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Carotid plaque, a subclinical precursor of vascular events:

The Northern Manhattan Study

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Abstract

Background—Carotid atherosclerosis is a known biomarker associated with future vascular disease. The risk associated with small, nonstenotic carotid plaques is less clear. The objective of this study was to examine the association between maximum carotid plaque thickness and risk of vascular events in an urban multiethnic cohort.

Methods—As part of the population-based Northern Manhattan Study, carotid plaque was analyzed among 2,189 subjects. Maximum carotid plaque thickness was evaluated at the cutoff level of 1.9 mm, a prespecified value of the 75th percentile of the plaque thickness distribution. The primary outcome measure was combined vascular events (ischemic stroke, myocardial infarction, or vascular death).

Results—Carotid plaque was present in 1,263 (58%) subjects. After a mean follow-up of 6.9 years, vascular events occurred among 319 subjects; 121 had fatal or nonfatal ischemic stroke, 118 had fatal or nonfatal myocardial infarction, and 166 died of vascular causes. Subjects with maximum carotid plaque thickness greater than 1.9 mm had a 2.8-fold increased risk of combined vascular events in comparison to the subjects without carotid plaque (hazard ratio, 2.80; 95% CI, 2.04–3.84). In fully adjusted models, this association was significant only among Hispanics. Approximately 44% of the low-risk individuals by Framingham risk score had a 10-year vascular risk of 18.3% if having carotid plaque.

Conclusions—Maximum carotid plaque thickness is a simple and noninvasive marker of subclinical atherosclerosis associated with increased risk of vascular outcomes in a multiethnic cohort. Maximum carotid plaque thickness may be a simple and nonexpensive tool to assist with vascular risk stratification in preventive strategies and a surrogate endpoint in clinical trials.

Carotid artery atherosclerosis is a strong predictor for future ischemic stroke as a result of both luminal stenosis and plaque rupture.[1,2] Carotid atherosclerosis also has been associated with an increased risk of cardiovascular disease.[3,4] The degree of carotid stenosis is a strong marker of the risk of stroke and has been used to select patients for interventional procedures among asymptomatic subjects.[5] The role of nonstenotic and "vulnerable" atherosclerotic plaque has been recognized as an important factor to identify patients at high risk to develop stroke and

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other ischemic vascular events.6,7 High-resolution B-mode ultrasound could help identify "vulnerable" individuals at high risk for vascular events beyond the Framingham vascular risk factors.8-10 Carotid artery plaque and intima-media thickness (IMT) are markers of systemic subclinical atherosclerosis and strong predictors of incident myocardial infarct (MI) and ischemic stroke.11-13 Of the two, several studies suggest that carotid plaque may be a more powerful predictor of vascular outcomes than IMT.14,15

Although some population-based longitudinal studies, including the Atherosclerosis Risk in Communities (ARIC) Study,16 the Cardiovascular Health Study,17 and the Rotterdam Study, 18 have shown an association between nonstenotic carotid plaque and an increased risk of vascular events, the information from lower socioeconomic and diverse race–ethnic communities is sparse. In addition, the carotid scanning and reading protocols used in these studies are complex, lengthy, and therefore not practical for use in large epidemiologic studies or a busy clinical practice. In this study, we sought to determine the association between maximum carotid plaque thickness (MCPT) and the risk of ischemic stroke, MI, and vascular death in a prospective cohort study from an urban multiethnic community.

Methods

Subjects

The Northern Manhattan Study (NOMAS) is an ongoing population-based study designed to document the incidence of stroke, novel risk factors, and vascular outcomes in a multiethnic urban community.[19] The race–ethnic distribution of community residents is approximately 63% Hispanic, 20% black, and 15% white.

Selection of the prospective cohort

The methods of stroke-free participant recruitment and enrollment have been described previously.[20] Subjects were identified by random digit dialing and enrolled in a prospective study between 1993 and 2001 if they had never been diagnosed with stroke, were older than age 39 years, and resided in northern Manhattan for more than 3 months. The study was approved by the Columbia University Medical Center Institutional Review Board. All participants gave informed consent. A total of 3,298 subjects were enrolled.

Baseline data were collected through interviews of the community participants using standardized data collection instruments,[21] review of the medical records, and physical and neurologic examinations. Race–ethnicity was based on self-identification through a series of questions modeled after the US Census and the standard definitions outlined by Directive 15. Hypertension was defined as a systolic blood pressure ≥140 mm Hg or a diastolic blood pressure ≥90 mm Hg or a patient's self-report of a history of hypertension or use of antihypertensive medications. Diabetes mellitus was defined as fasting blood glucose >126 mg/dL or the patient's self-report of such a history or use of insulin or hypoglycemic medications. Cigarette smoking was categorized as non-smoker, former, or current smoker. Mild to moderate alcohol use was defined as current drinking of >1 drink per month and ≤2 drinks per day. Cardiac disease included history of angina, MI, coronary artery disease, atrial fibrillation, congestive heart failure, or valvular heart disease.

Assessment of maximum carotid plaque thickness

Carotid ultrasound was performed according to standard scanning and reading protocols by a trained and certified sonologist as detailed previously.22,23 Left and right carotid bifurcations and internal and common carotid arteries were examined for the presence of plaque. Plaque was defined as an area of focal wall thickening 50% greater than surrounding wall thickness confirmed by marking and comparing plaque thickness with the thickness of the surrounding

wall during scanning by electronic calipers. The plaque boundaries were traced manually from the digitized multiangled images and MCPT (in millimeters) was computed automatically by Image Pro software (Microsoft Inc., Redmond, WA). The MCPT reliability analyses were conducted among 110 stroke-free NOMAS subjects. The interrater intraclass correlation coefficient for MCPT was 0.87 and intrarater intraclass correlation coefficient 0.94. Pulsed Doppler ultrasound was performed to obtain peak systolic and end-diastolic velocities.

Follow-up and outcomes assessment

Follow-up evaluations were conducted annually by telephone to assess vital and functional status, intercurrent hospitalizations, and to screen for symptoms consistent with stroke, transient ischemic attack, or MI.[20] When symptoms were reported, participants were evaluated in person by a study neurologist or cardiologist. The examiners were blinded to the carotid measures.

Definitions of outcomes

Ischemic stroke was defined by the National Institute of Neurological Disorders and Stroke Classification of Cerebrovascular Diseases III. Patients with primary intracerebral or subarachnoid hemorrhage were excluded.20 Myocardial infarction was defined by criteria adapted from the Cardiac Arrhythmia Suppression Trial24 and the Lipid Research Clinics Coronary Primary Prevention Trial.[25] Causes of death were determined from death certificates, medical records of hospitalizations, family interviews, physicians caring for the patient, and health professionals. Causes of death were verified by a study physician and classified as vascular or nonvascular. Vascular causes of death were stroke, MI, heart failure, pulmonary embolus, cardiac arrhythmia, and other vascular causes. Nonvascular causes of death included accidents, cancer, pulmonary (pneumonia, chronic obstructive pulmonary disease, and so on), and other nonvascular causes.

Statistical analyses

The cut points of MCPT were prespecified into the following three categories: 1) no plaque (MPCT = 0); 2) with plaque but MCPT less than the 75th percentile of the MCPT distribution (1.9 mm); and 3) MCPT ≥75th percentile. MCPT was compared across demographic and vascular and lifestyle risk factor categories to identify potential confounders. The variables of interest were prespecified based on previous NOMAS results on the association of traditional vascular risk factors and risk of vascular events.[20] Variables with significant associations at the level of $p < 0.1$ in univariate models were included in the final multivariate models. Bonferroni correction was used to adjust for multiple comparisons. Kaplan-Meier curves were constructed to illustrate the vascular event-free survival between subjects with no plaque, with plaque but MCPT <75th percentile, and MCPT >75th percentile. The age-specific incidence rates of ischemic stroke, MI, and combined vascular events for various MCPT categories were expressed per 1,000 person-years. Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% CIs of MCPT. Models were adjusted for demographics (age, gender, race–ethnicity, and education) first and then adjusted for risk factors, including hypertension, diabetes, low-density lipoprotein and high-density lipoprotein levels, body mass index (kg/m^2), smoking, alcohol consumption, aspirin, and lipid-lowering medication. The 10-year risks of combined vascular events according to the Framingham risk score (FRS) categories[26] were computed for the plaque categories. The *p* values were calculated by two-sided normal approximation test based on product-limit survival estimators and their standard errors. All statistical analyses were performed using SAS version 8.02 (SAS Institute, Cary, NC).

Results

Carotid ultrasound was performed among 2,189 (66%) subjects at the time of baseline evaluation. Demographics and clinical characteristics of this group did not differ from the characteristics of the parent cohort.[20] The mean age in the cohort was 68 ± 10 years; 60% were women; 52% Caribbean Hispanics, 25% black, and 22% white. Carotid plaque was present in 1,263 (58%) subjects and was more prevalent among subjects older than 65 years; non-Hispanics; those with a history of hypertension, diabetes, or cardiac disease; current smokers; and those with low-density lipoprotein cholesterol ≥130 (table 1). The mean MCPT was 1.1 ± 0.9 mm (range, 0–8.0 mm; median, 1.0 mm) and the 75th percentile was 1.9 mm. Stenosis >40% was present in 69 subjects (4%), among whom only six had carotid stenosis of 60% to 79%, one had stenosis 80% to 99%, and none had occlusion.

After a mean follow-up of 6.9 years, ischemic stroke, MI, or vascular death occurred in 319 (14%) subjects; 121 had fatal or nonfatal ischemic stroke, 118 had fatal or nonfatal MI, and 166 died of other vascular causes. Age-adjusted incident rates for ischemic stroke, MI, and combined vascular events were 7.9, 7.7, and 19.3 events per 1,000 person-years, respectively. The incidence rates increased with age and increased MCPT level (table 2). The Kaplan-Meier curves for the vascular event-free intervals are presented for the subjects without plaque; with plaque and MCPT <1.9 mm; and MCPT ≥1.9 mm (figure e-1 on the *Neurology*® Web site at www.neurology.org).

In the unadjusted Cox regression model (table 3), MCPT ≥1.9 mm was associated with a 2.8-fold increased risk of combined events (HR, 2.76; 95% CI, 2.10–3.63) in comparison to the reference (no plaque). After adjusting for demographics and risk factors, this association remained significant (HR, 1.48; 95% CI, 1.05–2.10). MCPT ≥1.9 mm was associated with a 1.8-fold increased risk of ischemic stroke (HR, 1.79; 95% CI, 1.11–2.90), a 2.9-fold increased risk of MI (HR, 2.87; 95% CI, 1.73–4.78), and 3.3-fold increased risk of vascular death (HR, 3.28; 95% CI, 2.05–5.23). After adjustment for demographics and traditional vascular risk factors, these risks attenuated and were not significant (figure e-2).

Stratified analyses by age, sex, and race–ethnicity are presented in table 4. The association between MCPT ≥1.9 mm and the vascular risk was substantial in all age and sex strata in comparison to reference (no plaque). This was particularly pronounced among subjects older than 65 years (table 4, model 2). Men had an adjusted 2.3-fold increased risk of combined outcomes (model 2). Among Hispanics, MCPT ≥1.9 mm was associated with a significant adjusted 2.2- and 3.0-fold increased risk of combined outcome (models 3 and 2). Among whites and blacks, this risk was nonsignificant. All stratified analyses, except for Hispanics, were not significant in fully adjusted models (model 3).

The 10-year Framingham score risks of combined vascular events by plaque categories are presented in table 5. Approximately 44% of subjects with low FRS and plaque <1.9 mm (220/505 with low FRS) had a 10-year risk of 18.3% vs 5.8% among those without plaque. Approximately 12% of subjects in low FRS and MCPT ≥1.9 mm (62/505) had a 10-year risk of 24.7%. Those in the intermediate FRS category with plaque had a significant increased 10-year risk in comparison to those without plaque, but this risk remained within the same FRS category, except for those with MCPT ≥1.9 mm whose 10-year risk exceeded 20% (25.1%). The 10-year vascular risk among individuals with high FRS and plaque did not significantly differ in comparison to those high-risk individuals without plaque.

Discussion

Our results demonstrate an increased incidence of ischemic stroke, MI, and vascular death among stroke-free individuals with presence of small nonstenotic carotid plaques in an urban

population-based cohort. The age-adjusted incidence rate of combined vascular outcome in our study was 12/1,000 person-years for subjects without carotid plaque, 16/1,000 person-years for subjects with plaque but MCPT <1.9 mm, and 35/1,000 person-years for those with MCPT ≥1.9 mm. In addition, MCPT was a stronger predictor of MI and vascular death than of ischemic stroke, indicating that small, nonstenotic carotid plaque may be a marker of generalized atherosclerotic burden rather than a triggering lesion in the causative pathway of ischemic stroke. In ischemic stroke, however, other plaque characteristics such as ulcerations, surface irregularities, and morphologic composition may be more important than plaque size.[6-9,23,27] Presence of carotid plaque may considerably contribute to better estimation of the 10-year Framingham vascular risk. More than a half of individuals in low and moderate FRS categories can be reclassified into the higher risk category if their information on presence on carotid plaque is available. This may have a direct implication for the risk stratification and treatment in vascular preventive programs.

Previous studies have described the risk of vascular events conferred by the presence and severity of carotid plaque thickness in blacks and whites, but there are very few reports available for Hispanics. In our study, the amount of atherosclerosis overall was higher among whites and blacks than among Hispanics, but if carotid plaque was present, it had a significant impact on the vascular risk only among Hispanics. Hispanics with MCPT ≥1.9 mm had a three- to fourfold increased risk of vascular events in comparison to a one- to twofold increased risk among whites and blacks. We have previously shown that Hispanics had a higher incidence of stroke in comparison to other race–ethnic groups.[20] Taken together, these results may be of significant importance for the development of primary prevention programs for this vulnerable and the fastest growing minority population in the United States.[28]

Several large-population based studies[16-18] and numerous smaller studies have shown the significant association between the presence of carotid plaque and the risk of vascular events but predominantly in white populations.16-18 In ARIC,[16] the presence of carotid artery lesions without acoustic shadowing was predictive of the risk of ischemic stroke during the mean follow up of 8 years. The incidence rate of ischemic stroke was 2/1,000 person-years for women and 4/1,000 person-years for men. In our study, the incidence rate of ischemic stroke was noticeably greater than in the ARIC: 8/1,000 person-years in overall cohort (6/1,000 person-years for those without plaque and 11/1,000 person-years for those with MCPT >1.9 mm). Several reasons exist for this discrepancy. Age may be one of the most important contributing factors. The NOMAS cohort was on average 10 years older than the ARIC population. The ARIC study consisted of two race–ethnic groups, but the valid comparison of the associations of carotid plaque with the risk of stroke between whites and blacks could not be estimated as a result of its design. The study participants were enrolled by matching individuals by race–ethnicity to maximize the enrollment of blacks. In addition, they were enrolled from two different communities out of the four participating communities.[29] In the Cardiovascular Health study, a 1.7-fold increased risk of incident stroke was reported for the subjects with hypoechoic plaque over a mean follow up of 3.3 years.17

The comparison of the results from various populations must be considered with caution. Differences in demographics and risk factor profiles across different study populations and use of different measurements of subclinical atherosclerosis may have contributed to varying plaque size and its associated risk of vascular events. Furthermore, different mean follow-up time between the studies may bias the comparisons, because the studies with longer follow-up time tend to report falsely lower incidence rates resulting from competing mortality.[30] The NOMAS cohort is an elderly population with a heavy burden of atherosclerotic risk factors and therefore shorter life expectancy. Furthermore, the NOMAS cohort consists of predominantly Caribbean Hispanics and it may not be representative of other Hispanics or other race–ethnic minority groups. The environmental and genetic factors may differ among

various race–ethnic groups, including atheroma formation. In addition, it may be difficult to compare results among various studies because of the differences in plaque measurement methodologies.

Other carotid ultrasound imaging measures of subclinical atherosclerosis such as carotid plaque area, volume, and IMT have been used.[15,31-35] Although some methods (e.g., plaque area and volume) may be better in risk prediction than others,[15,31,35] the availability, ease of measurement, and cost will be of major importance in choosing imaging methodology for use in large epidemiologic studies. Imaging of carotid plaque and measurement of its maximal thickness is a simple noninvasive and cost-effective method. It can be obtained in <20 minutes. The ultrasound protocols of measuring IMT and plaque volume are more complex, time-consuming, expensive, and not readily available. Recent development of computerized, automated edge detection for IMT,36 plaque volume,[37] and first consensus document regarding the role of carotid IMT in research and clinical practice[38] may broaden the use of these methods among a wide range of individuals at increased vascular risk in the future.

Atherosclerosis is a chronic inflammatory disorder that involves a complex interaction among vascular, metabolic, and immune systems. Carotid plaque is a distinctive phenotype of atherosclerosis and may have a high likelihood of rupture, thrombotic complications, and rapid progression.[7,27] In contrast, IMT represents mainly hypertensive hypertrophy of the media and is under a substantial genetic control.[39,40] Carotid plaque, compared to IMT, is strongly influenced by environmental factors and less influenced by genetic factors.[40] The reasons responsible for the different heritability of carotid IMT and carotid plaque remain speculative. Smooth muscle cell proliferation and deposition of extracellular matrix material resulting in increased IMT may be a chronic adaptive process in the development of atherosclerosis, whereas formation of plaques represents an advanced lesion triggered by an acute inflammatory response. Several studies have provided evidence that carotid plaque predicts MI better than IMT.[14,31,35] It is also important to note, however, that many studies included plaque in the measurement of carotid IMT.[11-14,38] In some, the IMT measurement was dichotomized above and below a threshold level of IMT, which produced the effect of pooling subjects with plaques into the higher IMT level group because plaques tend to be more common in those with a thicker IMT.[14] Separate characterization of plaque and IMT is prudent to derive better information on vascular risk.[38]

Strengths of our study include the population-based design, the diverse ethnic population, long follow up, and systematic surveillance of vascular events. Several limitations may be noted. For any population-based study, the generalizability of the results to other populations is limited. The data on other measures such as plaque area or volume were not part of our standard ultrasound assessment and therefore not available. The associations of MCPT with specific ischemic stroke subtype (e.g., large-vessel, small-vessel, or cryptogenic stroke) were not ascertained. We did not account for the effect of the potential development of new risk factors on vascular risk during follow up. However, the prevalence of the risk factors such as hypertension and diabetes did not considerably change over time in our cohort.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Glossary

ARIC	Atherosclerosis Risk in Communities
FRS	Framingham risk score
IMT	intima-media thickness
MCPT	maximum carotid plaque thickness
MI	myocardial infarct
NOMAS	Northern Manhattan Study

Table 1

Baseline sociodemographics, vascular risk factors, and carotid plaque among 2,189 subjects from the Northern Manhattan Study cohort

	Percent (n)	Prevalence of carotid plaque, % (n)
Sociodemographics		
Age*		
≥65 y*	61.7 (1,351)	69.3 (936)
<65y	38.3 (838)	39.0 (327)
Sex		
Men	40.2 (880)	58.0 (510)
Women	59.8 (1,309)	57.5 (753)
Race		
White*	22.0 (470)	71.1 (334)
Black	25.2 (540)	64.1 (346)
Hispanic	52.8 (1,131)	49.4 (559)
Education* (high school)		
Complete	48.4 (1,059)	62.1 (658)
Incomplete	51.6 (1,130)	53.5 (605)
Conventional vascular risk factors		
Hypertension*		
Yes	72.5 (1,587)	61.3 (973)
No	27.5 (602)	48.2 (290)
Diabetes*		
Yes	21.3 (467)	64.9 (303)
No	78.7 (1,722)	55.8 (960)
Any cardiac disease*		
Yes	21.8 (476)	69.1 (329)
No	78.2 (1,713)	54.5 (934)
Cigarette* smoking		
Former	38.9 (853)	61.4 (524)
Current*	15.1 (329)	66.0 (217)
None	46.0 (1,007)	51.8 (522)
Alcohol consumption		
None	64.7 (1,414)	58.1 (821)
Mild to moderate	35.3 (771)	56.9 (439)
Body mass index (kg/m^2)		
≥30	27.6 (603)	56.7 (342)
<30	72.4 (1,581)	57.9 (916)

	Percent (n)	Prevalence of carotid plaque, % (n)
Low-density lipoprotein*		
≥130*	46.6 (997)	60.4 (602)
<130	53.4 (1,142)	55.3 (632)
High-density lipoprotein≥40		
Yes	65.9 (1,411)	57.3 (808)
No	34.1 (730)	58.4 (426)
Medications		
Aspirin		
Yes	29.5 (395)	17.6 (236)
No	70.5 (945)	12.6 (159)
Lipid lowering		
Yes	15.3 (205)	10.1 (133)
No	84.7 (1,132)	7.1 (75)

* Significant association with prevalence of plaque ($p < 0.005$).

Table 2

Age-adjusted and age-specific incidence rates per 1,000 person-years by MCPT levels

	Ischemic stroke				Myocardial infarction				Combined vascular events			
		MCPT levels (mm)				MCPT levels (mm)				MCPT levels (mm)		
		0	<1.9	≥1.9		0	<1.9	≥1.9		0	<1.9	≥1.9
Overall	7.89	6.35	7.16	11.26	7.66	4.51	7.12	13.42	19.27	12.17	16.36	34.59
40–64 y	2.85	1.91	2.56	10.47	0.63	0.48	1.28	0.49	3.80	2.39	3.84	14.01
65–74 y	7.52	8.91	5.58	7.81	8.41	6.58	6.97	13.68	17.11	16.27	14.09	22.85
≥75y	11.76	10.40	10.93	13.35	11.82	8.50	10.17	15.40	32.41	23.67	24.86	44.74

No plaque (0); with plaque and MCPT <1.9 mm (<75th percentile); and MCPT ≥1.9 mm (≥75th percentile) for ischemic stroke, myocardial infarction, and combined vascular events. MCPT = maximum carotid plaque thickness.

Table 3

Cox proportional hazard models of vascular outcomes for carotid plaque levels

Outcome	Cox model*	With plaque and MCPT <1.9, HR(95% CI)	With plaque and MCPT ≥1.9, HR(95%CI)
Ischemic stroke	(1)	1.12 (0.67–1.87)	1.79 (1.11–2.90)
	(2)	0.98 (0.58–1.66)	1.41 (0.85–2.34)
	(3)	0.78 (0.46–1.35)	1.12 (0.66–1.91)
Myocardial infarction	(1)	1.59 (0.91–2.77)	2.87 (1.73–4.78)
	(2)	1.24 (0.70–2.20)	2.10 (1.24–3.58)
	(3)	0.94 (0.52–1.69)	1.41 (0.81–2.45)
Vascular death	(1)	1.09 (0.61–1.94)	3.28 (2.05–5.23)
	(2)	0.83 (0.46–1.51)	2.21 (1.36–3.60)
	(3)	0.68 (0.37–1.25)	1.64 (0.98–2.75)
Combined vascular events	(1)	1.35 (0.95–1.92)	2.80 (2.04–3.84)
	(2)	1.07 (0.74–1.54)	2.02 (1.45–2.81)
	(3)	0.84 (0.58–1.23)	1.48 (1.05–2.10)

With plaque and MCPT <1.9 mm (<75th percentile) vs no plaque and MCPT ≥1.9 mm (≥75th percentile) vs no plaque. Reference maximum carotid plaque thickness (MCPT) = 0 (no plaque).

*Model: (1) MCPT only; (2) model (1) adjusted for age, gender, race-ethnicity, and education; (3) model (2) adjusted for hypertension, diabetes, any cardiac disease, alcohol consumption, current cigarette smoking, high-density lipoprotein, low-density lipoprotein, and body mass index levels, and use of aspirin and lipid-lowering medication.

MCPT = maximum carotid plaque thickness; HR = hazard ratio.

Table 4

Cox proportional hazard model of combined vascular outcomes for carotid plaque ≥1.9 mm vs no plaque: Stratified analyses by age, sex, and race-ethnicity

	MCPT ≥1.9 mm						
	Age		Sex		Race–ethnicity		
Cox model*	≤65y	>65y	Men	Women	White	Black	Hispanic
(1)	1.87 (1.32–2.65)	3.13 (1.35–7.25)	2.97 (1.85–4.76)	2.68 (1.75–4.11)	1.95 (1.00–3.77)	1.72 (1.01–2.92)	4.06 (2.48–6.66)
(2)	1.80 (1.26–2.56)	3.19 (1.36–7.47)	2.28 (1.40–3.73)	1.75 (1.12–2.74)	1.72 (0.88–3.36)	1.26 (0.73–2.20)	3.00 (1.80–5.00)
(3)	1.37 (0.95–1.99)	1.93 (0.77–4.84)	1.67 (0.99–2.84)	1.32 (0.82–2.11)	1.10 (0.53–2.26)	0.95 (0.52–1.73)	2.22 (1.30–3.78)

Values are HR (95% CI). Reference MCPT = 0 (no plaque).

*Model: (1) MCPT only; (2) model (1) adjusted for demographics and education; (3) model (2) adjusted for hypertension, diabetes, any cardiac disease, alcohol consumption, current cigarette smoking, high-density lipoprotein, low-density lipoprotein, and body mass index levels, use of aspirin, and lipid-lowering medication.

MCPT = maximum carotid plaque thickness; HR = hazard ratio.

Table 5

Ten-year risk of combined vascular outcomes by the Framingham Risk Score (FRS) categories and presence and thickness of carotid plaque

	Low FRS		Moderate FRS		High FRS	
	No. (%)	**10-year risk (%)**	**No. (%)**	**10-year risk (%)**	**No. (%)**	**10-year risk (%)**
Overall	505 (26)	11.4	920 (47)	15.6	541 (27)	26.0
No plaque	285 (56)	5.8	402 (44)	11.5	178 (33)	27.6
With plaque and MCPT <1.9 mm	220 (44)	18.3	518 (56)	18.6	364 (67)	25.0
p* Value		0.001		0.020		0.325
MCPT≥1.9 mm	62 (12)	24.7	173 (19)	25.1	157 (29)	30.7
p* Value		0.004		0.002		0.319

*Reference MCPT = 0.

MCPT = maximum carotid plaque thickness.