Exercise-Ankle Brachial Pressure Index with One-Minute Treadmill Walking in Patients on Maintenance Hemodialysis

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Background: The ankle-brachial pressure index (ABI) is widely used as a standard screening method for arterial occlusive lesion above the knee. However, the sensitivity of ABI is low in hemodialysis (HD) patients. Exercise stress (Ex-ABI) may reduce the false negative results.

Patients and Methods: After measuring resting ABI and toe-brachial pressure index (TBI), ankle pressure and ABI immediately after walking (Post-AP, Post-ABI) were measured using one-minute treadmill walking in 52 lower limbs of 26 HD patients. The definition of peripheral arterial occlusive disease (PAD) required an ABI value of less than 0.90, TBI value of less than 0.60, and decrease of more than 15% of the Post-ABI value and 20 mmHg of Post-AP in Ex-ABI. Computed tomographic angiography (CTA) was performed in 32 lower limbs of 16 HD patients. PAD is defined as presence of stenosis of more than 75% in the case of lesions from an iliac artery to knee on CTA.

Results: The accuracy of Ex-ABI (Sensitivity, 85.7%; Specificity, 77.7%) was higher than those of ABI (Sensitivity, 42.9%; Specificity, 83.3%) or TBI (Sensitivity, 78.6%; Specificity, 61.1%).

Conclusion: Ex-ABI with one-minute treadmill walking is the most useful tool for the screening of arterial occlusive lesions above the knee in maintenance HD patients.

Keywords: peripheral arterial disease, exercise, diagnosis, screening, hemodialysis

INTRODUCTION

Patients undergoing hemodialysis (HD) are likely to develop peripheral arterial occlusive disease (PAD) due to complicated causation. PAD in HD patients is characterized by diffuse stenotic lesions below the knee. However, one-third of HD patients with lesions below the knee also have stenotic lesions above the knee1 and their presence accelerates progress to critical limb ischemia (CLI). Early detection of PAD is the most important factor for the management of CLI in HD patients and various examinations are performed for this purpose. Generally, skin perfusion pressure (SPP) is useful for the evaluation of microangiopathy below the knee or ankle.1 On the other hand, ankle-brachial pressure index (ABI) is widely used as a standard screening method for macroangiopathy above the knee. However, in HD patients, false negative results due to medial arterial calcification have been reported, which is problematic.2,3 With this background in mind, the toe-brachial pressure index (TBI), which circumvents the effects of calcification, is recommended as a screening method. However, the sensitivity of ABI for PAD can be improved by inducing ischemia of the lower limbs with an exercise (Ex-ABI),4,5 and this
Table 1  Clinical characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Patients who underwent CTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of limbs</td>
<td>52</td>
<td>32</td>
</tr>
<tr>
<td>Number of patients</td>
<td>26</td>
<td>16</td>
</tr>
<tr>
<td>Gender (men/women)</td>
<td>17/9</td>
<td>10/6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.2 ± 10.6</td>
<td>67.2 ± 10.0</td>
</tr>
<tr>
<td>Etiology of kidney disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10 (38.5)</td>
<td>5 (31.1)</td>
</tr>
<tr>
<td>Others</td>
<td>17 (61.5)</td>
<td>11 (68.8)</td>
</tr>
<tr>
<td>Dialysis duration (years)</td>
<td>8.4 ± 7.3</td>
<td>10.1 ± 7.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20 (76.9)</td>
<td>13 (81.3)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>7 (26.9)</td>
<td>4 (25.0)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>6 (23.1)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Intermittent claudication (limbs)</td>
<td>17 (32.7)</td>
<td>14 (43.8)</td>
</tr>
<tr>
<td>ABI at rest</td>
<td>1.04 ± 0.22</td>
<td>0.98 ± 0.23</td>
</tr>
<tr>
<td>ABI &lt; 0.9</td>
<td>12 (23.1)</td>
<td>9 (28.1)</td>
</tr>
<tr>
<td>ABI &gt; 1.3</td>
<td>4 (7.7)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Stenotic lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of limbs</td>
<td>16 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>11 (68.8)</td>
<td></td>
</tr>
</tbody>
</table>

ABI: ankle brachial pressure index; CTA: computed tomographic angiography (%)

Exercise-ABI in HD Patients

After measuring resting ABI and TBI, AP and ABI were measured immediately post-walking (Post-AP and Post-ABI) using the computerized treadmill system (CASE 12, Marquette Electronics, Milwaukee, WI, USA) following a protocol. Each patient’s 12-lead electrocardiogram and heart rate were monitored throughout the walking protocol for one minute (2.4 km/h, 12%). However, the walking speed was reduced to 2.0 km/h when the patient was more than 70 years old or was a low left ventricular function case. The supervising physician could stop the walking protocol based on the following criteria:

1. the development of significant symptoms such as chest pain or dizziness;
2. marked systolic hypotension or hypertension (more than 250/120 mmHg or a decrease in systolic blood pressure or HR in spite of increasing workload);
3. the development of dangerous or potentially dangerous arrhythmias; and
4. ST-segment deviations (horizontal or a downsloping depression of more than 80 ms from the J point) or elevation.

Room temperature was set at 25°C.

The definition of PAD required an ABI value of less than 0.90, TBI value of less than 0.60, and decrease more than 15% of the Post-ABI value and 20 mmHg of Post-AP in Ex-ABI. However, the result of Ex-ABI was judged to be test negative when the Post-AP was more than 120 mmHg.

Computed tomographic angiography (CTA) was performed in 16 patients (32 limbs) who gave informed consent on a non-HD day. To study the sensitivity and specificity of various measurements (ABI, TBI and Ex-ABI), PAD is defined as the presence of stenosis of more than 75% in the case of lesions from an iliac artery to knee on CTA (PAD-AK). CTA was performed with a 16-detector-row CT scanner (Aquilion 16; Toshiba Medical, Tokyo, Japan). The scanning range was planned with a scout view and included the entire vascular tree from the abdominal aorta to ankles. A total of 100 mL of contrast media (Proscope 300, Tokyo, Japan) was administered with an automated injector (Stellant; Medrad, Pennsylvania, USA) at a flow rate of 3 mL/sec through a 16 to 22-G needle that was placed in a superficial vein or blood access.

The presence of intermittent claudication was determined by walking impairment questionnaire. Hypertension was diagnosed when a study subject had received medical treatment for hypertension.
artery disease was defined as a previous history of angina pectoris or myocardial infarction. Cerebrovascular disease was defined as a previous history of clinical cerebral infarction or hemorrhage.

Data are presented as mean ±SD. A paired t-test was used for between before and after one-minute treadmill walking comparisons. Comparison of test positive rate between 3 measurements was performed using chi-square test in 3 × 2 tables. Significance was defined as P less than 0.05. All statistical analyses were performed using commercially available statistical software (StatMate III Ver.3.16, ATMS, Tokyo, Japan).

**RESULTS**

The mean ABI and TBI at rest were 1.04 ± 0.22 and 0.61 ± 0.22, respectively. All HD patients were performed Ex-ABI using one-minute treadmill walking. In the Ex-ABI, though brachial pressure increased significantly (7.0 ± 16.0 mmHg, p < 0.01), Post-AP decreased significantly (−26.6 ± 31.0 mmHg, p < 0.01). As a result, Post-ABI decreased significantly (−25.3 ± 21.9%, p < 0.01) (Fig. 1).

In test positive rate, though TBI (38.5%) was no significant difference compared with ABI (23.1%), Ex-ABI (42.3%) was higher than ABI (p < 0.05) (Fig. 2).

Of 26 HD patients, 16 patients gave informed consent. Basic characteristics of the 16 patients who underwent CTA are listed (Table 1). Nine of 32 limbs examined showed an ABI of less than 0.9. The sensitivity of ABI set at 0.9 for detecting PAD-AK was only 42.9%, although the specificity was 83.3% (positive predictive value, 66.7%; negative predictive value, 66.5%). Eighteen of 32 limbs examined showed TBI of less than 0.6. The sensitivity of TBI set at 0.6 for detecting PAD-AK was 78.6%, and specificity was 61.1% (positive predictive value, 61.1%; negative predictive value, 78.6%). Sixteen of 32 limbs examined showed positive finding in Ex-ABI. The sensitivity of Post-ABI set at −15% and Post-AP set at −20 mmHg for detecting PAD-AK was 85.7%, and the specificity was 77.8% (positive predictive value, 75.0%; negative predictive value, 87.5%) (Table 2).

**DISCUSSION**

In Japan, standard Ex-ABI testing involves walking on a treadmill inclined by 12% at a speed of 2.4 km/hr for 5 minutes. However, Ohta, et al. and Sugimoto et al. proposed to shorten the duration of walking from 5 to one minute. An advantage of this proposal is that Ex-ABI can be determined to detect PAD safely with a low exercise load in patients with heart disease or elderly patients with reduced exercise tolerance, while maintaining high diagnostic accuracy with a sensitivity of 78.8% and specificity of 93.8%. In this study, macroangiopathy in the lower limbs of HD patients were evaluated by Ex-ABI with one-minute treadmill walking for the first time.

In healthy individuals, the blood flow demand of lower limb skeletal muscles due to walking was met by increasing cardiac output and blood distribution to the skeletal muscles. At this time, as Post-AP increased simultaneously with brachial pressure, no change was measured in Post-ABI. However, in HD patients in this study, brachial pressure increased after walking, but Post-AP and ABI markedly decreased. These decreases in Post-AP and ABI are suggested to occur as blood in the skeletal muscles rapidly returns through veins to the right atrium by a milking action during walking, but the arterial blood supply is insufficient to...
Table 2  Sensitivity and specificity of three non-invasive measurements for peripheral artery occlusive lesion above the knee in HD patients

<table>
<thead>
<tr>
<th></th>
<th>ABI</th>
<th>TBI</th>
<th>Ex-ABI</th>
</tr>
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<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>42.9</td>
<td>78.6</td>
<td>85.7</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>83.3</td>
<td>61.1</td>
<td>77.8</td>
</tr>
</tbody>
</table>

ABI: ankle brachial pressure index; TBI: toe brachial pressure index; Ex: exercise

balance this venous return and fails to fill the arteries. Therefore, decreases in Post-AP and ABI strongly suggest the presence of a stenotic lesion in the lumen of a lower limb artery, causing a decrease in the blood flow reserve to areas below the lesion.

Generally, ABI is widely used for the evaluation of blood flow reserve in PAD not only in HD patients, but also all patients, because of the high diagnostic accuracy with a specificity of 100% and maximum sensitivity of 95%. In HD patients, however, it has been reported that the sensitivity of an ABI less than 0.9 was very low at 29%, while the specificity was 100% for the detection of PAD. This is primarily due to medial arterial calcification, which causes deviations in the normal value of ABI to the right. According to our study, more abnormal findings could be induced by the Ex-ABI than ABI. Priority should be placed on high sensitivity for screening. Therefore, Ex-ABI is considered to be a better screening test than ABI for the detection of PAD-AK.

TBI is the brachial pressure divided by the great toe pressure and can be used as an index of lower limb macroangiopathy similarly to ABI. Since calcification rarely extends to toe arteries, TBI has been suggested to be a substitute for ABI in HD patients. According to our study, more abnormal findings could be observed by Ex-ABI than by TBI. This result suggests that PAD can be detected earlier using Ex-ABI, which is less affected by medial arterial calcification, than by ABI or TBI.

In HD patients, positive findings could be more readily detected using Ex-ABI than ABI or TBI. However, the percentage of false-positive results in positive results should be clarified. Although Ex-ABI after one-minute exercise has a high diagnostic accuracy in non-HD patients, it is unclear whether this tool can be directly applied to HD patients. We performed CTA in the subjects whenever possible, and compared the findings with the diagnostic results of the 3 measurements.

As a result, the sensitivity and specificity of Ex-ABI were higher than those of ABI or TBI.

SPP is the most useful for evaluating below the knee or ankle microangiopathy. For the evaluation of above the knee stenotic lesions, ABI is considered to be useful, but its sensitivity has been reported to be low in HD patients. In this study, Ex-ABI in HD patients overcame this problem of ABI on screening for above the knee stenotic lesions by increasing the positive result rate and reducing the false-positive rate.

**STUDY LIMITATIONS**

With CTA, it is difficult to visualize lumens with blood flow within severe calcification lesions. In addition, the possibility that patients with multi-vessel occlusive lesions below the knee affected the diagnostic accuracy of each measurement cannot be excluded.

**CONCLUSION**

Ex-ABI with one-minute treadmill walking is most useful tool for a screening of arterial occlusive lesion above the knee in maintenance HD patients.

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**DISCLOSURE STATEMENT**

The authors declare that they have no competing interests.

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