Evaluation of the Associations between Vascular Endothelial Function and Coronary Artery Stenosis in Patients with Elevated Blood Pressure during Coronary Angiography

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ABSTRACT

Objectives: The aim of the present study is to explore the correlation between vascular endothelial function and coronary artery stenosis in non-hypertensive patients with elevated blood pressure under stress.

Methods: This study included 1141 patients suspected of having coronary artery disease (CAD) without hypertension. Coronary arteriography and ultrasonic detection were used to measure the flow-mediated dilatation (FMD) function in the brachial artery. Patients were divided into 2 groups according to coronary angiography: experiment group, patients with blood pressure ≥ 140/90 mm Hg; control group, patients with blood pressure <140/90 mm Hg. The correlation between vascular endothelial function and coronary artery stenosis was observed.

Results: The majority of the patients in the control group were found to have either normal coronary arteries or stenosis ≤50%. Patients in the experiment group (those with invasive blood pressure [IBP] ≥140/90 mm Hg) were more likely to have some degree of coronary artery stenosis. Specifically, there were significantly more patients with >50% stenosis in the experiment when compared with the control group (P < .05). The FMD in the experiment group was significantly lower than that in the control group (P < .05).

Conclusion: The non-hypertensive patients with elevated blood pressure under stress had coronary artery stenosis, which was associated with vascular endothelial dysfunction.

INTRODUCTION

Coronary vascular endothelial function plays a pivotal role in the development, progression, and clinical manifestations of coronary artery disease (CAD) [Ludmer 1986]. CAD has multiple classic risk factors, including aging, hypertension, diabetes mellitus, smoking, and hyperlipidemia [Modan 1985; DeFronzo 1991]. The presence of multiple metabolic derangements in certain subjects has also been associated with a threefold increased risk of coronary heart disease, myocardial infarction, and stroke, and a three- to five-fold increased risk of cardiovascular death [Hurst 2003; Isomaa 2001; Olijhoek 2004].

One defining characteristic of non-diseased vascular tissue is endothelial release of nitric oxide (NO), which inhibits platelet aggregation, attenuates inflammation, decreases cellular proliferation, and induces local vascular smooth muscle vasodilation [Deanfield 2007]. Functional changes in coronary arteries precede lesion formation and become more pronounced with disease progression [Luscher 1995; Ludmer 1986; Schachinger 1995]. Endothelial dysfunction occurs as a response to injury to oxidized low-density lipoproteins [Deanfield 2007; Tanner 1991], hypertension [Luscher 1987; Linder 1990; Panza 1990], increased blood glucose [Cosentino 1997; Johnstone 1993], and oxygen-derived free radicals [Mugge 1991]. Endothelial dysfunction is a key process in atherosclerosis and has been reported in chronic mild fasting hyperhomocysteinemia in subjects free of vascular disease [Cosentino 1997; Johnstone 1993]. There is a strong and frequent association between arterial hypertension and CAD. Hypertension induces endothelial dysfunction, exacerbates the atherosclerotic process, and contributes to making the atherosclerotic plaque more unstable. People with hypertension have a 3-4 times higher risk of coronary disease than those with normal blood pressure. Thus, early control of blood pressure is very important for delaying the occurrence of coronary artery atherosclerosis in patients. In our clinical work, coronary artery stenosis was found in non-hypertensive patients with elevated blood pressure under stress such as tension, fear, or irritation, especially in patients with a significant rise in blood pressure because of tension in coronary angiogram. Thus, the purpose of the present study is to evaluate the correlations between vascular endothelial function and coronary artery stenosis in non-hypertensive patients with elevated blood pressure under stress.

METHODS

Study Population
Between October 2004 and October 2011, 1141 consecutive patients (age 56.7 ± 11.3; 589 male, 552 female) who were admitted to our hospital for coronary angiography were studied. Vasoreactive medications including calcium–channel blockers, ACE inhibitors, and long-acting nitrates were withheld for over 24 hours before the start of the study. The protocol of this study was approved by the institutional Human Investigation Review Committee, and written informed consent was obtained from all patients before enrollment into the study. We excluded patients with a history of hypertension, acute myocardial infarction or old myocardial infarction, and coronary stent implantation or coronary artery bypass surgery.
Coronary Artery Stenosis in Patients—Yu

**Table 1. Baseline Characteristics of the Study Population***

<table>
<thead>
<tr>
<th></th>
<th>IBP &lt;140/90 mm Hg (n = 507)</th>
<th>IBP ≥140/90 mm Hg (n = 634)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>55±12</td>
<td>56±11</td>
<td>.45</td>
</tr>
<tr>
<td>Male sex, n</td>
<td>291</td>
<td>298</td>
<td>.24</td>
</tr>
<tr>
<td>Height, cm</td>
<td>174.2±11.7</td>
<td>172.4±10.3</td>
<td>.19</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>75.2±14.3</td>
<td>77.5±16.2</td>
<td>.21</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.4±3.2</td>
<td>26.3±4.1</td>
<td>.18</td>
</tr>
<tr>
<td>Smoking, n</td>
<td>56</td>
<td>72</td>
<td>.11</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>67±10</td>
<td>66±10</td>
<td>.32</td>
</tr>
<tr>
<td>LDL-C, mg/dL</td>
<td>131±35</td>
<td>128±32</td>
<td>.16</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>47±12</td>
<td>45±10</td>
<td>.25</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>158±51</td>
<td>161±47</td>
<td>.18</td>
</tr>
<tr>
<td>Systolic BP, mm Hg†</td>
<td>133±16</td>
<td>132±16</td>
<td>.32</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg†‡</td>
<td>73±9</td>
<td>72±9</td>
<td>.21</td>
</tr>
</tbody>
</table>

*Data are expressed as mean ± SD of the patients. BMI indicates body mass index; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; BP: blood pressure.
†Blood pressure was taken at 1 hour before coronary angiography.
‡t-Mann-Whitney test.

**Study Design**

The blood pressure of the patients was taken during angiography. Patients with invasive blood pressure (IBP) ≥140/90 mm Hg were assigned to the experiment group, and patients with IBP >140/90 mm Hg were assigned to the control group. Coronary angiography results were divided into three grades: normal (coronary artery stenosis was not detected), stenosis <50%, and stenosis >50%.

**Coronary Angiography**

Coronary angiography was performed by appointed cardiologists and angiograms were analyzed at a core lab. Left and right coronary angiography was performed via the femoral and radial artery. Readers were blinded to patients’ identity and the severity of coronary artery stenosis was expressed by diameter method. Identification of CAD and assessment of its extent and severity were the indications for cardiac catheterization.

**Measurements of Flow-Mediated Dilatation in the Brachial Artery**

Patients were studied under quiet conditions in a temperature-controlled room after 30 minutes of supine rest. Flow-mediated dilatation (FMD) was measured by use of Doppler high-resolution ultrasound and electrocardiogram (ECG) was recorded at the same time. Briefly, optimal brachial artery images were obtained approximately 2 and 3 cm above the antecubital fossa. This location was marked, and all subsequent images were obtained at the same location. The exact distance of the measured point on the skin surface from the antecubital fossa was recorded in each patient to ensure that the same segment of the brachial artery was measured at each time point during follow-up. A forearm blood-pressure cuff was placed distal to the antecubital fossa and inflated to 300 mm Hg for 4 minutes. End-diastolic diameter was measured at baseline and at approximately 60–90 seconds after cuff deflation. Endothelium-dependent vasomotion was determined by the maximal brachial artery diameter after exactly 60 seconds of reactive hyperemia compared with the baseline vessel diameter, and was expressed as percent FMD: (diameter max – diameter baseline)/diameter baseline ×100%.

**Statistical Analysis**

All measurements and analysis of all measures were done in a blinded fashion. Data were entered into Excel and analyzed with SPSS 15.0 (SPSS, Chicago, IL, USA). Data are expressed as mean ± SE. Comparisons between the experiment and control group were performed with an unpaired t test or Pearson’s χ² test to demonstrate potential associations with FMD. P < .05 was considered statistically significant.

**RESULTS**

**Patient Characteristics**

A total of 1141 patients (589 male, 552 female) with a mean age of 56.7 ± 11.3 were enrolled and assigned to the experiment group (n = 634) or the control group (n = 507) according to their IBP (Table 1).

**Result of Coronary Arteriography**

Coronary arteriography was performed in order to determine whether elevated blood pressure under stress would have an effect on CAD. As shown in Table 2, the majority of the patients in the control group were found to have either normal coronary arteries or stenosis <50%. Patients in the experiment group (those with IBP >140/90) were more likely to have some degree of coronary stenosis. Specifically, there were significantly more patients with >50% stenosis in the experiment when compared with the control group (P < .05).

**Effect of Elevated Blood Pressure Under Stress on Vascular Endothelial Function**

The effect of elevated blood pressure under stress on vascular endothelial function is shown in Table 3. There was
no significant difference in baseline brachial artery dimensions between the control and experiment groups. FMD was significantly lower (4.42 ± 0.15) in the 634 subjects with IBP ≥140/90 mm Hg compared with the 507 subjects with IBP <140/90 mm Hg (4.65 ± 0.40).

### DISCUSSION

Psychological pressure-induced temporal stress condition is common when patients receive coronary angiography. Stress is an organism’s response to a stressor such as an environmental condition or a stimulus. Previous studies have demonstrated that stress can affect vascular endothelial function in spontaneously hypertensive rats. The stress state can affect multiple systems, such as blood pressure, arteriosclerosis, blood fat, blood sugar by changing the body’s neuroendocrine, endothelial function, and behavior [Seeman 2001]. Therefore, stress has been recognized as a major risk factor for hypertension, coronary heart disease, diabetes, and hyperlipidemia [Ducher 2006; Jiang 2008].

Previous reports have noted a correlation between abnormalities in FMD of the brachial artery and the presence of CAD by coronary angiography [Neunteufl 1997; Schroeder 1999]. In this study, we demonstrated for the first time that there are associations between coronary artery stenosis and FMD in patients with elevated blood pressure under stress, which includes tension and fear. The results show that patients with significantly increased blood pressure always have coronary artery stenosis and there were significantly more patients with stenosis >50% than with a normal coronary artery. In addition, FMD was significantly lower in individuals with coronary artery stenosis compared with those who had a normal coronary artery. Furthermore, FMD was an independent predictor of coronary artery stenosis.

The mechanism that hypertension leads to coronary atherosclerotic cardiopathy is unclear. It has been reported that vascular endothelial injury can cause endothelium-derived relaxing factors (EDRFs) to decrease and endothelium-derived contracting factors (EDCFs) to increase, thus leading to a decrease of endothelium-dependent dilatation and elevated blood pressure [Drexler 1999]. It has been recognized that endothelial dysfunction is closely related to initiation and progression of coronary atherosclerotic diseases and cardiac events [Bissinger 2011]. Therefore, FMD of patients in both groups was measured and the result suggests that endothelial function in patients with elevated blood pressure is significantly lower than in patients with normal blood pressure, demonstrating that there is endothelial dysfunction and coronary artery stenosis in non-hypertensive patients with elevated blood pressure under stress.

In conclusion, the current study shows that endothelial dysfunction can be found in the early period of hypertension. Non-hypertensive patients with elevated blood pressure under stress are in an early period of hypertension, which can lead to endothelial dysfunction and coronary artery stenosis. One limitation of this study is that the subjects were not evaluated to see if they were experiencing stress during the coronary angiography. However, further studies are needed to define the mechanisms and clinical implications of vascular effects.

### REFERENCES


