Cardiovascular morbidity and mortality vary among different ethnic groups. People of Indian subcontinental, or South Asian, origin (SA) in Britain and North America have higher coronary heart disease (CHD) prevalence and mortality, experiencing events at a younger age and slower declines in premature CHD mortality than other groups.5–7 (Figure S1A, available in the online Data Supplement at http://hyper.ahajournals.org). Conventional risk factors, such as diabetes mellitus, obesity, and hypertension, fail to explain these ethnic differences fully.5 In contrast, African Caribbeans (AfCs) have lower CHD mortality than Europeans despite higher rates of hypertension, diabetes mellitus, and stroke2,6,7 (Figure S1B). Despite sharing excess hypertension and diabetes mellitus, a similar heritage, and genetic background with AfCs, blacks have a different vascular profile further along the epidemiological transition to atheromatous disease than AfCs.7,8

There has been little comparative data on arterial function of these populations. Aortic pulse wave velocity (aPWV), an index of arterial stiffness, is a powerful independent predictor of cardiovascular events and death.9–12 We studied aPWV and its determinants in a sample of men from 3 ethnic groups to investigate the following questions. First, do differences in aPWV across ethnic groups parallel their known coronary risk profiles, and, if so, do proximal and distal aPWVs measured by more precise magnetic resonance (MR) imaging differ similarly? Second, are serum vitamin D or aldosterone concentrations related to aPWV as a risk marker, and do they influence cross-ethnic aPWV differences?

**Methods**

Participants were 198 men aged 40 to 80 years of AfC, SA, and European origin in Manchester, United Kingdom, who had already been recruited to the European Male Ageing Study.13 The participants had to be free of severe chronic or acute disease of active malignant renal or liver origin. Ethnicity was defined by participants’ self-reporting and 3 of 4 grandparents being of the same ethnic origin. Original recruitment was through volunteers by advertising in community centers and media in Manchester for SA and AfC groups and by general practice register sampling for Europeans.
Main Study
All of the participants had noninvasive oscillometric arterial stiffness and blood pressure (BP) measurement in the morning after avoiding caffeine, tobacco, and heavy meals 3 hours before their visit, as well as alcohol from the night before. Using a standard protocol, BP was measured using a validated Omron semiautomatic device on the left upper arm, sitting, 3 times after 5 minutes rest in a temperature-controlled room. The values from the last 2 measurements were averaged and recorded.

The Arteriograph (TensioMed, Budapest, Hungary) device was used to measure arterial stiffness indices, including total aPWV (aPWV\(_{AG}\)), estimated central (aortic) augmentation index (aoAlx), and central systolic BP (SBP). The device records pressure waves in the brachial artery with an arm cuff and estimates the aortic pulse wave transit time between the aortic root and bifurcation from the time interval between the peaks of forward and reflection pressure waves in each cardiac cycle using a commercial algorithm. It assumes that the corresponding aortic path is approximated by sternal notch-to-pubis distance on body surface.

Arrival times of the aortic pulse waves were computed from the 3 transit-times measured by the Arteriograph (as externally estimated arterial pathway) showed that the latter would overestimate the real aortic path and that it was possible to predict MR-measured total aortic lengths from a regression model derived from age and height. Consequently, the Arteriograph measurements were performed a minimum of 2 times on the left arm after ≥5 minutes of rest supine after BP measurement. Central augmentation pressure was derived from aoAlx and central pulse pressure. The coefficient of variation (intraobserver correlation) for Arteriograph aPWV\(_{AG}\), aoAlx, and central SBP for separate sessions in our laboratory were 5% (0.87), 14% (0.83), and 5% (0.90).

Liquid chromatography-tandem mass spectrometry was used to measure 25(OH)D3 on frozen serum samples, as described previously. Serum aldosterone was measured using radioimmunoassay (Coat-A-Count aldosterone; Siemens Medical Solutions Diagnostics, Los Angeles, CA).

MRI Substudy
A subsample of the men in the main study free from diabetes mellitus and cardiovascular medications and without previous histories of cardiovascular events was invited for the MR study and seen under the same conditions. The MR protocol for PWV measurement used a 1.5-T Philips Intera scanner (Philips Medical Systems, Best, the Netherlands) to acquire 2 consecutive nonbreath hold, through-plane, velocity-encoded, phase-contrast transverse aortic cine images, one from the aortic arch at the level of pulmonary artery and the other 2 cm above the aortic bifurcation (Figure 1). Image analysis was performed offline with the same analyst blinded to patient identities. Arrival times of the aortic pulse waves were computed from the 3 flow-time curves recorded at the 3 points: P\(_1\), P\(_2\), and P\(_3\) (Figure 1), from which 3 transit-times could be derived for P\(_1\)P\(_2\), P\(_2\)P\(_3\), and P\(_1\)P\(_3\). The lengths of corresponding aortic paths were measured on MRIs. This enabled measurement of 3 PWV values, over the aortic arch (archPWV\(_{MR}\)), descending aorta (desPWV\(_{MR}\)) and the overall segment (aoPWV\(_{MR}\)) (Figure 1). Intraobserver coefficient of variation was 7.8% (0.91) for archPWV\(_{MR}\), 3.4% (0.96) for desPWV\(_{MR}\), and 2.5% (0.98) for aoPWV\(_{MR}\), when MRI analysis was repeated for 10 participants.

Improving aPWV\(_{AG}\) Estimation With MRI Aortic Lengths
Comparison of the MR-measured total aortic lengths (ie, aortic root to bifurcation) to the surface sternal notch-pubis length used by Arteriograph (as externally estimated arterial pathway) showed that the latter would overestimate the real aortic path and that it was possible to predict MR-measured total aortic lengths from a regression model derived from age and height. Consequently, the Arteriograph aPWV\(_{AG}\) was recalculated using the transit time measured by the device and the length of aortic path estimated by the aforementioned regression model.

Statistical Analysis
Data were analyzed by R statistical package version 2.11.1. ANOVA was used to compare means of parametric (and transformed skewed) variables across ethnic groups. PWV and hormonal corre-

![Figure 1. Magnetic resonance aortic sagittal view shows 3 aortic paths (P1, P2, P3, and P1, P2, P3), for which the 3 pulse wave velocities, pulse wave velocity (PWV) aortic arch segment (arch-PWV\(_{arch}\)), PWV descending aorta segment (des-PWV\(_{des}\)), and PWV aortic overall segment (ao-PWV\(_{ao}\)), were measured in a subsample of 47 men. AV indicates aortic valve; Bif, aortic bifurcation.](image-url)
Table 1. General, Hemodynamic, and Metabolic Characteristics of the Participants With Univariate Analysis (n=198) in Mean±SD or Median (Interquartile Range)

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (N=198)</th>
<th>MR Subsample (N=47)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AIC (N=67)</td>
<td>SA (N=68)</td>
</tr>
<tr>
<td>Age, y</td>
<td>55±10</td>
<td>55±10</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8 (12%)</td>
<td>24 (35%)</td>
</tr>
<tr>
<td>Hypertension Tx</td>
<td>8 (12%)</td>
<td>10 (15%)</td>
</tr>
<tr>
<td>Dyslipidemia Tx</td>
<td>6 (9%)</td>
<td>13 (19%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>12 (19%)</td>
<td>11 (17%)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>84±11.0</td>
<td>79±110</td>
</tr>
<tr>
<td>Height, cm</td>
<td>174±6</td>
<td>170±6</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28±3</td>
<td>27±3</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>130±16</td>
<td>124±14</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>82±11</td>
<td>78±9</td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>48±10</td>
<td>46±9</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>98±12</td>
<td>94±11</td>
</tr>
<tr>
<td>cSBP, mm Hg</td>
<td>127±20</td>
<td>125±19</td>
</tr>
<tr>
<td>cPP, mm Hg</td>
<td>46±11</td>
<td>45±11</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>65±8</td>
<td>68±11</td>
</tr>
<tr>
<td>archPWVagg, m/s</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>desPWVagg, m/s</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>aPWVAG or MRI, m/s</td>
<td>6.8 (1.7)</td>
<td>7.6 (2.4)</td>
</tr>
<tr>
<td>aAoAix, %</td>
<td>27±13</td>
<td>33±13</td>
</tr>
<tr>
<td>cAP, mm Hg</td>
<td>13±9</td>
<td>16±9</td>
</tr>
<tr>
<td>FPG, mmol/L</td>
<td>5.3 (0.9)</td>
<td>5.6 (1.5)</td>
</tr>
<tr>
<td>Creatinine, mmol/L</td>
<td>95±14</td>
<td>85±14</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>5.0±1.1</td>
<td>4.7±0.8</td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>1.4 (0.5)</td>
<td>1.1 (0.3)</td>
</tr>
<tr>
<td>TC/HDL ratio</td>
<td>3.6±0.9</td>
<td>4.4±1.1</td>
</tr>
<tr>
<td>25 (OH)D, nmol/L</td>
<td>30 (16)</td>
<td>18 (15)</td>
</tr>
<tr>
<td>Aldosterone, pmol/L</td>
<td>180 (137)</td>
<td>295 (160)</td>
</tr>
</tbody>
</table>

*Data show significant P values.  
†Data show  χ² P values.  
‡Data show P values from ANOVA on reverse-transformed pulse wave velocity values and log transforms of other marked variables.

Adjusted mean (SE) aPWVAG in SAs was ~0.5 m/s (0.2 m/s) higher than in AfCs and Europeans (Table 2), whereas AIC adjusted aoAix and central augmentation pressure were 7% (2%) and 3.6 mm Hg (1.0 mm Hg) lower than SAs and 7% (2%) and 2.5 mm Hg (1.0 mm Hg) less than Europeans. Thus, SAs had higher aPWVAG for given levels of age and distending pressures. Excluding diabetes mellitus or replacing SBP with mean arterial pressure did not change the ethnic
effects for \( \text{aPWV}_{AG} \) and \( \text{aoAIx} \); entering heart rate in the \( \text{aPWV} \) model (Model A, Table 2) slightly weakened but did not remove them (data not shown).

**Hormones**

Vitamin D and aldosterone were significantly different across the groups (Table 1 and Figure 3A and 3B). Adjusted for age, weight, season of blood sampling, and vitamin D supplement use, mean (SE) 25(OH)D in SAs was 21 nmol/L (3 nmol/L) and AfCs 14 nmol/L (3 nmol/L) lower than Europeans and in SAs was lower by 7 nmol/L (2 nmol/L) than AfCs (\( P<0.001 \) for all).

Compared with AfCs, aldosterone was 85 pmol/L (20 pmol/L) higher in SAs (\( P<0.001 \)) and 51 pmol/L (21 pmol/L) higher in Europeans (\( P=0.015 \)) after adjusting for antihypertensive use and body mass index. SAs had 34 pmol/L (22 pmol/L) higher aldosterone than Europeans, but this was not significant (\( P=0.13 \)) after adjustments. There was borderline inverse correlation between aldosterone and 25(OH)D (\( \rho = -0.14; \) \( P=0.06 \)).

**Arterial Stiffness-Hormonal Relations**

Neither hormone was correlated with BPs, PWV, and \( \text{aoAIx} \) in univariate analysis. Adjusted for age, SBP, and diabetes mellitus, 25(OH)D was inversely related to \( \text{aPWV}_{AG} \) (B [SE]= -0.013 [0.004]; \( P<0.001 \)) but not \( \text{aoAIx} \) (data not shown). With similar adjustments, the participants in tertiles 2 and 3 of 25(OH)D had 0.3 m/s (0.2 m/s; \( P=0.1 \)) and 0.5 m/s (0.2 m/s; \( P=0.015 \)) lower \( \text{aPWV}_{AG} \), respectively, compared with tertile 1. The correlations between aldosterone and 25(OH)D were insignificant in similar models. Entering 25(OH)D in the model removed statistical ethnic differences in \( \text{aPWV}_{AG} \); such results were not observed for aldosterone (Table 2). An interaction term between ethnicity and 25(OH)D in these models was not significant (data not shown). Age adjustment was the main factor making the 25(OH)D-\( \text{aPWV}_{AG} \) relationship significant, notably in those 50 years of age (Figure 3C).

**MRI Substudy**

MRI study participants consisted of 16 Caribbean, 13 Pakistani, and 18 European men whose age, body mass index, brachial BP, or central BP differed significantly with this relatively small sample size (Table 1). After adjusting for age and SBP, mean (SE) desPWV\( _{MR} \) in SAs was 0.7 m/s (0.3 m/s) and 0.8 m/s (0.3 m/s) higher than in AfCs and Europeans, respectively; archPWV\( _{MR} \) was not statistically different (Table 3). This pattern of ethnic difference in desPWV\( _{MR} \) in the MR study replicates the result for the \( \text{aPWV}_{AG} \) in the total sample (Figure 2A through 2B), but the pattern for archPWV\( _{MR} \) is different (Figure 2C). Adjusted for age and SBP, higher aldosterone tertiles were associated with greater archPWV\( _{MR} \) but not desPWV\( _{MR} \) (Table 3); this remained significant after adjusting for ethnicity.

**Discussion**

The results suggest firstly that SA men had higher \( \text{aPWV} \) than AfCs and Europeans for the same levels of age and brachial/central distending pressures, thus reflecting the known CHD population risk differences across ethnic groups. Despite slightly higher peripheral BPs, AfCs had lower \( \text{aPWV} \) paralleling currently lower CHD risk in Britain and the Caribbean region. Second, the MR substudy showed that pathology in the more elastic descending aortic segment, but not that of the aortic arch, may be related to CHD risk. Third, serum 25(OH)D was inversely related to \( \text{aPWV} \) independent of age and SBP; hence, poor vitamin D status may account for some of the ethnic differences in \( \text{aPWV} \) and, potentially, therefore, some vascular disease in the population as a whole. Randomized trials to test that hypothesis are scarce.19

Studies comparing arterial stiffness in SAs, AfCs, and Europeans, particularly in community samples, are few. Our previous population-based work focused on comparing risks across glucose tolerance with relatively small numbers of controls found no difference in Doppler-measured \( \text{aPWV} \) down the descending aorta in AfC (10.1 m/s), Gujarati SA (10.5 m/s), and European (9.7 m/s) groups after adjusting for age and sex.9 However, those data were not adjusted for BPs, which were higher in AfCs. Two studies reported higher arterial stiffness estimated by reflection wave indices among SAs.
healthy and poststroke SA subjects compared with their European counterparts. Neither measured aPWV.

We found no significant aPWV differences between AfCs and Europeans. Similar results were found in different populations of black and white adults, using Doppler-measured aortic-femoral PWV,22 central aPWV,23 or arterial compliance by the Windkessel method.24 However, 2 other studies using the Complior device reported higher carotid-femoral PWV in younger Brazilians of African descent25 and for British AfCs compared with Europeans.26 The above inconsistencies may be attributed to different techniques, study populations, statistical approaches, and arterial paths or length estimation methods used for PWV measurement, as we found in a recent European pooling project.27 Here we measured aPWV over a central aortic path.

Data on the relationship between vitamin D and PWV is scarce and limited to chronic kidney disease patients, with inverse relationships found.28–30 Our study appears to be the first to report such an association in a community-dwelling, multiethnic sample. A recent randomized trial (n=49) found a fall in carotid-femoral PWV among black teenagers given 2000 IU/d of vitamin D3 compared with those on 400 IU/d.31 These pilot results suggest promise for vitamin D as an intervention in black populations. Other data from disease-free or asymptomatic subjects primarily relate to endothelial function measured by brachial flow-mediated dilation,32 which was positively correlated with serum 25(OH)D and improved on supplementation in deficient cases.33

In our data, vitamin D was also negatively related to total cholesterol/high-density lipoprotein cholesterol ratio, fasting plasma glucose, and aldosterone. Including these variables in the regressions did not remove the independent correlation of vitamin D and aPWV (data not shown).

Effects of vitamin D on arterial stiffness may be via a variety of mechanisms, including endothelial function, renin-angiotensin system inhibition, regulation of parathyroid hor-

Figure 3. A and B, Box-plots for circulating 25(OH)D and aldosterone among ethnic groups. AfC indicates African Caribbean; SA, South Asian; WE, European. C, Aortic pulse wave velocity (aPWV) estimated noninvasively by the arteriograph device (aPWV\textsubscript{AG}) by 25(OH)D tertiles in 4 age groups among total sample. Thick horizontal lines are medians; bottom and top box borders are 25th and 75th percentiles; and whiskers are data range (Qrt indicates quartile).
mone, vascular calcification, and matrix metalloproteinase activity. Paradoxically, pharmacological doses of some vitamin D receptor activators (e.g., calcitriol) may cause arterial calcification and stiffness in experimental models, whereas others (e.g., paricalcitol) do not.

Arterial stiffness here was greater among SA men, with lower aPWV values from both noninvasive and MR measures in AfCs despite slightly higher BPs. Because the data parallel CHD risk in these ethnic groups, aPWV may, therefore, add precision to risk estimation from BP alone. Vitamin D insufficiency may explain part of the ethnic differences in aPWV and cardiovascular risk.

### Study Limitations

Although the participants were community-dwelling men, they were recruited as volunteers. The study sample is, therefore, not fully representative, although their BP and metabolic profiles are similar to those reported previously. Similarly, our MR substudy results should be interpreted with caution, because the numbers in each group are small. However, the MR subsamples were free of known vascular disease, so these novel data generate hypotheses on the relative roles of regional differences in aortic PWV in relation to vascular events. In cross-sectional data, cause and effect between low vitamin D or higher aldosterone levels and arterial stiffness cannot be assessed, and are in part confounded by the ethnic data. Participants were also not on standardized sodium diets.

### Perspectives

Arterial stiffness here was greater among SA men, with lower aPWV values from both noninvasive and MR measures in AfCs despite slightly higher BPs. The data parallel

### Sources of Funding

The work was a part of M.R.’s PhD project supported by a Biotechnology and Biological Sciences Research Council–related Faculty Strategic Studentship and Overseas Research Students Awards Scheme awards from the University of Manchester and partly supported by Wellcome Trust Clinical Research Facility. The MRI scans were funded by Magnetic Resonance Imaging Facility and the National Institute for Health Research, Manchester Biomedical Research Centre.

### Disclosures

None.

### References


Ethnic Differences in Aortic Pulse Wave Velocity Occur in the Descending Aorta and May Be Related to Vitamin D

Mohammad-Reza Rezai, A. Michael Wallace, Naveed Sattar, Joseph D. Finn, Frederick C.W. Wu and J. Kennedy Cruickshank

Hypertension. 2011;58:247-253; originally published online June 13, 2011; doi: 10.1161/HYPERTENSIONAHA.111.174425

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/58/2/247

Data Supplement (unedited) at:
http://hyper.ahajournals.org/content/suppl/2011/06/10/HYPERTENSIONAHA.111.174425.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org/subscriptions/
Online Supplement

Ethnic differences in aortic pulse wave velocity occur in the descending aorta and may be related to vitamin D

Mohammad-Reza Rezai1*, A. Michael Wallace3, Naveed Sattar3, Joseph D. Finn2, Frederick C.W. Wu2, J. Kennedy Cruickshank1

1. Cardiovascular Research Group, University of Manchester, Manchester Academic Health Science Centre, UK
2. Andrology Research Unit, Developmental & Regenerative Biomedicine Research Group, University of Manchester, Manchester Academic Health Science Centre, UK
3. Department of Clinical Biochemistry, Glasgow Royal Infirmary, Glasgow, UK

Short title: Aortic stiffness & vitamin D, a multi-ethnic study

Corresponding author:
Professor JK Cruickshank
Cardiovascular Research Group
Core Tech Facility, 46 Grafton Street
University of Manchester, M13 9NT, UK
Email: elinep@manchester.ac.uk
Tel : +44(0)161-275-1191 and 275-1191-1203
Fax: +44(0)161-275-1183
Email : kennedy.cruickshank@manchester.ac.uk
Figure S1. a) Men’s CHD prevalence by age and three ethnic groups in England, 2008, (adapted from data in 1) and b) Men’s stroke mortality trends, 1979-2003 by country of birth in England and Wales (adapted from data in 1, 2)