Pulse Pressure in Youth and Carotid Intima-Media Thickness in Adulthood

The Cardiovascular Risk in Young Finns Study

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Background and Purpose—Large pulse pressure associates with atherosclerosis, but it is unclear if it contributes to the development of atherosclerosis or if atherosclerosis leads to pulse pressure widening. We examined whether exposure to large pulse pressure in childhood predicts carotid artery intima-media thickness in adulthood.

Methods—Carotid intima-media thickness was measured in 2146 adults in the Cardiovascular Risk in Young Finns Study. These subjects have blood pressure data available dating back to their childhood (baseline in 1980, ages 3 to 18 years).

Results—Baseline pulse pressure measured in adolescence was significantly related to carotid intima-media thickness measured in adulthood 21 years later ($r=0.123, P<0.0001$). The relation remained significant ($P=0.0029$) in models adjusted for age, sex, adolescent mean arterial pressure, adult systolic pressure, adult pulse pressure, body mass index, smoking, physical activity, and carotid artery diameter. Each 10 mm Hg increment in pulse pressure was associated with a 0.008-mm (95% CI, 0.003 to 0.013 mm) increase in carotid intima-media thickness.

Conclusions—Exposure to wide pulse pressure in adolescence may induce changes that contribute to carotid artery intima-media thickening. (Stroke. 2009;40:00-00.)

Key Words: atherosclerosis ■ carotid intimal medial thickness ■ epidemiology

Large pulse pressure is a risk factor for cardiovascular disease. The underlying mechanism for this relation is unclear, but it is possible that the pulsatile component of blood pressure contributes to the development of atherosclerosis. In line, studies have shown direct associations between pulse pressure and carotid intima-media thickness (IMT). The causality of this association, however, is unclear. It is unknown whether a large pulse pressure is related to subsequent thickening of IMT or whether the increase in IMT leads to pulse pressure widening. In the Young Finns cohort, systolic blood pressure measured in adolescence predicts carotid IMT in adulthood, but the role of pulse pressure is unknown. To gain more insight on youth determinants of adult vascular health, the current analyses examined whether pulse pressure levels in youth are related to carotid artery IMT in adulthood.

Methods

The Young Finns Study included 3596 3- to 18-year-old youths at baseline in 1980. In 1980, blood pressure was measured from 3 year olds (N=302) with an ultrasound device (Arteriosonde 1020; Roche) and in others with a standard mercury sphygmomanometer. In 2001, blood pressure was measured with a random zero sphygmomanometer (and with an automatic oscillometric sphygmomanometer during the ultrasound examination). Pulse pressure was calculated as the difference between systolic blood pressure and diastolic blood pressure. The number of subjects with complete data was 2146. Ultrasound studies to measure carotid IMT were performed as previously reported. Group comparisons were made using the $t$ test or $\chi^2$ test. Multivariable regression models were used to examine the associations between youth pulse pressure and adult IMT.

Results

The characteristics are shown in Table 1. Blood pressure values measured with the random zero sphygmomanome-
baseline IMT was a predictor of the change in pulse pressure. In women with coronary artery disease followed for 3.2 years, increased baseline pulse pressure was associated with progression of coronary atherosclerosis.

Pressure pulsation may directly influence atherosclerosis by a number of mechanisms. High pulsation may induce endothelial dysfunction. Cyclic strain may enhance adhesion of monocytes to endothelial cells and modulate gene expression in smooth muscle cells and monocytes/macrophages.

Our study has limitations. Brachial pulse pressure overestimates true central pulse pressure because of pressure amplification. Although adolescent pulse pressure was significantly associated with IMT in adulthood, the association was rather weak. Increased carotid IMT can be seen in children with risk factors; therefore, it is possible that the early increase in pulse pressure in the adolescents is a result rather than a cause of increased carotid IMT. Bearing these limitations in mind, however, our results provide further evidence for the hypothesis that the pulsatile component of blood pressure has a role in the development of increased carotid IMT.

Table 1. Characteristics of 2146 Study Subjects*

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>32 (range, 24–39)</td>
<td>32 (range, 24–39)</td>
</tr>
<tr>
<td>No.</td>
<td>961</td>
<td>1185</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.0±4.0</td>
<td>24.5±4.5</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>30</td>
<td>19</td>
</tr>
<tr>
<td>IMT, mm</td>
<td>0.591±0.100</td>
<td>0.570±0.083</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>121±12</td>
<td>112±12</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>73±11</td>
<td>74±11</td>
</tr>
<tr>
<td>Mean blood pressure, mm Hg</td>
<td>89±10</td>
<td>83±10</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>48±10</td>
<td>44±9</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>54±6</td>
<td>44±7</td>
</tr>
</tbody>
</table>

*The values are mean±SD or percentages.
†Blood pressure measured using a random zero device (sitting position).
‡Blood pressure measured using an automatic oscillometric device (supine position).

All comparisons P<0.0001 between sexes (except age, P=0.8).

Figure. Carotid IMT (mean±SEM) measured in adulthood across pulse pressure quintiles measured 21 years earlier in adolescence.

Table 2. Multivariable Relations Between Pulse Pressure Measured in Adolescence (12–18 Year Olds) and Carotid IMT Measured in Adulthood (33–39 Year Olds)*

<table>
<thead>
<tr>
<th>Model</th>
<th>β±SE</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Age, sex</td>
<td>0.0062±0.0023</td>
<td>0.0075</td>
</tr>
<tr>
<td>B. A+adolescent mean arterial pressure</td>
<td>0.0079±0.0023</td>
<td>0.0008</td>
</tr>
<tr>
<td>C. B+adult mean arterial pressure</td>
<td>0.0067±0.0023</td>
<td>0.0050</td>
</tr>
<tr>
<td>D. C+adult pulse pressure</td>
<td>0.0074±0.0024</td>
<td>0.0021</td>
</tr>
<tr>
<td>E. D+adolescent body mass index</td>
<td>0.0065±0.0025</td>
<td>0.0081</td>
</tr>
<tr>
<td>F. E+adult body mass index</td>
<td>0.0079±0.0025</td>
<td>0.0029</td>
</tr>
</tbody>
</table>

*N=940 to 1108 (varies because some variables missing). Regression coefficient denotes the increase in IMT in millimeters associated with each 10 mm Hg increment in pulse pressure.

References
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