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Adolescence Risk Factors Are Predictive of Coronary Artery Calcification at Middle Age

The Cardiovascular Risk in Young Finns Study

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Objectives The purpose of this study was to examine the roles of adolescence risk factors in predicting coronary artery calcium (CAC).

Background Elevated coronary heart disease risk factor levels in adolescence may predict subsequent CAC independently of change in risk factor levels from adolescence to adulthood.

Methods CAC was assessed in 589 subjects 40 to 46 years of age from the Cardiovascular Risk in Young Finns Study. Risk factor levels were measured in 1980 (12 to 18 years) and in 2007.

Results The prevalence of any CAC was 19.2% (27.9% in men and 12.2% in women). Age, levels of systolic blood pressure (BP), total cholesterol, and low-density lipoprotein cholesterol (LDL-C) in adolescence, as well as systolic BP, total cholesterol, diastolic BP, and pack-years of smoking in adulthood were higher among subjects with CAC than those without CAC. Adolescence LDL-C and systolic BP levels predicted CAC in adulthood independently of 27-year changes in these risk factors. The multivariable odds ratios were 1.34 (95% confidence interval: 1.05 to 1.70; $p = 0.02$) and 1.38 (95% confidence interval: 1.08 to 1.77; $p = 0.01$), for 1-SD increase in adolescence LDL-C and systolic BP, respectively. Exposure to both of these risk factors in adolescence (defined as values at or above the age- and sex-specific 75th percentile) substantially increased the risk of CAC (multivariable odds ratio: 3.5 [95% confidence interval: 1.7 to 7.2; $p = 0.007$]) between groups with no versus both risk factors.

Conclusions Elevated adolescence LDL-C and systolic BP levels are independent predictors of adulthood CAC, indicating that adolescence risk factor levels play an important role in the pathogenesis of coronary heart disease. (J Am Coll Cardiol 2012;60:1364–70) © 2012 by the American College of Cardiology Foundation

The development of coronary heart disease (CHD) starts in childhood decades before clinical symptoms. The presence of preclinical atherosclerotic lesions in adolescents and young adults and their associations with CHD risk factors have been shown in autopsy studies (1).

Coronary artery calcium (CAC) is a sign of coronary atherosclerosis (2) most frequently present in advanced lesions and older individuals (3). The amount of calcified

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plaque correlates with the total amount of atherosclerotic plaque (4), and there is a direct association between CAC and CHD events (5–7). The presence of atherosclerotic plaque is confirmed by a positive scan finding, whereas the absence of detectable CAC on computed tomography (CT) among asymptomatic subjects implies that the presence of atherosclerotic plaque is substantially less likely (3,4,8).

The CARDIA (Coronary Artery Risk Development in Young Adults) study has demonstrated that early adulthood risk factors, including dyslipidemia, high blood pressure (BP), cigarette smoking, and elevated plasma glucose, are associated with increased coronary calcification 2 decades later in middle age independently of contemporary risk factors (9,10). In the Muscatine study, elevated body mass index (BMI) in childhood was associated with adult CAC (11). However, it is unclear whether exposure to other risk factors in adolescence is predictive of increased CAC in adulthood and whether adolescence risk exposure has an independent effect after taking into account a change in risk factors. The residual effect of adolescence CHD risk factor exposures on CAC risk would have implications for primary prevention programs (12). Childhood risk factors, such as dyslipidemia and elevated BP, have been associated with increased preclinical carotid atherosclerosis in adulthood (13–15), but no direct evidence exists linking adolescence lipid and BP levels to coronary atherosclerosis in adulthood. In the present study, we aimed to examine the roles of adolescence risk factors in predicting CAC 3 decades later in adulthood. To distinguish the effects of adolescence risk factor exposure from that of adult exposure, we estimated the residual effect due to adolescence risk exposure by taking into account the change in CHD risk factors from adolescence to adulthood (16). The study subjects were 589 participants in the prospective Cardiovascular Risk in Young Finns Study.

Methods

For detailed methods, please see the Online Appendix.

Participants. The Cardiovascular Risk in Young Finns Study is an ongoing follow-up study of atherosclerosis risk factors of Finnish children and young adults. The first cross-sectional survey was conducted in 1980 on 3,596 participants 3 to 18 years of age. The latest adult follow-up survey was conducted in 2007, in which 2,204 individuals participated (17). In 2008, a cardiac CT study to measure CAC was conducted for 589 individuals, then 40 to 46 years of age. This was a convenience sample; the 3 oldest cohorts from 3 centers with a possibility to perform CAC imaging were invited (N = 711), and the attendance rate was 80%. Risk factor levels among those who participated and those who did not are shown in Online Table 1. Sixty-two participants were taking antihypertensive medication, 19 were taking lipid-lowering medication, 4 used injected insulin, and 2 were taking oral medication for diabetes. No significant difference in results was observed after these participants were excluded from the analyses. Participants gave written informed consent, and the study was approved by local ethics committees.

Clinical characteristics. BMI was calculated as: BMI = weight in kilograms/height in meters squared (kg/m^2). BP was measured using a standard mercury sphygmomanometer in 1980 and a random zero sphygmomanometer in 2007. Smoking was defined as daily smoking in adolescence and/or in adulthood. Pack-years of smoking were calculated as the number of cigarette packs smoked daily multiplied by the duration of daily smoking in years.

Abbreviations and Acronyms

BMI = body mass index
BP = blood pressure
CAC = coronary artery calcium
CHD = coronary heart disease
CI = confidence interval
CRP = C-reactive protein
CT = computed tomography
HDL-C = high-density lipoprotein cholesterol
LDL-C = low-density lipoprotein cholesterol
OR = odds ratio

Biochemical analyses. Venous blood samples were taken after an overnight fast. Standard methods were used to determine total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglyceride concentrations. Low-density lipoprotein cholesterol (LDL-C) was calculated indirectly using the Friedewald formula. In 1980, serum insulin was measured using a modification of the immunoassay method. In 2007, serum insulin concentrations were measured by a microparticle enzyme immunoassay kit. Serum high-sensitivity C-reactive protein (CRP) was analyzed with a turbidimetric immunoassay kit.

CAC scoring. CT scans were performed at 3 study locations: Turku, Tampere, and Kuopio, Finland. The scans were performed with a GE Discovery VCT 64-slice CT/positron emission tomography device (GE Healthcare, Milwaukee, Wisconsin) (Turku), a Philips Brilliance 64-slice CT device (Philips Medical Systems, Best, the Netherlands) (Tampere), and a Siemens Somatom Sensation 16-slice CT device (Siemens Healthcare, Erlangen, Germany) (Kuopio). CAC scores were calculated using the Agatston method for each coronary artery (18). The coefficient of variation for intraobserver measurements was 4%. Absence of CAC was defined as an Agatston score of 0 and presence of CAC as an Agatston score of 1 or greater (9). A phantom with deposits of known calcium concentration was also scanned twice using 3 projections at all of the study centers, and the calcium scores from these scans were compared. The coefficient of variation between all of the phantom scans was 3.9%.

Statistical methods. Logistic regression analysis adjusted for sex and age was used to test how risk factors predict the presence or absence of CAC. A series of multivariable logistic regression models were fitted, positing the dichotomous CAC variable (0 = absence of CAC, 1 = presence of CAC) as the outcome. First, a stepwise multivariable model adjusting for age, sex, and all continuous adolescence risk factors was fitted. Second, a multivariable model in-

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cluding sex, age, all significant adolescence variables from the stepwise model (systolic BP and LDL-C), and change in risk factor levels between adolescence and adulthood (adult level–adolescence level) for these variables was fitted. This model was finally adjusted with adolescence and adulthood levels of BMI, insulin, and CRP as well as pack-years of smoking. Odds ratios (ORs) were standardized for a 1-SD increase in risk factor levels. Spearman correlation coefficients were used to assess associations between adolescence and adulthood risk factor levels and regional CAC scores. Adolescence risk factor variables were available for all 589 participants (587 for lipid variables). Adulthood risk factor variables were available for 569 participants (565 for lipid variables) (i.e., there were 20 individuals with CT scan data who had not participated in the latest adulthood follow-up field clinics).

The combined effect of LDL-C and systolic BP in adulthood versus adolescence on CAC prevalence was studied by dividing the participants into 9 groups according to the presence or absence of high levels of LDL-C, systolic BP, or both in adolescence and adulthood. High levels of LDL-C and systolic BP were defined as values at or above the age- and sex-specific 75th and 80th percentiles with similar results (data shown for the 75th percentile). The effect of multiple high-risk factor levels on prevalence of CAC was studied by a multivariable logistic regression model adjusted for sex and age. A significance level of 0.05 was used for all analyses. The statistical analyses were performed with SAS software version 9.2 (SAS Institute Inc., Cary, North Carolina).

Results

The mean age of participants at follow-up was 42.7 ± 2.4 years, and 44.5% were male. The prevalence of CAC was 19.2%. Total CAC scores of 1 to 100, 101 to 400, and >400 were measured in 16.7%, 1.9%, and 0.7% of the subjects, respectively; 3.4% of men and 3.7% of women had CAC scores above the age- and sex-specific 95th percentile based on large U.S. population data (19).

To study the representativeness of the participating study population, a comparison between the participants and nonparticipants within the 3 oldest cohorts was conducted (Online Table 1). No significant differences between the participants and nonparticipants were found.

Adolescence and adulthood risk factor levels are shown in Table 1. Individuals with CAC were more often male and older than individuals without CAC. They also had higher systolic BP, total cholesterol, and non–HDL-C levels in both adolescence and adulthood, a higher total cholesterol to HDL-C ratio and higher LDL-C levels in adolescence, and higher diastolic BP levels in adulthood. Individuals with CAC had significantly higher pack-years of smoking than individuals without CAC.

In age- and sex-adjusted logistic regression models, the significant ORs for adult CAC were 1.37 (95% confidence interval [CI]: 1.11 to 1.69; p = 0.003) for a 1-SD change in

Table 1 Adolescence and Adult Characteristics by CAC Status in Adulthood in the Cardiovascular Risk in Young Finns Study

	Adolescence (Age 12–18 Yrs)			Adult (Age 39–45 Yrs)		
	CAC Absent	CAC Present	p Value*	CAC Absent	CAC Present	p Value*
n	476	113		460	109	
Male, %	39.7	64.6	<0.0001	39.5	65.4	<0.0001
Age, yrs	14.7 ± 2.4	15.2 ± 2.5	0.02	41.7 ± 2.4	42.2 ± 2.5	0.03
Weight, kg	51.9 ± 12.0	56.3 ± 13.8	0.14	78.7 ± 17.3	83.8 ± 17.7	0.43
BMI, kg/m^2	19.6 ± 2.9	20.3 ± 3.2	0.12	26.9 ± 5.1	27.5 ± 4.7	0.41
Systolic BP, mm Hg	116 ± 10	120 ± 12	0.02	122 ± 16	129 ± 15	0.02
Diastolic BP, mm Hg	70.4 ± 9.8	70.7 ± 9.4	0.84	76.6 ± 12.0	81.7 ± 12.3	0.01
Total cholesterol, mmol/l†	5.14 ± 0.92	5.26 ± 0.90	0.01	5.14 ± 0.92	5.48 ± 1.07	0.04
LDL-C, mmol/l	3.23 ± 0.77	3.41 ± 0.80	0.003	3.18 ± 0.81	3.43 ± 0.92	0.09
HDL-C, mmol/l	1.55 ± 0.31	1.51 ± 0.30	0.65	1.32 ± 0.31	1.32 ± 0.34	0.34
Triglycerides, mmol/l	0.73 ± 0.35	0.74 ± 0.32	0.55	1.48 ± 1.0	1.63 ± 0.91	0.93
Non-HDL-C, mmol/l	3.6 ± 0.8	3.8 ± 0.9	0.004	3.8 ± 0.9	4.2 ± 1.0	0.02
Total cholesterol/HDL-C	3.4 ± 0.7	3.6 ± 0.9	0.01	4.0 ± 1.2	4.4 ± 1.3	0.33
Triglycerides/HDL-C	0.5 ± 0.3	0.5 ± 0.3	0.66	1.2 ± 0.9	1.4 ± 0.9	0.80
CRP, mg/l	1.0 ± 3.2	1.1 ± 3.7	0.87	1.9 ± 2.9	2.9 ± 10.1	0.15
Insulin, mU/l	13.1 ± 5.8	12.6 ± 5.1	0.84	9.1 ± 8.4	12.0 ± 15.9	0.07
Daily smoking, %	16.2	18.9	0.97	16.4	18.3	0.99
Pack-years of smoking				3.3	4.9	0.007
Antihypertensive medication				11.3	11.7	0.93
Lipid-lowering medication				3.2	4.9	0.40

Values are n, %, or mean ± SD. For triglycerides, CRP, and insulin, the p values were calculated for log-transformed values. *p Values are from logistic regression models adjusted for age and sex (except the model for sex, which was adjusted for age only, and the model for age, which was adjusted for sex only). †1 mmol/l = 38.66976 mg/dl.

BMI = body mass index; BP = blood pressure; CAC = coronary artery calcium; CRP = high-sensitivity C-reactive protein; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.

Table 2 ORs and 95% CIs for CAC in Adulthood in a Multivariable Logistic Regression Model (N = 563) Adjusted for All of the Listed Variables

	OR	95% CI	p Value
Age	1.09	0.99–1.20	0.09
Male	2.52	1.56–4.05	0.0001
Adolescence LDL-C	1.34	1.05–1.70	0.02
Adolescence systolic BP	1.38	1.08–1.77	0.01
ΔLDL-C	1.07	0.84–1.37	0.58
ΔSystolic BP	1.25	0.98–1.60	0.08

Increase in ORs for 1-year increase in age and 1-SD increase in LDL-C, systolic BP, ΔLDL-C, and Δsystolic BP. Adolescence risk markers that were not included in the final model included BMI, HDL-C, triglycerides, insulin, CRP, and smoking.

CAC = coronary artery calcium; CI = confidence interval ΔLDL-C = change in LDL-C between adolescence and adulthood; OR = odds ratio; ΔSystolic BP = change in systolic blood pressure between adolescence and adulthood; other abbreviations as in Table 1.

adolescence LDL-C and 1.31 (95% CI: 1.04 to 1.63; p = 0.02) for 1-SD change in adolescence systolic BP. In a multivariable analysis adjusted for sex, age, and change in LDL-C and systolic BP levels between adolescence and adulthood, both LDL-C and systolic BP measured in adolescence remained independent predictors of adult CAC (Table 2). Changes in these risk factors between adolescence and adulthood were not significant predictors of adult CAC. The effects of adolescence LDL-C and systolic BP remained statistically significant after further adjustment for adolescence and adulthood levels of BMI, insulin, and CRP, and pack-years of smoking (p = 0.04 for LDL-C and p = 0.01 for systolic BP). Substituting LDL-C with non–HDL-C did not significantly alter the results.

We further examined the combined effects of high (values at or above the age- and sex-specific 75th percentile) LDL-C and systolic BP levels on the prevalence of adult CAC. In a multivariable logistic regression model adjusted for age and sex, the number of adolescence risk factors was significantly associated with CAC. The OR was 3.5 (95% CI: 1.7 to 7.2; p = 0.002) between groups with zero versus both risk factors, whereas the effect of adult risk factors was nonsignificant: OR: 1.1 (95% CI: 0.5 to 2.5; p = 0.27) between groups with zero versus both risk factors.

We also examined the relationships between established risk algorithms, the Framingham Risk Score calculated using adulthood risk factors (10-year risk of the development of CHD) (20) and the Pathobiological Determinants of Atherosclerosis in Youth score (21) calculated using the adolescence risk factors and adult CAC scores. In bivariate analysis, the adult CAC score correlated significantly with the Framingham score (Spearman's r = 0.22; p < 0.0001) and with the Pathobiological Determinants for Atherosclerosis in Youth score (r = 0.15; p = 0.0002). In a multivariable logistic regression model, both scores were significant predictors of adult CAC (Framingham score, p < 0.0001; Pathobiological Determinants for Atherosclerosis in Youth score, p < 0.05).

The distribution of CAC was examined by assessing the regional CAC scores in the 113 subjects with prevalent calcium (total score >0). The highest average CAC scores were found in the left anterior descending and right coronary arteries (Online Table 2). The correlations of regional CAC scores with adolescence and adulthood LDL-C and systolic BP levels are shown in Table 3. In general, LDL-C in adolescence correlated more strongly with the regional scores than LDL-C in adulthood. Both adolescence and adulthood systolic BP values correlated with total CAC scores, but no significant relationships were seen for regional scores.

Discussion

We demonstrate that elevated adolescence levels of LDL-C and systolic BP are predictive of CAC in adulthood nearly 3 decades later. These associations remained significant after further adjustment for the longitudinal change in these risk factors. The data thus suggest that exposure to adverse levels of LDL-C and systolic BP in adolescence contribute to the development of CAC in adulthood and

Table 3 Age- and Sex-Adjusted Spearman's Correlations Coefficients Between Risk Variables (LDL-C and Systolic Blood Pressure) and Regional Calcium Scores

	r Value	p Value	r Value	p Value
	Adolescence LDL-C		Adulthood LDL-C	
Total score	0.130	0.002	0.082	0.05
LAD	0.158	0.0001	0.109	0.01
LMA	0.094	0.02	0.027	0.53
LCX	0.037	0.38	0.019	0.66
RCA	0.102	0.01	0.043	0.30
	Adolescence Systolic BP		Adulthood Systolic BP	
Total score	0.090	0.03	0.103	0.01
LAD	0.065	0.12	0.065	0.12
LMA	0.051	0.22	0.027	0.53
LCX	0.075	0.07	0.016	0.71
RCA	0.019	0.65	0.071	0.09

LAD = left anterior descending artery; LCX = left circumflex artery; LMA = left main artery; RCA = right coronary artery; other abbreviations as in Table 1.

that these effects are independent of adult levels of LDL-C and systolic BP. This is in line with the findings that we reported using carotid artery intima-media thickness as a surrogate marker for atherosclerosis (13).

One previous study examined whether childhood risk factor levels are predictive of CAC in adulthood (11). As part of the Muscatine Study, Mahoney et al. (11) examined 384 individuals and observed a significant association between increased BMI at ages 8 to 18 years (mean age, 15 years) and CAC measured at the mean age of 33 years. Significant associations between childhood exposure to adverse lipids or BP and CAC were not observed in the Muscatine data, although individuals in whom CAC subsequently developed had nonsignificantly higher levels of total cholesterol in childhood. Compared with the Muscatine study, we had a slightly larger sample size and information on HDL-C that enabled us to calculate LDL-C concentration. Other markers of subclinical atherosclerosis that have been associated with childhood levels of systolic BP and LDL-C include decreased carotid artery elasticity (22) and increased brachial-ankle pulse wave velocity (23).

We used a modeling approach suggested by De Stavola et al. (16) to examine the independent effects of adolescence LDL-C and systolic BP levels on adult CAC. The inclusion of both adolescence risk factors and adult risk factors in the same model would only quantify the direct effect of adolescence risk factors on the outcome because part of the effect of adolescence risk is indirect via the mediating effect of current risk due to tracking. Therefore, we re-specified the model into a mathematically equivalent alternative form, using adolescence risk factors and the change in risk factor level from adolescence to adulthood as the predictor variables. The effect estimate for the adolescence risk factors quantifies the total effect of the adolescence risk factors, whereas the effect estimate for change in risk factor level quantifies the additional influence mediated by the change in risk factor level from adolescence to adulthood. Previously, the effect of change in risk factor levels on CAC was studied in the CARDIA study in which the 15-year change in systolic BP from young adulthood to middle age (mean ages, 25.1 and 40.3 years, respectively) remained an independent predictor of CAC (9). In the present study, change in systolic BP from adolescence to adulthood remained a borderline significant predictor of adult CAC when adjusted for adolescence systolic BP and LDL-C ($p = 0.08$), but was not as important as the adolescence measure. Together, these longitudinal data suggest that maintaining low systolic BP levels throughout life is important in the prevention of subsequent coronary atherosclerosis.

We also found a significant association between the combined effect of LDL-C and systolic BP in adolescence and subsequent CAC. This finding was consistent with previous observations indicating that the presence of multiple risk factors may lead to acceleration of atherosclerosis in young people (1,13,22). The prevalence of CAC in our study was 19.2%. Previous studies of subjects of similar age have reported CAC prevalences of 13.3% to 20.6% (9,11). Most CAC was found in the left anterior descending artery, which is consistent with previous data (24). Individuals who had been exposed to both elevated LDL-C and high systolic BP in adolescence had approximately a 2-fold increased risk of CAC than unexposed individuals (CAC prevalence ~40%), and this association was observed regardless of adulthood levels. This observation suggests that early exposure to these risk factors plays an important independent role in the development of adult CAC. In line with this, baseline risk factor levels in young adults of the CARDIA study were equally or more predictive of CAC in middle age than the subsequent levels (9). Similarly as seen here with the CAC score, we observed that the effects of childhood LDL-C level and systolic BP remained independently associated with an elevated carotid intima-media thickness when adjusted for the adulthood LDL-C and BP levels. These observations may indicate hypothetical vulnerability phases for atherosclerosis during development. Supporting age-dependent effects, we recently showed, using data from 4 longitudinal studies, that risk factor measurements obtained at or after 9 years of age are predictive of subclinical atherosclerosis in adulthood (25). Additionally, risk variables measured in childhood have a tendency to maintain their rank order into adulthood (26–28). This may explain that measurements of single risk variables seem to be as informative as the risk load in identifying groups of children who are at increased risk of atherosclerosis as adults (13).

The roles of LDL-C and elevated BP in the pathogenesis of CHD are well established. Elevated BP is known to accelerate atherosclerosis, collagen synthesis, and arterial smooth muscle hyperplasia and hypertrophy (29). The rate of movement of LDL-C particles from plasma into the arterial wall depends on the plasma concentration of LDL-C (30). Lowering LDL-C levels by statin therapy is associated with decreased CHD-related events (31). A recent consensus statement from the American Heart Association regarding the guidelines for therapy in boys older than 10 years of age and girls after menarche favored use of statins when diet and exercise fail to achieve the set goals for lipid levels, especially for boys with multiple risk factors (32). In the statement, LDL-C levels of ≥3.35 mmol/l are considered high and drug therapy should be considered for those with average levels of ≥4.9 mmol/l. The 75th percentile for LDL-C in youth in our study was 3.6 to 4.2 mmol/l.

The definition of hypertension in children and adolescents according to the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents is based on BP percentiles (33). Children with systolic and/or diastolic BP that is at or above the 95th percentile for age, sex, and height are considered hypertensive, whereas those with BP levels that are at or above the 90th percentile but lower than the 95th percentile are prehypertensive. In our study, the 75th percentile was 112 to 133 mm Hg. Therapy for pediatric

hypertension includes lifestyle changes and antihypertensive drugs in children with secondary hypertension or those who have an insufficient response to lifestyle modifications. In the present study, the combination of high BP and LDL-C in adolescence was especially unfavorable for the development of adult CAC, even with levels that are somewhat lower than the recommended cut points for therapy. Therefore, our results support the prevention and treatment of high LDL-C and BP levels in adolescents.

Substantive research has demonstrated the potential importance of CRP in risk prediction in adults. In this study, adolescence CRP was not associated with adult CAC. This is consistent with our previous data showing a lack of association between childhood CRP and adult carotid artery intima-media thickness (34,35). This suggests that youth CRP may not be a useful marker for the prediction of adult subclinical atherosclerosis. Recent epidemiological observations using the Mendelian randomization approach have not been able to demonstrate a causal relationship between CRP and CHD (35). Exposure to adolescence smoking was similar in individuals in whom CAC subsequently developed but they had higher lifetime exposure to smoking (higher pack-years) than individuals who remained free of CAC. Smoking was previously linked with CAC among young adults in the CARDIA study (9). One possible mechanism explaining the association between LDL-cholesterol and pack-years of smoking and CAC is smoking-induced LDL oxidation. The percentages of daily smokers as well as the LDL-C concentrations were almost identical in adolescence and adulthood. Similar smoking rates are explained by the fact that the prevalence of smoking peaks at 20 years of age and decreases thereafter (unpublished observations). Concerning LDL-C, there has been a significant declining secular trend between 1980 and 2007 that counteracts an age-associated increase (26–28).

Study limitations. Because the study subjects are young adults, we were not able to study associations between adolescence risk factor exposures and cardiovascular events. Instead, we measured CAC with CT as an indicator of atherosclerosis. The CT scans were performed at 3 centers using different devices. The scan protocols, however, were similar, and the images were analyzed by 1 reader blinded to participants' details. A phantom with deposits of known calcium concentration was scanned in the 3 study centers, and no significant differences were found between the phantom scans. Also, use of contrast CT angiography to study noncalcified plaque was not feasible because this was an asymptomatic young population. Previously, we and others (13–15) have shown that childhood adiposity is associated with increased carotid intima-media thickness and decreased arterial elasticity in adulthood. In the present study, however, we were unable to demonstrate an association between BMI measured in adolescence and subsequent CAC. Similarly, we found no association between other metabolic risk factors, such as adolescence levels of insulin and HDL-C with adult CAC. Our study may have been underpowered to detect such associations. Therefore, the negative results need to be interpreted with caution. As expected in this relatively young population, the prevalence of CAC was quite low. However, compared with a large U.S. population (19), the prevalence of subjects with elevated age-dependent values (above the 95th percentile) was rather similar in our population. We observed a sex difference in the prevalence of CAC, which may be due to risk factor levels, sex hormone levels, or other factors. Finally, genetic susceptibility (36) and all of the risk factors possibly contributing to the development of CAC, such as air pollution (37), were not studied.

Conclusions

Elevated LDL-C and systolic BP levels in adolescence may induce permanent effects on coronary arteries, which contribute to the development of future atherosclerosis. Our data add to the evidence base that adolescence risk factor levels play an important role in the pathogenesis of CHD.

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Key Words: adolescents ■ coronary calcium ■ risk factors.

APPENDIX

For a supplemental Methods section and supplemental tables, please see the online version of this article.