Risk Factors Identified in Childhood and Decreased Carotid Artery Elasticity in Adulthood: The Cardiovascular Risk in Young Finns Study

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Risk Factors Identified in Childhood and Decreased Carotid Artery Elasticity in Adulthood
The Cardiovascular Risk in Young Finns Study

Markus Juonala, MD, PhD; Mikko J. Järvisalo, MD, PhD; Noora Mäki-Torkko, BM; Mika Kähönen, MD, PhD; Jorma S.A. Viikari, MD, PhD; Olli T. Raitakari, MD, PhD

Background—Exposure to risk factors in childhood may have long-term influences on vascular function. We examined the relationship between risk factors identified in childhood and arterial elasticity assessed in adulthood.

Methods and Results—Carotid artery compliance (CAC), Young’s elastic modulus (YEM), and stiffness index (SI), 3 measures of large-artery elasticity, were assessed with noninvasive ultrasound in 2255 healthy white adults aged 24 to 39 years participating in a population-based cohort study and who had risk factor data available since childhood. In multivariate models, childhood obesity (skinfold thickness) predicted decreased CAC (P<0.001), increased YEM (P<0.01), and increased SI (P<0.01) in adulthood. Childhood blood pressure was inversely associated with CAC (P<0.001) and directly associated with YEM (P<0.001). The number of risk factors identified in childhood, which included high LDL cholesterol (at or above 80th percentile), elevated blood pressure, skinfold thickness, low HDL cholesterol (at or below 20th percentile), and smoking, was related inversely with CAC (P<0.001) and directly with YEM (P<0.001). These associations remained highly significant after adjustment for the number of risk factors identified in adulthood (P=0.005 for CAC and P<0.001 for YEM).

Conclusions—Cardiovascular risk factors identified in childhood and adolescence predict decreased carotid artery elasticity in adulthood. These data suggest that risk factors operating in early life may have sustained deleterious effects on arterial elasticity. (Circulation. 2005;112:1486-1493.)

Key Words: risk factors ■ elasticity ■ obesity ■ atherosclerosis ■ epidemiology

Ultrasonographically assessed arterial elasticity is a useful means to study early pathophysiological changes in the arteries relevant to the development of atherosclerosis.1 Risk factors such as high LDL cholesterol, elevated blood pressure, obesity, and smoking have been associated with decreased arterial elasticity in cross-sectional studies.2–4 Furthermore, decreased arterial elasticity has been implicated as an independent predictor of cardiovascular events in high-risk individuals.5 These observations thus suggest that reduced arterial elasticity may reflect increased atherosclerotic burden.

Although the clinical complications of coronary heart disease mainly occur in middle age or later in life, atherosclerosis has its roots in childhood. Recent observations by us6 and others7,8 have consistently shown that risk factors identified in childhood predict the occurrence of preclinical carotid atherosclerosis in adulthood. On the other hand, previous observations concerning the relationship between risk factors in childhood/adolescence and arterial elasticity later in life have been controversial. In the Bogalusa Heart Study,9 childhood blood pressure correlated with pulse-wave velocity (PWV) in adulthood, whereas in the Atherosclerosis Risk in Young Adults (ARYA) study,10 no association between adolescent blood pressure and adult PWV was observed. Therefore, to gain more insight on childhood determinants of adult vascular health, we measured 3 indices of arterial elasticity—carotid artery compliance (CAC), Young’s elastic modulus (YEM), and stiffness index (SI)—in 2255 adults aged 24 to 39 years. These individuals were participants of the prospective Cardiovascular Risk in Young Finns Study for whom risk factor data were available since their childhood.

Methods

The Cardiovascular Risk in Young Finns Study is an ongoing, multicenter, follow-up study of atherosclerosis risk factors of Finnish children and young adults. A cross-sectional survey was conducted in 1980 for 3596 subjects aged 3, 6, 9, 12, 15, and 18 years.11 In 2001, we reexamined these individuals, then aged 24 to 39 years. The loss to follow-up was approximately 34%. In the present study,
we have analyzed the associations of risk factors measured in childhood and adulthood with carotid artery elasticity indices assessed in adulthood. Subjects gave written informed consent, and the study was approved by local ethics committees.

**Clinical Characteristics**

Height and weight were measured, and body mass index (BMI) was calculated. Skinfold thicknesses (in childhood) were measured by Harpenden calipers (Holtain and Bull-British Indicators instruments) to 0.2-mmreadings in 1980. The combined thickness of 3 skinfold measurements (subcapsular, triceps, and biceps) was used in the analysis. Blood pressure was measured from the brachial artery with a standard mercury sphygmomanometer in 1980. In 3-year-olds, blood pressure was measured with an ultrasound device. The mean of 3 measurements was used in the analysis. In 2001, brachial blood pressure was measured during the ultrasound study with an automated sphygmomanometer (Omron M4, Omron Matsusaka Co). The mean of 2 measurements was used in the analysis. Smoking habits were ascertained with a questionnaire in subjects aged 12 years or older. Smoking was modeled as a dichotomous variable (smoking/nonsmoking). Smoking was defined as regular cigarette smoking on a weekly basis or more often in adolescents, and in adults, it was defined as smoking on a weekly basis or regular smoking in the past.

**Biochemical Analyses**

For the determination of serum lipid levels, venous blood samples were drawn after an overnight fast. All lipid determinations were done in duplicate in the same laboratory. Standard enzymatic methods were used for serum total cholesterol, triglycerides, and HDL cholesterol. LDL cholesterol concentration was calculated by the Friedewald formula. Fasting plasma high-sensitivity C-reactive protein (CRP) concentrations were analyzed by latex turbidimetric immunoassay (Wako Chemicals GmbH). The lower detection limit reported for the assay was 0.06 mg/L. Glucose concentrations were analyzed enzymatically (glucose dehydrogenase, Olympus Diagnostica GmbH). In 1980, serum insulin was measured with a modification of the immunoassay method of Herbert et al. In 2001, serum insulin was measured by microparticle enzyme immunoassay kit (Abbott Laboratories, Diagnostic Division, Dainabot). Details of these methods have been described previously.

**Carotid Artery Studies**

Ultrasound studies were performed with Sequoia 512 ultrasound mainframes (Acuson) with 13.0-MHz linear-array transducers between September 2001 and January 2002. The left carotid artery was scanned according to a standardized protocol. Several moving-image clips of the beginning of the carotid bifurcation and the common carotid artery with a duration of 5 seconds were acquired and stored in digital format for subsequent offline analysis. The digitally stored scans were analyzed by one reader blinded to subjects’ details (M.J.). Carotid artery intima-media thickness was measured as described previously.

To assess carotid artery elasticity indices, the best-quality cardiac cycle was selected from the 5-second image clips. The common carotid diameter 10 mm from the carotid bifurcation was measured from the B-mode images with ultrasound calipers at least twice in end diastole and end systole, respectively. The means of the measurements were used as the end-diastolic and end-systolic diameters. Carotid Artery Studies

Ultrasound and concomitant brachial blood pressure measurements were used to calculate the following indices of arterial elasticity: CAC = (\(D_{d} - D_{s}\))\(/(P_{s} - P_{d})\), \(YEM = (|P_{s} - P_{d}| \times D_{s})\)/\(D_{d}\), \(SI = \ln(P_{d}/P_{s})\)/\(D_{s}\), where \(D_{d}\) is the diastolic diameter, \(D_{s}\) is the systolic diameter, \(P_{s}\) is systolic blood pressure, \(P_{d}\) is diastolic blood pressure, and IMT is carotid artery intima-media thickness.

CAC measures the ability of the arteries to expand as a response to pulse pressure caused by cardiac contraction and relaxation, whereas YEM gives an estimate of arterial stiffness that is independent of wall (intima-media) thickness. SI has been developed to reduce the impact of the curvilinear pressure-stiffness relationship on arterial stiffness and is therefore considered to be relatively independent of blood pressure. These indices correlated highly significantly (\(P < 0.001\)) with each other, with Pearson’s correlation coefficients of \(r = -0.71\) between CAC and YEM, \(r = -0.73\) between CAC and SI, and \(r = 0.88\) between YEM and SI. Carotid artery wall thickness correlated weakly with CAC in men \((r = -0.06, P = 0.051)\) but not in women \((r = -0.01, P = 0.64)\). Wall thickness was not related to SI either in men \((r = 0.03, P = 0.28)\) or in women \((r = -0.03, P = 0.20)\).

To assess reproducibility of ultrasound measurements, we reexamined 57 subjects 3 months after the initial visit (2.5% random sample). The between-visit coefficient of variation was 2.7% for carotid artery diastolic diameter, 16.3% for CAC, 19.5% for YEM, and 16.6% for SI.

**Statistical Methods**

The comparisons between men and women and between study dropouts and participants were performed with \(t\) tests. The bivariate relationships between risk factors and carotid artery elasticity were examined by Pearson’s correlation analysis. To examine the effect of multiple risk factors on arterial elasticity, we calculated a risk score, defined as the number of risk factors. Risk factors were defined as values at or above the age- and sex-specific 80th percentile for LDL cholesterol, systolic blood pressure, skinfold thickness (childhood), and BMI (current); at or below the 20th percentile for HDL cholesterol; and smoking. The mean number of risk factors was 0.9 (range 0 to 5) in childhood and 1.3 (range 0 to 5) in adulthood. Because smoking was only evaluated in children aged 12 years or older, we repeated all analysis using a risk score that did not include smoking as a risk variable and obtained essentially similar results.

To evaluate which childhood risk variables were independently associated with carotid elasticity indices, we used multivariate regression analysis. Similarly, multivariate modeling was used to examine which current risk variables were independent correlates for elasticity indices. Variables in initial stepwise multivariate models included age, sex, and childhood current LDL cholesterol, HDL cholesterol, triglycerides, BMI (in childhood models, skinfold thickness), systolic blood pressure, insulin, and smoking. In current models, CRP and glucose were also analyzed.

Next, we examined whether each of those childhood risk variables that turned out to be significantly related to adult elasticity indices had an independent effect after the effect of the current risk variable in question was taken into account. To accomplish this, we calculated the change in regression coefficient between childhood risk variable and elasticity index after introducing the current risk variable into the same model. All analysis were performed with the Statistical Analysis System, SAS (version 8.1), and statistical significance was inferred at a 2-tailed probability value <0.05. When performing multiple bivariate correlations between elasticity indices and risk variables, we applied the Bonferroni correction by adjusting the probability values (the probability value of each bivariate correlation analysis was multiplied by the number of correlations being tested). Values for triglycerides, insulin, and CRP were log-transformed before analyses owing to skewed distributions.

**Results**

The representativeness of the present study cohort was tested by comparing its baseline (1980) characteristics with the dropouts. There were more males than females among dropouts, and the dropouts were younger than participants in both genders. Otherwise, when dropouts and participants were compared with age-adjusted analysis, there were no statistically significant differences in total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, blood pressure, or BMI (Table 1). Table 2 summarizes the mean values of carotid artery elasticity indices in men and women. Men had lower CAC and higher YEM, SI, and carotid diameters than
TABLE 1. Baseline Characteristics (in 1980) of Participants and Dropouts in the Follow-Up (in 2001)

<table>
<thead>
<tr>
<th></th>
<th>Participants (n=1012)</th>
<th>Dropouts (n=752)</th>
<th>Participants (n=1243)</th>
<th>Dropouts (n=589)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in 1980*</td>
<td>10.7†</td>
<td>9.9</td>
<td>10.7*</td>
<td>10.1</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L‡</td>
<td>5.02</td>
<td>5.05</td>
<td>5.19</td>
<td>5.12</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L‡</td>
<td>3.2</td>
<td>3.22</td>
<td>3.33</td>
<td>3.29</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L‡</td>
<td>1.48</td>
<td>1.5</td>
<td>1.5</td>
<td>1.47</td>
</tr>
<tr>
<td>Triglycerides, mmol/L‡</td>
<td>0.75</td>
<td>0.74</td>
<td>0.79</td>
<td>0.79</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg‡</td>
<td>114</td>
<td>112</td>
<td>112</td>
<td>112</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg‡</td>
<td>69</td>
<td>69</td>
<td>69</td>
<td>69</td>
</tr>
<tr>
<td>BMI, kg/m²‡</td>
<td>17.9</td>
<td>17.7</td>
<td>17.8</td>
<td>17.9</td>
</tr>
<tr>
<td>Smoking prevalence, %§</td>
<td>21.7</td>
<td>27.0</td>
<td>16.3</td>
<td>18.8</td>
</tr>
</tbody>
</table>

*P<0.05, †P<0.001, t tests applied between participants and dropouts to examine differences in age. §Differences between participants and dropouts were examined with regression analysis adjusted with age (P always >0.05). Smoking prevalences in 15- to 18-year-old subjects; differences between participants and dropouts were examined with χ² test (P always >0.05).

TABLE 2. Mean Values of Ultrasound Measurements (n=2255)

<table>
<thead>
<tr>
<th></th>
<th>Men (n=1012)</th>
<th>Women (n=1243)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>31.7±5.0</td>
<td>31.7±5.0</td>
</tr>
<tr>
<td>Carotid artery diastolic diameter, mm</td>
<td>6.02±0.51</td>
<td>5.50±0.45</td>
</tr>
<tr>
<td>CAC, %/10 mm Hg</td>
<td>2.00±0.66</td>
<td>2.31±0.78</td>
</tr>
<tr>
<td>YEM, mm Hg-mm</td>
<td>334±152</td>
<td>280±153</td>
</tr>
<tr>
<td>SI</td>
<td>5.60±1.95</td>
<td>5.30±2.50</td>
</tr>
</tbody>
</table>

Plus-minus values are mean±SD. All comparisons (t tests) between men and women P<0.001, except for age.

Women. Elasticity indices correlated strongly with age in both sexes (Figure 1).

Childhood Risk Factors and Carotid Artery Elasticity
Correlation coefficients between risk factors and CAC are shown in Table 3. Childhood systolic blood pressure, BMI, insulin, and skinfold thickness correlated inversely with CAC both in men and in women (Table 3). When the CAC variable was substituted with YEM, we found significant direct correlations between YEM and childhood triglycerides (P<0.001), blood pressure (P<0.001), skinfold thickness (P<0.001), insulin (P<0.001), and BMI (P<0.001). SI correlated directly with childhood triglycerides (P<0.001), blood pressure (P<0.001), skinfold thickness (P<0.001), insulin (P<0.001), and BMI (P<0.001).

In multivariate models, childhood skinfold thickness and systolic blood pressure predicted decreased CAC and increased YEM in adulthood. Childhood skinfold thickness was also directly related to adult SI (Table 4). Childhood BMI was directly associated with YEM (P=0.002) when included in the multivariate model instead of skinfold thickness.

A decreasing trend in CAC (P<0.001) and an increasing trend in YEM (P<0.001) was observed across the groups with an increasing number of childhood risk factors (Figure 2). The association between the number of childhood risk factors and SI was of borderline significance (P=0.07).

Current Risk Factors and Carotid Artery Elasticity
In univariate analysis, current LDL cholesterol, triglycerides, blood pressure, BMI, and insulin correlated inversely with CAC in both sexes. In men, CRP was also inversely correlated with CAC (Table 3). LDL cholesterol (P<0.001), triglycerides (P<0.001), blood pressure (P<0.001), BMI (P<0.001), insulin (P<0.001), and glucose (P<0.001) were directly related to YEM in both sexes. In men, CRP (P<0.001) was inversely associated with YEM. LDL cholesterol (P<0.001), triglycerides (P<0.001), BMI (P<0.001), and insulin (P<0.001) correlated directly with SI in both sexes. In addition, in men, blood pressure (P<0.001) and CRP (P<0.001) were directly related to SI. In multivariate models, current LDL cholesterol, systolic blood pressure, and insulin were inversely related to CAC and directly related to YEM and SI. BMI correlated directly with YEM (Table 5).

Independent Effect of Childhood Risk Factors
Childhood systolic blood pressure, skinfold thickness, and risk score were significantly associated with carotid elasticity in adulthood. Each of these childhood risk variables also correlated significantly with the correspondent current risk factor variable, with correlation coefficients ranging between r=0.2 and r=0.3 (P always <0.001). To examine how the associations between childhood risk and adult carotid elasticity changed when the effect of adult risk was taken into account, we calculated the associations of these variables with elasticity indices before and after adjustment for current risk factors. Figure 3 shows the unadjusted and adjusted regression coefficients and their 90% CIs for CAC. Overall, the effect of childhood risk factors on adult CAC was
The effect of current risk factors was 50% when the effects of current risk factors were taken into account. The effect of childhood risk score remained highly significant when the current risk score was introduced into the same regression model (\(P < 0.005\)). The effect of childhood systolic blood pressure remained of borderline significance (\(P = 0.08\)) when the current blood pressure was introduced.

The association between childhood risk score and YEM (\(P < 0.001\)) also remained significant after adjustment with the current risk score. Furthermore, the effect of childhood blood pressure on YEM (\(P = 0.003\)) remained significant when adjusted with current blood pressure.

Discussion

Risk factors that operate in early life may have long-term effects on arterial physiology. We found that skinfold thickness and blood pressure measured in childhood and adolescence predicted decreased carotid artery elasticity in adulthood. Moreover, we demonstrated that the number of risk factors identified in childhood correlated inversely with carotid artery elasticity in adulthood. Our observations thus suggest that childhood risk factors predict decreased carotid artery elasticity in adulthood.

We assessed 3 indices (CAC, YEM, and SI) that may reflect different aspects of arterial elasticity16,17 with consistent results concerning the associations between risk variables and elasticity parameters.

Obesity in children and young adults has been associated with decreased arterial elasticity.4,18 Nevertheless, to the best of our knowledge, this is the first study indicating that childhood obesity has predictive value for decreased arterial elasticity in adulthood. There are different potential mechanisms to explain the association between childhood obesity and decreased arterial elasticity in adults. Obesity-associated hyperinsulinemia has been shown to decrease arterial elasticity.15 Consistently, we observed that insulin levels measured in adulthood were associated independently with carotid artery elasticity. Second, obesity might decrease arterial elasticity through inflammation. Overweight has been related with low-grade inflammation,19 and recently, Yasmin et al20 showed that CRP correlates directly with arterial stiffness. In
In the present study, CRP correlated inversely with arterial elasticity in a univariate model in men. However, because of a strong correlation with BMI, this relationship did not remain significant in multivariate models. Finally, elevation in leptin levels, a hormone that plays a key role in the regulation of appetite and body weight, has been related to impaired arterial distensibility in children.21

In addition to obesity, elevated systolic blood pressure measured in childhood was an independent predictor of arterial elasticity in young adults. Elevated blood pressure accelerates atherosclerosis, collagen synthesis, and arterial smooth muscle hyperplasia and hypertrophy, which contributes to decreased arterial elasticity.19 Our findings suggest that high blood pressure levels operating in childhood may induce adverse vascular effects. In an analysis from the Bogalusa Heart Study,9 high childhood blood pressure was an independent predictor of increased ankle-brachial PWV in young adults. Their study group consisted of 835 black and white adults aged 24 to 44 years with an average follow-up of 26.5 years. Conversely, in the ARYA study,10 blood pressure measured at the mean age of 13.5 years did not predict carotid-femoral PWV in 527 white adults aged 27 to 30 years. The present results among a substantially larger cohort of 2255 white young adults in the 21-year follow-up are in line with the observations from the Bogalusa Heart Study. We assessed carotid artery elasticity indices ultrasonically. PWV used in the 2 above-mentioned studies measured the speed of transmission of pulse pressure wave between 2 arteries to determine an index of the average elastic state of the vessel pathway. These 2 methods have been shown to correlate with each other, which supports the concept that they measure similar arterial properties.22 Therefore, the discrepancy with the results from the ARYA study is probably not due to methodological issues. Instead, it may be explained by differences in blood pressure measurements. We measured blood pressure using a standardized protocol in the entire cohort, whereas values in the ARYA study were obtained from school health records.

The number of risk factors identified in childhood was significantly associated with decreased CAC and increased YEM. Risk factors included in the model were high LDL cholesterol, low HDL cholesterol, obesity, elevated blood pressure, and smoking. The present results are in line with earlier observations that showed that the presence of multiple risk factors may lead to acceleration of atherosclerosis in young people.6,23 This finding may have implications in the prevention of cardiovascular disease, because these risk factors (apart from smoking) are mainly metabolically linked,
and previous reports have suggested that they tend to cluster in childhood.\textsuperscript{24}

Current risk factors showed a stronger relation to elasticity indices than childhood risk factors. For example, \approx 14\% of the variance in CAC was explained by risk variables measured in childhood, whereas 24\% of the variance in CAC was explained by current risk variables. Risk factors show significant tracking, and therefore, the relationship between childhood risk and later reduced arterial elasticity could be explained in part by tracking of risk factor values from childhood to adulthood. However, the fact that childhood risk factors continued to be significant predictors of CAC and YEM even after adjustment for adult risk factors suggests a direct relation between childhood risk factors and arterial elasticity.

We have previously shown that childhood risk factors correlate with carotid artery intima-media thickness, a structural marker of subclinical atherosclerosis, rather independently of current risk factors.\textsuperscript{6} In the present study, adjustment for current risk factors attenuated the effect of childhood risk factors on adult arterial elasticity approximately by half. This may suggest that structural changes in the arterial wall represent lifetime exposure to risk factors, whereas a functional change in arterial elasticity may be dynamic and more dependent on current risk factor status. In line with this assumption, intervention studies have shown that arterial elastic properties are rapidly influenced with nitrates, calcium channel blockers, and ACE inhibitors and possibly with statins.\textsuperscript{1,25–27}

An important limitation of the present study is the blood pressure measurement method. The pulse pressure used in the equations to calculate elasticity indices was measured from the brachial artery. It would be ideal to study the pulse pressure from the artery in question, because the use of brachial pressures may overestimate pulse pressure in central arteries.\textsuperscript{28} This increase is a consequence of pulse-wave reflection from the periphery, which augments the peak of the pressure wave in peripheral arteries close to the reflection sites. PWV is closely related to age. Therefore, the difference between central and peripheral pulse pressure is likely to be similar between study subjects within a narrow age range, as in the present study. Moreover, Borow and Newburger\textsuperscript{29} have shown an excellent correlation of $r=0.98$ between systolic blood pressures and $r=0.97$ between diastolic pressures measured invasively from ascending aorta and noninvasively from brachial artery. The close positive relationship between brachial pulse pressure and the relative diameter increase of carotid artery during systole, as shown by Reneman et al,\textsuperscript{30} also supports the assumption that brachial pulse pressure can

<table>
<thead>
<tr>
<th>Risk Variable</th>
<th>Mean±SD</th>
<th>CAC, β±SE</th>
<th>YEM, β±SE</th>
<th>SI, β±SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>31.7±5.0</td>
<td>-0.036±0.003‡</td>
<td>8.7±0.6†</td>
<td>0.096±0.010‡</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>44.4</td>
<td>-0.135±0.030†</td>
<td>21.7±6.4†</td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.28±0.84</td>
<td>-0.047±0.015*</td>
<td>8.9±3.1*</td>
<td>0.146±0.049*</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>116±13</td>
<td>-0.228±0.015‡</td>
<td>36.9±3.3†</td>
<td>0.153±0.049*</td>
</tr>
<tr>
<td>Insulin, μU/mL</td>
<td>7.7±5.6</td>
<td>-0.079±0.015‡</td>
<td>10.0±3.5*</td>
<td>0.218±0.050‡</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.0±4.4</td>
<td>3.5* 0.218</td>
<td>15.7±3.7‡</td>
<td></td>
</tr>
<tr>
<td>Model $R^2$</td>
<td></td>
<td>24% 23% 7%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(\beta\)-Values are regression coefficients for a 1-unit change in age and a 1-SD change in continuous variables.

Initial stepwise regression models included age, sex, LDL cholesterol, HDL cholesterol, triglycerides, systolic blood pressure, skinfold thickness, insulin, CRP, glucose, and smoking as independent variables. The nonsignificant predictors did not act as confounders, because the significant relations shown were not affected by inclusion or exclusion of these variables.

$^*P<0.01, †P<0.001, ‡P<0.0001$. 

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3}
\caption{Regression coefficients (adjusted for age and sex) and their 90\% CIs for associations of childhood risk score ($P<0.001$), systolic blood pressure ($P<0.001$), and skinfold thickness ($P<0.001$) with CAC (upper lines). Lower lines show the same associations after adjustment for current risk score, blood pressure, and BMI, respectively. After these adjustments, the association between childhood risk score and CAC remained significant ($P=0.005$), whereas the effect of childhood blood pressure became borderline significant ($P=0.08$). Childhood skinfold thickness was not associated with CAC ($P=0.16$) when adjusted for adult BMI. When risk scores were calculated, risk factors were defined as values at or above the age- and sex-specific 80th percentile for LDL cholesterol, systolic blood pressure, skinfold thickness (childhood), and BMI (current), values at or below the 20th percentile for HDL cholesterol, and smoking.
}\end{figure}
be used to derive CAC. Accordingly, techniques similar to those in the present study are commonly used in cardiovascular research. The between-visit variations for arterial elasticity indices was rather high (between 15% and 20%), as also observed in previous reports. This is, in part, due to the fact that several variables, including arterial diameter and blood pressure measurements, are used to derive these indices. We observed small variation in the carotid artery diameter measurements (2.7%), however, which suggests that much of the long-term variation in elasticity indices is due to physiological fluctuation and not to measurement error. The reproducibility of elasticity measurements is improved by the use of computerized edge-detection analysis of sequential image frames. With this method, Selzer et al reported very low coefficients of variation of 1.2% in carotid diameter measurements. Because of the large variability in blood pressure measurements (coefficient of variation 6% to 9%), coefficients of variation for elasticity indices ranged between 11% and 15%. The large variation in elasticity indices is a limitation, and the results must be interpreted with caution. The noise in the data is likely to weaken the observed relationships. Therefore, the associations observed between risk factors and arterial elasticity may be underestimated. Another potential limitation is the nonparticipation in the follow-up study. However, baseline risk factors (in 1980) were similar among participants and dropouts in the 21-year follow-up. Thus, the present study cohort appears to be representative of the original study population.

In conclusion, childhood risk factors predict decreased carotid artery elasticity 21 years later in adulthood. Therefore, risk factors operating early in life may have sustained deleterious effects on vasculature.

Acknowledgments

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References


