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Association of Carotid Atherosclerosis and Left Ventricular Hypertrophy

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Objectives. **This study was undertaken to determine the prevalence of carotid atherosclerosis in a large group of asymptomatic hypertensive and normotensive adults and to examine its relation to the presence of left ventricular hypertrophy.**

Background. **Both electrocardiographic and echocardiographic left ventricular hypertrophy predict an increased risk of cardiovascular events and mortality, including cerebrovascular disease, but the mechanism of association is unknown.**

Methods. **Four hundred eighty-six (277 normotensive and 209 untreated hypertensive) adults, free of clinical evidence of cardiovascular disease, were studied prospectively with echocardiography to determine left ventricular mass and carotid ultrasound to detect atherosclerosis and to measure common carotid artery dimensions.**

Results. **Carotid atherosclerosis was present in 16% of normotensive and 23% of hypertensive participants ($p < 0.05$) and was associated with older age, higher systolic and pulse pressures and larger left ventricular mass index ([mean ± SD] 91 ± 19 vs. 82 ± 18 g/m^2, $p < 0.0001$). The difference in mass persisted after adjustment for baseline differences in age and blood pressure. Subjects with left ventricular hypertrophy were twice as likely to have carotid atheromas (35% vs. 18%, $p < 0.01$). Logistic regression analyses, including standard risk factors, indicated that only age and left ventricular mass index independently predicted the presence of carotid plaque, both in the entire study group and when normotensive and hypertensive subjects were considered separately.**

Conclusions. **We believe that the present study provides the first evidence that higher left ventricular mass as detected by echocardiography is associated with the presence of carotid plaque. The association between cardiac hypertrophy and systemic atherosclerosis may contribute to the pathogenesis of the high incidence of vascular events that is well documented in patients with left ventricular hypertrophy.**

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The predictive value of both electrocardiographic (ECG) (1) and, as a more sensitive measure, echocardiographic (2) evidence of left ventricular hypertrophy for subsequent cardiovascular morbidity and mortality is well established in the general population (3), among hypertensive patients (2,4,5) and among catheterized patients with or without coronary artery disease (6,7). Progress has been made in elucidating mechanisms underlying the relation between left ventricular hypertrophy and complications from ischemic heart disease, including impairment of coronary vascular reserve (8–11), more extensive coronary atherosclerosis (12), an increased risk of ventricular arrhythmias (13–15) and greater susceptibility of hypertrophied myocardium to ischemic damage (16).

Additional observations have documented a relation between ECG (17) or echocardiographic (18) left ventricular hypertrophy and the subsequent risk of stroke. Recent longitudinal data from the Framingham Study (18) demonstrate a stepwise increase in the risk of transient ischemic attack and stroke by quartile of left ventricular mass indexed by height independent of blood pressure, serum lipids and smoking history in both men and women. Although the mechanism of this association is unknown, indirect ECG evidence of left ventricular hypertrophy was found to be associated with increased carotid wall thickness and more prevalent carotid stenoses among elderly subjects participating in the Cardiovascular Health Study (19). Available studies have not evaluated the possible association between the more sensitive echocardiographic measurement of left ventricular mass and the presence of atherosclerosis in the carotid circulation, which is now amenable to noninvasive study.

Preliminary data from our laboratory (20) have identified an increased prevalence of carotid atherosclerosis in subjects with echocardiographic left ventricular hypertrophy independent of standard risk factors. Thus, the present study was undertaken to determine the prevalence of carotid atherosclerosis in a large group of asymptomatic hypertensive and

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normotensive adults and to examine its relation to the presence of left ventricular hypertrophy.

Methods

Study subjects. The study included 486 adults: 277 normotensive subjects from employed populations enrolled by defined recruitment schemes into ongoing longitudinal studies (21,22) and 209 untreated hypertensive patients from either the work site–based studies or referred from the Hypertension Center of The New York Hospital-Cornell Medical Center. One hundred forty-nine patients had essential hypertension (systolic pressure ≥140 mm Hg or diastolic pressure ≥90 mm Hg); 43 had borderline or "white coat" hypertension (elevated clinical blood pressure with normal ambulatory blood pressure [awake blood pressure <134/90 mm Hg (23)]); and 17 had isolated systolic hypertension (systolic pressure ≥160 mm Hg and diastolic pressure <90 mm Hg). All 486 subjects were asymptomatic and free of clinical evidence of coronary artery or cerebrovascular disease. The presence of valvular heart disease was excluded by Doppler echocardiography. Eighty-three hypertensive patients (40%) had never received pharmacologic antihypertensive therapy; the remaining 126 patients were studied without medication for periods of 3 weeks to several years. The study was performed in accordance with protocols approved by the Committee on Human Rights in Research of Cornell University Medical College.

Echocardiography. All subjects underwent M-mode, two-dimensional and Doppler echocardiography performed by a research technician using commercially available echocardiographs equipped with 2.5- and 3.5-MHz transducers. Left ventricular dimensions were obtained from two-dimensionally guided M-mode tracings according to recommendations of the American Society of Echocardiography (24). Studies were coded and read in batches that mixed tracings for normotensive and hypertensive subjects, with no information about subject age, gender, blood pressure or body size. Measurements were performed for up to six cycles using a digitizing tablet and were averaged. Left ventricular mass was calculated using the Penn convention (25). Whenever M-mode cycles were unsuitable, left ventricular measurements were obtained from the two-dimensional study using the approach recommended by the American Society of Echocardiography (26). Left ventricular hypertrophy was considered present if the left ventricular mass indexed by body surface area exceeded 125 g/m^2 in men or 110 g/m^2 in women (2,4,27). The 95% confidence interval of reproducibility of left ventricular mass measurement performed 5 years apart in 117 normotensive adults was ±23 g after adjustment for biologic influences of changes in weight, blood pressure and dietary salt intake (28).

Carotid ultrasound. Imaging of both carotid arteries was performed in all subjects using a Biosound Genesis II system (OTE Biomedica, Florence, Italy) equipped with a 7.5-MHz imaging transducer. With the subject supine with slight hyperextension of the neck, the common carotid artery, carotid bulb and bifurcation were identified. The carotid bulb and proximal portions of the external and internal carotid arteries were imaged in multiple projections to maximize detection of irregularities in the vessel walls. Carotid atherosclerosis was defined as the presence of a discrete plaque at least 50% greater than the surrounding wall within any segment of either carotid artery (29). Carotid plaque size was quantified by computer-assisted measurement of plaque thickness on two-dimensional frames (Fig. 1).

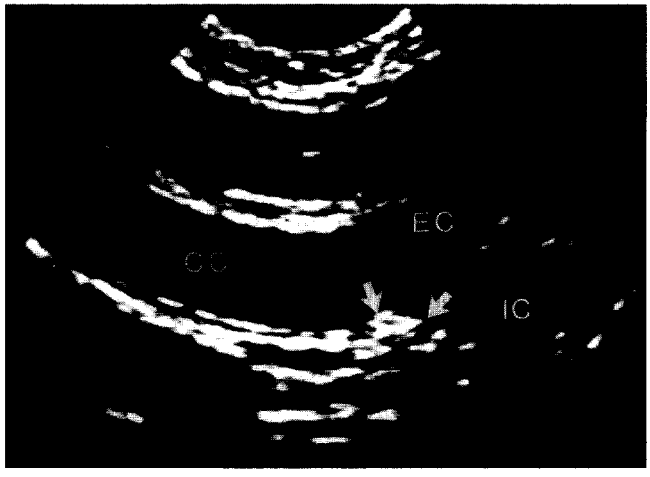


Figure 1. Two-dimensional image of the distal common carotid artery (CC), carotid bulb and bifurcation in a 60-year old woman. An atherosclerotic plaque 2.6 mm in maximal thickness is highlighted by the **arrows;** distal common carotid wall thickness was 0.7 mm. EC = external carotid artery; IC = internal carotid artery.

Two-dimensionally guided M-mode tracings of the distal common carotid artery ~1 cm proximal to the bulb were recorded on 0.5-in. videotape, as previously described (30). The videotape was subsequently reviewed, and suitable frames for measurement of M-mode images were obtained in real time using a frame grabber (Imaging Technology, Inc.) interfaced with a high resolution (640 × 480 pixel) video monitor and stored on diskettes. The axial resolution of the M-mode system is 0.2 mm.

All carotid measurements were performed on stored images using a mouse-driven computer program after calibration for depth. Measurements included end-diastolic (minimal diameter) wall thickness, defined as the combined thickness of the apparent intimal–medial layers of the far wall (31), and end-diastolic and peak-systolic (maximal diameter) internal dimensions obtained by continuous tracing of the intimal–luminal interface of the near and far walls of the common carotid artery (Fig. 2). All measurements were performed over several cycles and averaged. The ultrasound measurement of carotid wall thickness has been validated by Pignoli et al. (31) and Gamble et al. (32) using gross and histopathologic reference standards. In our laboratory, reproducibility of carotid wall thickness measurements has been shown to be high with regard to both intraobserver (r = 0.98, SEE 0.04 mm) and interobserver (r = 0.97, SEE 0.05 mm) variabilities (30). Wall thickness of the distal common carotid artery was never measured at the level of a discrete plaque.

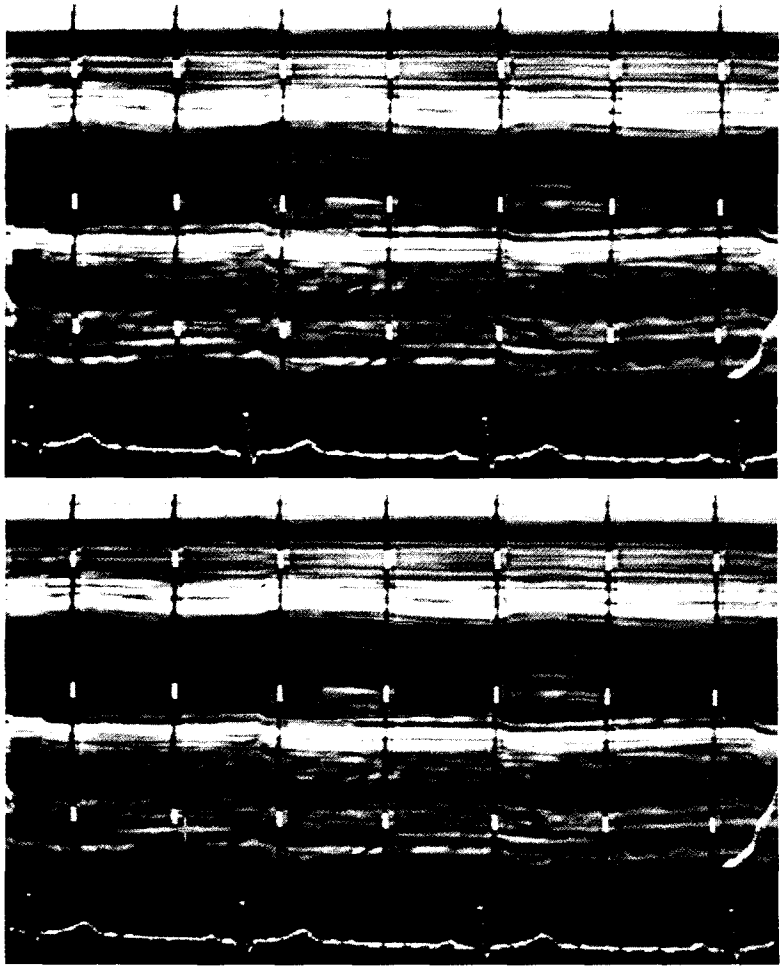


Figure 2. Two-dimensionally guided M-mode ultrasound tracing of the distal common carotid artery in a 68-year old man. **Top**, Intimal–medial thickness of the far wall (indicated between the **red arrows**) measured at end-diastole (minimal diameter). **Bottom**, Continuous tracing of intimal–luminal interfaces of the near and far walls to detect minimal and maximal diameters is indicated by the **red lines**. **Depth markers** are 1 cm apart.

Statistical methods. Data were analyzed with the Crunch[4] Statistical Package (Crunch Software Corp.). Mean values are presented with 1 SD as the index of dispersion and were compared by the Student *t* test. Differences in prevalences between two groups were compared by a chi-square test with the Yates continuity correction. Significant differences in baseline variables between groups with and without plaque were taken into account by means of analysis of covariance. Independent predictive effects of risk factors for plaque were determined using logistic regression analysis.

Results

Subject characteristics. Clinical characteristics of the normotensive and hypertensive subgroups are compared in Table 1. Hypertensive subjects were significantly older, more likely to be women and more overweight. There was a more than threefold increase in the prevalence of left ventricular hypertrophy (using gender-specific criteria) among the hypertensive group as well as an increased prevalence of carotid plaque.

Carotid atherosclerosis was present in 19% of subjects, and the clinical features of the 94 subjects with plaque are compared with those of the 392 subjects without plaque in Table 2. Subjects with plaque were significantly older, more likely to be hypertensive, had higher systolic and pulse pressures and exhibited a strong trend ($p = 0.06$) toward a higher prevalence of current or former cigarette smoking than those without plaque. The two groups were similar with regard to diastolic pressure and serum lipid levels.

Plaque was present in 21.6% of women and 18.5% of men. The similarity in prevalence may reflect the offsetting influences of differences in risk factors, with women being older (56 ± 14 vs. 50 ± 12 years, $p < 0.00005$) and more likely to be hypertensive (52% vs. 39%, $p < 0.01$) than men but having higher high density lipoprotein levels (61 vs. 51 mg/dl, $p < 0.00005$) and a similar smoking history.

Relation of carotid plaque to cardiac and vascular geometry. Absolute and relative left ventricular and common carotid wall thicknesses were greater in the group with carotid atherosclerosis (Table 3). Left ventricular mass and, more significantly, left ventricular mass index were accordingly larger. After adjustment for baseline differences in age and systolic blood pressure between the two groups using analysis of covariance, significant differences persisted in left ventricular (0.90 vs. 0.86 cm, $p < 0.05$)

Table 1. Clinical Features of Subjects With and Without Hypertension

	Normotensive Subjects (n = 277)	Hypertensive Subjects (n = 209)	p Value
Age (yr)	49 ± 12	56 ± 13	< 0.00005
Gender (% male)	72	60	< 0.01
Race (% white)	77.5	80	NS
Body surface area (m^2)	1.88 ± 0.21	1.89 ± 0.23	NS
Body mass index (kg/m^2)	25.8 ± 4.0	26.6 ± 4.3	< 0.05
Blood pressure (mm Hg)			
Systolic	121 ± 12	156 ± 22	< 0.00005
Diastolic	74 ± 8	92 ± 11	< 0.00005
Pulse	47 ± 9	63 ± 18	< 0.00005
Creatinine (mg/dl)	1.0 ± 0.2	1.0 ± 0.2	NS
Glucose (mg/dl)	84 ± 22	89 ± 31	NS
Total cholesterol (mg/dl)	220 ± 41	225 ± 46	NS
HDL cholesterol (mg/dl)	54 ± 16	55 ± 16	NS
Smoking (%)			NS (0.25)
Former	33	34	
Current	14	9	
Left ventricular hypertrophy (%)	4	14	< 0.005
Carotid plaque (%)	16	23	< 0.05

Data presented are mean value ± SD or percent of patients. HDL = high density lipoprotein.

and carotid (0.82 vs. 0.77 mm, $p < 0.05$) wall thicknesses and in left ventricular mass (168 vs. 155 g, $p < 0.01$) and mass index (88 vs. 82 g/m^2, $p < 0.01$). There was a twofold increase in the prevalence of carotid atherosclerosis among subjects with left ventricular hypertrophy compared with those without (35% vs. 18%, odds ratio 2.47 [95% confidence interval 1.08 to 4.94], $p < 0.01$) (Fig. 3). In a logistic regression analysis that included age, blood pressure, serum cholesterol, smoking history and left ventricular mass in the equation, only age ($p = 0.00005$), left ventricular mass ($p = 0.005$) and current smoking ($p = 0.05$) were independently related to the presence of carotid atherosclerosis (Table 4).

Subdivision of the subjects into quintiles of left ventricular mass index (Fig. 4) suggested a continuous relation between left ventricular mass and the likelihood of carotid atherosclerosis rather than a threshold effect. Consistent with this interpretation, left ventricular hypertrophy, defined as a categoric variable, did not add significantly ($p = 0.3$) to the predictive value of age for the presence of carotid plaque in a similar logistic regression analysis.

Associations with plaque in normotensive and hypertensive subjects. Among normotensive subjects, those with plaque (n = 45) differed from those without plaque (n = 232) in age (60 ± 12 vs. 46 ± 11 years, $p < 0.00005$), systolic blood

Table 2. Clinical Features of Subjects With and Without Carotid Atherosclerosis

	Plaque (n = 94)	No Plaque (n = 392)	p Value
Age (yr)	61 ± 11	49 ± 12	< 0.00005
Gender (% male)	63	68	NS
Body surface area (m^2)	1.87 ± 0.22	1.88 ± 0.22	NS
Body mass index (kg/m^2)	25.8 ± 3.3	26.2 ± 4.3	NS
Blood pressure (mm Hg)			
Systolic	145 ± 27	134 ± 23	< 0.0005
Diastolic	83 ± 13	81 ± 13	NS
Pulse	62 ± 20	52 ± 14	< 0.0005
Hypertension (%)	52	41	< 0.05
Creatinine (mg/dl)	1.0 ± 0.2	1.0 ± 0.5	NS
Glucose (mg/dl)	85 ± 23	86 ± 28	NS
Total cholesterol (mg/dl)	224 ± 48	223 ± 42	NS
HDL cholesterol (mg/dl)	54 ± 14	55 ± 16	NS
Smoking (%)			NS (0.13)
Former	40	32	
Current	14	11	

Data presented are mean value ± SD or percent of patients. HDL = high density lipoprotein.

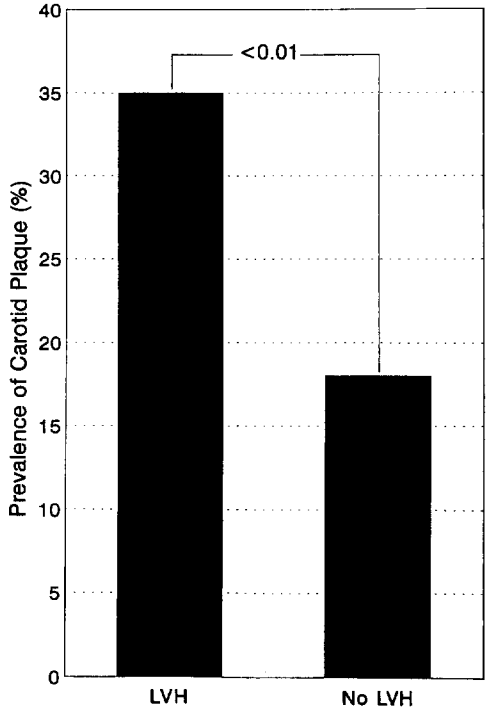
Table 3. Cardiac and Vascular Structure of Subjects With and Without Carotid Atherosclerosis

	Plaque (n = 94)	No Plaque (n = 392)	p Value
LV end-diastolic dimension (cm)	5.0 ± 0.5	5.0 ± 0.5	NS
Septal thickness (cm)	0.96 ± 0.13	0.92 ± 0.13	< 0.005
Posterior wall thickness (cm)	0.92 ± 0.12	0.86 ± 0.12	< 0.00005
Relative wall thickness	0.37 ± 0.06	0.35 ± 0.06	< 0.001
LV mass (g)	170 ± 44	155 ± 41	< 0.005
LV mass index (g/m^2)	91 ± 19	82 ± 18	< 0.0001
Carotid end-diastolic diameter (mm)	5.9 ± 0.7	5.5 ± 0.8	< 0.0001
Carotid wall thickness (mm)	0.88 ± 0.21	0.76 ± 0.18	< 0.00005
Carotid relative wall thickness	0.30 ± 0.07	0.28 ± 0.06	< 0.005

Data presented are mean value ± SD. LV = left ventricular.

pressure (127 ± 14 vs. 120 ± 11 mm Hg, $p < 0.005$) and pulse pressure (52 ± 11 vs. 46 ± 8 mm Hg, $p < 0.005$). There were no differences in gender, diastolic pressure or serum lipids, but a history of smoking was more common among subjects with plaque (60% vs. 43%, $p < 0.05$). Left ventricular mass index was larger in the group with plaque (85 ± 15 vs. 77 ± 16 g/m^2, $p < 0.005$) because of significant increases in left ventricular wall thicknesses but not chamber diameter. The prevalence of left ventricular hypertrophy was higher in the group with plaque (11% vs. 2%, $p < 0.005$). After analysis of covariance taking baseline differences in age and blood pressure into account, left ventricular mass remained significantly higher in the group of normotensive subjects with plaque (162 vs. 146 g, $p < 0.02$). In a logistic regression analysis, only age ($p = 0.00005$) and left ventricular mass ($p = 0.01$) were independently related to carotid plaque (Table 4).

Figure 3. Prevalence of atherosclerotic plaque within the extracranial carotid arteries was higher among subjects with (15 [35%] of 43) than in those without (79 [18%] of 443) echocardiographic evidence of left ventricular hypertrophy (LVH).



Similarly, compared with the 160 hypertensive patients without plaque, the 49 patients with plaque were older (62 ± 10 vs. 54 ± 13 years, $p < 0.00005$) and had higher systolic (162 ± 25 vs. 154 ± 20 mm Hg, $p < 0.05$) and pulse (72 ± 21 vs. 61 ± 16 mm Hg, $p < 0.0001$) pressures but did not differ in gender, diastolic blood pressure, serum lipids or smoking history. Left ventricular mass was greater in the hypertensive patients with plaque (96 ± 21 vs. 88 ± 18 g/m^2, $p < 0.05$) and, along with age ($p = 0.0002$), remained an independent correlate of plaque ($p = 0.05$) in multivariate analyses involving standard risk factors for atherosclerosis (Table 4).

As a further test of the consistency of results, analyses were performed in the 228 subjects drawn from the larger of our work site studies (22) and by dividing the subjects into two groups on the basis of a median age of 50 years. In all analyses, left ventricular mass and mass index were significantly greater in the group with than without plaque.

Discussion

Left ventricular mass and carotid atherosclerosis. We believe that the present study provides the first evidence that the presence of carotid artery plaque is associated with increased echocardiographic left ventricular mass and with ventricular hypertrophy considered as a categoric variable. When considered with well established risk factors for extracranial carotid atherosclerosis, only age (29,33), left ventricular mass index and smoking history are independent predictors of the presence of carotid plaque. Furthermore, left ventricular mass remained a predictor of carotid plaque in multivariate analyses performed in separate normotensive and hypertensive strata of our subjects, in the younger and older halves of our study subjects and in subjects from a work site–based project with a defined sampling strategy as well as in a more selected group of adults. The strong association that we observed between cerebrovascular atherosclerosis and left ventricular mass provides a potential pathophysiologic link to explain both the increased risk of vascular events, including stroke and transient

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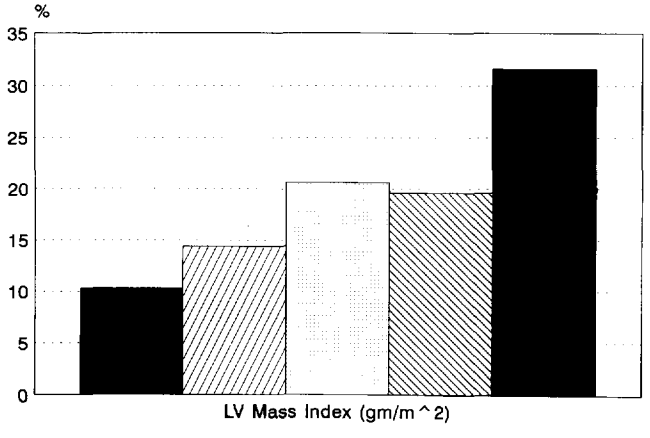
Table 4. Multivariate Correlates of Carotid Artery Plaque

	All Subjects (n = 486)			Normotensive Subjects (n = 277)			Hypertensive Patients (n = 209)		
	Beta Coefficient	SE	p Value	Beta Coefficient	SE	p Value	Beta Coefficient	SE	p Value
Age	0.083	0.014	0.0000	0.088	0.020	0.0000	0.072	0.019	0.0002
Systolic blood pressure	−0.005	0.007	0.51	−0.001	0.018	0.97	−0.007	0.011	0.45
Cholesterol	−0.004	0.003	0.22	−0.001	0.005	0.78	−0.006	0.004	0.17
Left ventricular mass	0.010	0.003	0.005	0.013	0.005	0.01	0.021	0.011	0.05
Smoking history									
Former vs. never	0.321	0.292	0.27	0.286	0.420	0.50	0.286	0.419	0.50
Current vs. never	0.777	0.401	0.05	0.752	0.525	0.51	0.757	0.633	0.23

ischemic attacks in subjects with ECG or echocardiographic left ventricular hypertrophy noted in several previous studies (2–4,17,18,34) and the converse ability of asymptomatic carotid bruits to predict cardiac morbid events (35).

Risk factors for carotid atherosclerosis. Previous population-based studies examining standard risk factors, such as serum lipids, cigarette smoking and hypertension, as potential determinants of extracranial carotid atherosclerosis have had varying results. Among Finnish men studied in Kuopio, smoking conferred a threefold increase in risk of carotid plaque, whereas hypertension was unrelated to atherosclerosis (36). In the Rotterdam Elderly Study (37), subjects with isolated systolic hypertension had a threefold higher prevalence of carotid plaque than age-matched control subjects (15% vs. 5%) with a similar serum lipid concentration and smoking history, but this difference did not achieve statistical significance. In an age-matched case-control analysis from the Atherosclerosis Risk in Communities (ARIC) Study (38), smoking and hypertension were associated with the highest risk for carotid atherosclerosis after adjustment for other risk factors. An association between carotid plaque and hypertension has been more consistently observed in studies of clinical series of largely symptomatic patients (39–41).

Figure 4. Prevalence of atherosclerotic plaque within the extracranial carotid arteries increased significantly ($p < 0.005$) from the lowest quintile of left ventricular (LV) mass index (<68.5 g/m^2) to the highest (>97.6 g/m^2).



In the present study of asymptomatic normotensive and hypertensive subjects, most of whom were recruited from work site–based populations, subjects differed from those without carotid plaque in age, systolic and pulse pressures, as well as the prevalence of hypertension among traditional risk factors. Our finding that age and smoking history among traditional risk factors were independent predictors of carotid atherosclerosis in multivariate analyses is also compatible with the results of previous studies. The elimination of arterial pressure as an independent predictor of carotid plaque in an analysis that also considered left ventricular mass may reflect the known positive relation between blood pressure and ventricular mass and the possibility suggested by studies using ambulatory pressure monitoring that left ventricular mass may be a better measure of long-term blood pressure than are rest blood pressure measurements themselves (42).

The lack of a significant difference in the present study in serum lipids between subjects with and without plaque may be attributable to a variety of factors, including their healthy, asymptomatic status; the relatively low mean level of serum cholesterol; the inclusion of a significant proportion of women (43); and the possibility that recent shifts in diet may have reduced lipid levels in some subjects from those that prevailed during the protracted process of development of atheroma.

Mechanism of association. The mechanism underlying the association between left ventricular hypertrophy and carotid atherosclerosis is uncertain. Similar to the results of the present study, we recently reported (30) parallel increases in ventricular and vascular wall thicknesses in hypertensive patients, which, although related to blood pressure, remained significant independently of age and conventional blood pressure measurements, suggesting that additional factors promote cardiac and vascular growth. However, the impact of arterial pressure on both organs may have been underestimated as a result of the known limitations of rest as opposed to ambulatory measurements of blood pressure levels (42). Alternatively, changes in arterial properties due to vascular growth or atherosclerosis may cause earlier return of reflected pressure waves to the central circulation or elevation of effective arterial elastance that may stimulate increases in left ventricular mass and relative wall thickness (44,45) without a detectable alteration in systolic or diastolic arterial pressure. The increased

carotid wall thickness in a segment unaffected by discrete atheroma in our subjects with plaque may represent either the vascular hypertrophy that we have found to be associated with these abnormalities of arterial dynamics or early generalized atherosclerosis (46,47). Although hypertension is a risk factor for the development of stroke, the striking increase in risk associated with left ventricular hypertrophy appears to be independent of conventional blood pressure measurements (17,18).

In addition to these hemodynamic mechanisms, it is possible that asymptomatic coronary atherosclerosis—which would be expected to be more prevalent in patients with carotid atherosclerosis (39)—might have contributed to the development of increased left ventricular mass in our patients with carotid plaque. Thus, transient experimental coronary occlusion stimulates myocardial growth (48), and clinical studies document increased ventricular mass in patients with coronary stenoses (7,49,50). Given the strong association between carotid plaque and subsequent myocardial infarction in the Kuopio Heart Disease Risk Factor Study (51,52), our findings may provide a noninvasive window on more generalized atherosclerosis in subjects with left ventricular hypertrophy.

Clinical implications. Several potential clinical implications of the present study need to be clarified by longitudinal study. Whether subjects with both asymptomatic carotid atherosclerosis and abnormal left ventricular geometry are at higher risk than those with either abnormality alone needs to be verified by long-term follow-up. Other studies examining the prognostic importance of echocardiographic left ventricular hypertrophy have provided little (4) or no data (6) concerning the risk of developing symptomatic cerebrovascular disease. Similarly, initial reports of the ability of atherosclerosis in the carotid circulation detected by ultrasound to predict myocardial infarction (51,52) have not considered left ventricular mass as a covariate predisposing to this adverse outcome. At present, detection of cardiac or vascular abnormalities indicative of preclinical cardiovascular disease (44,53) often prompts intervention aimed at reversing or at least retarding progression of morphologic abnormalities by lowering blood pressure or serum lipids, cessation of smoking or dietary change to reduce salt intake or induce weight loss. Although the impact of normalization of left ventricular mass or regression of carotid atherosclerosis on clinical outcome has not been conclusively established, preliminary data (54) suggest that normalization of left ventricular mass by antihypertensive treatment is associated with a reduced risk of subsequent events.

Study limitations. A potential limitation of the current study concerns the previous use of pharmacologic agents to lower blood pressure in a substantial proportion of the hypertensive patients because several classes of antihypertensive agents have been shown to reduce left ventricular mass over periods as short as several months (55). A reduction in left ventricular mass among previously treated hypertensive patients might be expected to weaken the association of carotid atherosclerosis with left ventricular hypertrophy because such treatment would be expected to have a much slower, if any, effect on the presence of plaque. This suggests that the observed association between atherosclerosis and left ventricular mass may have been understated.

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References

1. Kannel WB, Gordon T, Offutt D. Left ventricular hypertrophy by electrocardiogram: prevalence, incidence, and mortality in the Framingham study. Ann Intern Med 1969;71:89–105.
2. Casale PN, Devereux RB, Milner M, et al. Value of echocardiographic measurements of left ventricular mass in predicting cardiovascular morbid events in hypertensive men. Ann Intern Med 1986;105:173–8.
3. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. N Engl J Med 1990;322:1561–6.
4. Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in men and women with essential hypertension. Ann Intern Med 1991;114:345–52.
5. Mensah GA, Pappas TW, Koren MJ, Ulin RJ, Laragh JH, Devereux RB. Comparison of the classification of severity of hypertension by blood pressure level and by World Health Organization criteria in the prediction of concurrent cardiac abnormalities and subsequent complications in essential hypertension. J Hypertens 1993;11:1429–40.
6. Ghali JK, Liao Y, Simmons B, Castaner A, Cao G, Cooper RS. The prognostic role of left ventricular hypertrophy in patients with or without coronary artery disease. Ann Intern Med 1992;117:831–6.
7. Bolognese L, Dellavesa P, Rossi L, Sarasso G, Bongo AS, Scianaro MC. Prognostic value of left ventricular mass in uncomplicated acute myocardial infarction and one-vessel coronary artery disease. Am J Cardiol 1994;73:1–5.
8. Houghton JL, Frank MJ, Carr AA, von Dohlen TW, Prisant LM. Relations among impaired coronary flow reserve, left ventricular hypertrophy and thallium perfusion defects in hypertensive patients without obstructive coronary artery disease. J Am Coll Cardiol 1990;15:43–51.
9. Treasure CB, Klein JL, Vita JA, et al. Hypertension and left ventricular hypertrophy are associated with impaired endothelium-mediated relaxation in human coronary resistance vessels. Circulation 1993;87:86–93.
10. Antony I, Nitenberg A, Foult J-M, Aptcar E. Coronary vasodilator reserve in untreated and treated hypertensive patients with and without left ventricular hypertrophy. J Am Coll Cardiol 1993;22:514–20.
11. Schwartzkopff B, Motz W, Frenzel H, Vogt M, Knauer S, Strauer BE. Structural and functional alterations of the intramyocardial coronary arterioles in patients with arterial hypertension. Circulation 1993;88:993–1003.
12. Young W, Gofman JW, Tandy R. The quantitation of atherosclerosis. II. Quantitative aspects of the relationship of blood pressure and atherosclerosis. Am J Cardiol 1960;6:294–9.
13. Levy D, Anderson KM, Savage DD, Balkus SA, Kannel WB, Castelli WP. Risk of ventricular arrhythmias in left ventricular hypertrophy: the Framingham Heart Study. Am J Cardiol 1987;60:560–5.
14. McLenachan JM, Henderson E, Morris KI, Dargie HJ. Ventricular arrhythmias in patients with hypertensive left ventricular hypertrophy. N Engl J Med 1987;317:787–92.
15. Ghali JK, Kadakia S, Cooper RS, Liao Y. Impact of left ventricular hypertrophy on ventricular arrhythmias in the absence of coronary artery disease. J Am Coll Cardiol 1991;17:1277–82.
16. Koyanagi S, Eastham CL, Harrison DG, Marcus ML. Increased size of myocardial infarction in dogs with chronic hypertension and left ventricular hypertrophy. Circ Res 1982;50:55–62.
17. Kannel WB. Prevalence and natural history of electrocardiographic left ventricular hypertrophy. Am J Med 1983;75 Suppl 3A:4–11.
18. Bikkina M, Levy D, Evans JC, et al. Left ventricular mass and risk of stroke in an elderly cohort: the Framingham Heart Study. JAMA 1994;272:33–6.
19. O'Leary DH, Polak JF, Kronmal RA, et al. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. Stroke 1992;23:1752–60.

20. Roman MJ, Spitzer M, Pini R, Pickering TG, Devereux RB. The association of carotid atherosclerosis and increased left ventricular mass in hypertension [abstract]. J Am Coll Cardiol 1992;19:86A.
21. de Simone G, Devereux RB, Roman MJ, Schlussel Y, Alderman MH, Laragh JH. Echocardiographic left ventricular mass and electrolyte intake predict arterial hypertension. Ann Intern Med 1991;114:202–9.
22. Schnall PL, Schwartz JE, Landsbergis PA, Warren K, Pickering TG. Relation between job strain, alcohol and ambulatory blood pressure. Hypertension 1992;19:488–94.
23. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH: How common is white coat hypertension? JAMA 1988;259:225–8.
24. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.
25. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. Circulation 1977;55: 613–8.
26. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989;2:358–67.
27. Devereux RB, Casale PN, Kligfield P, et al. Performance of primary and derived M-mode echocardiographic measurements for detection of left ventricular hypertrophy in necropsied subjects and in patients with systemic hypertension, mitral regurgitation and dilated cardiomyopathy. Am J Cardiol 1986;57:1388–93.
28. de Simone G, Ganau A, Verdecchia P, Devereux RB. Echocardiography in arterial hypertension: when, why and how. J Hypertens 1994;12:1129–36.
29. Salonen R, Seppanen K, Ravramara R, Salonen JT. Prevalence of carotid atherosclerosis and serum cholesterol levels in Eastern Finland. Arteriosclerosis 1988;8:788–92.
30. Roman MJ, Saba PS, Pini R, et al. Parallel cardiac and vascular adaptation in hypertension. Circulation 1992;86:1909–18.
31. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. Circulation 1986;74:1399–1406.
32. Gamble G, Beaumont B, Smith H, et al. B-mode ultrasound images of the carotid artery wall: Correlation of ultrasound with histologic measurements. Atherosclerosis 1993;102:163–73.
33. Tell GS, Howard G, McKinney WM. Risk factors for site specific extracranial carotid artery plaque distribution as measured by B-mode ultrasound. J Clin Epidemiol 1989;42:551–9.
34. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Left ventricular mass and incidence of coronary heart disease in an elderly cohort. The Framingham Heart Study. Ann Intern Med 1989;110:101–7.
35. Heyman A, Wilkinson WE, Heyden S, et al. Risk of stroke in patients with cervical arterial bruits: a population study in Evans County, Georgia. N Engl J Med 1980;302:838–41.
36. Salonen JT, Salonen R. Association of serum low density lipoprotein cholesterol, smoking and hypertension with different manifestations of atherosclerosis. Int J Epidemiol 1990;19:911–7.
37. Bots ML, Hofman A, de Bruyn AM, de Jong PTVM, Grobbee DE. Isolated systolic hypertension and vessel wall thickness of the carotid artery: the Rotterdam Elderly Study. Hypertension 1993;13:64–9.
38. Heiss G, Sharrett AR, Barnes R, Chambless LE, Szklo M, Alzola C, and the ARIC Investigators. Carotid atherosclerosis measured by B-mode ultrasound in populations: associations with cardiovascular risk factors in the ARIC Study. Am J Epidemiol 1991;134:250–6.
39. Crouse JR, Toole JF, McKinney WM, et al. Risk factors for extracranial carotid atherosclerosis. Stroke 1987;18:990–6.
40. Rubens J, Espeland MA, Ryu J, et al. Individual variation in susceptibility to extracranial carotid atherosclerosis. Arteriosclerosis 1988;8:389–97.
41. Handa N, Matsumoto N, Maeda H, et al. Ultrasonic evaluation of early carotid atherosclerosis. Stroke 1990;21:1567–72.
42. Devereux RB, Pickering TG, Harshfield GA, et al. Left ventricular hypertrophy in patients with hypertension: importance of blood pressure responses to regularly recurring stress. Circulation 1983;68:470–6.
43. Tell GS, Crouse JR, Furberg CD. Relation between blood lipids, lipoproteins, and cerebrovascular atherosclerosis: a review. Stroke 1988;19:423–30.
44. Saba PS, Roman MJ, Pini R, Ganau A, Devereux RB. Relation of carotid pressure waveform to left ventricular anatomy in normotensive subjects. J Am Coll Cardiol 1993;22:1873–80.
45. Saba PS, Roman MJ, Pini R, Devereux RB. Relations of effective arterial elastance to carotid and left ventricular structure [abstract]. Am J Hypertens 1993;6:40A.
46. Glagov S, Zarins C, Giddens DP, Ku DN. Hemodynamics and atherosclerosis: insights and perspectives gained from studies of human arteries. Arch Pathol Lab Med 1988;112:1018–31.
47. Wikstrand J, Wiklund O. Quantitative measurements of atherosclerotic manifestations in humans. Arterioscler Thromb 1992;12:114–9.
48. Fujita M, Mikuniya A, McKown DP, McKown MD, Franklin D. Regional myocardial volume alterations induced by brief repeated coronary occlusion in conscious dogs. J Am Coll Cardiol 1988;12:1048–53.
49. Pech HJ, Witte R, Romaniak R, Pars RA, Portsmann W. Left ventricular mass in coronary artery disease without hypertension. Br Heart J 1974;36: 362–7.
50. Gould KL, Lipsomb K, Hamilton GW, Kennedy JW. Relation of left ventricular shape, function and wall stress in man. Am J Cardiol 1974;39: 627–34.
51. Salonen JT, Salonen R. Ultrasound B-mode imaging in observational studies of atherosclerotic progression. Circulation 1993;87 Suppl II:II-56–65.
52. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease. Arterioscler Thromb 1991;11:1245–9.
53. Devereux RB, Alderman MH. The role of preclinical cardiovascular disease in the evolution from risk factor exposure to development of morbid event. Circulation 1993;88:1444–55.
54. Yurenev AP, Dyakonova HG, Novikov ID, et al. Management of essential hypertension in patients with different degrees of left ventricular hypertrophy: multicenter trial. Am J Hypertens 1992;5:182S–9S.
55. Dahlof B, Pennert K, Hansson L. Reversal of left ventricular hypertrophy in hypertensive patients: a metaanalysis of 109 treatment studies. Am J Hypertens 1992;5:95–110.