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ORIGINAL PAPER

Ethnicity differences in geometric remodelling and myocardial composition in hypertension unveiled by cardiovascular magnetic resonance

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Aims Hypertensive patients of African ancestry (Afr-a) have higher incidences of heart failure and worse clinical outcomes than hypertensive patients of European ancestry (Eu-a), yet the underlying mechanisms remain misunderstood. This study investigated right (RV) and left (LV) ventricular remodelling alongside myocardial tissue derangements between Afr-a and Eu-a hypertensives.

Methods and results 63 Afr-a and 47 Eu-a hypertensives underwent multi-parametric cardiovascular magnetic resonance. Biventricular volumes, mass, function, mass/end-diastolic volume (*M*/*V*) ratios, T2 and pre-/post-contrast T1 relaxation times, synthetic extracellular volume, and myocardial fibrosis (MF) were measured. 3D shape modelling was implemented to delineate ventricular geometry. LV and RV mass (indexed to body-surface-area) and M/V ratio were significantly greater in Afr-a than Eu-a hypertensives (67.1 ± 21.7 vs. 58.3 ± 16.7 g/m^2, 12.6 ± 3.48 vs. 10.7 ± 2.71 g/m^2, 0.79 ± 0.21 vs. 0.70 ± 0.14 g/mL, and 0.16 ± 0.04 vs. 0.13 ± 0.03 g/mL, respectively; $P < 0.03$). Afr-a patients showed greater basal interventricular septum thickness than Eu-a patients, influencing LV hypertrophy and RV cavity changes. This biventricular remodelling was associated with prolonged T2 relaxation time (47.0 ± 2.2 vs. 45.7 ± 2.2 ms, $P = 0.005$) and higher prevalence (23% vs. 4%, $P = 0.001$) and extent of MF [2.3 (0.6–14.3) vs. 1.6 (0.9–2.5) % LV mass, $P = 0.008$] in Afr-a patients. Multivariable linear regression showed that modifiable cardiovascular risk factors and greater end-diastolic volume, but not ethnicity, were independently associated with greater LV mass.

Conclusion Afr-a hypertensives had distinctive biventricular remodelling, including increased RV mass, septal thickening and myocardial tissue abnormalities compared with Eu-a hypertensives. From this study, modifiable cardiovascular risk factors and ventricular geometry, but not ethnicity, were independently associated with greater LV myocardial mass.

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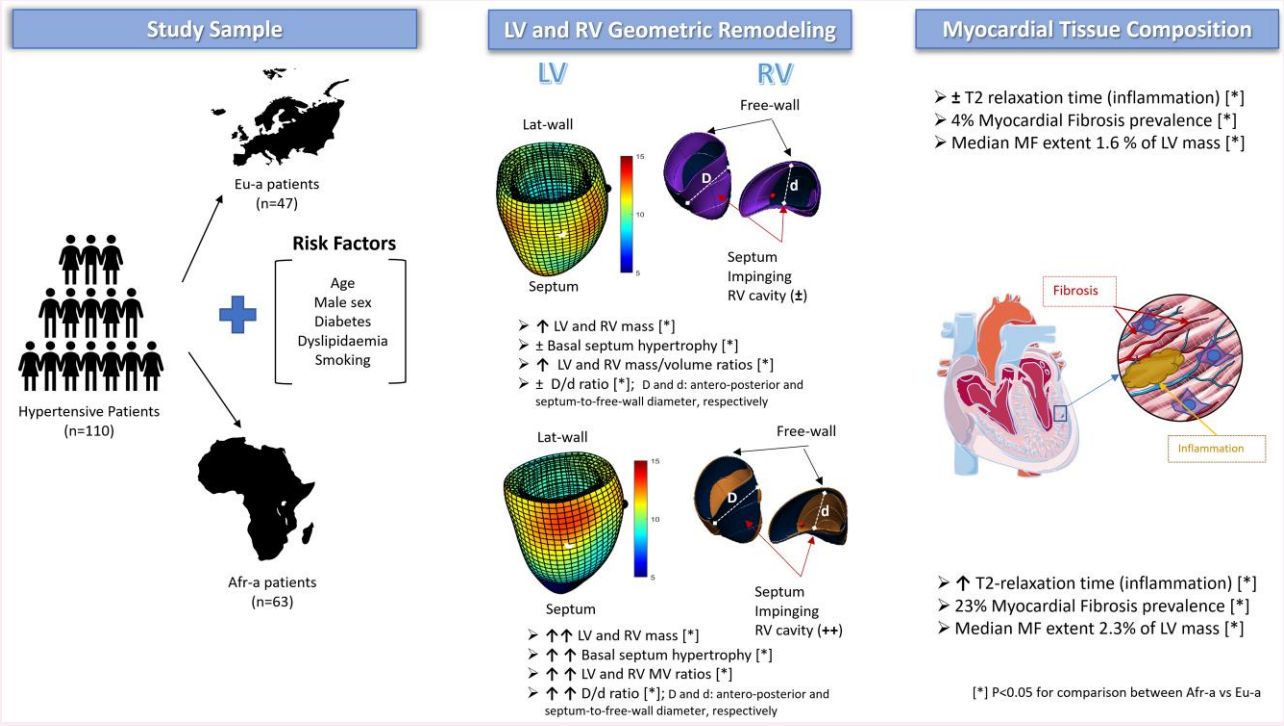
Graphical Abstract



Keywords hypertension • ventricular remodelling • heart failure • ethnicity • myocardial fibrosis • inflammation

Introduction

Systemic hypertension is a major global health concern, particularly in patients of African ancestry (Afr-a). Large population-based studies reported a higher likelihood of heart failure (HF) and worse clinical outcomes in Afr-a hypertensive patients compared with patients of European ancestry (Eu-a).[1–4] This observation was largely attributed to higher prevalence of left ventricular (LV) hypertrophy and remodelling in Afr-a patients.[3–7] A better understanding of the interplay between ethnicity, hypertension, and cardiac remodelling is paramount for implementing personalized interventional and risk stratification strategies to tackle HF. In this respect, two main aspects remain poorly understood, which our study sought to explore. Our first primary outcome is whether the greater LV hypertrophy and remodelling in Afr-a patients is paralleled by changes in the myocardial composition, such as inflammation or myocardial fibrosis (MF). Our second primary outcome is to investigate the relationship between ethnicity and right ventricular (RV) remodelling. Both features are key players in HF development and adverse clinical outcomes.[8–11] Cardiovascular magnetic resonance (CMR) is well poised to investigate biventricular remodelling and myocardial composition in hypertensive patients given its unparalleled ability to non-invasively delineate ventricular geometry and interrogate myocardial structure. We therefore studied Afr-a and Eu-a hypertensive patients undergoing multi-parametric CMR to investigate ethnic differences in myocardial composition and ventricular geometry.

Methods

Study population

Between November 2019 and November 2021, 123 consecutive hypertensive patients were prospectively assessed. Ethnicity was recorded as Afr-a if both parents self-identified as African descendants or Eu-a if both parents self-identified as European descendants. Inclusion criteria are as follows: (i) ≥18 years; (ii) hypertension diagnosed on previous treatment and/or daytime ambulatory blood pressure (or home blood pressure averaged over seven days) >135mmHg systolic or >85mmHg diastolic[12]; (iii) presence of LV hypertrophy and/or LV dysfunction; and (iv) under stable antihypertensive treatment for the last 12 months. Exclusion criteria are as follows: (i) Myocardial infarction or coronary artery revascularization; (ii) primary cardiomyopathy; (iii) inflammatory heart disease; (iv) congenital heart disease; (v) severe renal failure (<30mL/min^{-1}/m^2); and (vi) refusal to provide informed consent. In parallel, 48 healthy volunteers of either ethnicity were also included in the study. Anthropometric, body mass index (BMI), fat mass, and fat-free masses were calculated as previously reported.[13] The term race is defined by the National Institutes of Health[14] as 'a social construct used to group people. Race divides human populations into groups often based on physical appearance, social factors, and cultural backgrounds'. The term ethnicity is defined by Lewis *et al.*[15] as 'cultural factors such as language, religion, cuisine, ancestry, and nationality that specific communities share. Ethnicity is also considered a social construct that individuals may change as their community and personal dynamics change'. In this article, we are investigating ethnic differences rather than racial.

Cardiovascular magnetic resonance

All patients underwent 1.5-T CMR (Aera-Magneton, Siemens Healthcare, Erlangen, Germany) as part of their diagnostic workup. Imaging acquisition protocol and parameters are detailed in the Supplementary data online.

Image analysis

Images were analysed offline by an experienced operator (18 years) using commercially available cardiovascular software (CVI42 v5.14.2, Circle Cardiovascular Imaging Inc., Calgary, Canada), following current

recommendations.[16,17] The CVI42 software also uses machine-learning–enabled segmentation that enhanced precision for image analysis. RV mass was measured at end-systole to facilitate discrimination between endocardial and epicardial borders. RV trabeculae were excluded from mass. Ventricular volumes and masses were normalized to body-surface-area (Mosteller's formula) and height (m). Global LV circumferential and longitudinal strains were measured using two-chamber, four-chamber, and short-axis stacks of cine images.[18] T2-, native (pre-contrast) and post-contrast T1 relaxation times, and synthetic extracellular volume (s-ECV) were measured in the mid-interventricular septum.[17] On post-contrast images, late-gadolinium-enhancement (LGE) was deemed present if visible in two orthogonal views or on the same image orientation after swapping the phase frequency direction. LGE extent was quantified as myocardium with signal-intensity >5 standard deviations (SDs) than normal.[19] LGE was expressed as a percentage of LV mass (%LV mass). Segmental pulse-wave-velocity (PWV) was measured by combining high-temporal resolution free-breathing phase-contrast velocity-encoded images of the ascending and proximal descending aorta (aortic flow transit time) and parasagittal cine images of the ascending-descending aorta (mid-vessel path length) by an in-house developed software (see Supplementary data online).

Ventricular shape computational modelling

3D computational analysis of LV and RV geometry was carried out as previously described.[20,21] This approach generated personalized biomechanical meshes of the ventricles. Statistical shape models were built by principal component analysis to delineate modes (geometric signatures) of ventricular shape variation across patients. Linear discriminatory analysis was applied to identify LV or RV modes for ethnicity classification[22] (see Supplementary data online).

Statistical analysis

Continuous and categorical variables were expressed as mean ± SDs or median and interquartile range (25th–75th percentiles), and frequency (%), respectively. Normal distribution of continuous variables was assessed by histograms or *QQ* plots. Continuous variables were compared between Afr-a and Eu-a groups by independent samples Student's *t*-tests or Mann–Whitney tests, as appropriate. Categorical variable differences between the two groups were tested by contingency tables and chi-square or Fisher's exact test, as appropriate. Pearson's and Spearman's rho correlation coefficients (*r*) were used to assess the correlation between continuous variables. Multivariable linear regression analysis was used to assess the association between LV or RV mass and covariates. Risk factors considered for differential remodelling profiling between Afr-a and Eu-a patients were traditional cardiovascular factors (e.g., age, diabetes, hyperlipidaemia, smoking, and male sex) and remodelling parameters such as hypertension duration and mean blood pressure (MBP). Given the cross-correlation between LV and RV parameters, models were developed without (Model A) and with (Model B) the contralateral ventricular parameters, in addition to covariates known to influence myocardial mass.[1–5,22] To avoid collinearity (i.e. variance inflation factor > 5), only BMI, but not fat-free mass/fat mass, was introduced in the models, while LV or RV end-diastolic volume were introduced separately.[23] Interaction terms between ethnicity and sex were also inserted into the multivariable regression models to test for potential effect modification by sex on ethnicity-induced LV/RV hypertensive remodelling. Statistical analysis was conducted with Stata v16.1 (Stata Corp, College Station, Texas, USA). We deemed statistical significance at $\alpha = 0.05$. Interaction terms were considered significant at $P < 0.1$.[24] By multivariable regression, our study with 110 participants was powered at the 0.85 level to detect an independent association between LV or RV mass and ethnicity after controlling for seven risk factors. The effect size of the independent association was considered small to moderate according to Cohen's convention ($f2 = 0.1$) and type-I error was pre-specified at 0.05. An *F*-test for the squared multiple partial correlation coefficient with *k* degrees of freedom (where *k* is the total number of variables used in the multivariable regression model) was used for power considerations.[25,26] Power calculation was performed with G*Power v3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany).[27] We also calculated the intra- and inter-rated intra-class correlation coefficient [alongside 95% confidence intervals (CIs)] in 10 randomly chosen patients for measurements of LV mass by the same or two independent raters, by using two-way random-effects models. Absolute agreement of individual ratings was estimated.[28]

Results

Study population

Among the initially screened 123 patients, three patients (2.4%) were excluded because of hypertrophic cardiomyopathy, one patient was on dialysis, five patients did not complete CMR scan (claustrophobia or technical reasons), and four patients refused study participation. Eventually, 110 hypertensives were included in the study with 47/110 (42%) Eu-a patients and 63/110 (58%) Afr-a patients (*Figure 1*). In addition, 16 Afr-a and 32 Eu-a age- and sex-matched healthy volunteers were recruited. Ethics approval was issued by King's College London (REC: 15/NS/0030) and all study participants provided written informed consent.

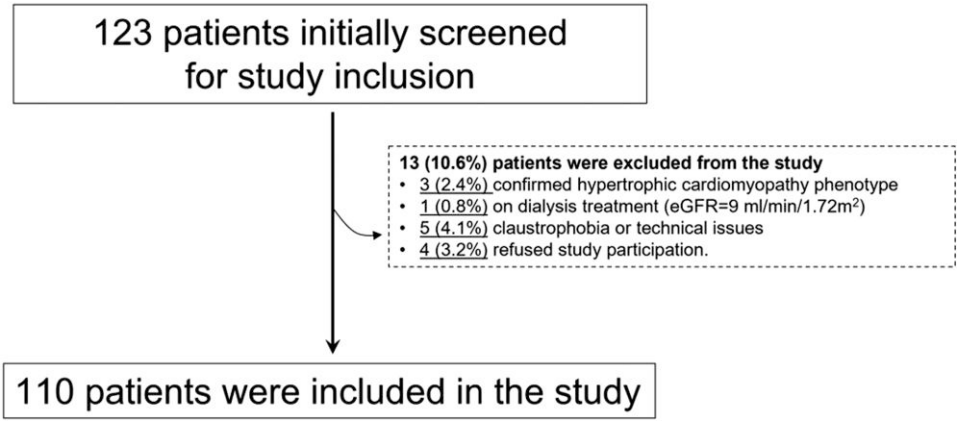


Figure 1 Study flow. eGFR, estimated glomerular filtration rate

Table 1 Baseline characteristics

Variable	European ancestry ($n = 47$)	African ancestry ($n = 63$)	*P*-value
Demographics and CVRFs			
Age (years)	44 ± 14	49 ± 12	0.033
Male sex, *n* (%)	30(64)	35(56)	0.437
Diabetes, *n* (%)	6(13)	13(21)	0.274
Dyslipidaemia, *n* (%)	10 (21)	11(17)	0.614
Active smokers, *n* (%)	7(15)	0(0)	0.002
Anthropometric and body composition measures			
Weight (kg)	90 ± 20	94 ± 17	0.362
Height (m)	1.73 ± 0.12	1.73 ± 10	0.916
Body surface area (m^2)	2.0 ± 0.4	2.1 ± 0.2	0.138
Body mass index (kg/m^2)	30.3 ± 6.4	31.4 ± 5.6	0.378
Fat mass (kg)	32.8 ± 13.7	36.0 ± 13.2	0.227
Fat-free mass (kg)	57.6 ± 9.7	57.7 ± 11.0	0.936
Haemodynamic parameters			
Systolic BP (mmHg)	138 ± 18	143 ± 21	0.179
Diastolic BP (mmHg)	85 ± 14	91 ± 14	0.025
Mean BP (mmHg)	103 ± 14	107 ± 21	0.226
Heart rate (bpm)	74 ± 18	71 ± 13	0.371
Medical therapy			
Hypertension duration (months)	30(12–120)	37(6–96)	0.756
ACEi or ARB, *n* (%)	18(38)	33(52)	0.110
Calcium antagonists, *n* (%)	18(38)	35(56)	0.052
Diuretics, *n* (%)	11(23)	27(43)	0.026
Beta-blockers, *n* (%)	11(23)	13(21)	0.760

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CVRFs, cardiovascular risk factors.

Baseline characteristics

The baseline characteristics of the study participants are summarized in *Table 1*. Afr-a patients were, on average, 5 years older than their Eu-a counterparts; however, other risk factors were similarly distributed between the two groups, except for smoking which was more prevalent in Eu-a patients. Anthropometric and body composition measures were also comparable between the two groups. Afr-a had higher diastolic blood pressure (DBP) than Eu-a patients, while systolic blood pressure and MBP were comparable between the two ethnicities. Afr-a hypertensives were more likely to receive diuretics as an anti-hypertensive drug than Eu-a hypertensives. The baseline characteristics of age- and sex-matched healthy volunteers are summarized in Supplementary data online, *Table S1*.

LV and RV remodelling

LV/RV remodelling findings are summarized in *Table 2*. Segmental PWV was higher in Afr-a than Eu-a patients, reflecting an increased aortic stiffness. LV volumes (indexed to body-surface-area or height), LV systolic function, (including global circumferential and longitudinal strains), as well as peak filling rate (a metric of diastolic function), were comparable between Eu-a and Afr-a patients. However, LV mass and mass/end-diastolic volume ratio (*M*/*V*) were significantly greater in the Afr-a than in Eu-a hypertensives (*Table 2*; *Figure 2*). Moreover, the interventricular septum was thicker in Afr-a compared with Eu-a patients (*Table 2*; *Figure 2*). From the linear regression analysis, the difference in interventricular septal thickness between the two groups was not attenuated after controlling for age, sex, hypertension duration, dyslipidaemia, and smoking (mean difference = 1.69 mm, 95% CI: 0.024–3.35, $P = 0.047$). Likewise, RV volumes and systolic function were similar between Afr-a and Eu-a patients, while RV mass and *M*/*V* were significantly greater in the former group (*Table 2*; *Figure 2*). The ethnicity-specific biventricular mass difference was confirmed after controlling for anti-hypertensive treatments, age, and smoking status (see Supplementary data online, *Tables S2–S4*). In contrast to hypertensive patients, Afr-a and Eu-a healthy volunteers showed comparable biventricular masses and *M*/*V* ratios while PWV was lower in Afr-a than Eu-a patients (see Supplementary data online, *Table S5*). To further support our hypothesis on ethnic-specific hypertensive remodelling, we conducted adjusted comparisons. Multivariable regression analysis confirmed that African ethnicity was associated with higher RV mass (adjusted coefficient = 0.617, 95% CI: 0.245–3.90, $P = 0.029$), which was indexed to body-surface-area and controlled for a number of variables including age, sex, and BMI (see Supplementary data online, *Table S7*). Given the sex differences in LV/RV remodelling in hypertensive patients,[29,30] *ad hoc* interaction terms between sex and ethnicity were also investigated in our multivariable regression models as additional fixed-effects independent variables (sex × ethnicity). However, there was no evidence of a differential effect of sex on ethnicity-induced LV/RV remodelling ($P > 0.1$ for all interaction terms tested) among hypertensive patients within our study.

Table 2 Cardiovascular magnetic resonance results

Variable	European ancestry ($n = 47$)	African ancestry ($n = 63$)	*P*-value
Arterial afterload			
PWVasc-desc (m/s)	6.97 ± 2.82	8.16 ± 2.71	0.044
LV measures indexed by body surface area			
LV-EDV (mL/m^2)	84 ± 18	88 ± 19	0.280
LV-ESV (mL/m^2)	35 ± 13	38 ± 15	0.277
LV mass (g/m^2)	58.3 ± 16.7	67.1 ± 21.7	0.028
LV mass/LV-EDV (g/mL)	0.70 ± 0.14	0.79 ± 0.21	0.009
LV-EF (%)	59 ± 7	58 ± 9	0.491
LV measures indexed by height			
LV-EDV (mL/m)	101 ± 25	108 ± 24	0.181
LV-ESV (mL/m)	42 ± 17	47 ± 19	0.174
LV mass (g/m)	70 ± 24	83 ± 28	0.016
LV filling/ejection rate and strain measures			
Peak ejection rate (mL/s)	435 ± 191	452 ± 176	0.634
Peak filling rate (mL/s)	432 ± 139	433 ± 174	0.965
Peak circumferential strain (%)	−19.92 ± 3.94	−19.46 ± 4.20	0.573
Peak longitudinal strain (%)	−10.87 ± 3.55	−10.29 ± 3.80	0.424
RV measures indexed by body-surface-area			
RV-EDV (mL/m^2)	82 ± 17	80 ± 14	0.575
RV-ESV (mL/m^2)	33 ± 11	32 ± 8	0.878
RV mass (g/m^2)	10.7 ± 2.71	12.6 ± 3.48	0.004
RV mass/RV-EDV (g/mL)	0.13 ± 0.03	0.16 ± 0.04	<0.001
RV-EF (%)	60 ± 7	60 ± 7	0.920
RV measures indexed by height			
RV-EDV (mL/m)	98 ± 23	99 ± 19	0.929
RV-ESV (mL/m)	40 ± 13	40 ± 11	0.935
RV mass (g/m)	13 ± 4	16 ± 5	0.001
Atrial size			
Left atrial surface (cm^2/m^2)	11.5 ± 2.9	11.8 ± 2.1	0.606
Left atrial surface (cm^2/m)	13.7 ± 3.1	14.5 ± 2.7	0.172
Right atrial surface (cm^2/m^2)	10.9 ± 2.1	10.4 ± 2.4	0.297
Right atrial surface (cm^2/m)	12.9 ± 2.2	12.8 ± 2.9	0.799
Average IVS thickness			
Average IVS thickness (mm)	9.14 ± 0.11	10.7 ± 0.06	<0.001
Average IVS thickness (mm/m^2)	4.52 ± 0.05	5.02 ± 0.03	0.002
Myocardial tissue characterization			
Native T1 relaxation time (ms)	1007.7 ± 79.6	999.6 ± 35.7	0.480
Synthetic ECV	0.26 ± 0.04	0.26 ± 0.04	0.921
T2 relaxation time (ms)	45.7 ± 2.2	47.0 ± 2.2	0.005
LGE, *n* (%)	2(4)	14(23)	0.001
LGE extent (% of LV mass)	1.6(0.9–2.5)	2.3(0.6–14.3)	0.008†

ECV, extracellular volume; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; IVS, interventricular septum; LGE, late gadolinium enhancement; LV, left ventricle; PWVasc-desc, pulse wave velocity of ascending and proximal descending aorta; RV, right ventricle; †Mann-Whitney and (interquartile range).

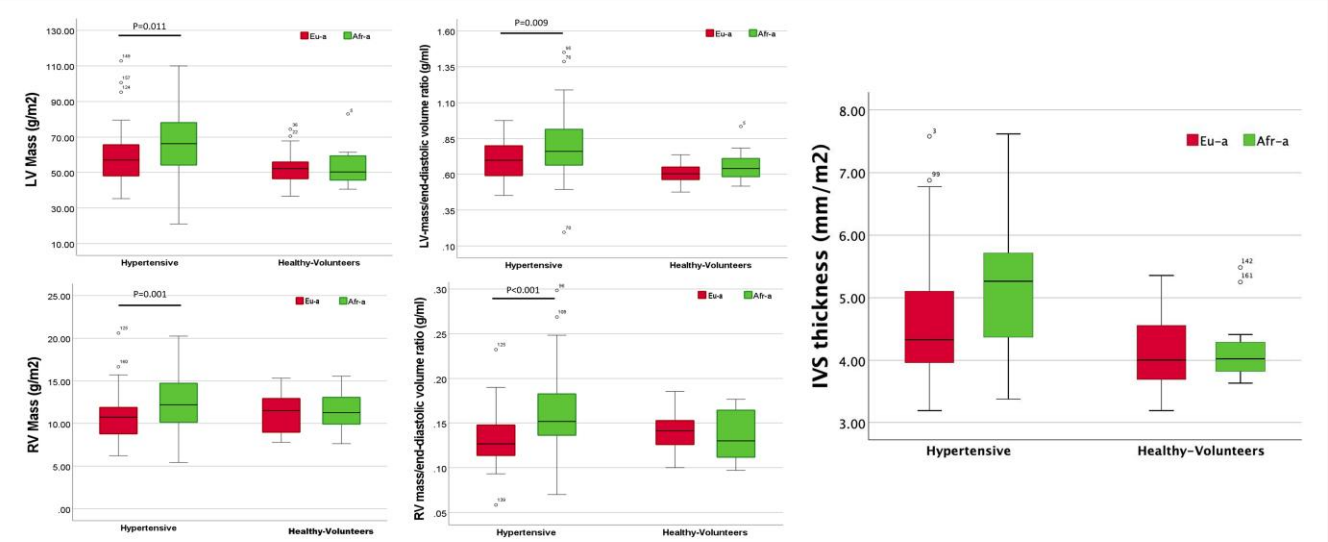


Figure 2 Ventricular mass, mass/end-diastolic volume ratio, and interventricular septum thickness differences between Afr-a and Eu-a ethnicity among hypertensive patients and healthy volunteers.

Ventricular shape modelling

3D statistical shape modelling portrays the main geometric biventricular differences between the two ethnicities. African ethnicity was associated with a localized increase of basal septal thickness with no substantial changes in mid-to-apical-wall thickness compared to Eu-a patients. As such, in Afr-a patients, the higher LV mass was driven by basal septal thickening, whereas Eu-a patients had more homogeneous LV hypertrophy. In Afr-a patients, the thickened septum impinged the RV cavity prompting a distinctive RV geometric pattern, i.e. smaller septal-to-free-wall diameter but greater anterior–posterior diameter as compared with Eu-a patients (*Graphical Abstract*). Linear discriminatory analysis showed a good yield in cross-validation analyses (area-under-the-curve of 0.712 for the LV and 0.722 for the RV; both $P \leq 0.001$). This finding implies that ethnicity was correctly classified in 71.2% and 72.2% of patients (on average) based on the main geometric signatures of the LV and RV, respectively. Given the importance of basal septal thickening in ventricular shape differences between the two ethnicities, we investigated the association between basal septal thickness and PWV. We found a positive relationship between basal septal thickness and PWV in Afr-a (beta-coefficient = 0.309, $P = 0.025$) but not in Eu-a (beta-coefficient = 0.046, $P = 0.747$) hypertensive patients.

Myocardial tissue composition

Afr-a and Eu-a patients had comparable native myocardial T1 relaxation times and s-ECV. However, T2 relaxation time was significantly higher in Afr-a than Eu-a hypertensives (*Table 2*). In the whole cohort, MF by LGE was observed in 16/110 patients (14%) with a median MF extent of 2.29% of LV mass (1.11–9.95% LV mass). The pattern and distribution of MF are shown in *Figure 3*. The interventricular septum and mid-wall were the most prevalent location and patterns of MF, respectively. Of importance, MF was observed in 2/47 Eu-a (4%) and 14/63 Afr-a (23%) hypertensive patients ($P = 0.001$), and its extent was greater in Afr-a patients ($P = 0.008$) (*Table 2*). When patients were dichotomized based on MF presence, patients with MF (MF[+]) had higher biventricular volumes, mass, and *M*/*V* ratios but lower systolic function than those without MF (MF[−]). Moreover, MF[+] patients had higher T2 relaxation times and s-ECV than MF[−] (see Supplementary data online, *Table S6*).

Associative measures of LV and RV mass

Correlations between demographic, anthropometric, haemodynamic parameters, geometric and functional measures of the left and right ventricles are shown in *Figure 4*. Given that ethnic disparity in ventricular remodelling was driven by an increase in myocardial mass, we carried out multivariable linear regression analysis to underpin the main determinants of LV and RV mass. We found that diabetes, smoking, and greater LV end-diastolic volume were independently associated with higher LV mass after correction for major confounders, including ethnicity and RV parameters (Model A and Model B; *Table 3*). Likewise, diabetes and higher RV end-diastolic volume were independently associated with greater RV mass after correction for major confounders, including ethnicity and LV end-diastolic volume (Model A and Model B; *Table 3*). Finally, measurement of LV mass showed excellent consistency, both in terms of intra- (0.995, 95% CI: 0.979–0.999, $n = 10$) and inter-rater (0.988, 95% CI: 0.957–0.977, $n = 10$) reproducibility.

Discussion

To the best of our knowledge, this is the first study pinpointing that Afr-a hypertensive patients have greater RV mass and concentric remodelling than their Eu-a counterparts, mirroring the remodelling pattern in the LV. We also found that Afr-a patients had more pronounced basal interventricular septal thickness than Eu-a patients, which may prompt an increase in LV mass and changes in RV geometry. Previous studies have supported this hypothesis. Yalçin *et al.*[31] hypothesized that basal septal hypertrophy could be a clinical biomarker for cardiac remodelling since the 'septal wall is speculated to be the first LV wall to become hypertrophic', which is also supported by other cross-sectional studies.[32–34] Furthermore, the literature has also highlighted greater IVS thickening[35] and LV mass index in Afr-a patients.[35,36] With this in mind, the findings from our study, supported by sophisticated 3D shape modelling, may formulate an interesting hypothesis that could explain inter-ethnicity differences in LV and RV hypertensive remodelling. This distinctive biventricular mass pattern was paralleled by higher myocardial T2 relaxation times and more prevalent and extensive MF in Afr-a than Eu-a patients (*Graphical Abstract*). From this study, modifiable cardiovascular risk

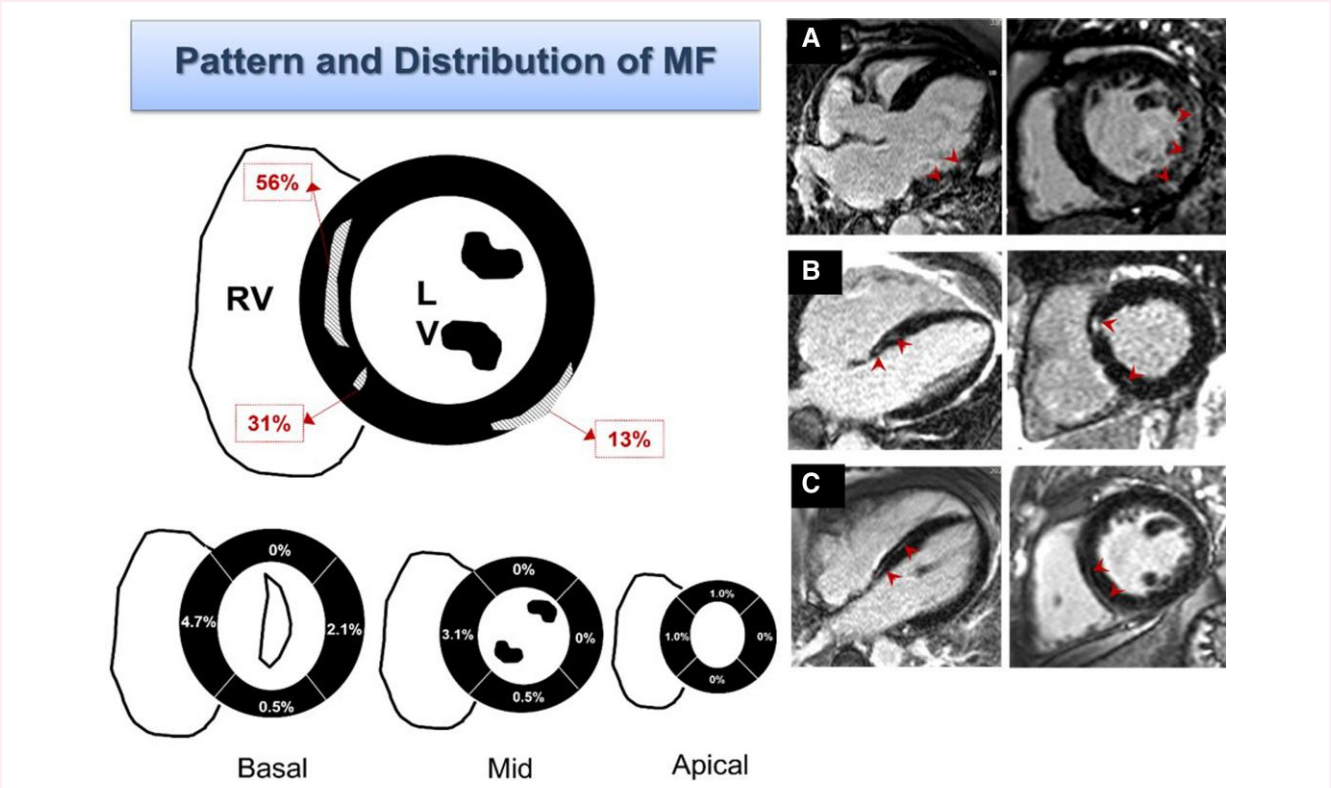


Figure 3 Pattern and distribution of myocardial fibrosis in Afr-a and Eu-a patients. Upper and lower cartoons show the pattern and distribution of MF, respectively, in the 16 patients (both Afr-a and Eu-a) with LV LGE in the LV walls (anterior, inferior, and lateral walls and interventricular septum). Patterns of LGE are expressed on a per-patient basis (upper cartoon). The distribution of MF by LGE is expressed on a per-region basis (lower cartoon) as percentage (%) of LGE-positive regions over the LV regions ($n = 192$). Representative Afr-a patients with sub-epicardial (*A*), patchy (*B*), and mid-wall (*C*) LGE (arrowheads) are also shown. LV, left ventricle; RV, right ventricle; MF, myocardial fibrosis.

factors, and ventricular geometry, but not ethnicity, were independently associated with higher LV mass. This finding was further corroborated by the fact that age- and sex-matched Eu-a and Afr-a healthy volunteers showed closely comparable LV volumes and masses.

Ethnicity and ventricular remodelling in hypertension

Compelling evidence indicates that LV concentric remodelling or hypertrophy occurs more often in Afr-a than Eu-a hypertensive patients, conferring an accrued risk of HF.[1–7] In our study, Afr-a was associated with greater LV and RV mass with no substantial differences in ventricular size, resulting in greater concentric remodelling (i.e. *M*/*V* ratio). The 3D statistical model also revealed that higher LV mass in Afr-a patients was due to basal septum hypertrophy, while in Eu-a patients, there was a more homogenous increase in myocardial mass. The interventricular septum is particularly sensitive to pro-hypertrophic stimuli, given the greater radius of curvature and sympathetic innervation.[31,37] Of note, prior studies reported that Afr-a patients have higher sympathetic activation than Eu-a patients.[38] Moreover, in our study, PWV in the proximal aorta was greater in Afr-a than in Eu-a patients, and we also found a positive association between PWV and basal septal thickness in the Afr-a ($P = 0.025$) but not Eu-a ($P = 0.747$) hypertensives, in line with prior studies.[39] The basal septum hypertrophy altered the RV geometry by shortening the septal-to-free-wall dimension, with a compensatory increase in the anteroposterior diameter (*Graphical Abstract*). These geometric signatures enabled differentiation in patients' ethnicity in 70% of cases by simply interrogating LV or RV anatomy. Prior studies in smaller cohorts of Eu-a individuals reported higher RV mass and concentric remodelling in hypertensive patients than controls,[9] advocating in-parallel ventricular interdependency through the shared septum and epicardial fibres as the main driver for the increased RV mass in hypertension.[10,11,40] This is likely the mechanism responsible for higher RV mass and concentric remodelling in Afr-a patients in our study. Although initial RV hypertrophy may be adaptive, it may eventually lead to RV dilatation and dysfunction, paralleling the transition from compensatory to maladaptive hypertrophy seen in the LV[1–3,8,41] or pulmonary arterial hypertension.[42,43] A final noteworthy point is when including interaction terms between sex and ethnicity (additional fixed-effects independent variables) in our multivariable regression analysis, there was no evidence of a differential effect of sex on ethnicity-induced LV/RV hypertensive remodelling.

Ethnicity and myocardial tissue abnormalities

The more pronounced biventricular geometric remodelling in Afr-a patients was associated with prolonged myocardial T2 relaxation time (though within normal range), as well as higher prevalence and extent of MF compared with Eu-a patients. Prolonged T2 relaxation time reflects an increased free-water content in the myocardium,[44] likely underpinning subtle myocardial inflammation in the Afr-a group. Given that native T1 relaxation time was similar between the ethnicities may reflect the lower sensitivity of this biomarker in capturing subtle

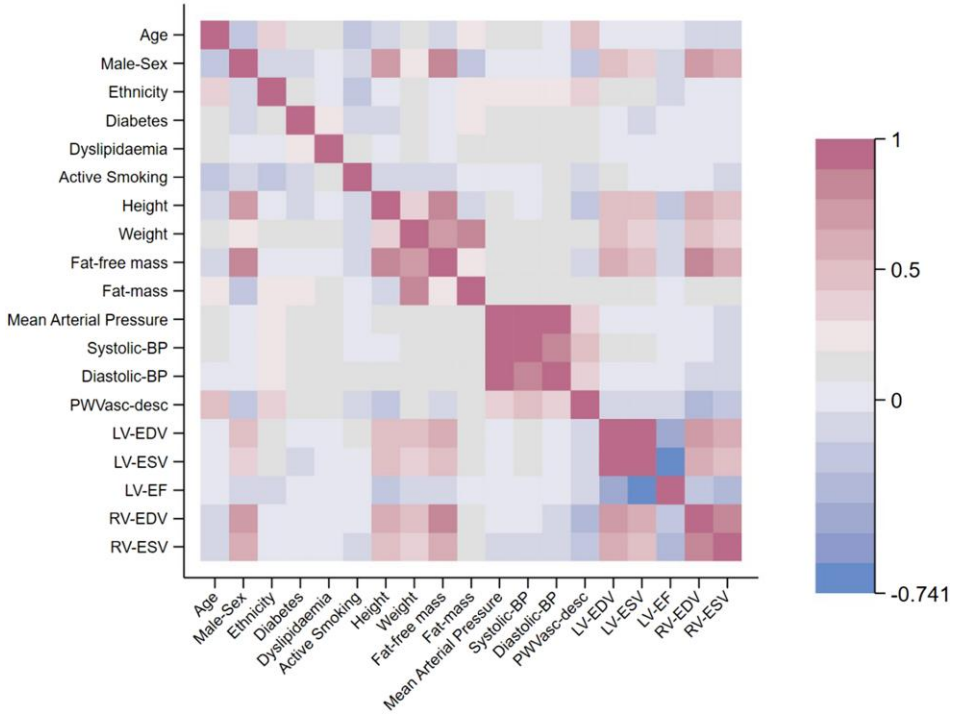


Figure 4 Heat-map of correlation coefficients. Correlations between demographic, anthropometric, haemodynamic parameters, and geometric and functional measures of LV and RV are shown in the heatmap. BP, blood pressure; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; LV, left ventricle; PWVasc-desc, pulse wave velocity of ascending and proximal descending aorta; RV, right ventricle.

increases in free-water content.[44–46] Low-grade persistent systemic inflammation is a key feature of hypertension[47] mediated by activation of renin–angiotensin–aldosterone system and mineralocorticoid pathways. We, and other groups, have previously shown elevated plasma aldosterone levels in Afr-a hypertensive patients, which not only concur to increase myocardial mass but are also associated with low-grade myocardial inflammation.[48] Of note, Afr-a patients had significantly higher prevalence (23% vs. 4%) and extent (~50% higher) of MF than Eu-a patients, which was mainly located in the hypertrophied ventricular septum.

Although the cross-sectional nature of our study prevents us from mechanistic interpretations, low-grade myocardial inflammation and enhanced arterial afterload may contribute to greater MF in Afr-a patients. When patients were dichotomized based on MF by LGE, MF[+] patients had higher biventricular volumes, mass, and concentric remodelling but lower LV systolic function than MF[−] patients. Moreover, T2 relaxation time and s-ECV were higher in MF[+] patients. Kuruvilla *et al.*[45] and Treibel *et al.*[46] reported MF by LGE in 5% and 28% of Eu-a patients with hypertension, respectively, which diverges substantially from 14% prevalence observed in our cohort. This discrepancy can be ascribed to technical and population differences between studies. For instance, Treibel *et al.* included LGE in the papillary muscles, which was not counted in our study because of the partial volume averaging, which is likely when imaging these small complex structures by standard 2D-LGE images.[49] Finally, myocardial s-ECV, an estimate of extravascular–extracellular myocardial compartment, was similar between Afr-a and Eu-a patients, despite a higher prevalence of MF by LGE in the former. This apparent incongruency can be ascribed to two main factors. First, s-ECV was measured in one mid-ventricular short-axis slice and, thereby, small LGE areas in the septum were not necessarily included in s-ECV calculation. Second, hypertension-mediated myocyte hypertrophy likely opposed extracellular expansion due to interstitial fibrosis resulting in a neutral effect on s-ECV.[17,45,46]

Associative measures of myocardial mass

Given that ethnic differences in ventricular remodelling were driven by an increase in myocardial mass, we carried out multivariable linear regression analysis to identify the main associates of myocardial mass. We found modifiable cardiovascular risk factors and end-diastolic volume were independent associates of greater LV or RV mass and that ethnicity was independently associated with greater RV mass, supporting our hypothesis of ethnic-specific hypertensive remodelling. These findings were substantiated by similar biventricular volumes, masses, and *M*/*V* ratios in Afr-a and Eu-a healthy volunteers.

Our data align with prior evidence, supporting that ethnic disparities in ventricular remodelling are largely mediated by clustering of cardiovascular risk factors in Afr-a patients rather than genetic background.[1–4] In our cohort, Afr-a had higher DBP and tended to have higher fat mass and more prevalent diabetes. Diabetes was associated with higher LV and RV mass in multivariable models, aligning with prior evidence substantiating the pro-hypertrophic role of insulin resistance and diabetes.[50] These findings may have far-reaching consequences for HF prevention in Afr-a individuals by underlining the importance of lifestyle changes, better control of modifiable cardiovascular risk factors, and early hypertension screening.

Limitations

A referral bias is likely in our study given that patients were recruited in a tertiary referral centre, limiting the generalizability of our results. Any extrapolation of our findings should be conducted with caution. Our research utilized a cross-sectional design, meaning we lacked

Table 3 **Model A and Model B parameters**

Variable	Model A for LV mass (adjusted $R^2 = 0.591$)			Model B for LV mass (adjusted $R^2 = 0.617$)			Model A for RV mass (adjusted $R^2 = 0.512$)			Model B for RV mass (adjusted $R^2 = 0.635$)		
	Beta-coefficient	*t*-statistic	*P*-value	Beta-coefficient	*t*-statistic	*P*-value	Beta-coefficient	*t*-statistic	*P*-value	Beta-coefficient	*t*-statistic	*P*-value
Age (years)	0.21	0.215	0.831	0.015	0.153	0.879	−0.122	−1.104	0.275	−0.096	−0.876	0.385
Male sex	0.208	2.570	0.013	0.143	1.414	0.164	0.131	1.135	0.262	0.069	0.596	0.554
Diabetes	0.363	3.775	<0.001	0.286	2.824	0.007	0.308	2.934	0.005	0.298	2.164	0.032
Dyslipidaemia	0.014	0.141	0.889	0.043	0.445	0.658	−0.141	−1.319	0.193	−0.158	−1.502	0.140
Smoking	0.164	1.763	0.084	0.218	2.270	0.028	−0.138	−1.285	0.205	−0.195	−1.798	0.079
African ancestry	0.187	1.896	0.064	0.173	1.710	0.094	0.144	1.290	0.203	0.063	0.550	0.585
Hypertension duration (months)	−0.047	−0.460	0.648	−0.025	−0.237	0.814	0.064	0.543	0.590	0.047	0.400	0.691
BMI (kg/m^2)	−0.046	−0.472	0.639	−0.068	−0.710	0.481	0.009	0.86	0.939	0.003	0.030	0.976
MAP (mmHg)	0.097	1.026	0.310	0.097	0.985	0.329	0.206	1.931	0.059	0.136	1.245	0.219
LV-EDV (mL)	0.504	4.418	<0.001	0.430	3.170	0.003	NA	NA	NA	NA	NA	NA
LV mass (g)	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.278	1.907	0.062
LV-EF (%)	−0.169	−1.845	0.071	−0.121	−1.098	0.277	NA	NA	NA	−0.004	−0.034	0.973
RV-EDV (mL)	NA	NA	NA	NA	NA	NA	0.565	4.829	<0.001	0.459	3.492	0.001
RV mass (g)	NA	NA	NA	0.223	1.953	0.057	NA	NA	NA	NA	NA	NA
RV-EF (%)	NA	NA	NA	−0.096	−0.921	0.362	−0.033	−0.337	0.738	0.001	−0.034	0.973

BMI, body mass index; EDV, end-diastolic volume; EF, ejection fraction; LV, left ventricle; MAP, mean arterial pressure; RV, right ventricle; NA, not applicable.

longitudinal serial CMR measurements as hypertension progressed in our study participants. This limitation prevents us from inferring causality and accentuates uncertainty surrounding hypertension duration, both of which are significant drawbacks to interpreting our findings. However, the uncertainty regarding hypertension duration was somewhat mitigated, as all patients were hypertensive upon study enrolment and were receiving anti-hypertensive treatment for the past 12 months. Multivariable models explained about 60% of the LV and RV mass variance; thus likely, other potentially relevant variables (unmeasured confounders) were not included in the models. Moreover, subtle increase in T2 relaxation times in Afr-a patients, compared with Eu-a patients, does not qualify for inflammation based on clinical standards but may suggest low-grade, sub-clinical inflammatory changes. Furthermore, despite controlling for differences in hypertension severity between ethnic groups, residual confounding cannot be excluded. Finally, our study included only 110 hypertensive patients, and therefore, larger prospective studies are needed to confirm our preliminary results.

Conclusion

Afr-a hypertensive patients had distinctive, more pronounced biventricular remodelling, including increased RV mass and septal thickening and subtle myocardial tissue abnormalities compared with Eu-a hypertensive patients. From this study, modifiable cardiovascular risk factors, and ventricular geometry, but not ethnicity, were independently associated with higher LV mass.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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Conflict of interest: P.-G.M. is a consultant at Perspectum Diagnostics Ltd (Oxford, UK)

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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