Assessment of the Arterial Stiffness Index as a Clinical Parameter for Atherosclerotic Coronary Artery Disease

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ABSTRACT

Background: Arterial stiffening increases both the systolic blood and pulse pressures, which is known to be a major contributor to atherosclerosis and the most important cause of cardiovascular disease. The aims of this study were to assess the feasibility of the arterial stiffness index (ASI), using a computerized oscillometric device, by comparison with the pulse wave velocity (PWV), and to investigate its usefulness to patients with clinical coronary artery disease. Methods: 60-consecutive patients, who underwent coronary angiography and who’s aorto-femoral PWV were obtained with a Judkins catheter, were the subjects of this study. The ASI was obtained for all patients, using CardioVision® MS-2000 (IMDP, Las Vegas, NV), with cuff pressure on the brachial artery. The ASI were obtained as follows: 1) at the baseline (ASI-B), 2) after hyperemia induced by compression of the arm with cuff pressure for 5 minutes (ASI-H), 3) after having taken sublingual nitroglycerin (ASI-N). Results: 34-patients had significant coronary artery disease (CAD) from the coronary angiography findings. All the ASI were positively correlated to the PWV, and were also higher in patients with CAD (ASI-B, 85.9±57.8 vs. 48.2±24.5, p=0.001; ASI-H, 98.1±49.8 vs. 48.1±21.3, p=0.00; ASI-N, 66.7±55.7 vs. 33.2±27.9, p=0.002). The ASI-H was mostly well correlated to the PWV and the severity of CAD (PWV, r=0.49, p=0.00; severity, r=0.52, p=0.00). The ASI was increased after hyperemia in patients with CAD (85.9±57.8 to 98.1±49.8, p=0.01), but was not significantly changed in those without CAD (48.2±24.5 to 48.1±21.3, p=0.68). The ASI-N was decreased in all patients. Conclusions: The Arterial Stiffness Index, measured non-invasively by computerized oscillometry, was feasible and useful for detection of atherosclerotic coronary disease. Especially, the difference in the ASI between patients with and without CAD was more apparent after hyperemia. These findings suggest that in addition to stiffening of the arterial wall itself, the impairment of flow mediated vasodilation, due to endothelial dysfunction, further increases the arterial stiffness. (Korean Circulation J 2004;34(7):677-683)

KEY WORDS: Compliance; Coronary atherosclerosis; Oscillometry.

Introduction

Stiffening of the arterial tree increase the systolic blood pressure (BP), and simultaneously decreases the diastolic BP, resulting in a wide ranging pulse pressure (PP). Many studies have shown that the arterial stiffness, when determined invasively, is the most important cause of cardiovascular complications and a major contributor to atherosclerosis, and thus to strokes, myocardial infarctions and renal failure. However, invasive techniques are of limited value for the screening and risk stratification of clinical cardiovascular disease. So, considering the increasing emphasis placed on primary prevention of cardiovascular diseases, the development of non-invasive techniques to identify high risk patients and to assess the prognosis of future atherosclerotic burden is very important. Recently, a new clinical device, the CardioVision®...
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MS-2000 (IMDP, Las Vegas, NV) was developed to simultaneously measure the arterial stiffness index (ASI), brachial arterial BP and PP. Thus, the aims of this study were to evaluate the feasibility of ASI, using the computerized oscillometric device, by comparison with the pulse wave velocity (PWV), via femoral arterial catheterization, and investigate the association between clinical coronary artery disease and the ASI.

Methods

Study populations

60-consecutive patients (30 men and 30 women; mean age=66±7 years), who underwent coronary angiography and who’s arterial pulse wave was recorded with a right Judkins catheter were the subjects of this study. Patients that had had a myocardial infarction or acute coronary syndrome within the last 3 months, valvular heart disease, arrhythmia, decreased left ventricular function (ejection fraction<50%) or chronic renal failure were excluded. All patients refrained from caffeine containing beverages, alcohol and smoking for at least 4 hours prior to the study. All vasoactive medications were discontinued in all patients for at least 12 hours prior to the study.

Coronary angiography

Routine biplane coronary angiography, using the Judkins technique, was performed in all patients. Significant coronary artery stenosis was defined as >50% narrowing in the vessel diameter on the coronary angiogram. All patients were divided into either those with coronary artery disease (defined as at least one vessel with coronary artery stenosis ≥50%) or those without coronary artery disease. The severity of the coronary artery disease (CAD) was based on the number of stenotic coronary vessels.

Pulse wave velocity obtainment

After diagnostic coronary angiography in all patients, the pulse waves and electrocardiograms were recorded at the aortic arch and right femoral artery with a Judkins catheter. The time delay between the arrivals of pulse waves at these 2 points was obtained by gating to the peak of the R-wave of the electrocardiogram. The distance traveled by the pulse wave was measured with the Judkins catheter length, then the PWV calculated as the distance/time (m/sec).

Measurement of arterial stiffness index

Assessment of the arterial stiffness was performed non-invasively with the CardioVision®MS-2000 (IMDP, Las Vegas, NV). This device provides the BP, PP and brachial artery stiffness. It utilizes a computerized oscillometric method of BP measurement and through a press-

![Figure 1. Measurement of the arterial stiffness index (ASI). BP: blood pressure.](image-url)
sure sensor attached to the BP cuff (Figure 1). In all patients, the ASI was measured as follows: 1) at rest as the baseline (ASI-B), 2) after hyperemia induced by compression of the arm with cuff pressure for 5 minutes (ASI-H), 3) after having taken 0.5 mg nitroglycerin sublingually (ASI-N).

Statistics
For descriptive purposes, all data are presented as the mean value ± SD and relative frequencies, as indicated. Differences in the mean values between those patients with and without CAD were analyzed using ‘Student T-tests’. Comparison of the arterial stiffness indices in each group was performed using ‘paired t-tests’. A p-value of < 0.05 was considered statistically significant.

Results
Clinical characteristics
The baseline clinical characteristics of the patients are summarized in Table 1. The patients with CAD were older than those without (65 ± 7 years versus 54 ± 10 years, \( p = 0.00 \)). Most patients had hypertension (86.7%), and the frequencies of hypertension and diabetes were higher in the patients with CAD than in those without.

| Table 1. Baseline characteristics of the study patients |
|---------------------------------|----------------|----------------|-----|
| Number of patients | 26 | 34 | \( p = 0.00 \) |
| Averaged age (years)* | 54 ± 10 | 65 ± 7 | 0.008 |
| Men: Women | 13 : 13 | 16 : 18 | |
| Diabetes | 4 (15%) | 10 (29%) | |
| Hypertension | 21 (81%) | 31 (91%) | 0.73 |
| Dyslipidemia | 12 (46%) | 8 (53%) | |
| Smoking | 5 (19%) | 4 (1.1%) | |
| BMI (>25 kg/m²) | 12 (46%) | 10 (29%) | |
| Medication | 10 (38%) | 32 (94%) | 0.005 |
| SBP (mmHg) | 128 ± 15 | 143 ± 26 | 0.008 |
| DBP (mmHg) | 76 ± 9 | 80 ± 13 | 0.18 |
| MBP (mmHg) | 113 ± 16 | 114 ± 23 | 0.73 |
| HR (/min) | 66 ± 12 | 68 ± 12 | 0.65 |
| PP (mmHg) | 52 ± 11 | 63 ± 12 | 0.005 |
| PWV (m/sec) | 10.4 ± 2.4 | 14.0 ± 2.9 | 0.00 |

BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, PP: pulse pressure, PWV: pulse wave velocity

Figure 2. Age was one of the greatest factors affecting the arterial stiffness index (ASI). PWV: pulse wave velocity, B: baseline, H: hyperemia, N: nitroglycerin, \( p < 0.05 \).
Of note, the difference in the pulse pressure was mediated mainly by a higher systolic BP in the patients with CAD (143±26 mmHg versus 128±15 mmHg, p = 0.008). As known previously, the PWV was higher in patients with CAD than in those without (14.0±2.9 m/sec versus 10.4±2.4 m/sec, p=0.00) and well correlated to the severity of CAD (r=0.53, p=0.00, Figure 5).

**Correlation between pulse wave velocity and arterial stiffness index**

Both the PWV and ASI increased with aging (Figure 2). The ASI also increased with the PWV after adjusted for age, but only the ASI-H had a positive correlation with the PWV (r=0.29, p=0.03). The strong factors affecting

### Table 2. Correlations with the arterial stiffness index (ASI)

<table>
<thead>
<tr>
<th></th>
<th>ASI-B</th>
<th>ASI-H</th>
<th>ASI-N</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>0.76</td>
<td>0.68</td>
<td>0.69</td>
</tr>
<tr>
<td>DBP</td>
<td>0.39</td>
<td>0.33</td>
<td>0.47</td>
</tr>
<tr>
<td>PP</td>
<td>0.81</td>
<td>0.65</td>
<td>0.56</td>
</tr>
<tr>
<td>Age</td>
<td>0.48</td>
<td>0.54</td>
<td>0.34</td>
</tr>
</tbody>
</table>

p<0.05 in all cases. B,H,N: baseline, hyperemia, nitroglycerin. SBP (mmHg): systolic blood pressure, DBP (mmHg): diastolic blood pressure, PP (mmHg): pulse pressure

### Table 3. Comparison of the arterial stiffness index (ASI)

<table>
<thead>
<tr>
<th></th>
<th>CAD (−)</th>
<th>CAD (+)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASI-B</td>
<td>48.2±24.5</td>
<td>85.9±57.8</td>
<td>0.001</td>
</tr>
<tr>
<td>ASI-H</td>
<td>48.1±21.3</td>
<td>98.1±49.8</td>
<td>0.000</td>
</tr>
<tr>
<td>ASI-N</td>
<td>33.2±27.9</td>
<td>36.4±11.3</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Figure 3. Changes in the arterial stiffness index (ASI) in patients without coronary artery disease. B: baseline, H: hyperemia, N: nitroglycerin. *: p=0.68, †: p=0.00

Figure 4. Changes in the arterial stiffness index (ASI) in patients with coronary artery disease. B: baseline, H: hyperemia, N: nitroglycerin. *: p=0.01, †: p=0.00

Figure 5. Correlation between the arterial stiffness index (ASI) and the severity of coronary artery disease. PWV: pulse wave velocity, B: baseline, H: hyperemia, N: nitroglycerin.
the ASI were the systolic BP and PP (Table 2).

**Arterial stiffness index and coronary artery disease**

All the ASI were higher in patients with CAD than in those without (Table 3). In patients without CAD, there were no differences between the ASI-B and ASI-H, and the ASI decreased after having taken nitroglycerin (Figure 3). Compared with the patients without CAD, there were some differences in the response to hyperemia and nitroglycerin in patients with CAD. After hyperemia, the ASI increased (85.9 ± 57.8 to 98.1 ± 49.8, p=0.01) and after having taken nitroglycerin, the ASI decreased (85.9 ± 57.8 to 66.7 ± 55.7, p=0.00, Figure 4). All the ASI were positively correlated to the severity of CAD, and the ASI-H was especially strongly correlated with the PWV ($r=0.52$, p=0.00, Figure 5). Comparing the diagnostic accuracy between the ASI-B, ASI-H and ASI-N, the ASI-H with a cut-off value of 45 was most valuable; the sensitivity, specificity and diagnostic accuracy were 74.4, 88.2 and 78.3%, respectively, which were not inferior to those of treadmill test.

**Discussion**

Even when atherosclerotic vascular disease is advanced, it remains clinically silent if the blood flow is maintained. It is very useful to detect imminent clinical atherosclerotic coronary artery, with non-invasive methods, for the prevention of its clinical manifestations and complications. In the present study, the feasibility of the ASI was evaluated as a parameter of clinical atherosclerotic coronary artery disease. Furthermore, the severity of atherosclerosis in the coronary bed was found to correlate positively with the ASI on the brachial artery, which agreed well with previous studies.9,10 Recently, a new clinical testing device, the CardioVision®MS-2000 (IMDP, Las Vegas, NV), was developed to simultaneously measure the arterial BP, PP and arterial stiffness index. The changes in the stiffness of the large arteries, such as the aorta and its major branches, largely account for the changes in the systolic and diastolic BP and PP. In the computerized oscillometric method, the cuff is filled with air, and the cuff volume change can be measured as a change in the inner pressure. Because of the arterial pressure-volume properties, when the cuff pressure equals the mean BP, the elastic modulus of the brachial artery is at a minimum (i.e. the expendability of the artery is at its greatest). Therefore, when the cuff pressure decreases to the mean BP, the artery increases in elasticity and the arterial volume change caused by the PP of the blood vessel increases. Thus, this device determines the BP and arterial stiffness according to the arterial volume pattern changes caused by the steady decreasing cuff pressure.7,8 The arterial distensibility, defined as the ratio of change of volume to the change in pressure (or the slope of the pressure volume curve), has been described as a marker for predicting vascular disease in studies.9-11 The distensibility of both the large and small arterial systems serves as a cushion to buffer the pulsatile pressure and flow. A reduced buffering capacity leads to amplification of the reflected pressure waves and a more rapid PWV. The CardioVision®MS-2000 device was based on these mechanisms, and the ASI was found to correlate well to the PWV in our study. Atherosclerosis refers to a concentric hyaline thickening of the arterial and arteriolar wall, together with endothelial dysfunction, smooth muscle cell proliferation, deposition of lipid, and accumulation of collagen, elastin and proteoglycans. Endothelial dysfunction, with a release of nitric oxide, produces vasoconstriction, which reduces the compliance. As atherosclerosis progresses, the tunica media thickens and the tunica intimas becomes rigid, thus reducing the arterial elasticity.12-14 Reduced arterial distensibility has been shown to be associated with atherosclerotic events.15-17 Stefanadis et al18 found that coronary ischemic disease was substantially associated with increased aortic stiffness. When arteries are stiffer and the PWV higher, the reflected waves arrive earlier and augment the central systolic BP, rather than the diastolic BP, which increases the left ventricular workload and compromises the coronary
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blood flow. With increasing age, the function-al and structural changes in the arterial wall influence the reac-
tivity of the arteries and accelerate the atherogenic pro-
cess, with an average age for myocardial infarction of 62 
years. In this study, in addition to the traditional me-
thod, the measurement of the ASI after and with nitro-
glycerin, to some extent, indicated a relationship between 
the arterial endothelial and smooth muscle functions. 
Our study agreed towel with previous studies, in which 
the arterial stiffness was inversely correlated to age. 
It was our assumption that all patients had some impair-
ment in their flow-mediated vasodilation because they 
were all older and had other atherosclerotic risk factors. 
Therefore, the patients with CAD also had more signi-
ficant endothelial dysfunction. The ASI was rather in-
creased after hyperemia. Hypertension has also been well 
known as another cardiovascular risk factor, which may 
influence the arterial stiffness. Diabetes has been re-
ported to accelerate arterial stiffness, whereas the roles 
of dyslipidemia and tobacco smoking are unclear. In 
our study patients, the frequencies of hypertension 
and diabetes were higher in patients with CAD, but these 
were not significantly different.

Study limitation

The limitations of this study were the relatively small 
study population and the patients with CAD were older 
than those without, but by controlling for age, the patients 
with CAD had higher ASI than those without. Thirdly, 
the patients were not controlled for comorbid diseases in 
the analysis, as most patients had hypertension and a 
few had other diseases.

Clinical implication

In this study, the ASI was found to be a feasible method 
for the assumption of clinical coronary artery disease. 
After hyperemia, induced by compression with cuff pres-
sure, its diagnostic accuracy was increased. Thus, the use 
of the ASI is suggested as an easy, non-invasive screen-
ing and risk stratification method for the assessment of 
clinical atherosclerotic coronary artery disease.

Conclusion

In conclusion, the ASI, as measured by non-invasive 
computerized oscillometry, provides a sensitive technique, 
which serves as a parameter for assessing the athero-
scrotic changes in coronary vessels. The difference in 
the ASI, especially between patients with and without CAD, 
was more apparent after hyperemia. These findings sug-
gest that in addition to stiffening of the arterial wall itself, 
the impairment of flow-mediated vasodilation, due to 
endothelial dysfunction, further increases the arterial 
stiffness.

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