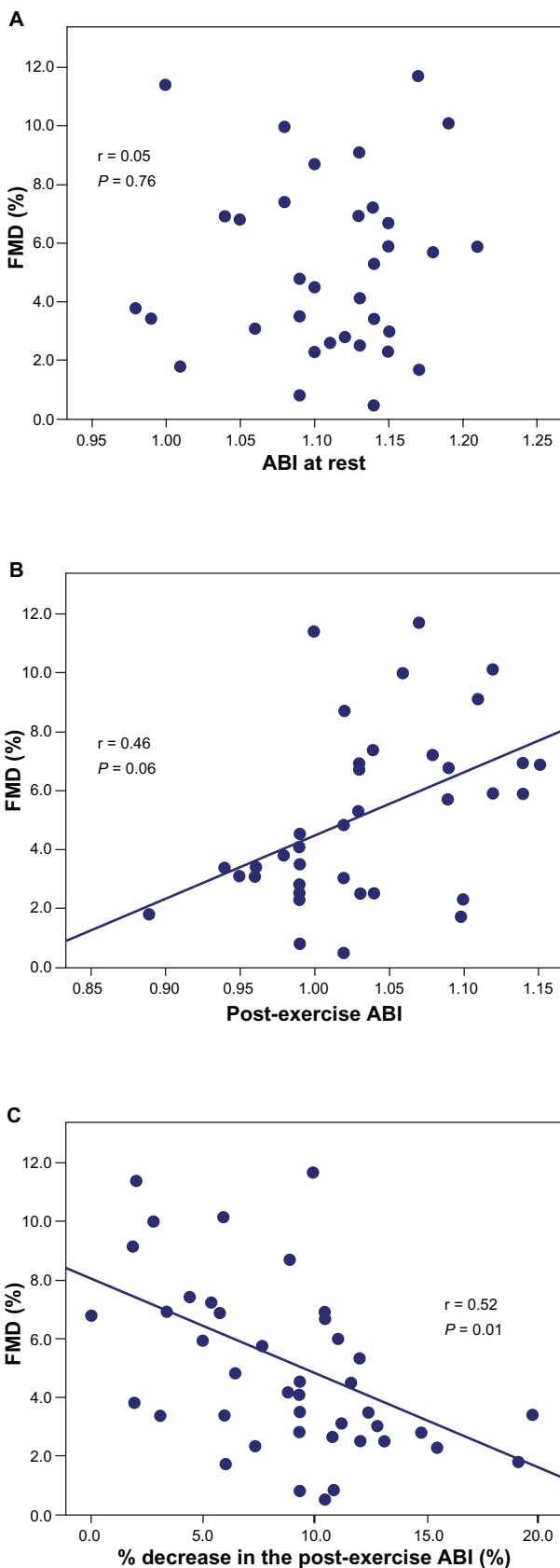
The mean FMD was  $5.24\% \pm 3.0\%$ , the mean ABI at rest was  $1.11 \pm 0.06$ , and the mean ABI after exercise was  $1.04 \pm 0.06$ . The mean reduction in post-exercise ABI from baseline readings was  $8.6\% \pm 4.8\%$  (Table 1).

No correlation was found between FMD and ABI at rest ( $r = 0.054$ ,  $P = 0.76$ ). However, a weak correlation was found between FMD and post-exercise ABI ( $r = 0.46$ ,  $P = 0.06$ ). A strong correlation was observed between FMD and the percentage decrease in post-exercise ABI compared to baseline readings ( $r = -0.52$ ,  $P = 0.01$ , Fig. 1). These associations could not be explained on the basis of individual differences in age, systolic blood pressure, or a history of angina pectoris, diabetes, or smoking.

Furthermore, multiple linear regression analysis was used to generate a prediction equation for FMD using the percentage decrease in post-exercise ABI [FMD =  $-0.32 \times$  (% decrease in post-exercise

**Table 1.** Characteristics of study population.

Characteristic	
Age	$66.2 \pm 6.7$
Body mass index (kg/m <sup>2</sup> )	$23.2 \pm 4.0$
Systolic blood pressure (mmHg)	$136 \pm 18$
ABI at rest	$1.11 \pm 0.06$
ABI after exercise	$1.04 \pm 0.06$
Percentage of reduction in post-exercise ABI (%)	$8.6 \pm 4.8$



**Figure 1.** Relationships between FMD and (A) ABI at rest, (B) ABI after exercise and (C) the percentage decrease in the post-exercise ABI.

ABI) + 8.00,  $R^2 = 0.25$ ,  $P = 0.001$ ]. Significant correlations were observed between the ultrasound imaging-measured FMD and the predicted FMD ( $R^2 = 0.27$ ,  $P = 0.001$ ).

## Discussion

The present study shows that an increased reduction in post-exercise ABI is associated with decreased FMD in elderly patients. Additionally, we developed a prediction model for FMD using the post-exercise ankle-brachial blood pressure. These results suggest that post-exercise ABI, that is, the exercise-induced ankle-brachial pressure mismatch, may be used as a simple surrogate parameter for the determination of endothelial function.

## Previous studies and advantages

Generally speaking, endothelial function and blood pressure are closely associated. Elevated systolic brachial pressure has been shown to contribute significantly to endothelial dysfunction, which is associated with increasing vasoconstriction. On the other hand, a functional alteration in the endothelium has been shown to result in high systolic brachial pressure. Notably, an exaggerated brachial pressure response to exercise is a sign of early stage endothelial dysfunction. Mirat et al suggested that impairment of endothelial function exists in normotensive subjects with exaggerated systolic brachial pressure during the maximal treadmill test.<sup>8</sup> Tzemos et al have shown that treated hypertensive subjects with an exaggerated brachial pressure response had endothelial dysfunction, as shown using a simple 3-minute exercise step-test. Further, we have previously demonstrated that a low-level exercise-induced increase in brachial blood pressure, but not resting blood pressure, is representative of endothelial dysfunction in postmenopausal females.<sup>9</sup> In the present study, we found that ABI, the ratio of ankle blood pressure to brachial pressure, dropped after exercise in patients with endothelial dysfunction.<sup>10</sup> To the best of our knowledge, this is the first study showing an association between ABI and endothelial function. Akopov et al have shown that the synthesis of nitric oxide, important for endothelial-mediated flow regulation, is also impaired in PAD to an extent related to the fall in post-exercise ABI.<sup>11</sup> These findings partly support our results.



## Clinical implications

Endothelial dysfunction is considered an early marker for sub-clinical atherosclerosis. Importantly, endothelial dysfunction has the potential for reversal with risk management or lipid-lowering therapy. Therefore, to improve prevention policies, all practitioners should pay attention to the presence of endothelial dysfunction, especially among participants with atherosclerotic risk factors.

The measurement of ABI has emerged as a simple surrogate marker for atherosclerosis and is highly predictive of total cardiovascular mortality. Several studies have demonstrated that ABI measured immediately post-exercise enhances this sensitivity. In a prospective cohort study, Feringa et al reported that a reduction in post-exercise ABI could identify patients who have normal resting ABI values but are at increased risk of long-term mortality.<sup>12</sup> Our study provides new insights into the potential benefits of measuring post-exercise ABI for identifying subclinical participants with endothelial dysfunction.

## Limitations

Our study had several limitations. First, we assessed endothelial function only at 1 point in time. Second, we did not obtain relevant clinical data for atherosclerotic risk factors likely to affect endothelial function, such as low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and hemoglobin A1c level. Finally, the number of patients was too small. Only a large-scale clinical trial can provide definitive evidence on this interesting clinical topic.

## Conclusions

To summarize, a reduction in post-exercise ABI from baseline readings is associated with endothelial dysfunction in elderly. Post-exercise ABI appears to be a simple and reliable surrogate marker for endothelial dysfunction in the elderly, although larger studies are required for validation.

## Disclosure

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors

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