

Ethnic differences in carotid and left ventricular hypertrophy

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Objectives Afro-Caribbean subjects have a higher prevalence of hypertension, a lower prevalence of ischaemic heart disease and a higher premature mortality compared to White Europeans. Left ventricular hypertrophy (LVH) is also more prevalent in Afro-Caribbeans even at similar levels of blood pressure. It is widely believed that carotid artery intima-media thickening (IMT) represents an early marker for the development of atheroma, and carotid IMT and LVH are associated in White populations. Whether the relationship between carotid IMT and LVH is similar in Black subjects is unknown.

Methods Thirty-eight subjects were studied using carotid and femoral ultrasonography and echocardiography; 19 Afro-Caribbean and 19 White European subjects were matched for age, sex and mean 24 h systolic blood pressure.

Results The Afro-Caribbean group had a significantly greater left ventricular mass index (LVMI) compared to the White European: 136.4 ± 6.1 versus 112.4 ± 6.2 g/m², $P < 0.01$. However, carotid IMT, carotid diameter, femoral IMT and femoral diameter were similar between the groups: 0.75 ± 0.02 versus 0.77 ± 0.04 mm, 6.54 ± 0.15 versus 6.56 ± 0.16 mm, 0.66 ± 0.03 versus 0.68 ± 0.03 mm and 8.40 ± 0.33 versus 8.25 ± 0.23 mm, respectively.

Conclusions Afro-Caribbean subjects with similar blood pressures have similar mean carotid and femoral IMTs compared to White Europeans, in spite of marked differences in LVMI. Whether this reflects a discrepancy in the degree of cardiovascular risk for similar levels of LVMI or whether this is a reflection of an altered pattern of target organ damage associated with hypertension in Afro-Caribbean subjects is unclear. *J Hypertens* 20:539–543 © 2002 Lippincott Williams & Wilkins.

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Introduction

Studies from both the UK and the USA have shown that the prevalence of hypertension is higher in Black than in White populations [1–3], as is the prevalence of left ventricular hypertrophy (LVH) [4,5], which has been demonstrated to be a powerful predictor of increased morbidity and mortality [6]. This may partly explain why Black hypertensives die earlier than Whites [7–9].

Carotid artery intima-media thickening is widely believed to represent an early marker for atherosclerosis. An increased carotid intima-media thickness (IMT) has been found to be associated with increasing age [10], male sex [11], hypertension [11–13], cigarette smoking [11], hypercholesterolaemia [11,14] and raised homocysteine levels [15], all of which are known cardiovascular risk factors. Measurement of carotid IMT has been used to study the presence and progress of atheroma [16,17] and to monitor the efficacy of lipid-lowering therapy [18–20]. The importance of an in-

creased carotid IMT is highlighted by many prospective studies that have demonstrated its value in predicting myocardial infarction and stroke [21–26].

Carotid IMT and LVH are associated with each other [10,27] and, if the former truly represents early atherosclerosis, this association may provide further insights into the increased cardiovascular morbidity and mortality observed with LVH. Black hypertensives, with their increased prevalence of LVH might be expected to also have an increased carotid IMT, which in turn may indicate an increased atherosclerotic burden and help to explain their greater cardiovascular mortality. The present study was designed to test this hypothesis.

Methods

Thirty-eight subjects were studied; 19 Afro-Caribbean and 19 White European subjects referred to the Peart-Rose Clinic at St Mary's Hospital for assessment of hypertension were matched for age (within 5 years), sex and mean 24 h systolic blood pressure (within

5 mmHg). All patients had normal systolic function determined by two-dimensional echocardiography and no clinical or Doppler evidence of valvular stenosis or regurgitation. Patients were excluded if they had a history of ischaemic heart disease, congestive cardiac failure, peripheral vascular disease, diabetes melitus (a previous diagnosis of diabetes or they had a fasting plasma glucose of greater than 7.8 mmol/l on two occasions), alcohol abuse (greater than 30 units of alcohol per week) or an abnormal haematological or biochemical profile. No patient had been previously treated with antihypertensive or lipid-lowering therapy. Each subject underwent carotid and femoral ultrasonography, echocardiography and 24 h ambulatory blood pressure monitoring.

Blood pressure

Blood pressures were measured using an automated monitor (Sentron, CR Bard, Lombard, Illinois, USA). The mean of three sitting measurements made 2 min apart was taken as the blood pressure.

Twenty-four hour ambulatory blood pressure monitoring was performed using Spacelabs 90207 machines (Space Labs Inc, Redmond, Washington, USA). The accuracy of this method has been validated [28]. Measurements were made every 30 min throughout the day and hourly at night. During the test, patients were asked to maintain their normal activities; they were asked to keep their arms still during cuff inflation. Ambulatory monitoring was deemed acceptable if more than 90% of readings were recorded. Mean blood pressure was calculated from the readings over the whole 24 h period. Daytime was taken to be between 0600 h and 2400 h and night-time from 2400 h to 0600 h.

Carotid and femoral artery ultrasound

High resolution ultra-sound imaging was performed by a single ultrasonographer using an Ultramark 4 scanner (Advanced Technologies Laboratories, Washington, USA) with a high resolution 7.5 MHz linear array scan head. All images were coded and stored in original digital quality for offline analysis.

Common carotid scanning was performed with the subject in the supine position, with the neck extended and rotated 45° to the contralateral side. Carotid bulb dilation served as a landmark indicating the border between distal common carotid artery and the bifurcation area. A 10 mm length between 5 and 15 mm proximal to the carotid bulb was imaged. For the determination of common carotid IMT and lumen diameter (D), longitudinal images of the distal common carotid focused on the far wall were utilized. Using electrocardiography (ECG) gating, images from each of three projections (posterior oblique, lateral and anterior

oblique) were frozen at end diastole. In analogous fashion, both femoral arterial systems were scanned with the subjects in the supine position, hips extended and externally rotated approximately 30°. Images of right and left distal common femoral arteries from each of two projections (anterolateral and anteromedial) were frozen at end diastole.

At study completion, all images were measured by a single observer using a purpose-designed, user-directed image analysis program. The observer was blinded to subject identity and category. IMT was measured as the distance from the leading edge of the lumen-intima interface to the leading edge of the media-adventia interface of the far wall, over a 5–15 mm length in the distal vessel, from each of the images. Far wall IMT was then determined as the median distance between blood-to-intima and media-to-adventia interfaces within the selected segment. Where the image analysis program failed to clearly delineate the relevant interfaces, five estimates of IMT were made using a mouse-controlled on-screen cross-hair, and the median was calculated. Lumen diameter for each image was taken as the median of five mouse-controlled measures of the distance from the leading edge of the intima-lumen interface of the near wall to the leading edge of the lumen-intima interface of the far wall.

The mean values of all six measures were taken as common carotid IMT and D for each subject. The mean values of four measures were taken as femoral IMT and D for each subject. Common carotid and femoral, intima media area (IMA) and circumferential tensile stress (CTS) were calculated according to the following formulae:

$$\text{Vessel IMA (mm}^2\text{)} = \pi(D \times \text{IMT} + \text{IMT}^2)$$

$$\text{Vessel CTS (mmHg)} = \text{DBP} \times D/\text{IMT}$$

where DBP denotes diastolic blood pressure.

Six subjects underwent repeated carotid and femoral ultrasonography, after an interval of 1–4 weeks. These were performed by the same ultrasonographer and the same observer directed off-line measurements of IMT and D . Between scan reproducibility, expressed as mean difference \pm SD (mm), was 0.01 ± 0.03 for common carotid IMT, -0.02 ± 0.17 for common carotid D , 0.01 ± 0.03 for femoral IMT, and 0.05 ± 0.23 for femoral D .

Echocardiography

Echocardiography was performed with the subject in the left lateral position using a phased-array sector scanner (General Electric Pass II, 3.3 MHz transducer; General Electric, Milwaukee, Wisconsin, USA). Inter-

ventricular septal wall thickness (IVS), posterior wall thickness (PWT) and left ventricular internal diameter (LVID) were measured from the left ventricular short axis view using two-dimensional guided M-Mode echocardiography. Measurements were made at end-diastole in accordance with the Penn convention. Three consecutive cardiac cycles were measured and average values obtained. Left ventricular mass was calculated using the cubed formula, which has been previously validated [29]:

$$\text{LV mass} = 1.04[(\text{IVS} + \text{LVID} + \text{PWT})^3 - \text{LVID}^3] - 14 \text{ g}$$

This was then divided by body surface area to give a value for left ventricular mass index (LVMI).

Statistical analysis

Where appropriate, hypothesis testing was performed using an unpaired Student's *t*-test and *P*-values calculated. All descriptive data are expressed as mean \pm SEM.

Results

The results are shown in Tables 1–3. Age, sex ratio and blood pressure were similar by design. The mean total cholesterol level, high-density lipoprotein cholesterol level and prevalence of cigarette smoking were also similar between the two groups. Afro-Caribbean patients were heavier, although this difference did not reach statistical significance. IVS, PWT and LVMI were significantly greater in the Afro-Caribbean compared to the White European group. Fifty-eight percent of Afro-Caribbean subjects had LVH compared to 26% of the White European group. However, in spite of these differences in cardiac structure, carotid and femoral IMT were similar between the two groups. No patient had any carotid plaques, defined as a focal thickening > 1.3 mm.

Discussion

The principal findings of the present study were the similarity of carotid and femoral IMT in the two groups

Table 2 Blood pressure, echocardiographic and electrocardiography (ECG) measurements

	Afro-Caribbean (<i>n</i> = 19)	White European (<i>n</i> = 19)
Systolic blood pressure (mmHg)	164.4 \pm 3.4	162.8 \pm 4.3
Diastolic blood pressure (mmHg)	100.1 \pm 1.9	99.1 \pm 2.1
Heart rate (b.p.m.)	67.4 \pm 2.2	69.6 \pm 2.1
24 h systolic blood pressure (mmHg)	150.7 \pm 3.3	150.2 \pm 3.3
24 h diastolic blood pressure (mmHg)	98.4 \pm 2.1	95.5 \pm 1.8
24 h (b.p.m.)	73.1 \pm 1.6	74.6 \pm 1.8
IVS (cm)	1.09 \pm 0.03	0.96 \pm 0.03*
LVID (cm)	5.03 \pm 0.10	4.91 \pm 0.09
PWT (cm)	1.15 \pm 0.03	1.01 \pm 0.03*
LVMI (g/m ²)	136.4 \pm 6.1	112.4 \pm 6.2*
ECG LVH (SV1 + RV5)	32.5 \pm 2.5	29.1 \pm 1.8

Data are means \pm SEM. **P* < 0.01 compared with Afro-Caribbean group. IVS, interventricular septal wall thickness; LVID, left ventricular internal diameter; PWT, posterior wall thickness; LVMI, left ventricular mass index; LVH, Left ventricular hypertrophy.

despite a markedly increased LVMI in the Afro-Caribbean group. To our knowledge, this is the first study to show an ethnic dissociation between LVH and carotid IMT. This is an intriguing finding and raises a number of issues. First, what does carotid intima-media thickening actually represent? The close correlation with many cardiovascular risk factors [10–15] and association with stroke and myocardial infarction [21–26] suggest that it may represent early atheroma; however, an increased carotid IMT has been found in young, fit athletes [30], which raises questions about its reliability as a cardiovascular risk marker. Ultrasound is unable to distinguish between intima and media [31] making IMT a 'lumped' parameter reflecting both intimal (atheroma) and medial changes (remodelling). It has been hypothesized that at low levels of IMT, thickening may represent an adaptive response to changes in shear stress, lumen diameter, tensile stress and pressure instead of atherosclerotic thickening, while beyond a certain level IMT probably represents atherosclerosis [32]. The degree of carotid IMT observed in both groups in the present study is in the range that is generally accepted to represent atherosclerosis but there may be underlying ethnic differences in the normal ratio of intimal to medial thickness. In a study of Canadians of South Asian, Chinese and White European origin, carotid IMT was correlated with ischaemic heart disease within each ethnic group but was thicker in the White Europeans than the South Asians despite a lower prevalence of ischaemic heart disease [33]. This suggests that normal values need to be indexed according to ethnicity. The two previous studies comparing carotid IMT in White and Black subjects provide conflicting information. The Atherosclerosis Risk In Communities study found that Black men had thinner carotid IMT than White men, but no differences were observed in women [34]; conversely, the Insulin Resistance Atherosclerosis

Table 1 General characteristics of subjects

	Afro-Caribbean (<i>n</i> = 19)	White European (<i>n</i> = 19)
Age (years)	45.3 \pm 2.3	46.4 \pm 2.4
Male/female	12/7	12/7
Height (cm)	169.3 \pm 2.0	168.4 \pm 1.6
Weight (kg)	80.5 \pm 4.0	72.6 \pm 2.7
Duration of hypertension (months)	37.0 \pm 8.9	34.4 \pm 8.0
Smoking habit (never/ex/current)	11/3/5	9/5/5
Total cholesterol (mmol/l)	5.53 \pm 0.28	5.67 \pm 0.30
Triglycerides (mmol/l)	1.67 \pm 0.59	1.43 \pm 0.17
HDL cholesterol (mmol/l)	1.38 \pm 0.10	1.37 \pm 0.09

Data are means \pm SEM. No differences were statistically significant. HDL, High-density lipoprotein.

Table 3 Carotid and femoral artery measurements

	Afro-Caribbean (n = 19)	White European (n = 19)
Intima-media thickness, distal common carotid (mm)	0.75 ± 0.02	0.77 ± 0.04
Internal diameter, distal common carotid (mm)	6.54 ± 0.15	6.56 ± 0.16
Intima-media area, distal common carotid (mm ²)	17.38 ± 0.73	17.77 ± 1.12
Circumferential tensile stress, distal common carotid (mmHg)	880.2 ± 34.3	884.3 ± 50.3
Intima-media thickness, femoral (mm)	0.66 ± 0.03	0.68 ± 0.03
Internal diameter, femoral (mm)	8.40 ± 0.33	8.25 ± 0.23
Intima-media area, femoral (mm ²)	19.12 ± 1.52	19.06 ± 1.13
Circumferential tensile stress, femoral (mmHg)	1303.8 ± 69.4	1248.6 ± 69.2

Data are means ± SEM. No differences were statistically significant.

Study observed that common carotid IMT was greater in Blacks than non-Hispanic Whites [35]. However, neither of these studies measured 24 h ambulatory blood pressure or assessed left ventricular structure and subjects in the present study had never been treated with antihypertensive or lipid-lowering therapy. Indeed, the relative importance of LVH in Black and White populations also needs addressing. The observation of LVH as a predictor of an increased cardiovascular morbidity and mortality largely comes from White populations [36,37]; although there is also data suggesting that an increased LVMI also predicts an adverse prognosis in Black populations [38], this does not mean that the same degree of LVH necessarily imparts the same risk in both groups. There is evidence to suggest that Black subjects have an increased LV wall thickness from a young age [39] and across a wide range of blood pressures [40] and this may be a normal variation. It may be that a greater degree of LVH in Black subjects compared to Whites confers the same level of cardiovascular risk. This explanation would fit with the discrepancy in LVMI and carotid IMT observed in the present study. However, there is an alternative explanation. It is known that Black hypertensives are at higher risk of renal failure [41], cardiac failure [42,43] and stroke [44] than Whites but are at lower risk of ischaemic heart disease [45]. The incidence of renal failure, cardiac failure and stroke have a marked relationship with blood pressure levels, but blood pressure has a less impressive relationship with atherosclerosis which underlies ischaemic heart disease. It is possible that carotid IMT reflects atherosclerosis and is a better marker for ischaemic heart disease than other cardiovascular complications of hypertension. There is certainly evidence to support a close correlation between carotid and coronary atherosclerosis [46,47] and the observations of the present study may therefore be consistent with the known ethnic variation in the different cardiovascular complications of hypertension in these populations. It is important to remember that these patient groups are matched for blood pressure and so are not a reflection of Black and White groups in the community. Black populations have high-

er blood pressures and if a typical Black population were studied (i.e. not matched for blood pressure), the higher mean blood pressure might be expected to result in a greater mean IMT than a corresponding White population; therefore the observations of a similar IMT in the Black and White groups in the present study and a higher incidence of stroke in Black populations are not incompatible.

In summary, Afro-Caribbean subjects with similar blood pressures have similar mean carotid and femoral IMTs compared to White Europeans, in spite of marked differences in LVMI. Whether this reflects a discrepancy in the degree of cardiovascular risk for similar levels of LVMI in Black and White subjects or whether this is a reflection of an altered pattern of target organ damage associated with hypertension in Afro-Caribbean subjects is unclear. A long-term prospective study assessing the association of carotid and left ventricular structure with cardiovascular end points in different ethnic populations is required to properly address this issue.

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