Lifetime Fruit and Vegetable Consumption and Arterial Pulse Wave Velocity in Adulthood
The Cardiovascular Risk in Young Finns Study

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Background—The relationships between childhood lifestyle risk factors and adulthood pulse wave velocity (PWV) have not been reported. We studied whether childhood and adulthood lifestyle risk factors are associated with PWV assessed in adulthood.

Methods and Results—The study cohort comprised 1622 subjects of the Cardiovascular Risk in Young Finns Study followed up for 27 years since baseline (1980; aged 3 to 18 years) with lifestyle risk factor data available since childhood. Arterial PWV was measured in 2007 by whole-body impedance cardiography device. Vegetable consumption in childhood was inversely associated with adulthood PWV ($\beta=-0.06, P=0.02$), and this association remained significant ($\beta=-0.07, P=0.004$) when adjusted for traditional risk factors (high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, systolic blood pressure, body mass index, and smoking). Vegetable consumption was also an independent predictor of PWV in adulthood when adjusted for lifestyle or traditional risk factors ($\beta=-0.08, P=0.002$ and $\beta=-0.07, P=0.0007$, respectively). Persistently high consumption of both fruits and vegetables from childhood to adulthood was associated with lower PWV compared with persistently low consumption ($P=0.03$ for both). The number of lifestyle risk factors (the lowest quintile for vegetable consumption, fruit consumption, physical activity, and smoking) in childhood was directly associated with PWV in adulthood ($P=0.001$). This association remained significant when adjusted for the number of lifestyle risk factors in adulthood ($P=0.003$).

Conclusions—These findings suggest that lifetime lifestyle risk factors, with low consumption of fruits and vegetables in particular, are related to arterial stiffness in young adulthood.

Key Words: epidemiology ■ lifestyle ■ atherosclerosis ■ risk factors

Clinical Perspective on p 2528

Arterial pulse wave velocity (PWV), a marker of central arterial stiffness, is generally accepted as an independent predictor of cardiovascular events and all-cause mortality.11 In the prevention of CVD, it may be possible to identify subjects at a high CVD risk by measuring PWV. We and others have demonstrated that traditional cardiovascular risk factors from childhood to adulthood are associated with PWV in young adulthood.12,13 Dietary habits and physical activity may also have an impact on the process of arterial stiffening. It has been shown that high intake of isoflavones or phytoestrogens may reduce arterial stiffness in middle-aged and elderly people.14,15 Moderate alcohol consumption has cross-sectionally been associated with lower PWV in both sexes.16,17 PWV has also been shown to be associated inversely with...
cardiorespiratory fitness in young adults, and moderate aerobic exercise may reduce large-artery stiffness.

To the best of our knowledge, no information has been published about the associations between childhood lifestyle risk factors and PWV in young adulthood. Therefore, the aim of the present study was to evaluate the relationship of lifestyle risk factors (vegetable consumption, fruit consumption, butter use, alcohol consumption, smoking, and physical activity) measured in childhood and adulthood with PWV in young adulthood. We measured PWV in 1622 white adults aged 30 to 45 years. These individuals were participants of the prospective Cardiovascular Risk in Young Finns Study followed up for 27 years since 1980, for whom risk factor data were available since their childhood (aged 3 to 18 years).

Methods

Subjects

In 1980, a total of 4320 children and adolescents aged 3, 6, 9, 12, 15, and 18 years were randomly chosen from the Finnish national population register to obtain a sample that would represent Finnish children and adolescents reasonably well. In practice, girls and boys of each age cohort in each study community (5 university cities in Finland with medical schools and 12 rural communities in their vicinity) were separately placed in random order on the basis of the unique personal identification number. Every kth girl and every kth boy in each community was selected so that the sample consisted of the required number of boys and girls. The varying k factors were determined on the basis of sample size and the total number of boys and girls in the different age cohorts in each community. A total of 3596 (83.1%) of those invited participated in the first cross-sectional study. During the follow-up, 76 subjects have died; 2 of these deaths were due to atherosclerotic disease. The study flow chart is shown in Figure 1. All subjects provided written informed consent, and the study was approved by the local ethics committees.

Clinical Characteristics and Risk Variables

Height and weight were measured, and body mass index was calculated. Blood pressure was measured from the brachial artery with standard methods as described previously. The mean of 3 measurements was used in the analysis. For the determination of serum lipoprotein levels, venous blood samples were drawn after an overnight fast. All determinations were performed with the use of standard methods reported previously.

Questionnaires using self-reports were completed to collect data on dietary habits, alcohol consumption, smoking, and physical activity. Information on dietary habits was obtained with a nonquantitative food frequency questionnaire. For subjects aged 3 to 9 years, the data were requested from the parents. At the age of 12 to 18 years, study subjects answered the questions themselves, assisted by their parents when necessary. To examine the frequency of fruit and vegetable consumption, the subjects were asked to complete a questionnaire on habitual dietary choices for the past month with 6 response categories: 1 = daily, 2 = almost every day, 3 = a couple of times per week, 4 = about once a week, 5 = a couple of times per month, and 6 = more seldom. The response categories were converted into times of consumption per month (1 = 35; 2 = 25; 3 = 10; 4 = 4; 5 = 2; 6 = 0). In 2007, a more detailed quantitative food frequency questionnaire providing an estimate of food consumption in grams per day was introduced. Subjects were also asked whether they use butter or butter-based spreads on bread. Habitual use of butter or butter-based spread on bread was defined as a risk factor. The dietary variables chosen for this analysis are indicators of 2 major dietary patterns, health conscious and traditional, identified in this study population. The health-conscious pattern was positively correlated with fruit and vegetable consumption, and this pattern was more predominant among female subjects. Dietary patterns remained stable from childhood to adulthood (Spearman correlation, r = 0.32 for traditional and r = 0.38 for health conscious) and especially among older subjects. These patterns were also associated with cardiovascular risk factors.

In 2001 and 2007, participants were asked to report their consumption of 0.33-L cans or bottles of beer, glasses (12 cL) of wine, and 4-cL shots of liquor or spirits during the past week. These doses are comparable to ~14 g of alcohol (=1 U). The values of different beverages consumed during the past week were summed to determine the total alcohol consumption. The distribution of the continuous alcohol consumption variable was strongly skewed and could not be normalized with logarithmic transformation. Therefore, the variable was categorized. The categorization of the participants according to daily ethanol consumption (average amount through the week) was performed as follows: (1) no alcohol consumption during the last week, (2)
23 Arterial PWV Studies

We used a whole-body impedance cardiography device (CircMon, JR Medical Ltd) to determine PWV. CircMon includes a whole-body impedance cardiography channel, a distal impedance plethysmogram channel, and an ECG channel. When the pulse pressure wave enters the aortic arch and the diameter of the aorta changes, the whole-body impedance decreases. The CircMon software measures the time difference between the onset of the decrease in the whole-body impedance signal and subsequently in the distal plethysmogram signal from a popliteal artery at knee joint level. The measurement is triggered by the R wave of the ECG. The PWV can be determined from the distance and the time difference between the 2 recording sites. The repeatability index and the reproducibility index were good (99% and 87%, respectively).26 A detailed description of the method12,27 and the validation study27 has been reported previously.

24 Statistical Methods

The comparisons between study participants and nonparticipants (subjects lost to follow-up or excluded) were performed with the use of age- and sex-adjusted regression analysis for continuous variables and the \( \chi^2 \) test for categorical variables.

To study the effects of risk variables on PWV, we calculated age- and sex-specific Z scores for fruit consumption, vegetable consumption, physical activity, and alcohol consumption at each study year. The Z score values were used to account for the possible biases caused by age, sex, and secular trends in risk factors. Childhood risk variable load was assessed by calculating the average of Z scores from the years 1980, 1983, and 1986. In these analyses, only measurements conducted at the ages of 3 to 18 years were included. Smoking was modeled as a dichotomous variable (no or yes) if subjects have smoked in at least 1 of the follow-ups. Adulthood risk variable load was assessed by calculating the average of measurements in 2001 and 2007.

The univariable relationships between load variables and PWV in childhood and adulthood were examined by regression analysis. To investigate whether sex or age modifies the associations between risk variables and PWV, we included sex \( \times \) risk variable and age \( \times \) risk variable interaction terms in the regression models. We have previously shown with this cohort that traditional risk factors in childhood (systolic blood pressure [SBP] and glucose) and adulthood (SBP, triglycerides, and insulin) were independent predictors of PWV in adulthood.12 Therefore, to study whether the effects of lifestyle risk factors are independent of traditional risk factors, we fitted a multivariable model also including data on those traditional risk factors. To study whether the effects of childhood lifestyle risk factors are independent of current risk factors, we fitted a multivariable model also including adulthood data on those risk factors with significant effects in the childhood multivariable model. In regression analysis, we used a heart rate–specific Z score for PWV because heart rate may be a confounding factor.28

To examine the effect of multiple lifestyle risk factors on PWV, we calculated the number of lifestyle risk factors. Lifestyle risk factors were defined as values at or below the age- and sex-specific 20th percentile for vegetable consumption, fruit consumption, physical activity index, and smoking. The mean number of risk factors was 0.7 (range, 0 to 4) in childhood and 0.8 (range, 0 to 4) in adulthood. Because smoking was only evaluated in children aged 12 years or older, we repeated all analyses using the number of risk factors that did not include smoking as a risk variable and obtained essentially similar results. Linear regression analysis was used to test the associations between the number of risk factors and the linear trend in PWV.

We calculated quintiles of fruit and vegetable consumption to study whether increase in fruit and vegetable consumption in childhood and adulthood is associated with PWV in adulthood. We used linear regression to test for trend in PWV across quintiles of fruit and vegetable consumption. In addition, as subgroup analyses, we used t tests to assess whether subjects persistently in the lowest quintile of fruit and vegetable consumption in childhood and adulthood differed from those persistently in the highest quintile of fruit and vegetable consumption.

All analyses were performed with SPSS for Windows (release 16.0.2, SPSS Inc). Statistical significance was inferred at a 2-tailed \( P \) value \(< 0.05\).

25 Results

The characteristics of study participants (n = 1622) and nonparticipants (n = 1974) are shown in Table 1. A comparison of baseline (1980) values showed that nonparticipants were
Table 2. Multivariable Relationships Between Childhood (Ages 3 to 18 Years) Risk Factor Load and PWV

<table>
<thead>
<tr>
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<th></th>
<th></th>
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<tbody>
<tr>
<td>Sex</td>
<td>0.32 (0.05)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>0.30 (0.01)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vegetable consumption</td>
<td>-0.06 (0.03)</td>
<td>0.02</td>
</tr>
<tr>
<td>Fruit consumption</td>
<td>-0.01 (0.03)</td>
<td>0.57</td>
</tr>
<tr>
<td>Butter use*</td>
<td>0.05 (0.05)</td>
<td>0.07</td>
</tr>
<tr>
<td>Smoking†</td>
<td>-0.005 (0.07)</td>
<td>0.84</td>
</tr>
<tr>
<td>Physical activity index</td>
<td>-0.02 (0.03)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

More often male and had higher SBP and body mass index than participants.

There were no interactions with age, except between SBP and PWV in adulthood. The association between SBP and PWV was statistically significant (P<0.0001) in all age groups, but older subjects had higher β values (0.24 to 0.479). Sex did not modify the associations between risk variables and PWV, except for vegetable consumption in childhood. Vegetable consumption in childhood was inversely related to PWV in both males and females, but in females the association was lower and not statistically significant (β=−0.12, P=0.002 and β=−0.02, P=0.58, respectively). Fruit consumption (β=−0.04, P=0.08), butter use (β=0.04, P=0.09), smoking (β=0.003, P=0.89), and physical activity index (β=−0.03, P=0.26) were not associated with PWV in childhood. In adulthood, vegetable consumption and fruit consumption were statistically significantly related to PWV (β=−0.09, P=0.001 and β=−0.06, P=0.03, respectively). The association of alcohol consumption, smoking, and physical activity index with PWV in adulthood was not statistically significant (β=0.03, P=0.20; β=−0.03, P=0.22; and β=−0.05, P=0.07, respectively).

Table 2 shows the results of the multivariable regression models in childhood. Vegetable consumption was an independent predictor of PWV in childhood as adjusted with lifestyle risk factors or traditional risk factors (β=−0.06, P=0.02 and β=−0.07, P=0.004, respectively). In adulthood (Table 3), vegetable consumption was also the only lifestyle risk factor that was an independent predictor of PWV when adjusted for lifestyle or traditional risk factors. The association with smoking in adulthood became nonsignificant when the associations of traditional risk factors were taken into account (Table 3). The association between childhood vegetable consumption and PWV was borderline significant (β=−0.05, P=0.05) in the multivariable model when adjusted for adulthood vegetable consumption (β=−0.07, P=0.002), age (β=0.28, P<0.0001), and sex (β=0.32, P<0.0001).

An increasing trend in adulthood PWV was observed across the groups with increasing number of childhood lifestyle risk factors (P=0.001; Figure 2A). This association remained significant when adjusted for the number of lifestyle risk factors in adulthood (P=0.003; Figure 2B).

Increase in fruit and vegetable consumption had an inverse association with PWV in childhood (P for trend across quintiles of fruit and vegetable consumption=0.04 and 0.005, respectively) and in adulthood (P for trend=0.03 and 0.003, respectively). There was also a significant difference (0.47 m/s; P=0.03) when those in the lowest quintile of vegetable consumption in both childhood and adulthood were compared with those persistently in the highest quintile (Figure 3A). Subjects in the highest quintile of fruit
consumption in both childhood and adulthood had significantly lower PWV in adulthood than those persistently in the lowest quintile (difference in PWV of 0.46 m/s; P = 0.03; Figure 3B).

Discussion

We found that the number of lifestyle risk factors identified in childhood correlated directly with adulthood PWV. We observed that high fruit and vegetable consumption is associated with lower adulthood PWV, especially if the consumption is persistently high from childhood to adulthood. We also found that vegetable consumption in both childhood and adulthood is an independent predictor of adulthood PWV.

To the best of our knowledge, this is the first study to demonstrate the associations between childhood lifestyle risk factors and adulthood PWV. Traditional childhood CVD risk factors have previously been shown to predict PWV in adulthood.12,13 With regard to childhood lifestyle factors and PWV, current knowledge is limited to cross-sectional data. Sakuragi et al29 have reported a cross-sectional association between childhood adiposity and physical activity and PWV.

Previous studies have reported inverse associations between plant-derived compounds and arterial stiffness in middle-aged and older adults.14,15 High fruit and vegetable consumption has also been related to reduced CVD risk in prospective settings with middle-aged and elderly subjects.5–7 Our present findings are in agreement with the previous studies and suggest that fruit and vegetable consumption is associated with the process of arterial stiffening in young adulthood. Subjects consuming high quantities of fruits and vegetables had slower PWV than those with low consumption. The difference in PWV was more evident if subjects had a high fruit and vegetable consumption from childhood to adulthood compared with those who had a persistently low consumption. The differences in PWV between the highest and the lowest quintile were 0.47 m/s for vegetable consumption and 0.46 m/s for fruit consumption. These
differences may be clinically meaningful because Blacher et al\textsuperscript{30} reported an all-cause mortality adjusted odds ratio of 1.39 in patients with end-stage renal failure, and Vlachopoulos et al\textsuperscript{11} demonstrated the all-cause mortality risk to increase by >10% in low- and high-risk patients for each PWV increase of 1 m/s.

We showed in our previous study that age, sex, SBP, childhood glucose, adulthood triglycerides, and adulthood insulin levels were independent predictors of adulthood PWV.\textsuperscript{12} The pathophysiology related to these traditional risk factors has been discussed in the earlier report. To evaluate whether lifestyle risk factors have an independent effect on PWV, we used multivariate regression models including traditional and lifestyle risk factors. Notably, vegetable consumption was an independent predictor of adulthood PWV. This independent association strengthens the hypothesis that vegetable consumption has a favorable influence on the process of arterial stiffening.

The association between fruit consumption and PWV was relatively weak in adulthood, and this statistically significant finding may possibly be due, at least in part, to the large number of participants. However, the magnitude of the association was quite similar to that previously reported between traditional risk factors and PWV (for example, $\beta$ values for triglycerides of 0.065 to 0.07).\textsuperscript{12,13} Frequent fruit consumption can be considered to represent a conscious intention toward healthy food choices, particularly in the 1980s, when not all fruits were available throughout the year in Finland. Therefore, the associations observed with frequent fruit consumption may reflect the effect of an overall healthier diet, and the effect of fruit consumption may be diluted by other lifestyle changes. This highlights the relevance of the present findings.

We found a borderline significant inverse univariable association between adulthood physical activity and adulthood PWV. However, when adjusted for other risk factors, physical activity did not associate independently with PWV in our cohort. The dilution of the association between physical activity and PWV in the multivariable model may be explained by the fact that physical activity modulates traditional risk factors (eg, high-density lipoprotein cholesterol and triglycerides) in this cohort.\textsuperscript{31} The possible favorable influence of physical activity on PWV may therefore not be direct but rather mediated through a modification of traditional risk factors. It is also important to keep in mind that other lifestyle risk factors could be confounders in these analyses.

The stiffness of large arteries increases with age. The mechanism of the stiffening process is complex,\textsuperscript{32,33} including structural changes of the vascular wall as well as elastocalcinosis, overproduction of collagen, and degradation and remodeling of normal elastin, as caused by repeated mechanical load and inflammation. Structural stiffening may alter endothelial function and thereby further worsen the stiffening. Endothelial dysfunction reduces the expression of nitric oxide, thus increasing vascular smooth muscle cell tone and arterial stiffness.\textsuperscript{32,33} Furthermore, increased local activity of the renin-angiotensin-aldosterone system enhances vascular hypertrophy, reduces elastin synthesis, and increases oxidative stress and fibrosis.\textsuperscript{32} The impact of fruit and vegetable consumption (and thus of nutrients and phytochemicals such as potassium, flavonoids, folate, vitamins, and dietary fiber) on this complex pathophysiological process is largely unknown. Nevertheless, the antioxidative and anti-inflammatory effects, reduction of triglycerides and very-low-density lipoprotein, as well as enhanced glucose tolerance, reduced insulin resistance, and reversed endothelial dysfunction are possible underlying pathophysiological mechanisms.\textsuperscript{6,7,32} Functional aspects of fruits and vegetables, such as low glycemic load, low energy density, and high water content, may also play a role in this process.\textsuperscript{6,14}

Our study has some limitations. First, the food frequency questionnaire used provides the fruit and vegetable consumption frequency only as times per month and is therefore possibly an imprecise estimate (leading to underestimation of associations) because current dietary recommendations are ≥4 to 5 servings per day.\textsuperscript{34} Another potential limitation is the nonparticipation in the follow-up study. However, baseline lifestyle risk factors in 1980 were mainly similar among participants and nonparticipants, with the exception of SBP and body mass index, which were slightly higher in nonparticipants. This significant difference can be explained at least in part by the large number of participants because the absolute difference was quite small. Therefore, the present study cohort appears to be fairly representative of the original study population. It is also a limitation that taking an average of $Z$ scores over ages might oversimplify these data, although age did not modify the associations between risk factors and PWV in childhood. The approach evaluating the association between the number of risk factors and PWV in this study has not been validated. This limits the interpretation of the results and warrants validation in separate cohorts in future studies.

Self-reported retrospective data on diet, alcohol, smoking, and physical activity will have bias. However, as reported previously, validation studies showed significant correlations between information obtained by the food frequency questionnaire and the 48-hour recall\textsuperscript{34} and between physical activity index and maximal cycle ergometer test.\textsuperscript{35} Kentala et al\textsuperscript{16} showed a significant association between self-reports of smoking (a measure similar to that used in our study) and biochemical measurements. These findings support the validity of the self-reports. Because our study cohort was ethnically homogeneous, the generalizability of our results is limited to white European subjects. It is also important to remember that observational studies cannot establish causality, and the impact of both baseline values and the changes in risk factors during follow-up may have been underestimated or overestimated because of possible regression dilution bias.

In conclusion, lifetime lifestyle risk factors, most specifically vegetable consumption, are associated with arterial stiffness measured by PWV. The decrease in PWV appears to be more pronounced if dietary habits remain favorable from childhood to adulthood. These findings highlight the importance of emphasizing dietary habits as early as in childhood in the primary prevention of CVD.
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Disclosures
None.

References

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CLINICAL PERSPECTIVE

The primary prevention of cardiovascular diseases should be started in childhood because the atherosclerotic process develops silently for decades before clinical events such as myocardial infarction or stroke occur. Epidemiological studies have shown that it may be possible to modify cardiovascular disease risk by favorable lifestyle changes (eg, healthy diet, adequate physical activity, smoking restriction). However, a limited amount of information is available on childhood lifestyle risk factors and cardiovascular disease risk in adulthood. The Cardiovascular Risk in Young Finns Study is an ongoing 5-center follow-up study of atherosclerosis risk factors in Finnish children and adolescents. Participants were followed up since 1980 and had lifestyle risk factor data since childhood (3 to 18 years). Arterial pulse wave velocity was determined in young adulthood (aged 30 to 45 years) because it is a marker of arterial stiffness and an independent predictor of cardiovascular events and all-cause mortality. We showed that high fruit and vegetable consumption was associated with lower pulse wave velocity. The decrease in pulse wave velocity was more evident if the consumption of fruits and vegetables remained high from childhood to adulthood. It is also important to modify all lifestyle risk factors (low fruit consumption, low vegetable consumption, low physical activity, and smoking) in childhood because multiple risk factors led to increased arterial stiffness in this study. These findings highlight the importance of emphasizing lifestyle as early as in childhood in the primary prevention of cardiovascular disease.
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