AJNR

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A.D. Mackinnon, P. Jerrard-Dunne, L. Porteous and H.S. Markus

AJNR Am J Neuroradiol 2010, 31 (10) 1951-1955
doi: https://doi.org/10.3174/ajnr.A2214
http://www.ajnr.org/content/31/10/1951

ORIGINAL RESEARCH

A.D. Mackinnon
P. Jerrard-Dunne
L. Porteous
H.S. Markus

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BACKGROUND AND PURPOSE: Carotid IMT is widely used as a surrogate marker for atherosclerosis. Prospective studies in largely white populations demonstrate that it is strongly associated with carotid plaque and is an independent predictor of stroke. There are few data from black populations. In a previous study, we showed that carotid IMT is increased in black individuals in the UK. The purpose of this study was to confirm this with a larger sample size and to establish whether raised IMT in black stroke-free individuals is associated with increased carotid plaque.

MATERIALS AND METHODS: High-resolution sonography was used to measure the CCA-, BIF-, and ICA-IMT and plaque in 306 black and 281 white healthy individuals recruited by random community sampling from London, U.K. Mean CCA-IMT was determined by using a semiautomated computer program that detects the blood/intima borderline and the media/adventitia borderline with the use of a gray-value algorithm.

RESULTS: CCA-IMT was higher in black compared with white individuals after controlling for cardiovascular risk factors and socioeconomic status ($\beta = 0.050$; 95% CI, 0.024–0.076; $P < .001$). BIF- and ICA-IMT were also increased in black subjects. In contrast, carotid plaque was more common in white individuals (OR, 2.90; 95% CI, 1.41–5.96; $P = .004$).

CONCLUSIONS: The lack of correlation between increased IMT and carotid plaque in black individuals implies that IMT should not currently be used as a surrogate marker of atherosclerosis in black populations. It suggests that the increased IMT seen in black individuals may not represent early atherosclerosis.

ABBREVIATIONS: BIF = carotid bifurcation; BMI = body mass index; CCA = common carotid artery; CI = confidence interval; DM = diabetes mellitus; ICA = internal carotid artery; IMT = intima-media thickness; IRAS = Insulin Resistance Atherosclerosis Study; LBIF = left carotid bifurcation; LCCA = left CCA; Max = maximum; OR = odds ratio; RBIF = right carotid bifurcation; RCCA = right CCA; SE = standard error; UK = United Kingdom

Individuals of African and African Caribbean descent living in the United States and the United Kingdom have a markedly increased risk of stroke compared with white individuals.[1,2] Differences in stroke subtype have also been identified, particularly an increase in small-vessel-disease stroke.[3,4]

One method of assessing cerebral arterial damage in a community population is measurement of CCA wall thickness. High-resolution B-mode sonography allows the measurement of arterial wall IMT and identification of the presence and thickness of any atheromatous plaque. This can be performed simply and noninvasively in large community populations.

Carotid IMT has been shown to correlate well with the pathologic intima-media complex[5] and is now widely used as a surrogate marker for atherosclerosis. This is based on prospective studies linking IMT to clinical cardiovascular events. However, these data are derived almost entirely from white populations.[6-8] In particular, there are very few prospective data from black populations. In white individuals, increased IMT is strongly associated with increased carotid plaque.[9,10] However, data from black populations suggest this may not be the case with reduced carotid plaque and large-vessel atherosclerosis.[11,12] This dissociation between IMT and plaque seen in black individuals suggests that increased IMT in blacks may not relate directly to increased atherosclerosis. This has important implications for the use of IMT as a surrogate marker for atherosclerosis in black populations.

In a community-based population, we aimed to determine whether carotid IMT and carotid plaque were increased in black compared with white stroke-free individuals living in London, United Kingdom. In the same population in a small sample size (89 black men), we previously found increased CCA-IMT in black compared with white individuals.[13] We have extended our sample size to allow us to look at not only IMT but also the prevalence of plaque in this population and to compare risk-factor profiles for increased IMT in the 2 ethnic groups.

Materials and Methods

Subjects

Individuals aged 35–85 years were randomly selected from 7 family practices in South London. In the United Kingdom, all individuals,

Received July 26, 2009; accepted after revision May 13, 2010.

From Clinical Neurosciences, St. George's University of London, London, United Kingdom.

This study was supported by a Programme Grant from the Stroke Association (Prog 3).

Preliminary data previously presented at: European Stroke Conference, May 29-June 1, 2007; Glasgow, United Kingdom.

Please address correspondence to Hugh Markus, MD, Clinical Neurosciences, St. George's University of London, Cranmer Terrace, Tooting, London SW17 0RE, United Kingdom; e-mail: hmarkus@sgul.ac.uk

Indicates article with supplemental on-line tables.

DOI 10.3174/ajnr.A2214

healthy or not, are registered with a family practice. An initial sample size of 600 (300 white and 300 black individuals) was sought. A brief questionnaire was sent to 2806 individuals; this questionnaire asked about their ethnicity and whether they would participate in the study. Nine hundred nine (32%) replies were received. Ninety-two letters were returned because individuals were no longer at that address, and 6 individuals had died. Of the respondents, 678 (75%) agreed to participate and were sent an appointment date, and 615 attended the study. Seven of these were neither white nor of African Caribbean descent and were excluded. Sixteen individuals with a history of stroke or TIA were also excluded, leaving 592 individuals included in the study. Of these, 307 were black (African 83, African Caribbean 224) and 285 were white. The study was approved by the local research ethics committee.

A cardiovascular interview and examination were performed. Risk factors recorded included any history of arterial hypertension, diabetes mellitus, myocardial infarction, stroke or transient ischemic attack, angina, peripheral vascular disease, and smoking. Adult socioeconomic status was coded according to the UK Registrar General's classification (I, Professional; II, Managerial and Technical; III, Skilled; IV, Partly Skilled; and V, Unskilled).[14] BMI was calculated. Three blood pressure measurements were obtained with subjects in the supine position and were averaged to obtain a mean systolic and diastolic blood pressure. "Hypertension" was defined as mean systolic blood pressure >140 mm Hg or mean diastolic pressure >90 mm Hg or self-reported use of antihypertensive medications.

In 5 subjects (1 African Caribbean and 4 white individuals), technically adequate images of the carotid artery could not be obtained. Carotid IMT and plaque measurements were, therefore, obtained on 306 black (African 83, African Caribbean 223) and 281 white subjects.

Imaging Protocol

Carotid artery imaging was performed with an S800 carotid duplex machine by using a 7-MHz transducer (Philips Healthcare, Best, the Netherlands). Each examination cycle included sequential, longitudinal, and transverse views of the CCA, the BIF, and the proximal ICA. All sonographic examinations were stored on a Super-Video Home System for subsequent off-line processing. Settings for depth-gain compensation, preprocessing, persistence, and postprocessing were held constant. Images were recorded at 60-dB log compression, and gain was adjusted so that the arterial wall–internal wall interface was just visible. Video images were captured at a standard point in systole of the cardiac cycle by triggering to the electrocardiogram. The frozen video images were digitized as bitmaps and transferred for further analysis to a PC. Images were analyzed with the researchers blinded to patient identity and ethnicity. CCA-IMT was measured on the far wall at the straight portion of the CCA, starting 20 mm proximal to the tip of the flow divider. The intraluminal diameter of the CCA (in systole) was measured 2.5 cm proximal to the tip of the flow divider. We made 2 different measurements of CCA-IMT: mean and maximum CCA-IMT. Mean CCA-IMT was obtained from a length of CCA by using a semiautomated computer analysis system that detects the blood/intima borderline and the media/adventitia borderline (Fig 1) with the use of a gray-value algorithm.[15] Distances between these 2 borderlines were measured along a line orthogonal to the arterial wall. Single IMT values were obtained from pixel-to-pixel measurements on neighboring lines perpendicular to the vertical line and then averaged and expressed as the mean IMT. Maximum IMT at a single point within the CCA, BIF, and ICA was determined visually from the frozen image. "Carotid plaque" was defined as a focal thickening ≥1.8 mm in the BIF or ICA.

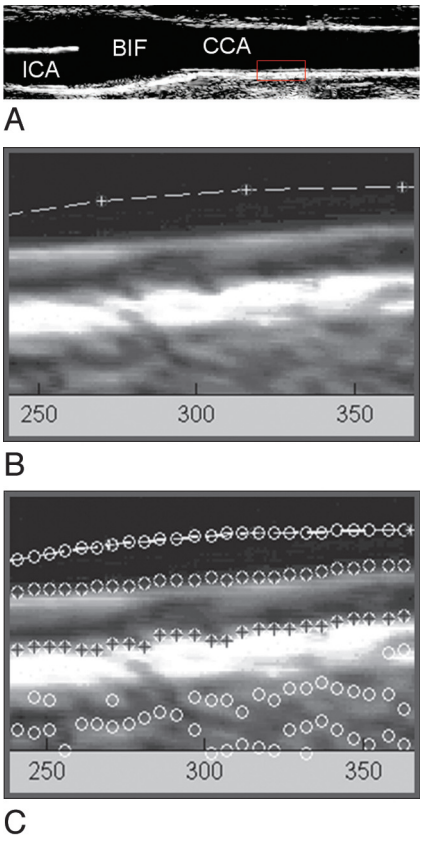

Fig 1. High-resolution B-mode sonography of the carotid artery demonstrating the far wall IMT. *A,* A characteristic longitudinal 2D sonogram of the CCA, BIF, and proximal ICA. The rectangle marks the arterial wall segment of the CCA, which is detailed and magnified in *B* and *C. B,* The dashed line above the blood/intima borderline spans the distance over which the IMT is to be measured. *C,* The gray value–based edge detection software delineates both blood/intimal and medial/adventitial borderline.[15]

In 29 individuals, reproducibility of measurements was estimated. These subjects returned for a further scan separated by 1 month. These scans were analyzed in a similar manner, with the researchers blinded to subject identity and whether the scan was a first or repeat scan. The regression coefficient was 0.78 ($P < .0001$) between mean CCA-IMT measurements and 0.81 ($P < .0001$) between maximum CCA-IMT measurements. The SD of repeated measurements[16] on the same subject was 0.060 mm for mean IMT measurements and 0.128 mm for maximum IMT measurements.

Statistical Analysis

Data were analyzed with the Statistical Package for the Social Sciences (SPSS, Chicago, Illinois). CCA-IMT measurements were obtained on all subjects. BIF-IMT was obtainable on 250 of 281 (89%) white and 222 of 306 (73%) of black subjects. ICA-IMT was obtainable in 192 of 281 (68%) white and 120 of 306 (39%) black subjects. Age- and sex-adjusted IMT measurements were obtained for all 3 carotid (CCA, BIF, and ICA) segments. Multivariate comparisons were performed only on the complete CCA-IMT dataset.

Analysis between CCA-IMT and cardiovascular variables was performed by using multiple linear regression. Estimated marginal means for CCA-IMT were obtained by using the general linear model. Socioeconomic status was entered as a nonlinear variable by use of dummy variables. Socioeconomic classes I and II were combined be-

Table 1: The demographics and risk factors in the 2 ethnic groups[a]

	Black Individuals ($n = 306$)	White Individuals ($n = 281$)	P Value[b]
Age (yr)	60.6 (9.3)	61.1 (8.0)	.825
Sex (men)	189 (61.8)	223 (79.4)	.000
Systolic blood pressure (mm Hg)	142.0 (17.8)	139.0 (19.4)	.011
Diastolic blood pressure (mm Hg)	85.3 (10.1)	83.7 (10.7)	.030
Antihypertensive therapy	129 (42.7)	46 (16.4)	.000
Hypertension	218 (71.2)	161 (57.3)	.000
Smoking: pack-years	6.7 (13.9)	21.9 (29.9)	.000
Current smoker	60 (19.6)	77 (27.4)	.000
Ex-smoker	69 (22.5)	106 (37.7)	
Never	177 (57.8)	98 (34.9)	
Diabetes mellitus	62 (20.3)	18 (6.4)	.000
Myocardial infarct	7 (2.3)	16 (5.7)	.114
Serum cholesterol (mmol/L)	5.1 (1.1)	5.5 (1.1)	.000
BMI (kg/m^2)	28.2 (5.8)	27.0 (5.3)	.067
Socioeconomic status			.000
I	11 (3.6)	12 (4.3)	
II	28 (9.2)	76 (27)	
IIIa	53 (17.3)	51 (18.1)	
IIIb	92 (30.1)	67 (23.8)	
IV	79 (25.8)	40 (14.2)	
V	43 (14.1)	35 (12.5)	

[a] Values are No. (%) or mean (± SD).
[b] Age- and sex-adjusted.

Table 2: Age and sex-adjusted carotid IMT and diameter measurements and prevalence of carotid plaque in the 2 ethnic groups[a]

	Black Individuals	White Individuals	P Value
Mean CCA-IMT (mm)			
LCCA	0.817 ± 0.009	0.771± 0.010	.001
RCCA	0.790 ± 0.008	0.729 ± 0.009	.000
Mean CCA	0.804 ± 0.008	0.750 ± 0.008	.000
Maximum CCA-IMT (mm)			
LCCA	0.970 ± 0.022	0.810 ± 0.021	.000
RCCA	0.899 ± 0.027	0.741 ± 0.015	.000
Mean CCA	0.940 ± 0.020	0.770 ± 0.015	.000
Maximum BIF/ICA-IMT (mm)			
LBIF	0.778 ± 0.020	0.685 ± 0.010	.000
RBIF	0.760 ± 0.020	0.657 ± 0.010	.000
Mean BIF	0.780 ± 0.020	0.676 ± 0.010	.000
Mean ICA	0.659 ± 0.010	0.574 ± 0.010	.000
CCA diameter (cm)			
LCCA	0.592 ± 0.005	0.618 ± 0.005	.000
RCCA	0.599 ± 0.004	0.624 ± 0.005	.000
Mean CCA	0.596 ± 0.004	0.621 ± 0.005	.000
Carotid plaque (No.) (%)	17 (5.6)	34 (12.1)	.004

[a] Values are mean ± SE. IMT results are from semiautomated analysis of an arterial segment giving a value of mean CCA-IMT and from the manual measurement of the single maximum value (maximum IMT) for CCA, BIF, and ICA. CCA diameters are from manual measurements taken during systole.

cause there were only 23 individuals in the former category. The proportion of variance (R^2) in CCA-IMT explained by conventional risk factors was determined in both ethnic groups. Analyses were performed for maximum CCA-IMT and for mean CCA-IMT. Comparisons for the presence or absence of carotid plaque were made by using binary logistic regression.

Results

Demographic and risk-factor differences between the black and white subjects are shown in Table 1. There was no difference in mean (±SD) age. There were more men in the white population (79.4% versus 61.8%). Therefore, analysis of differences between populations was age- and sex-adjusted. Black individuals were more likely to be taking antihypertensive medication (42.7% versus 16.4%, $P < .001$) and had higher systolic and diastolic blood pressures. They were more likely to have diabetes (20.3% versus 6.4%). White individuals were more likely to have a smoking history and had higher serum cholesterol levels. There was no significant difference in BMI between the 2 populations. Black individuals had lower socioeconomic status.

Mean values of left, right, and mean CCA-IMT for the black and white populations are shown in Table 2. Both maximum and mean IMT values were increased in black compared with white subjects after age and sex adjustment. This increase was seen for left, right, and averaged IMT measurements. The differences in CCA-IMT remained after adjusting for cardiovascular risk factors, socioeconomic status, and CCA diameter (On-line Table 1). Mean CCA-IMT remained significantly increased in black individuals after controlling for cardiovascular risk factors, including hypertension, diabetes, cholesterol, and pack-years smoked ($\beta = 0.049$; 95% CI, 0.024–0.074; $P < .001$). The strength of the association was unaltered after controlling for socioeconomic status ($\beta = 0.050$; 95% CI, 0.024–0.076; $P < .001$). Similarly, maximum CCA-IMT remained significantly increased in black individuals after controlling for cardiovascular risk factors ($\beta = 0.018$; 95% CI, 0.012–0.023; $P < .001$) and the association was similar after controlling for socioeconomic status ($\beta = 0.017$; 95% CI, 0.012–0.023; $P < .001$).

Mean CCA diameter was greater in whites than in blacks after controlling for age and sex (Table 2); the relationship persisted when cardiovascular risk factors were entered into the model. Scatterplots demonstrated a correlation between mean CCA-IMT and CCA diameter (black individuals, $r = 0.481$; white individuals, $r = 0.510$; both, $P < .001$). Because it could be a potential confounder, we repeated analyses also controlling for CCA diameter. Both mean and maximum CCA-IMT remained significantly increased in black individuals after controlling for CCA diameter in addition to cardiovascular risk factors and socioeconomic status ($\beta = 0.057$; 95% CI, 0.032–0.082; $P < .001$ and $\beta = 0.018$; 95% CI, 0.013–0.024; $P < .001$).

Further analysis was performed to determine the relationship between cardiovascular risk factors and CCA-IMT in the 2 ethnic groups separately (Table 3 and On-line Table 2). For the white cohort, on multivariate analysis, mean CCA-IMT was associated with age, diabetes, and a trend toward smoking. For the black cohort, mean CCA-IMT was associated with age, male sex, and diabetes. The association of diabetes with CCA IMT was greater in the white cohort. On multivariate analysis, maximum CCA-IMT was associated with age, male sex, diabetes, and smoking in the white cohort but only age in the black cohort. The proportion of variance in CCA-IMT explained by conventional risk factors was higher in the white cohort for maximum IMT (20% versus 11%) and only slightly higher for mean IMT (23% versus 20%) (Table 4).

BIF-/ICA-IMT measurements were obtained in 79% of the

Table 3: Relationship between cardiovascular risk factors and mean CCA-IMT in the 2 ethnic groups from univariate and multivariate regression analysis

	Black Individuals				White Individuals			
	Univariate		Multivariate (R^2 = 0.20)[a]		Univariate		Multivariate (R^2 = 0.23)[a]	
Risk Factor	B	*P*	B	*P*	B	*P*	B	*P*
Age	0.006	.000[b]	0.006	.000[b]	0.006	.000[b]	0.005	.000[b]
Male sex	0.052	.003[b]	0.037	.040[b]	0.021	.287	−0.034	.085
Hypertension	0.052	.006[b]	0.008	.674	0.065	.000	0.023	.168
Diabetes	0.082	.000[b]	0.043	.038[b]	0.118	.000[b]	0.126	.000b
BMI	0.001	.338	0.003	.096	0.003	.046[b]	0.003	.103
Cholesterol	−0.003	.731	0.002	.802	0.006	.466	0.006	.430
Smoking: pack-years	0.000	.736	0.000	.435	0.001	.005[b]	0.000	.068
Low social class	−0.020	.436	−0.047	.053	0.032	.071	0.015	.394

[a] R^2 = proportion of variance in IMT explained by conventional risk factors.
[b] $P = 0.05$.

white subjects and 56% of the black individuals. For both regions, age- and sex-adjusted IMT was higher in the black subjects (Table 2).

Carotid plaque was more prevalent in white individuals (age- and sex-adjusted: OR, 2.59; 95% CI, 1.38–4.89; $P = .003$), with the association persisting after controlling for cardiovascular, risk factors, including hypertension, diabetes, cholesterol, and pack-years smoked, and social class (OR, 2.90; 95% CI, 1.41–5.96; $P = .004$).

Discussion

The results from this study allow several conclusions to be drawn. First, in an English population, CCA-IMT is increased in black compared with white individuals after controlling for conventional cardiovascular risk factors, socioeconomic status, and CCA diameter. These differences were seen in both mean CCA-IMT measured over the whole arterial segment and maximum CCA-IMT. In contrast, carotid artery plaque is less prevalent in black individuals, with the relationship persisting after controlling for conventional cardiovascular risk factors and socioeconomic status. Finally, the risk factor profiles associated with a raised CCA-IMT may be different for black and white individuals. The implications of these findings are discussed below.

Carotid IMT is now a widely accepted surrogate marker of atherosclerotic disease and has been shown to independently predict both stroke and myocardial infarction. A recent meta-analysis of 8 observational studies with general population–based samples has shown that for an absolute carotid IMT difference of 0.1 mm, the risk of future myocardial infarction increases by 10%–15%, and the stroke risk increases by 13%–18%.[17] In our study, the mean age- and sex-adjusted arterial segment CCA-IMT, as measured by semiautomated software, was 0.05 mm higher and the mean maximum CCA-IMT, 0.17 mm higher in black individuals (Table 2). However, data from these prospective studies linking IMT to clinical cardiovascular events are derived from either white populations alone or combined black and white populations.[6-8] Very little prospective data from black populations concerns specific IMT risk estimates.

Our findings of an increased CCA-IMT but reduced plaque prevalence in black individuals suggest that the increased IMT seen in black individuals may not represent early atherosclerosis as it appears to do in white populations. To test this hypothesis, we extended the analysis to look for any cardiovascular-risk-factor interactions that might explain the increased CCA-IMT in black compared with white individuals. The proportion of variance in CCA-IMT explained by conventional risk factors was higher in the white cohort, especially for maximum CCA-IMT (20% versus 11%). For the black cohort, most explained variance in CCA-IMT was accounted for by age. In the white cohort, variance was explained by diabetes, smoking, and hypertension, as well as age. Furthermore, on multivariate analysis, the associations of CCA-IMT with diabetes were greater in the white compared with the black cohort.

The IRAS is a multicenter observational epidemiologic study of the relations among insulin resistance and risk factors in a multiethnic cohort. It has reported both an increased CCA-IMT in patients with diabetes, after adjustment for cardiovascular risk factors,[18] and more recently an increased CCA-IMT progression rate in these patients.[19] Although this was a multiethnic study and IRAS did adjust for ethnicity, they have not reported race-specific CCA-IMT estimates for patients with diabetes.

It has been suggested that hypertension may play a greater role in IMT in black populations and that the thickening seen may represent adaptive remodelling rather than true atherosclerosis. Furthermore, it is known that both intracranial atherosclerosis and cerebral small-vessel disease are more common in black than in white subjects.[3] It is possible that the increased CCA-IMT seen in blacks is a marker of both types of cerebral artery damage. Although we found associations with systolic blood pressure and increased CCA-IMT in both cohorts on univariate analysis, this did not persist when controlling for other risk factors, including diabetes.

A limitation of our study is that BIF-/ICA-IMT measurements were only obtainable in a subgroup of subjects. This partly reflects the higher BIF often seen in black subjects. Although incomplete, when this dataset was analyzed, the black population also had significantly increased BIF-/ICA-IMT compared with the white population. This demonstrates that the increase in IMT in blacks is seen throughout the carotid artery tree.

We also acknowledge that the prevalence of carotid plaque in our study is lower than that in other community-based

Table 4: Explained variance in CCA-IMT in the 2 ethnic groups

	Black Individuals: Explained Variance (R^2)		White Individuals: Explained Variance (R^2)	
Risk Factor	Mean CCA-IMT	Mean Max CCA-IMT	Mean CCA-IMT	Mean Max CCA-IMT
All	20%	11%	23%	20%
Age	15.6%	7.5%	12%	8.4%
Male sex	–	–	–	6.6%
Diabetes	1.4%	–	5.1%	1.5%
Smoking: pack-years	–	–	2.0%	–
Hypertension	–	–	1.5%	–
Low social class	–	–	–	1.7%
High social class	1.3%	–	–	–

Note:— – indicates no explained variance.

studies, despite a similar frequency of risk factors. This may, in part, reflect the definition of plaque in our study. Currently, there is no internationally accepted definition for plaque. Although our study commenced before the recent Mannheim Carotid Intima-Media Thickness Consensus (2004–2006),[20] our methodology is in line with the recommendations.

Conclusions

Our study shows that carotid IMT is increased, while carotid plaque is less prevalent, in black individuals compared with white individuals. Furthermore, conventional risk factors explain less of the variance in CCA-IMT in black compared with white individuals. The lack of correlation between increased IMT and carotid plaque in black individuals implies that IMT should not currently be used as a surrogate marker of atherosclerosis in black populations. Prospective studies are first required in large black populations to determine whether increased IMT relates to stroke and coronary heart disease risk in black subjects.

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