Impact of Carotid Artery Ultrasound and Ankle-Brachial Index on Prediction of Severity of SYNTAX Score

Nobutaka Ikeda, PhD; Norihiro Kogame, MD; Raisuke Iijima, PhD; Masato Nakamura, PhD; Kaoru Sugi, PhD

Background: Numerous reports have shown that both carotid artery ultrasound (carotid US) findings and ankle-brachial index (ABI) are associated with the prevalence of coronary artery disease. The relationship between carotid US findings and ABI and the complexity of coronary artery disease (as measured by SYNTAX [SX] score), was evaluated.

Methods and Results: The subjects included 496 consecutive patients who underwent carotid US, ABI analysis and initial coronary angiography. The mean common carotid artery intima-media thickness (mean IMT) was evaluated on carotid US. Patients with mean IMT ≥0.9 mm had significantly higher SX scores than patients without thickening (mean IMT <0.9mm; P<0.0001). Similarly, patients with low ABI (<0.9) had significantly higher SX scores than patients with ABI ≥0.9 (P<0.0001). When the patients were divided into 4 groups on the basis of mean IMT and ABI (group A, mean IMT <0.9 mm, ABI ≥0.9; group B, mean IMT <0.9 mm, low ABI; group C, mean IMT ≥0.9 mm, ABI ≥0.9; group D, mean IMT ≥0.9 mm, low ABI), the SX scores were significantly different. Among the patients in group D, 75% had coronary artery disease.

Conclusions: Carotid US and ABI are associated with SX score. The combination of carotid US and ABI provides useful information for predicting the complexity and presence of coronary artery disease. (Circ J 2013; 77: 712–716)

Key Words: Ankle-brachial index; Carotid intima-media thickness; Coronary disease; Peripheral vascular disease

The guidelines for conducting triage for cardiac catheterization recommend risk assessment and non-invasive testing.1–3 The effectiveness of non-invasive tests, however, is insufficient. Even if tests (including exercise or pharmacologic stress tests, radionuclide tests, ultrasound [US], computed tomography or other heart scans), are performed before coronary angiography, the diagnostic yield of elective cardiac catheterization is reported at <40%.4

Previous epidemiologic and clinical studies have shown a relationship between carotid artery US (carotid US) findings and the prevalence of coronary artery disease. Most studies use intima-media thickness (IMT) as an index of measurement.5–9 Similar to the IMT findings, previous reports have found that ankle-brachial index (ABI) provides meaningful information on the presence of coronary artery disease.10 More than half of the patients with peripheral artery disease have cardiovascular disease.11 This indicates that the demonstration of coronary artery disease is strengthened by an examination for generalized atherosclerosis. We previously reported the relationship between carotid US findings and coronary lesion complexity.12 No previous studies, however, have reported on the relationship between the complexity of coronary lesions and generalized atherosclerosis including ABI. Recently, the SYNTAX (SX) score, which represents lesion complexity, has been shown to be useful for decision-making and estimating prognoses among patients who have undergone coronary revascularization.13–18 In the drug-eluting stent era, early detection of multivessel coronary artery disease and complete revascularization improves prognosis of patients.19 In this study, we examined the potential efficacy of the combination of carotid US finding and ABI in predicting SX score.

Methods

The subjects included 496 consecutive patients who were admitted to Toho University Ohashi Medical Center and who underwent carotid US, ABI analysis and initial coronary angiography between December 2008 and January 2011. We retrospectively extracted these subjects from the database used for our previous report.12 Coronary angiography was performed to screen
for ischemic heart disease or cardiomyopathy and as a preoperative investigation for ischemic heart or valve disease. This study complied with the Declaration of Helsinki, and written informed consent was obtained from all patients.

### Carotid US

Using carotid US, the mean common carotid artery IMT was evaluated. High resolution B-mode, color Doppler, and pulse Doppler US of both carotid arteries were performed by an experienced sonographer with either one of the following US scanners (Aplio XV, Aplio XG, Xario; Toshiba, Tokyo, Japan) equipped with a 7.5-MHz linear array transducer. The sonographer and the interpreting cardiologist were blinded to the angiographic findings. Patients were examined in the supine position with their heads tilted backward. After the carotid arteries were located by transverse scans, the probe was rotated 90° to obtain and record longitudinal images of bilateral carotid arteries. High-resolution images were obtained of the far wall of the bilateral common carotid arteries, internal carotid arteries, and carotid bulbs, according to the recommendations of the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. IMT was defined as the distance between the leading edge of the lumen-intima echo and the leading edge of the media-adventitia echo (Figure 1). At least 3 measurements were taken over a 1-cm length of each common carotid artery, and measurements from both sides were averaged to obtain the mean IMT. When plaque was present in the segment used for measuring the mean IMT, the plaque thickness was averaged into the mean IMT measurement.

### Measurement of ABI

Each patient was evaluated in the supine position after resting for 5 min. ABI was measured in each leg using a volume plethysmograph (FORM/ABI; Colin, Komaki, Japan) while the patient remained in the same position. All recordings were performed while the patients were receiving their regular medication. For the purpose of this analysis, the lowest ABI obtained for either leg was taken as the ABI measurement for the patient.

### SX Score and Angiography

Coronary artery stenosis was defined as stenosis with a diameter ≥50%. On the basis of the baseline diagnostic angiogram, each coronary lesion producing stenosis with a diameter ≥50% in vessels ≥1.5 mm in diameter was scored separately, and these scores were combined to provide the overall SX score, which was calculated using the SX score algorithm. This algorithm is available on the SYNTAX website.

The SX scores were independently assessed by 2 experienced interventional cardiologists who were blinded to the carotid US and ABI data. They had experience with calculating the SX scores of more than 100 patients before assisting in the present study. The \( \kappa \) for inter-observer variability that was used to estimate the SX score was 0.75, whereas the \( \kappa \) for intra-observer variability was 0.709.

### Measurement of IMT

IMT was defined as the distance between the leading edge of the lumen-intima echo and the leading edge of the media-adventitia echo (Figure 1). At least 3 measurements were taken over a 1-cm length of each common carotid artery, and measurements from both sides were averaged to obtain the mean IMT. When plaque was present in the segment used for measuring the mean IMT, the plaque thickness was averaged into the mean IMT measurement.

### Table. Patient Characteristics

<table>
<thead>
<tr>
<th>Subject</th>
<th>Total</th>
<th>Mean IMT ≥0.9 mm</th>
<th>Mean IMT &lt;0.9 mm</th>
<th>P-value</th>
<th>ABI &lt;0.9</th>
<th>ABI ≥0.9</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>496</td>
<td>273 (55.0)</td>
<td>223 (45.0)</td>
<td>0.709</td>
<td>63 (12.7)</td>
<td>433 (87.3)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>310 (62.5)</td>
<td>173 (63.4)</td>
<td>137 (61.4)</td>
<td>0.070</td>
<td>37 (58.7)</td>
<td>273 (63.0)</td>
<td>0.578</td>
</tr>
<tr>
<td>Age (years)</td>
<td>69.2±11.4</td>
<td>73.2±9.5</td>
<td>64.4±11.7</td>
<td>&lt;0.0001</td>
<td>73.2±10.1</td>
<td>68.7±11.5</td>
<td>0.003</td>
</tr>
<tr>
<td>DM</td>
<td>88 (17.7)</td>
<td>55 (20.1)</td>
<td>31 (13.9)</td>
<td>0.070</td>
<td>16 (25.4)</td>
<td>70 (16.2)</td>
<td>0.076</td>
</tr>
<tr>
<td>Hypertension</td>
<td>281 (56.7)</td>
<td>177 (64.8)</td>
<td>104 (46.6)</td>
<td>&lt;0.0001</td>
<td>42 (66.7)</td>
<td>239 (55.2)</td>
<td>0.102</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>178 (35.9)</td>
<td>105 (38.5)</td>
<td>73 (32.7)</td>
<td>0.190</td>
<td>27 (42.9)</td>
<td>151 (34.9)</td>
<td>0.261</td>
</tr>
<tr>
<td>Mean IMT (mm)</td>
<td>0.90 (0.75–1.20)</td>
<td>1.15 (0.95–1.40)</td>
<td>0.75 (0.65–0.80)</td>
<td>&lt;0.0001</td>
<td>1.39 (0.90–1.70)</td>
<td>0.90 (0.75–1.10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ABI &lt;0.9</td>
<td>63 (12.9)</td>
<td>48 (17.6)</td>
<td>15 (6.7)</td>
<td>0.0004</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SYNTAX score</td>
<td>0 (0–12)</td>
<td>5 (0–23)</td>
<td>0 (0–8)</td>
<td>&lt;0.0001</td>
<td>14 (0–31)</td>
<td>0 (0–10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.3 (5.5–5.8)</td>
<td>5.4 (5–6)</td>
<td>5.3 (5.0–5.7)</td>
<td>0.060</td>
<td>5.6 (5.0–6.2)</td>
<td>5.3 (5.0–5.8)</td>
<td>0.080</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>181 (158–205)</td>
<td>181±40.8</td>
<td>184±33.8</td>
<td>0.528</td>
<td>173±46.6</td>
<td>184±36.2</td>
<td>0.043</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>102 (81–126)</td>
<td>101 (82–131)</td>
<td>103 (70–118)</td>
<td>0.390</td>
<td>99 (72–116)</td>
<td>103 (82–130)</td>
<td>0.355</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>51 (42–62)</td>
<td>53.3±14.8</td>
<td>53.4±15.7</td>
<td>0.930</td>
<td>49.9±15.0</td>
<td>54.0±15.1</td>
<td>0.129</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>108 (76–145)</td>
<td>108 (75–138)</td>
<td>107 (77–154)</td>
<td>0.162</td>
<td>110 (72–143)</td>
<td>108 (76–147)</td>
<td>0.754</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>102 (91–116)</td>
<td>102 (91–116)</td>
<td>101 (90–118)</td>
<td>0.680</td>
<td>107 (90–126)</td>
<td>101 (91–115)</td>
<td>0.134</td>
</tr>
</tbody>
</table>

Data given as n (%), mean±SD or median (interquartile range).

ABI, ankle-brachial index; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; IMT, intima-media thickness; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.
Results

Patient characteristics are listed in Table. The mean age was 69.2 years; 310 patients (62.5%) were male, 88 (17.7%) had diabetes mellitus, and 108 (21.8%) were current smokers. Patients with carotid mean IMT ≥0.9 mm had significantly higher SX scores than patients without thickening (mean IMT <0.9 mm) (5, 0–23 vs. 0, 0–3; P<0.0001). Similarly, patients with low ABI (<0.9) had significantly higher SX scores than patients with ABI ≥0.9 (14, 0–31 vs. 0, 0–10; P<0.0001). When the patients were divided into 4 groups (group A, mean IMT <0.9 mm, ABI ≥0.9; group B, mean IMT <0.9 mm, low ABI; group C, mean IMT ≥0.9 mm, ABI ≥0.9; group D, mean IMT ≥0.9 mm, low ABI), the SX scores of the groups were significantly different (group A, n=208: 0, 0–3; group B, n=15: 0, 0–16; group C, n=225: 2, 0–20; group D, n=48: 17, 1–35; P<0.0001; Figure 2). Among the patients in group D, 75%...
had coronary artery disease (SX score was not 0; Figure 3).

**Discussion**

The principal finding of the present study was that carotid US results and ABI are associated with the complexity of coronary artery disease. Furthermore, the combination of these 2 non-invasive tests makes the estimation of lesion complexity, as well as the detection of the presence of coronary artery disease, more accurate.

There is considerable overlap with regard to peripheral artery disease and cardiovascular disease, and previous studies have demonstrated that subjects with low ABI have a considerably higher prevalence of cardiovascular disease than those with normal ABI.\(^2\) Additionally, ABI can predict future coronary events, including total cardiovascular disease and all-cause mortality.\(^2\,4\)\(^5\,8\)\(^9\)\(^13\)\(^14\) There have been no reports, however, concerning the relationship between ABI and the complexity of coronary artery disease.

Many previous studies have demonstrated a relationship between carotid US findings and the prevalence or severity of coronary artery disease. These investigations have suggested that ABI and IMT could be useful surrogate markers for severity of coronary artery disease, based on the number of diseased coronary arteries, and to predict future cardiovascular events.\(^5\)\(^6\)\(^7\)\(^9\)\(^13\)\(^24\)\(^25\)\(^26\)

As far as we know, no studies have investigated the relationship between ABI, carotid US, and the complexity of coronary artery disease. Therefore, this is the first report to present the hypothesis that the evaluation of generalized atherosclerosis by mean IMT and ABI measurement indicates the complexity of coronary artery disease. In addition, the combination of the 2 non-invasive tests provides further precise information regarding lesion complexity, as well as the presence of coronary artery disease.

The mean IMT threshold used in this analysis corresponded to that in our previous report and to values ≥0.9 mm for most middle-aged men and women in the Atherosclerosis Risk in Communities study.\(^8\)\(^24\)\(^25\)\(^26\) But 55% of the present patients had mean IMT >0.9 mm. This finding can be explained by the nature of the present patients, who were candidates for elective coronary angiography. Conversely, we used a cut-off of 0.9 for ABI, according to the definition of the PARTNERS program.\(^11\) ABI <0.9 strongly suggests the presence of stenosis of a lower limb artery, but a mean IMT >0.9 mm does not equal the presence of stenosis of the carotid artery. Therefore, it is reasonable to hypothesize that a low ABI represents more advanced atherosclerosis than a slightly thicker mean IMT. Only 12.7% of the present patients had a low ABI <0.9, in contrast to the 55% with a mean IMT >0.9 mm. Nevertheless, the prevalence of coronary artery disease in patients with a low ABI <0.9 and with a mean IMT ≥0.9 mm was 67% and 56%, respectively, and the difference was not significant. This may mean that carotid US is a more useful test for detecting coronary artery atherosclerosis. The combination of the 2 non-invasive tests provides for better prediction of the presence and complexity of coronary artery disease. In addition, traditional risk factors (diabetes mellitus, hypertension, dyslipidemia and smoking) also help to stratify risk. In group A, 75 patients had no risk factor, and only 17.3% (n=13) of the patients had coronary artery disease. In contrast, 22 patients in group D had 2 and more risk factors, and 81.8% (n=18) had coronary artery disease. In particular, 11 patients with diabetes mellitus and other risk factors in group D had coronary artery disease: a very high prevalence (90.9%).

The REACH registry showed that the presence of polivascular disease is associated with poor prognosis and is an independent predictor of cardiovascular events.\(^2\)\(^7\) Furthermore, coronary artery disease with peripheral artery disease and multivessel disease with complex lesion morphology have been more frequently compared with isolated coronary artery disease.\(^8\)\(^26\) Conversely, recent clinical trials have clearly demonstrated that both the assessment of the classic categories, such as the number of diseased coronary arteries, and the complexity of coronary lesion morphology are useful for predicting major adverse cardiovascular and cerebrovascular events in patients who undergo percutaneous coronary intervention.\(^29\)\(^30\) Taken together, these previous findings seem to support the present findings: that group D (IMT ≥0.9 mm and ABI <0.9) was associated with both a greater probability of the presence of coronary artery disease and also with complex coronary artery disease (higher SX score). The present study suggests that we can detect both the presence of coronary artery disease and also complex coronary artery lesions using a combination of non-invasive methods. Furthermore, the present findings could be translated into a prediction of future cardiovascular events and may help in decision-making for treatment strategies, such as aggressive risk management and coronary revascularization.

**Study Limitations**

This study had some limitations. First, the completely occluded part of the carotid artery is not suitable for evaluating mean IMT. This fact may have affected the final results. Second, because the patients enrolled in the present study were candidates for elective coronary angiography, these subjects had a relatively greater risk than the healthy population. Therefore, it is not clear whether the present results would apply when screening the general asymptomatic population (eg, at a health checkup). Third, the present patients had relatively low SX scores, and >50% of patients had SX score of 0. Fourth, we did not have detailed data about medications or previous treatment for peripheral artery disease.

**Conclusions**

The combination of mean IMT and ABI provides useful information for predicting the complexity and prevalence of coronary artery disease. Large, prospective studies are still necessary to establish the link between these parameters and the complexity of coronary artery disease.

**Acknowledgments**

We thank the physiological laboratory staff for their excellent technical support.

**Disclosures**

None.

**References**


2. Fraker TD, Fihn SD, Gibbons RJ, Abrams J, Chatterjee K, Daley J, et al. 2007 chronic angina focused update of the ACC/AHA 2002 guidelines for the management of patients with chronic stable angina: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to develop the focused update of the 2002 guidelines for the manage-


