Correlation between Carotid Intima-Media Thickness, Carotid Peak Systolic Velocity and Pulse Wave Velocity in Patients with Coronary Artery Disease and Dyslipidemia

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Abstract

Background: Carotid intima-media thickness (IMT), carotid peak systolic velocity (PSV) and pulse wave velocity (PWV) are non-invasive predictors of future coronary artery disease (CAD). However, studies examining the association of these predictors are limited in patients with CAD and dyslipidemia.

Objective: To evaluate the correlation between carotid IMT, carotid PSV and PWV in patients with CAD and dyslipidemia.

Methods: Carotid B-mode ultrasound, Doppler flow velocity; PSV and brachial-ankle PWV were performed in patients who had clinical suspicions of CAD and in those patients with documented dyslipidemia who underwent coronary angiography (CAG) at the Chest Disease Institute from January 2006 to September 2006.

Results: 37 patients were studied; 22 in the non-CAD group and 15 in the CAD group. No significant differences in most of the demographic data were found between the groups. The only differences found were that the CAD group was older and predominantly male with a lower heart rate, lower low density lipoprotein (LDL) and lower high density lipoprotein (HDL). Mean carotid IMT, mean carotid PSV and mean PWV were comparable between the groups. No significant correlations between mean carotid IMT, mean carotid PSV and mean PWV were found in either group, with the exception of a correlation between mean carotid IMT and mean PWV in the non CAD group (r = 0.507, p = 0.016). However, the mean carotid IMT was higher in patients with 3 vessel or left main CAD than those with normal CAG (0.822 mm vs 0.548 mm; p = 0.005).

Conclusion: In patients with CAD and dyslipidemia, there was no correlation between carotid IMT, carotid PSV and brachial-ankle PWV. However, the carotid IMT was significantly higher in those patients with 3 vessel or left main CAD.

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Introduction

Atherosclerosis is a chronic inflammatory multi-stage process in the medium-sized and large-sized vessels that mainly result from endothelial dysfunction and accumulation of fat in the vessel wall. The continuous atherosclerotic process causes the narrowing of the luminal vessel wall and myocardial ischemic change is the final result. The slow progressive changes of atherosclerosis results in both structural and functional changes in the vessel wall. The long latent phase of atherosclerosis provides an ample opportunity to identify this process at an early stage, thus facilitating primary prevention.

In the last few years, there were reports that the carotid intima media thickness (IMT) detected by vascular ultrasound was correlated with pulse wave velocity (1-3). Pulse wave velocity reflects a functional consequence of atherosclerosis. Several studies have shown that carotid IMT is an excellent predictor of risk for future coronary artery disease (CAD) (1-3) and arterial stiffness determined by pulse wave velocity (PWV) is also a good predictor of future adverse cardiovascular events (4-7). Furthermore the presence and extent of CAD can change flow velocities of common and internal carotid arteries (8).
Previous studies have found that arterial stiffness increases with age,(9) hypertension (10), diabetes mellitus (11) and chronic renal failure (12). However no study has shown a correlation between carotid IMT, carotid peak systolic velocity (PSV) and pulse wave velocity in patients with coronary artery disease combined with another risk factor of dyslipidemia. Thus, the aim of this study was to assess the correlation between carotid IMT, carotid peak systolic velocity and pulse wave velocity in patients with CAD and dyslipidemia.

Methods
Study design: This was a cross-sectional analytic design Study.

From January 2006 to September 2006 we studied two groups of patients, those with a clinical suspicion of CAD and documented dyslipidemia and those patients who had dyslipidemia only, that underwent coronary angiography (CAG) at the Chest Disease Institute. The study involved 37 nonconsecutive patients from the inpatient and outpatient departments. They were divided into two groups: CAD group (n = 15) and non-CAD group (n = 22). The CAD groups were selected from chronic stable angina patients with dyslipidemia as the only risk factor who underwent elective coronary angiography. Subjects were excluded if they had a past history of coronary artery bypass graft, percutaneous transluminal coronary angioplasty, carotid artery disease with previous correction, peripheral artery disease or ankle-brachial index (ABI) < 0.9, cerebrovascular event, atrial fibrillation, complete heart block, pre-excitation syndrome, diabetes mellitus (DM), hypertension (HT), serum creatinine > 1.5 mg/dl and prior statin drug usage for more than 6 months. DM was defined as a fasting plasma glucose ≥126 mg/dl, a random plasma glucose ≥ 200 mg/dl or pharmacological treatment of DM. HT was defined as a systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥ 90 mmHg. Dyslipidemia was defined as either a mean low density lipoprotein (LDL) more than 100 mg/dl, a high density lipoprotein (HDL) less than 40 mg/dl, triglycerides more than 200 mg/dl or a patient with a history of dyslipidemia and on lipid lowering drugs less than 6 months. (13-15)

During the same period of the study, the non CAD group was selected from patients without a suggestive history of CAD, who had only dyslipidemia or was on lipid lowering drugs less than 6 months. An exercise stress test was performed in these subjects to exclude the presence of asymptomatic CAD since this was the control group in this study.

The study was approved by the ethics committee of the Chest Disease Institute and informed consent was obtained from all patients.

Carotid Ultrasonography
Measurement of carotid intima-media thickness was performed using high resolution ultrasound B-mode scan (Sonos 7500 USG) within 48 hours prior or after coronary angiography. Carotid IMT was taken as the distance between the leading edge of the first echogenic line of the far wall of the carotid artery (lumen-adventitia interface) and the leading edge of the second echogenic line (media-adventitia interface) 1 cm from the carotid bifurcation of the common carotid artery (Figure 1.1). Maximum detectable IMT excluding plaque (defined as focal increases in IMT > 50% of surrounding walls) was recorded as digital data using Xcelera echo version 1.2. The carotid IMT value was obtained from the computerized measurement of more than 95% of the segment (Figure 1.2). Three measurements were obtained from each side of the carotid. The mean of six values were used for further analysis. Carotid peak systolic velocity was measured 1 cm from the carotid bifurcation of the carotid artery (Figure 2). Three measurements were obtained from each side of the carotid. The mean of six values were used for further analysis. All scans were recorded as digital data for later interobserver and intraobserver analysis.

Pulse wave velocity
An automatic volume-plethysmography apparatus (BP-203 RPE II Colin, Japan) was used for detection of pulse wave velocity. The patients were examined in the supine position. Electrocardiogram electrodes were placed on both wrists.

Sphygmomanometer cuffs were wrapped around both arms just above the elbows and also just above both ankles. The cuffs were connected...
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Coronary angiography
Selective coronary angiography was performed by experienced cardiologists and analyzed by using quantitative coronary angiography (QCA) with an automated edge-detection system (CAAS II, Pie Medical Imaging). Non significant CAD was defined as the narrowing of the luminal coronary artery diameter less than 50% in one or more major epicardial coronary arteries, whereas stenosis ≥ 50% was classified as significant CAD. According to the number of diseased vessels, the CAD patients were classified into one of the following groups:

- Group 1: non-significant CAD
- Group 2: patients with 1 and 2 vessel CAD
- Group 3: patients with 3 vessel CAD or left main disease

Statistical analysis
Data were analyzed using SPSS 11.5 for windows. All descriptive data are presented as mean ± SD or as percentages. An unpaired T-test was used for analysis between the demographic data of the two groups. Correlation analysis was performed using Pearson correlation coefficient analysis. Correlation between severity of CAD and carotid IMT, pulse wave velocity, carotid peak systolic velocity and pulse pressure were tested by an ANOVA analysis. A p value < 0.05 is considered to be statistically significant.

Results
The baseline characteristics of the study group are shown in Table 1. There were essentially no statistical significant differences between the two groups (CAD vs non-CAD group), except for age, sex, heart rate, HDL and LDL. Older age and male patients were
found more in the CAD group which also had lower heart rates, HDL and LDL when compared to the non-CAD group.

The mean carotid IMT, PWV and carotid PSV in the two groups are shown in Table 2. The mean carotid IMT, mean PWV and mean carotid PSV were comparable between the two groups.

The relationship between the mean carotid IMT and mean PWV, mean carotid IMT and mean carotid PSV and mean PWV and mean carotid PSV in the two groups are depicted in Table 3. A significant correlation was found between mean carotid IMT and mean PWV in the non-CAD group ($r = 0.507, p = 0.016$) (Figure 3) but not in CAD group (Figure 4).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Non CAD group</th>
<th>CAD group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>6 (22.2)</td>
<td>11 (73.3)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.14 ± 5.0</td>
<td>55.67 ± 10.5</td>
<td>0.004*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.01 ± 9.5</td>
<td>65.20 ± 7.4</td>
<td>0.687</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.33 ± 4.3</td>
<td>24.62 ± 5.6</td>
<td>0.573</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>85.95 ± 9.8</td>
<td>88.13 ± 5.5</td>
<td>0.443</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>94.82 ± 14.1</td>
<td>94.20 ± 6.7</td>
<td>0.876</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>120.05 ± 10.5</td>
<td>111.97 ± 12.0</td>
<td>0.934</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>73.45 ± 8.5</td>
<td>72.00 ± 10.6</td>
<td>0.646</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>46.59 ± 7.2</td>
<td>47.73 ± 12.8</td>
<td>0.757</td>
</tr>
<tr>
<td>Heart rate (beat/min)</td>
<td>80.64 ± 11.1</td>
<td>68.40 ± 6.6</td>
<td>0.001*</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>265.91 ± 45.3</td>
<td>229.53 ± 105.7</td>
<td>0.159</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>132.50 ± 83.4</td>
<td>220.27 ± 334.5</td>
<td>0.244</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>54.45 ± 14.3</td>
<td>41.60 ± 11.1</td>
<td>0.006*</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>172.95 ± 43.3</td>
<td>139.6 ± 48.9</td>
<td>0.036*</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>94.82 ± 9.1</td>
<td>100.73 ± 12.9</td>
<td>0.110*</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.92 ± 0.18</td>
<td>1.03 ± 0.18</td>
<td>0.075</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>2 (9)</td>
<td>0 (0)</td>
<td>0.579</td>
</tr>
<tr>
<td>Family history of CAD (%)</td>
<td>4 (18)</td>
<td>3 (20)</td>
<td>0.848</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>71.32 ± 7.4</td>
<td>68.60 ± 11.8</td>
<td>0.438</td>
</tr>
</tbody>
</table>

Values in mean ± SD
CAD: coronary artery disease, SBP: systolic blood pressure, DBP: diastolic blood pressure, HDL: high density lipoprotein, LDL: low density lipoprotein, FBS: fasting blood sugar

Figure 3. Correlation between mean carotid intima-media thickness and mean pulse wave velocity in non-coronary artery disease group. Pearson’s correlation coefficient $r= 0.507, p=0.016$
The correlations between mean carotid IMT, mean PWV, mean carotid PSV and pulse pressure according to severity of CAD are shown in Table 4. A significant correlation was observed between mean carotid IMT and severity of CAD (p = 0.005). Analysis showed that mean carotid IMT was significantly different between the normal group with CAD and the 3 vessel or LM CAD group (p = 0.007).

**Discussion**

Development of non-invasive diagnostic tools for detection of subclinical atherosclerosis such as carotid IMT, carotid flow velocity, PWV etc. is a challenge in clinical cardiology practice. The easy and simple measurement of carotid IMT and flow velocity has become an attractive method. Assessment of aortic stiffness using PWV measured by an automated machine VP-100 (Colin Corporation®) has made the process very simple and a preferable substitute for the conventional carotid-femoral PWV for use in clinical applications.

**Table 2.** Carotid IMT, pulse wave velocity and carotid peak systolic velocity in the two groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Non-CAD group</th>
<th>CAD group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean carotid IMT (mm)</td>
<td>0.555 ± 0.060</td>
<td>0.661 ± 0.249</td>
<td>0.124</td>
</tr>
<tr>
<td>Mean PWV (cm/s)</td>
<td>1389.93 ± 194.4</td>
<td>1482.40 ± 178.4</td>
<td>0.151</td>
</tr>
<tr>
<td>Mean carotid PSV (cm/s)</td>
<td>54.05 ± 13.18</td>
<td>45.55 ± 11.67</td>
<td>0.052</td>
</tr>
</tbody>
</table>

IMT: intima-media thickness, PWV: pulse wave velocity, PSV: peak systolic velocity
CAD: coronary artery disease

**Table 3.** Correlation between Carotid IMT, pulse wave velocity and carotid peak systolic velocity in the two groups

<table>
<thead>
<tr>
<th></th>
<th>Non-CAD group</th>
<th>CAD group</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>p value</td>
<td>r</td>
</tr>
<tr>
<td>Mean carotid IMT and mean PWV</td>
<td>0.507</td>
<td>0.016&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mean carotid IMT and mean PSV</td>
<td>-0.096</td>
<td>0.671</td>
</tr>
<tr>
<td>Mean PSV and mean PWV</td>
<td>0.132</td>
<td>0.557</td>
</tr>
</tbody>
</table>

r: Pearson’s correlation coefficient
IMT: intima-media thickness, PWV: pulse wave velocity, PSV: peak systolic velocity
CAD: coronary artery disease

**Figure 4.** Correlation between mean carotid intima-media thickness and pulse wave velocity in coronary artery disease group. Pearson’s correlation coefficient r=0.311. p= 0.259
Table 4. Mean carotid IMT, pulse wave velocity, carotid peak systolic velocity and pulse pressure according to severity of CAD

<table>
<thead>
<tr>
<th>CAD</th>
<th>Mean carotid IMT (mm)</th>
<th>Mean PWV (cm/s)</th>
<th>Mean PSV (cm/s)</th>
<th>PP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n = 23)</td>
<td>0.548 ± 0.064</td>
<td>1398.58 ± 0.064</td>
<td>55.66 ± 13.01</td>
<td>46.65 ± 7.1</td>
</tr>
<tr>
<td>Non-significant (n = 3)</td>
<td>0.518 ± 0.070</td>
<td>1364.00 ± 204.3</td>
<td>38.05 ± 8.27</td>
<td>43.00 ± 9.8</td>
</tr>
<tr>
<td>1&amp;2 vessels (n = 6)</td>
<td>0.639 ± 0.151</td>
<td>1501.83 ± 235.2</td>
<td>43.63 ± 5.75</td>
<td>47.50 ± 17.8</td>
</tr>
<tr>
<td>3 vessels or LM (n = 5)</td>
<td>0.822 ± 0.350</td>
<td>1508.80 ± 81.5</td>
<td>52.61 ± 13.13</td>
<td>50.80 ± 9.9</td>
</tr>
<tr>
<td>p value</td>
<td>0.005*</td>
<td>0.461</td>
<td>0.118</td>
<td>0.741</td>
</tr>
</tbody>
</table>

PP: pulse pressure, CAD: coronary artery disease, IMT: intima-media thickness, PWV: pulse wave velocity, PSV: peak systolic velocity

In our demographic data patients in the CAD group were older than in the non-CAD group. Moreover, there were more male patients in the CAD group. These results conform to the increasing prevalence and severity of CAD with aging and earlier onset of symptoms in male patients (16). The lower heart rate in the CAD group was due to beta-blocker therapy which is the standard treatment for ischemic heart disease. Lower HDL and LDL in the CAD group imply more advanced atherosclerosis than in the non-CAD group.

In our investigation we studied the relationship between carotid IMT, carotid PSV, PWV and the presence of CAD in patients with clinical chronic stable angina who were admitted for elective coronary angiography and had only dyslipidemia as a risk factor. The results demonstrated that the relationship between mean carotid IMT and mean PWV, mean carotid IMT and mean carotid PSV were not significant in the two groups. However, there was a significant correlation between mean carotid IMT and mean PWV in the non-CAD group.

The correlations between mean PWV, mean carotid PSV and pulse pressure with the severity of CAD were not significant except for the correlation between mean carotid IMT and severity of CAD. A Significant correlation was found between the normal group and severe CAD group.

Ravi R Kasiliwal et al has shown a significant correlation between carotid IMT and brachial-ankle PWV in patients with CAD but no correlation in those without major atherosclerotic vascular disease. This suggests that the correlation between carotid IMT and brachial-ankle PWV becomes stronger with the increasing extent of atherosclerosis (17). Kumiko Kobayashi et al also found a significant correlation between carotid IMT and brachial-ankle PWV in atherosclerotic patients (18). But our study showed an inverse correlation probably because of the one risk factor of dyslipidemia as well as the small number of patients in this study. The significant correlation between mean carotid IMT and mean PWV in the non-CAD group with dyslipidemia suggests the population in this study had some structural and functional alterations due to the atherosclerosis process.

A previous study had analyzed the relationship of CAD with carotid doppler flow velocity in cases without significant carotid artery stenosis and found a significant correlation with the resistance index (RI) value of the common and internal carotid arteries (8). Our study did not demonstrate any correlations between mean carotid PSV and mean carotid IMT and between mean carotid PSV and mean PWV in either group which was probably due to the small population size.
Mean PWV and pulse pressure increased with the severity of CAD but did not show statistical significance. However risk of cardiovascular complications consistently increases in parallel with the increase in central aortic PWV (19). Dajiu Fukuda et al also demonstrated a significant correlation between brachial PWV and pulse pressure with the number of diseased coronary vessels (20).

Conclusion
In patients with 1 and 2 vessel CAD and dyslipidemia, there was no correlation between carotid IMT, carotid PSV and brachial-ankle PWV. However, the mean carotid IMT was significantly higher in those with 3 vessel or left main CAD.

Study limitations
Our study is limited by the small sample size. Larger studies are needed to confirm our findings and evaluate relative values of carotid IMT, carotid PSV and brachial-ankle PWV.

References

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การศึกษาความสัมพันธ์ระหว่างความหนาของชั้น intima media ของหลอดเลือดแดง carotid ความค่าเร่งคลื่นเสียงของหลอดเลือดแดง carotid และ pulse wave velocity ในผู้ป่วยโรคหลอดเลือดแดงที่มีไขมันในเส้นที่สูงเป็นปัจจัยเสี่ยง

ชินธารี ลกสวัสดิ์, พ.น. เกียรติไกร เจริญทิพย์, พ.น. สุข ภูมากมาย, พ.น.
กลุ่มงานอุดมศาสตร์ว่าจ้าง สถาบันโรคหัวใจ มหาวิทยาลัย

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างความหนาของชั้น intima media ของหลอดเลือดแดง carotid ความค่าเร่งคลื่นเสียงของหลอดเลือดแดง carotid และ pulse wave velocity ในผู้ป่วยโรคหลอดเลือดแดงที่มีไขมันในเส้นที่สูงเป็นปัจจัยเสี่ยง

วิธีการศึกษา: วัดความหนาของชั้น intima media ของหลอดเลือดแดง carotid ความค่าเร่งคลื่นเสียงของหลอดเลือดแดง carotid และ pulse wave velocity ในผู้ป่วยโรคหลอดเลือดแดงที่มีไขมันในเส้นที่สูงและได้รับการควบคุมว่าจ้างในสถาบันโรคหัวใจตั้งแต่เดือนมกราคมถึงกันยายน 2549

ผลการศึกษา: ผู้ป่วยทั้งหมด 37 คน โดยมีผู้ป่วย 22 คนอยู่ในกลุ่มไม่เป็นโรคหลอดเลือดแดงและ 15 คนอยู่ในกลุ่มเป็นโรคหลอดเลือดแดง กลุ่มเป็นโรคหลอดเลือดแดงสำหรับใหญ่เป็นผู้ชายและอายุมากกว่าและมีไขมัน, LDL และ HDL พบว่ากลุ่มที่ไม่เป็นโรคหลอดเลือดแดง ต่ำกว่ากลุ่มที่เป็นโรคหลอดเลือดแดง carotid และ pulse wave velocity ไม่แตกต่างกัน ไม่มีความสัมพันธ์ระหว่างความหนาของชั้น intima media ของหลอดเลือดแดง carotid ความค่าเร่งคลื่นเสียงของหลอดเลือดแดง carotid และ pulse wave velocity ในผู้ป่วยทั้งหมด พบความสัมพันธ์ระหว่างความหนาของชั้น intima media ของหลอดเลือดแดง carotid และ pulse wave velocity ในผู้ป่วยที่ไม่เป็นโรคหลอดเลือดแดง (r = 0.507, p = 0.016) อย่างไรก็ตาม ความสัมพันธ์ของความหนาของชั้น intima media ของหลอดเลือดแดง carotid ในกลุ่มเป็นโรคหลอดเลือดแดงตั้งแต่ 3 เซ็นติเมตรหรือ left main มากกว่าในกลุ่มไม่เป็นโรคหลอดเลือดแดงอย่างมีนัยสำคัญทางสถิติ (p = 0.005)

สรุป: ไม่มีความสัมพันธ์ระหว่างความหนาของชั้น intima media ของหลอดเลือดแดง carotid ความค่าเร่งคลื่นเสียงของหลอดเลือดแดง carotid และ pulse wave velocity ในผู้ป่วยโรคหลอดเลือดแดงที่มีไขมันในเส้นที่สูงเป็นปัจจัยเสี่ยง อย่างไรก็ตาม ไม่พบความสัมพันธ์ระหว่างความหนาของชั้น intima media ของหลอดเลือดแดง carotid มากกว่าในกลุ่มมีโรคหลอดเลือดแดงตั้งแต่ 3 เซ็นติเมตรหรือ left main ไม่มีความสัมพันธ์ของชั้น intima media ของหลอดเลือดแดง carotid มากกว่า