Predictors of Carotid Intima-Media Thickness Progression in Young Adults

The Bogalusa Heart Study

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Background and Purpose—We sought to evaluate the predictors of carotid intima-media thickness (CIMT) progression in young adults and to determine whether they differed between the sexes. Although risk factors for the progression of atherosclerosis in middle-aged and elderly adults are well known, they are less well understood in young adults. CIMT is a validated measure of subclinical atherosclerosis.

Methods—B-mode ultrasound images of the far walls of both carotid arteries were obtained in 336 young adults in the Bogalusa Heart Study, whose mean±SD age was 32.3±3.0 years. CIMT and risk factors were measured at baseline (1995–1996) and after 5.8±0.6 years. Multivariable regression was used to determine the predictors of CIMT progression.

Results—CIMT progression rates in women (0.015±0.024 mm/y) and men (0.020±0.027 mm/y) were not statistically different after controlling for body mass index ($P=0.155$). Smoking was a statistically significant predictor of common and composite CIMT progression in both sexes. In men, systolic blood pressure was an independent predictor of internal carotid and composite CIMT progression, fasting glucose predicted common CIMT progression, and family history predicted composite CIMT progression.

Conclusions—In young adults, smoking was a consistent predictor of short-term CIMT progression in men and women. Traditional risk factors also predicted CIMT progression in men. **(*Stroke*. 2007;38:900-905.)**

Key Words: aging ■ atherosclerosis ■ cardiovascular diseases ■ carotid arteries ■ smoking

Associations between cardiovascular risk factors and carotid intima-media thickness (CIMT), a marker of subclinical atherosclerosis, have been established across a wide spectrum of ages, including children and adults. The focus of these studies, however, has been on absolute CIMT rather than on changes in wall thickness over time. Longitudinal changes provide pathophysiological insight into atherogenesis and may predict future cardiovascular events.[1,2] Indeed, in the Bogalusa Heart Study, childhood risk factors were associated with CIMT in young adulthood, and an increasing risk factor burden was associated with increased aortic and coronary atherosclerosis found at autopsy in young adults.[1,3]

Although the risk factors for atherosclerosis progression are well known, their differential effect between the sexes is less well understood, especially in young adults and children.[1,4] In middle-aged and older women, serum triglycerides, presence of the metabolic syndrome, and pulse pressure predict CIMT progression compared with men, whereas physical activity and fibrinogen levels independently predict CIMT in middle-aged and older men but not in women.[5–9] Age, systolic blood pressure (SBP), fasting glucose, and smoking predict CIMT progression in both middle-aged and older men and women.[8,10] Although these conventional cardiovascular risk factors have been associated with increased CIMT in young adults, sex-related differences in the predictors of CIMT progression in young adults have not been described.[4,11] The purpose of this study was to evaluate the predictors of CIMT progression in young adults and to determine whether they differed between the sexes. Because the Bogalusa Heart Study is a longitudinal study of the natural history of atherosclerosis in children and young adults, it allows serial measurements of CIMT over time.

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Subjects and Methods

Study Participants and Design

The institutional review boards at Tulane University Health Sciences Center and the University of Wisconsin Medical School approved this study. The Bogalusa Heart Study is a biracial, longitudinal study of the natural history of atherosclerosis in the rural community of Bogalusa, La.[1,3,11] A detailed description of the study methods has been previously reported.[3,11] In the 1995 to 1996 survey, 519 participants (mean±SD age, 32±3 years; 71% white; 39% men) underwent B-mode ultrasonography of the carotid arteries with measurement of CIMT. In the 2000 to 2001 survey, CIMT was measured in 1204 participants (36±4 years old; 70% white; 43% men). This report includes a cohort of 336 subjects who were scanned in both surveys. This subgroup was not statistically different from the total study population in regard to sex, total cholesterol, age, SBP, body mass index (BMI), family history of coronary artery disease, tobacco use, fasting glucose, insulin, total cholesterol/HDL cholesterol, alcohol use, common CIMT, bulb CIMT, and internal CIMT.[12] Family history was defined in the Bogalusa Heart Study as a mother or father having a myocardial infarction, percutaneous coronary angioplasty, coronary artery bypass surgery, or angina pectoris at any age.

One white male participant reported that he experienced a myocardial infarction at the time of the 1995 to 1996 survey.[12] In addition, 10 subjects self-reported cardiovascular disease on a questionnaire at the 2000 to 2001 survey. Data from these 11 subjects were included in this study. The remaining study participants were free of clinical cardiovascular disease.

Study Procedures

Study-related protocols have been reported previously.[1,11] Images of the right and left common carotid arteries, carotid bulbs, and internal carotid arteries were acquired with a Toshiba SonoLayer SSH 160A ultrasound system (Toshiba Medical, Tokyo, Japan) and a 7.5-MHz linear-array transducer. Images were imaged and measured according to previously described protocols developed for the Atherosclerosis Risk in Communities Study.[11,13] A single reader conducted measurements with use of a semiautomated border-detection program.[11] At the 1995 to 1996 visit, 75 subjects underwent repeat assessments after 10 to 12 days, with a mean absolute difference of 0.05±0.03 mm for all CIMT segments, which is comparable to that in other CIMT studies.[14,15]

Statistical Analysis

Analyses were performed with SAS software (SAS Systems, Cary, NC). For each carotid segment, the average of the right- and left-sided far wall measurements was used to define the segmental maximum CIMT. "Composite" CIMT was defined as the average of the segmental maximum CIMT measurements ("mean max"). Missing data were handled conservatively by listwise deletion, such that both right- and left-sided measurements were required to determine common carotid, carotid bulb, and internal carotid artery values.[12] Cardiovascular risk factors and CIMT at each survey were described by mean±SD values and contrasted by paired *t* tests with Bonferroni's adjustment for multiple comparisons or Fisher exact test. Triglyceride values were corrected for outliers. The χ^2 test was used for between-group comparisons of categorical data. CIMT progression rates were estimated by determining the paired difference in CIMT values between surveys, annualized on the basis of the time between measurements. CIMT progression rates were contrasted between sexes and races according to a general linear model with adjustment for BMI and the Benjamini and Hochberg adjustment for multiple comparisons.[16] Predictors of CIMT progression were modeled separately for men and women. Each multiple linear-regression model of CIMT progression included the following independent variables from the 1995 to 1996 survey: age, BMI, fasting glucose, log insulin, SBP, total cholesterol/HDL cholesterol, race, alcohol use (yes/no), family history of heart disease (yes/no), and smoking status (yes/no) as previously reported.[11] Models also were adjusted for CIMT at the 1995 to 1996 survey because baseline CIMT was strongly correlated with CIMT progression ($r=-0.20$ to -0.30) by segment. SBP was used in the models because it had a stronger association with CIMT than did diastolic blood pressure in the Bogalusa Heart Study, and these 2 values were collinear.[11] The total-to-HDL cholesterol ratio was used instead of individual lipid values because this ratio has demonstrated the strongest associations with CIMT and is less sensitive to the fasting status of the subjects.

Additional models that included sex and baseline CIMT were created to evaluate whether the effects of smoking on CIMT progression were related to differences in the number of cigarettes smoked per day, years smoked, and smoking history (ie, current smoker, former smoker, never smoker).

Results

Subject Characteristics

Subject characteristics and CIMT values at each visit are provided in Table 1. At the time of the 1995 to 1996 survey, the 336 subjects were 32.4±3.0 years old (range, 25 to 37), 73% were white, and 62% were women. A family history of heart disease was reported by 64.1% of subjects. Use of alcohol was reported by 72.4% of subjects. There were 123 participants (36.7%) who reported cigarette use (mean, 16.2±9.9 cigarettes per day) for an average of 13.3±5.6 years. Follow-up was 5.8±0.6 years (range, 4 to 8). At the 2000 to 2001 survey, subjects were 38.2±2.9 years old (range, 31 to 43). Significant increases in BMI, fasting glucose, SBP, and all CIMT measurements were observed between the 2 visits.

CIMT Progression Rates

CIMT progression rates were as follows: common carotid=0.016±0.002 mm/y, carotid bulb=0.023±0.051 mm/y, internal carotid=0.009±0.041 mm/y, and composite CIMT=0.017±0.026 mm/y. CIMT progression rates did not differ significantly in women versus men: common CIMT=0.014±0.018 versus 0.019±0.020 mm/y ($P=0.103$), bulb=0.021±0.047 versus 0.025±0.055 mm/y ($P=0.513$), internal CIMT=0.007±0.038 versus 0.011±0.044 mm/y ($P=0.490$), and composite CIMT=0.015±0.024 versus 0.020±0.027 mm/y ($P=0.155$). Significant differences in CIMT progression between white and black participants also were not seen (data not shown). Progression rates by sex and race are in displayed in Table 2. Common CIMT progressed more slowly in white women than in black women, black men, and white men ($P<0.05$); however, after adjustment for multiple comparisons, theses differences were not statistically significant ($P=0.066$ to 0.096). Similarly, bulb CIMT progressed more rapidly in black men than in white women ($P=0.021$); however, after adjustment, this difference was not statistically significant ($P=0.126$).

Predictors of CIMT Progression

Predictors of segmental and composite CIMT progression for all participants are listed in Table 3. Although sex did not predict the progression of CIMT, there were differences between the sexes in predictors of CIMT progression. In women, smoking was a significant predictor of

TABLE 1. Participant Characteristics From the 1995–1996 and 2000–2001 Surveys

	Survey 1 1995–1996			Survey 2 2000–2001			Survey 1 vs Survey 2
	Men	Women	P_{adj}	Men	Women	P_{adj}	P_{adj}
Age	32.4 (2.8)	32.2 (3.0)	0.609	38.3 (2.9)	38.0 (2.9)	0.389	<0.001
BMI	28.1 (5.9)	27.6 (7.3)	0.574	29.9 (6.6)	29.1 (7.6)	0.410	<0.001
Glucose	81.4 (9.4)	78.8 (13.1)	0.073	87.6 (15.6)	84.9 (21.2)	0.289	<0.001
Insulin	12.8 (8.9)	12.2 (10.8)	0.629	15.0 (11.4)	12.1 (9.4)	0.021	0.174
Current smoker, %	36.4	36.7	0.999	32.8	33.5	0.800	0.445
SBP	117.1 (12.7)	110.5 (13.3)	<0.001	121.7 (14.0)	116.1 (14.5)	<0.001	<0.001
Total/HDL cholesterol ratio	4.9 (1.7)	3.9 (1.3)	<0.001	4.9 (1.6)	3.8 (1.0)	<0.001	0.553
HDL cholesterol	43.6 (14.7)	52.3 (13.4)	<0.001	43.1 (13.6)	53.2 (12.4)	<0.001	0.603
Triglycerides	127.9 (70.4)	101.3 (53.0)	0.585	122.4 (68.8)	95.9 (52.0)	0.373	0.327
LDL cholesterol	133.6 (39.9)	120.2 (29.8)	0.001	131.6 (38.9)	121.6 (31.8)	0.017	0.964
Common CIMT	0.683 (0.102)	0.658 (0.085)	0.037	0.797 (0.130)	0.746 (0.122)	0.001	<0.001
Bulb CIMT	0.910 (0.179)	0.834 (0.151)	<0.001	1.103 (0.386)	0.964 (0.277)	0.001	<0.001
Internal CIMT	0.705 (0.105)	0.670 (0.107)	0.030	0.793 (0.197)	0.707 (0.170)	0.002	<0.001
Composite CIMT	0.761 (0.094)	0.718 (0.087)	<0.001	0.884 (0.191)	0.800 (0.157)	<0.001	<0.001

All values mean (SD) unless otherwise noted.

common carotid and composite CIMT progression. Predictors with borderline statistical significance in women included smoking and SBP for the carotid bulb and age for common and composite CIMT. No independent predictors of internal CIMT were identified for women.

In men, smoking also predicted common and composite CIMT progression. SBP was an independent predictor of internal carotid and composite CIMT progression. Family history predicted composite CIMT progression, and fasting glucose predicted common CIMT progression. Predictors of borderline statistical significance in men included alcohol use for common CIMT, family history for bulb and internal CIMT progression, and BMI for internal carotid CIMT progression.

The percentage of smokers did not change between surveys and was similar among men and women at each survey (Table 1). Similarly, the number of cigarettes smoked per day, years of smoking, and smoking history were similar between the sexes. The association between the number of cigarettes smoked per day and CIMT progression was of borderline significance ($P=0.052$).

TABLE 2. CIMT Progression Rates

Site	Race and Sex	N	Mean ΔCIMT, mm/y	95% CI, mm/y
Common carotid	White men	93	0.019	0.015–0.023
	Black men	31	0.021	0.013–0.028
	White women	148	0.013	0.010–0.015
	Black women	57	0.018	0.013–0.024
Carotid bulb	White men	90	0.021	0.011–0.032
	Black men	30	0.034	0.009–0.060
	White women	145	0.022	0.015–0.028
	Black women	52	0.020	0.003–0.037
Internal carotid	White men	83	0.011	0.001–0.021
	Black men	26	0.014	0.001–0.026
	White women	136	0.009	0.001–0.016
	Black women	53	0.004	−0.002–0.010
Composite	White men	81	0.019	0.013–0.025
	Black men	26	0.027	0.016–0.030
	White women	138	0.014	0.010–0.019
	Black women	50	0.015	0.008–0.020

Discussion

Cross-sectional studies have established CIMT as a marker of atherosclerosis and have determined predictors for absolute CIMT and its progression.[1,2,8,10,11,17,18] In this study, we identified the predictors of CIMT progression in young (25- to 37-year-old) adults. The major finding was that smoking was the most consistent predictor of CIMT progression in both sexes and the only statistically significant predictor of composite CIMT progression in young women during an average follow-up of 5.8 years. In previous studies, smoking predicted CIMT in young women.[11,18] An earlier report from the Bogalusa Heart Study demonstrated that LDL cholesterol and BMI predicted absolute CIMT in young adults; however, smoking status was not incorporated in that analysis.[1] Autopsy studies of young adults in the Bogalusa Heart Study and the Pathobiological Determinants of Atherosclerosis in Youth Study demonstrated an association between coronary atherosclerosis and cigarette smoking.[3,19] In middle-aged and older populations, total years of cigarette smoking was the most significant independent predictor of severe carotid atherosclerosis.[20] In middle-aged adults in the Atherosclerosis Risk in Communities study, there was a linear relation between total pack-years of smoking and increased CIMT that persisted with adjustment for age and sex.[17]

TABLE 3. Predictors of CIMT Progression

Variable	Men β	Men 95% CI		Men P_{adj}	Women β	Women 95% CI		Women P_{adj}
a. Common Carotid Artery								
Intercept	−0.0242	−0.0833	0.0348	0.417	−0.0424	−0.0825	−0.0023	**0.038**
Age	0.0001	−0.0013	0.0015	0.874	0.0009	−0.0001	0.0018	0.065
BMI	0.0006	−0.0004	0.0017	0.221	0.0001	−0.0004	0.0007	0.640
Current drinker	−0.0089	−0.0181	0.0004	0.059	−0.0009	−0.0070	0.0053	0.777
Current smoker	0.0092	0.0007	0.0177	**0.035**	0.0064	0.0003	0.0125	**0.039**
Family history	0.0016	−0.0062	0.0094	0.687	0.0013	−0.0048	0.0073	0.682
Glucose	0.0005	0.0001	0.0010	**0.025**	0.0000	−0.0003	0.0003	0.979
Log insulin	−0.0021	−0.0247	0.0205	0.854	0.0034	−0.0140	0.0208	0.701
SBP	−0.0002	−0.0005	0.0002	0.351	0.0001	−0.0001	0.0004	0.301
Total/HDL cholesterol ratio	0.0005	−0.0018	0.0028	0.652	0.0014	−0.0009	0.0037	0.234
b. Carotid Bulb								
Intercept	−0.0248	−0.1849	0.1353	0.758	0.0350	−0.0714	0.1414	0.517
Age	0.0005	−0.0032	0.0042	0.789	0.0013	−0.0011	0.0038	0.281
BMI	−0.0007	−0.0035	0.0021	0.621	−0.0003	−0.0019	0.0013	0.748
Current drinker	0.0050	−0.0188	0.0289	0.675	−0.0125	−0.0290	0.0041	0.138
Current smoker	0.0171	−0.0053	0.0395	0.133	0.0157	−0.0007	0.0320	0.060
Family history	0.0184	−0.0022	0.0389	0.079	0.0008	−0.0155	0.0172	0.920
Glucose	−0.0004	−0.0016	0.0009	0.534	−0.0001	−0.0008	0.0006	0.771
Log insulin	0.0361	−0.0225	0.0948	0.223	0.0275	−0.0200	0.0749	0.254
SBP	0.0002	−0.0006	0.0011	0.564	−0.0007	−0.0013	0.0000	0.052
Total/HDL cholesterol ratio	−0.0005	−0.0064	0.0055	0.872	0.0019	−0.0042	0.0080	0.532
c. Internal Carotid Artery								
Intercept	−0.1409	−0.2931	0.0113	0.069	−0.0712	−0.1556	0.0131	0.097
Age	−0.0003	−0.0038	0.0031	0.842	0.0012	−0.0007	0.0031	0.208
BMI	−0.0022	−0.0049	0.0004	0.095	−0.0002	−0.0014	0.0011	0.809
Current drinker	0.0028	−0.0209	0.0264	0.815	0.0051	−0.0079	0.0181	0.436
Current smoker	0.0131	−0.0088	0.0350	0.237	0.0095	−0.0038	0.0229	0.160
Family history	0.0183	−0.0015	0.0382	0.069	0.0045	−0.0086	0.0175	0.502
Glucose	0.0009	−0.0003	0.0022	0.133	0.0003	−0.0002	0.0009	0.233
Log insulin	−0.0025	−0.0599	0.0549	0.931	0.0001	−0.0368	0.0370	0.996
SBP	0.0011	0.0003	0.0020	**0.008**	−0.0001	−0.0006	0.0005	0.831
Total/HDL cholesterol ratio	0.0014	−0.0043	0.0072	0.620	0.0034	−0.0024	0.0093	0.245
d. Composite								
Intercept	−0.0765	−0.1560	0.0031	0.059	−0.0248	−0.0785	0.0290	0.363
Age	−0.0001	−0.0019	0.0017	0.931	0.0011	−0.0001	0.0023	0.082
BMI	−0.0006	−0.0020	0.0008	0.380	0.0001	−0.0007	0.0009	0.867
Current drinker	−0.0013	−0.0134	0.0108	0.832	−0.0030	−0.0113	0.0053	0.474
Current smoker	0.0173	0.0059	0.0286	**0.003**	0.0110	0.0027	0.0194	**0.010**
Family history	0.0138	0.0036	0.0241	**0.008**	0.0020	−0.0064	0.0104	0.631
Glucose	0.0003	−0.0003	0.0009	0.342	0.0001	−0.0003	0.0004	0.726
Log insulin	0.0093	−0.0200	0.0387	0.527	0.0053	−0.0187	0.0294	0.662
SBP	0.0006	0.0001	0.0010	**0.009**	−0.0002	−0.0005	0.0002	0.303
Total/HDL cholesterol ratio	0.0007	−0.0023	0.0036	0.652	0.0023	−0.0007	0.0054	0.134

Bold values indicate $P<0.05$.

Smoking causes endothelial dysfunction, resulting in impaired endothelium-dependent peripheral and coronary vasodilation.[21] In vitro studies of cigarette smoke extract and nicotine have demonstrated decreased nitric oxide availability, resulting in vasodilatory dysfunction.[22] In both sexes, cigarette smoking causes the release of inflammatory cytokines, particularly interleukin-6 and tumor necrosis factor-α, increases leukocyte and platelet cell activation, and results in increased adhesion molecules and smooth muscle cell proliferation.[22] These factors initiate the pathway of atherosclerosis, ultimately resulting in atherosclerosis.

A major strength of this study is the description of prospective associations between prevalent cardiovascular risk factors and CIMT progression, in contrast to isolated cross-sectional associations between risk factors and absolute CIMT values, as described in most previous studies. This study underlines the importance of assessing risk factor profiles in young adults by demonstrating that risk factors are associated with the progression of subclinical atherosclerosis over a short time frame, even in individuals who are at low risk for such events. Although CIMT progression is not linear, short-term increases in CIMT that are related to risk factors probably are associated with increased cardiovascular risk. In this context, the increase in risk factors such as BMI, SBP, and fasting glucose as subjects aged between the 2 surveys is of concern. Rates of smoking remained constant.

This study characterized CIMT progression rates and their predictors in young adults. Although, SBP, fasting glucose, and family history predicted CIMT progression in young men but not in young women, this study had limited statistical power to identify all of the risk factors that might be associated with atherosclerosis progression.[11] Indeed, the association between SBP and CIMT progression in the carotid bulb in women was at the borderline of statistical significance.

Because this study identified baseline predictors of longitudinal CIMT progression, it is an association study and therefore is subject to selection bias. Very few subjects (n=3) had diabetes mellitus (fasting glucose >126 mg/dL). Furthermore, a family history of heart disease was present in 64% of subjects. This high value is explained by the broad definition of a family history of heart disease, which included any parental history of heart disease, rather than premature heart disease. In the 2000 to 2001 dataset, temporal drift in CIMT reading was not assessed. Although drift could have affected the absolute progression rates described in this article, comparisons between groups should be valid, because any drift would be expected to be similar between races and sexes. The laboratory that performed the CIMT measurements for this study is very experienced, and significant temporal drift has not been noted in other studies from this laboratory.[23,24]

Conclusions

In young adults, smoking was a consistent predictor of short-term CIMT progression in men and women. SBP, fasting glucose, and family history predicted CIMT progression in young men; however, larger longitudinal studies are needed to further define sex-related differences.

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Disclosures

None.

References

1. Li S, Chen W, Srinivasan SR, Bond MG, Tang R, Urbina EM, Berenson GS. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study. *JAMA*. 2003;290:2271–2276.
2. Hodis H, Mack W, LaBree L, Selzer R, Liu C, Liu C, Azen S. The role of carotid arterial intima-medial thickness in predicting clinical coronary events. *Ann Intern Med*. 1998;128:262–269.
3. Berenson GS, Srinivasan SR, Bao W, Newman WP III, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults: the Bogalusa Heart Study. *N Engl J Med*. 1998;338:1650–1656.
4. Oren A, Vos LE, Uiterwaal CS, Grobbee DE, Bots ML. Cardiovascular risk factors and increased carotid intima-media thickness in healthy young adults: the Atherosclerosis Risk in Young Adults (ARYA) Study. *Arch Intern Med*. 2003;163:1787–1792.
5. Stensland-Bugge E, Bonaa KH, Joakimsen O. Age and sex differences in the relationship between inherited and lifestyle risk factors and subclinical carotid atherosclerosis: the Tromso study. *Atherosclerosis*. 2001; 154:437–448.
6. Stensland-Bugge E, Bonaa KH, Joakimsen O, Njolstad I. Sex differences in the relationship of risk factors to subclinical carotid atherosclerosis measured 15 years later : the Tromso study. *Stroke*. 2000;31:574–581.
7. LaRosa JC. Triglycerides and coronary risk in women and the elderly. *Arch Intern Med*. 1997;157:961–968.
8. Ferrieres J, Elias A, Ruidavets JB, Cantet C, Bongard V, Fauvel J, Boccalon H. Carotid intima-media thickness and coronary heart disease risk factors in a low-risk population. *J Hypertens*. 1999;17:743–748.
9. Lassila HC, Tyrrell KS, Matthews KA, Wolfson SK, Kuller LH. Prevalence and determinants of carotid atherosclerosis in healthy postmenopausal women. *Stroke*. 1997;28:513–517.
10. Kuller L, Borhani N, Furberg C, Gardin J, Manolio T, O'Leary D, Psaty B, Robbins J. Prevalence of subclinical atherosclerosis and cardiovascular disease and association with risk factors in the Cardiovascular Health Study. *Am J Epidemiol*. 1994;139:1164–1179.
11. Urbina EM, Srinivasan SR, Tang R, Bond MG, Kieltyka L, Berenson GS. Impact of multiple coronary risk factors on the intima-media thickness of different segments of carotid artery in healthy young adults (the Bogalusa Heart Study). *Am J Cardiol*. 2002;90:953–958.
12. Stein JH, Douglas PS, Srinivasan SR, Bond MG, Tang R, Li S, Chen W, Berenson GS. Distribution and cross-sectional age-related increases of carotid artery intima-media thickness in young adults: the Bogalusa Heart Study. *Stroke*. 2004;35:2782–2787.
13. Bond M, Barnes R, Riley W, Wilmoth S, Chambless L, Howard G, Owens B, ARIC Study Group. High-resolution B-mode ultrasound scanning methods in the Atherosclerosis Risk in Communities Study (ARIC). *J Neuroimaging*. 1991;1:68–73.
14. Riley WA, Barnes RW, Applegate WB, Dempsey R, Hartwell T, Davis VG, Bond MG, Furberg CD. Reproducibility of noninvasive ultrasonic measurement of carotid atherosclerosis: the Asymptomatic Carotid Artery Plaque Study. *Stroke*. 1992;23:1062–1068.
15. Kanters SD, Algra A, van Leeuwen MS, Banga JD. Reproducibility of in vivo carotid intima-media thickness measurements: a review. *Stroke*. 1997;28:665–671.

16. Benjamini Y, Hochberg Y Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc.* 1995;B57:289–300.
17. Chambless LE, Folsom AR, Davis V, Sharrett R, Heiss G, Sorlie P, Szklo M, Howard G, Evans GW. Risk factors for progression of common carotid atherosclerosis: the Atherosclerosis Risk in Communities Study, 1987–1998. *Am J Epidemiol*. 2002;155:38–47.
18. Davis PH, Dawson JD, Mahoney LT, Lauer RM. Increased carotid intimal-medial thickness and coronary calcification are related in young and middle-aged adults: the Muscatine study. *Circulation*. 1999;100:838–842.
19. McGill HC Jr, McMahan CA. Determinants of atherosclerosis in the young: Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. *Am J Cardiol.* 1998;82:30T–36T.
20. Whisnant JP, Homer D, Ingall TJ, Baker HL Jr, O'Fallon WM, Wievers DO. Duration of cigarette smoking is the strongest predictor of severe extracranial carotid artery atherosclerosis. *Stroke*. 1990;21:707–714.
21. Puranik R, Celermajer DS. Smoking and endothelial function. *Prog Cardiovasc Dis*. 2003;45:443–458.
22. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. *J Am Coll Cardiol*. 2004;43:1731–1737.
23. Tang R, Hennig M, Thomasson B, Scherz R, Ravinetto R, Catalini R, Rubba P, Zanchetti A, Bond MG. Baseline reproducibility of B-mode ultrasonic measurement of carotid artery intima-media thickness: the European Lacidipine Study on Atherosclerosis (ELSA). *J Hypertens*. 2000;18:197–201.
24. Tang R, Hennig M, Bond MG, Hollweck R, Mancia G, Zanchetti A. Quality control of B-mode ultrasonic measurement of carotid artery intima-media thickness: the European Lacidipine Study on Atherosclerosis. *J Hypertens*. 2005;23:1047–1054.

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