

## RESEARCH

# Effects of age on left atrial volume and strain parameters using echocardiography in a normal black population

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## Abstract

**Objective:** Normal cut-off values for left atrial (LA) size and function may be altered by aging and ethnic differences. No age-related reference values for LA volumetric measurements or LA strain exist in Africans. We aimed to establish normal age-appropriate values of LA size and function in black Africans. Additionally, we studied the correlation between age, LA strain and volumetric parameters.

**Methods:** In this prospective, cross-sectional study of 120 individuals (mean age  $38.7 \pm 12.8$  years, 50% men), subjects were classified into four age groups: 18–29, 30–39, 40–49 and 50–70 years. LA volumes were measured by biplane Simpson's method, and Philips QLAB 9 (Amsterdam, The Netherlands) speckle-tracking software was used to measure LA peak strain in the reservoir ( $\mathcal{E}_R$ ) and contractile phase ( $\mathcal{E}_{CT}$ ).

**Results:** No significant differences in the maximum and minimum LAVi were noted among the four age categories ( $P=0.1$ ,  $P=0.2$ ). LA volumetric function assessment showed no difference in reservoir function between age groups ( $P>0.05$ ), conduit function decreased with advancing age ( $r=-0.3$ ,  $P<0.001$ ) and booster function displayed a significant increase with age (LA active emptying volume index,  $P=0.001$ ). There was a significant decrease in LA  $\mathcal{E}_R$  ( $P<0.0001$ ) in the older age groups, whereas  $\mathcal{E}_{CT}$  remained unchanged ( $P=0.27$ ).

**Conclusion:** Age-related changes in LA reservoir, conduit and contractile function in black Africans are similar to those observed in other populations, as was the trend of declining  $\mathcal{E}_R$  with advancing age. The preservation of  $\mathcal{E}_{CT}$  with increasing age requires further analysis.

## Key Words

- aging
- left atrium
- black population
- echocardiography

## Introduction

The left atrium (LA) has been described as a gauge of diastolic burden, and disturbances in its function can result in impairment of overall cardiac performance (1, 2). The function of the LA, determined by various echo methods, predicts clinical outcome and mortality in several cardiovascular disorders (3, 4, 5). Various echocardiographic techniques, including linear

dimensions of the LA, volumetric LA measurements and peak LA strain, have been studied to evaluate LA function (6, 7, 8, 9). The use of normative values from these techniques is essential to differentiate normality from milder disease in a variety of disease states. However, there are 2 important factors that may affect the interpretation of some of these measurements: age and ethnicity.

There are discrepant findings from a number of studies (using various echocardiographic techniques) relating to the effect of aging on LA function. The use of maximum LA volume as a surrogate of reservoir function in healthy subjects has revealed discordant results, with some studies reporting increments, whereas others report no change in LA volume (1, 6, 7, 10, 11, 12). The effect of age on conduit and booster function seems more predictable; several studies using volumetric analysis have demonstrated that a decline in LA conduit function occurs concomitantly with an increase in LA booster function. Most studies using speckle-tracking suggest that reservoir function seems to decline, as evidenced by a decrease in peak reservoir LA strain. However, controversy exists with regard to age-related change in LA contractile strain.

The probability for different population groups to have diverse normal ranges of LA echocardiographic measurements was accentuated by the findings of the recently reported Echo-NoRMAL study. In this study, the upper reference value for LA diameter was highest for Europeans and American blacks and was lowest for South Asians and Africans. The change in the upper reference values of LA diameter with increasing age was statistically significant for European, African and American black men. There are no age-related reference values for LA volumetric measurements or LA strain in Africans. This is potentially problematic as the use of certain measurements, including the widely advocated LA volume index, may result in inaccurate conclusions when interpreting measurements done in potentially normal or mild disease states. We thus sought to establish normal age-appropriate values of LA size and function in black Africans using volumetric measurements and speckle-tracking-derived longitudinal strain.

## Methods

### Study population

From January 2014 to June 2015, 190 normal subjects were screened at the echocardiography laboratory of Chris Hani Baragwanath Academic Hospital. This prospective, cross-sectional sub-study formed part of an ongoing study being conducted at our institution to provide normal echocardiographic reference ranges in people of African descent. The study population was recruited from unrelated staff at Baragwanath Hospital and volunteers who presented themselves to

the echocardiography laboratory after an advertisement about this study. All volunteers underwent a detailed history, physical examination, resting electrocardiogram and echocardiography. Individuals were included in the study if they were asymptomatic; lacked any known comorbidity; were not on chronic medication and had a normal physical examination, resting electrocardiogram and echocardiogram. Subjects were excluded if the quality of their images was poor or if either their 12-lead electrocardiogram or echocardiogram was abnormal.

The final sample comprised 120 individuals (60 women) between 18 and 70 years of age. The subjects were classified into four age groups: 18–29, 30–39, 40–49 and 50–70 years. All participants gave written informed consent, and the study received approval by the local ethics committee (M140114).

### Echocardiographic examination

Transthoracic echocardiography was performed by an experienced sonographer on a Philips iE33 system (Amsterdam, The Netherlands) using an S5-1 transducer. All the echocardiographic measurements were obtained from the standard left parasternal and apical views using a standardized protocol. An offline workstation (Xcelera, Philips) was used for data transfer and subsequent analysis.

### Two-dimensional and Doppler quantification

The American Society of Echocardiography chamber guidelines were used to perform linear chamber measurements (12). The biplane Simpson's method was used for calculation of LA volumes. LA volume was planimetered in the four-chamber and two-chamber views by tracing the endocardial border (pulmonary vein confluence and LA appendage were excluded) (12). Maximum LA volume ( $LA_{max}$ ) was obtained at the end of left ventricular (LV) systole, just prior to the opening of the mitral valve from the two-dimensional frame (13, 14). Pre-atrial volume ( $V_{pre-A}$ ) was acquired from the diastolic frame, just before mitral valve reopening as a result of contraction of the LA (13). The minimum volume of the LA ( $LA_{min}$ ) was assessed at the end of LV diastole from the lowest volume seen after contraction of the LA (13, 14).

The following formulas were used for LA phasic function assessment:

- Reservoir function: LA emptying fraction  
total =  $(LA_{max} - LA_{min}) / LA_{max} \times 100\%$ ; expansion  
index =  $(LA_{max} - LA_{min}) / LA_{min} \times 100\%$ .

- (2) Conduit function: Passive emptying volume =  $LA_{max} - V_{pre-A}$ ; passive LA emptying fraction =  $(LA_{max} - V_{pre-A}) / LA_{max} \times 100\%$ ; and conduit volume = LV stroke volume -  $(LA_{max} - LA_{min})$ .
- (3) Booster pump function: LA active emptying fraction =  $(LA_{pre-A} - LA_{min}) / LA_{pre-A} \times 100\%$ ; LA active emptying volume =  $V_{pre-A} - LA_{min}$  (13, 14, 15).

All LA volumetric parameters were indexed to body surface area (13).

A detailed diastolic function assessment was performed (16).

## 2D strain imaging

For speckle-tracking analysis, apical four- and two-chamber views were obtained in conjunction with end

expiratory breath-hold and stable electrocardiogram recording (3, 13, 17). Three consecutive beats were recorded and averaged at a rate of 60–80 frames per second (17). Offline semi-automated analysis of speckle-based strain was completed using Philips QLAB, version 9.0 software. A 3-point-and-click approach was used to trace the endocardial surface of the LA in both four-chamber and two-chamber views (17). An epicardial surface tracing was then automatically generated by the system (17). Once created, the region of interest was manually adjusted as required for the adequate speckle-tracking of myocardial segments.

The QLAB 9 speckle-tracking software divides the region of interest into seven segments in the two-chamber and the four-chamber views. It then generates the  $\epsilon$  curves for each myocardial segment and subsequently an average curve of all segments (17). From these strain curves, the peak LA strain

**Table 1** Baseline clinical and echocardiographic characteristics according to age.

Variable	Total (18–70) (n = 120)	Group 1 (18–29) (n = 34)	Group 2 (30–39) (n = 30)	Group 3 (40–49) (n = 27)	Group 4 (50–70) (n = 29)	P Value (ANOVA)
Age (years)	38.7 ± 12.8	23.5 ± 3.1	34.5 ± 2.8	43.2 ± 2.7	56.4 ± 6.42	<0.0001
Sex (female:male ratio)	60:60	16:18	13:17	15:12	16:13	0.73
Body mass index (kg/m <sup>2</sup> )	27.9 ± 5.8	25.9 ± 5.8 <sup>a,c</sup>	26.2 ± 4.1 <sup>b</sup>	31.1 ± 5.9	29.2 ± 5.6	0.0003
Body surface area (m <sup>2</sup> )	1.8 ± 0.2	1.8 ± 0.2 <sup>a</sup>	1.8 ± 0.2	1.9 ± 0.2	1.8 ± 0.2	0.040
Systolic blood pressure (mmHg)	121.9 ± 11.0	119.7 ± 10.5	118.9 ± 11.1	126.1 ± 9.9	123.8 ± 11.3	0.04
Diastolic blood pressure (mmHg)	76.3 ± 9.3	72.3 ± 9.0 <sup>a</sup>	76.4 ± 8.7	81.1 ± 7.3	76.5 ± 10.2	0.003
Heart rate (beats/min)	77.2 ± 12.6	78 ± 14	79 ± 13	77 ± 11	75 ± 13	0.468
End-diastolic diameter (mm)	42.7 ± 4.9	44 ± 4.3	43.2 ± 5.2	43 ± 5	41 ± 5.3	0.207
End-systolic diameter (mm)	27.1 ± 4.6	27.3 ± 5.4	28 ± 4	27 ± 4.4	26 ± 5	0.20
Interventricular septum end-diastolic diameter (mm)	9.3 ± 1.8	9 ± 2 <sup>a,c</sup>	9 ± 2	10 ± 1.4	10 ± 2.3	0.005
Left ventricular posterior wall diameter (mm)	9 ± 1.6	8 ± 2 <sup>c</sup>	9 ± 1.3	9.3 ± 1.3	10 ± 2	0.0017
End-diastolic volume index (mL/m <sup>2</sup> )	49.5 ± 13.6	53 ± 13 <sup>c</sup>	54 ± 15 <sup>d</sup>	50 ± 12.3	41 ± 11.4	0.0010
End-systolic volume index (mL/m <sup>2</sup> )	18.5 ± 5.9	20 ± 5 <sup>c</sup>	20 ± 6 <sup>d</sup>	19 ± 6.3 <sup>e</sup>	15 ± 5	0.0007
Ejection fraction (%)	63.1 ± 6.4	63.1 ± 5.6	62.8 ± 6.2	63.4 ± 7.2	63 ± 7.1	0.931
Relative wall thickness (ratio)	0.42 ± 0.1	0.37 ± 0.06 <sup>a,c</sup>	0.41 ± 0.07	0.44 ± 0.08	0.5 ± 0.12	0.0002
Left ventricular mass index (g/m <sup>2</sup> )	66.1 ± 18.0	62.2 ± 18.1	67.8 ± 19.3	65.9 ± 17	69.0 ± 18	0.474
E wave (cm/s)	78.5 ± 17.6	88 ± 17 <sup>c</sup>	76 ± 14	82.3 ± 19 <sup>e</sup>	68 ± 15	0.0001
A wave (cm/s)	58.9 ± 15.5	53 ± 16.4 <sup>c</sup>	54.2 ± 11.4 <sup>d</sup>	63 ± 15.2	67 ± 15	0.0003
Deceleration time (ms)	140.5 ± 53.4	145 ± 73	129 ± 41	134.2 ± 45	153.4 ± 44.3	0.278
E/A (ratio)	1.4 ± 0.4	1.6 ± 0.5 <sup>a,c</sup>	1.4 ± 0.3 <sup>d</sup>	1.4 ± 0.3 <sup>e</sup>	1.0 ± 0.3	<0.0001
E' medial (cm/s)	9.3 ± 2.8	12.0 ± 2 <sup>a,c</sup>	10.3 ± 3 <sup>b,d</sup>	8.1 ± 2.1	7 ± 2	<0.0001
E' lateral (cm/s)	14.1 ± 3.5	17.1 ± 3 <sup>a,c</sup>	15 ± 3 <sup>d</sup>	13 ± 3	11.1 ± 3	<0.0001
E/E' medial (ratio)	9.1 ± 2.7	8 ± 2 <sup>a,c</sup>	8 ± 2.2 <sup>b,d</sup>	11 ± 3	10.3 ± 3	<0.0001
E/E' lateral (ratio)	5.8 ± 1.5	5.3 ± 2 <sup>a</sup>	5.4 ± 1.3 <sup>b</sup>	7 ± 2	6.2 ± 1.3	0.0010
Average E/E' (ratio)	7.4 ± 1.83	6.5 ± 1.4 <sup>a,c</sup>	6.6 ± 1.4 <sup>b,d</sup>	8.5 ± 1.8	8.2 ± 1.7	<0.0001
S' medial (cm/s)	7.4 ± 1.5	8.0 ± 1.2	8.1 ± 2.0 <sup>d</sup>	7.3 ± 1.4	7 ± 1.3	0.005
S' lateral (cm/s)	8.7 ± 2.6	9.0 ± 3.0	9.2 ± 3.0	9.0 ± 3.0	8.0 ± 2.0	0.20

Data reported as mean ± s.d.

<sup>a</sup>Group 1 vs Group 3  $P < 0.05$ , <sup>b</sup>Group 2 vs Group 3  $P < 0.05$ , <sup>c</sup>Group 1 vs Group 4  $P < 0.05$ , <sup>d</sup>Group 2 vs Group 4  $P < 0.05$ , <sup>e</sup>Group 3 vs Group 4  $P < 0.05$ .

**Table 2** Left atrial volumetric and strain parameters with age.

Variable	Total (120)	Group 1 (18–29) (n=34)	Group 2 (30–39) (n=30)	Group 3 (40–49) (n=27)	Group 4 (50–70) (n=29)	P Value (ANOVA)
LA volumes						
Max-LAVi (mL/m <sup>2</sup> )	19.7 ± 5.9	18.4 ± 5.5	19.1 ± 4.7	22.0 ± 7.0	20.2 ± 6.2	0.10
Min-LAVi (mL/m <sup>2</sup> )	7.7 ± 3.2	7.3 ± 3.2	7.1 ± 2.6	7.8 ± 3.2	8.5 ± 3.6	0.27
Pre-A LAVi (mL/m <sup>2</sup> )	12.2 ± 4.4	10.9 ± 4.5 <sup>c</sup>	11.1 ± 3.6 <sup>d</sup>	12.4 ± 4.4	14.6 ± 4.3	0.003
LA reservoir function						
LA total EV (mL/m <sup>2</sup> )	12.2 ± 4.8	11.1 ± 4.2	12.1 ± 4.3	14.2 ± 5.8	11.6 ± 4.6	0.08
LAEF total (%)	59.9 ± 13.5	57.3 ± 13.3	61.9 ± 12.4	63.2 ± 14.1	57.9 ± 13.8	0.25
LA exp index (%) <sup>†</sup>	152.7 (109.5–228.8)	139.0 (111.5–218.1)	178.7 (115.4–234)	172.3 (231–114.9)	129.7 (92.4–242)	0.16
LA conduit function						
LA PEVi (mL/m <sup>2</sup> ) <sup>†</sup>	6.8 (4.7–9.0)	6.9 (4.7–9.0)	7.4 (6.0–10.2) <sup>d</sup>	8.6 (5.2–11) <sup>e</sup>	4.2 (3.1–6.1)	0.0008
Conduit vol (mL/m <sup>2</sup> ) <sup>†</sup>	17.8 (12.1–24.5)	19.9 (15.7–28.1)	20.9 (13.9–26.6)	14.6 (11.1–23.2)	15.4 (10.5–18.9)	0.01
LA PEF (%) <sup>†</sup>	36.8 (28–47)	38.7 (31.6–51) <sup>c</sup>	39.1 (31.4–51) <sup>d</sup>	40.2 (33.6–56) <sup>e</sup>	26 (17.3–35)	0.0001
LA pump function						
LA AEVi (mL/m <sup>2</sup> )	4.6 ± 2.6	3.7 ± 2.4 <sup>c</sup>	4.0 ± 2.3 <sup>d</sup>	4.6 ± 2.7	6.1 ± 2.6	0.001
LAEF Booster (%)	37.7 ± 13.9	32.6 ± 10.6	37.8 ± 12.5	39.7 ± 15.4	41.4 ± 15.8	0.07
LA strain						
$\mathcal{E}_R$ (%)	39.0 ± 8.3	40.7 ± 7.9 <sup>c</sup>	42.8 ± 8.5 <sup>d</sup>	39.4 ± 7.7 <sup>e</sup>	33.2 ± 5.5	<0.0001
$\mathcal{E}_{CT}$ (%)	–2.7 ± 2.5	–3.2 ± 3.0	–2.9 ± 2.5	–2.6 ± 2.2	–1.9 ± 2.1	0.27
Left atrial stiffness index						
$E/E'$ lateral/ $\mathcal{E}_R$	0.15 ± 0.05	0.13 ± 0.03 <sup>a,c</sup>	0.13 ± 0.04 <sup>b,d</sup>	0.17 ± 0.06	0.19 ± 0.05	<0.001

Data reported as mean ± s.d. or <sup>†</sup>median (IQR).

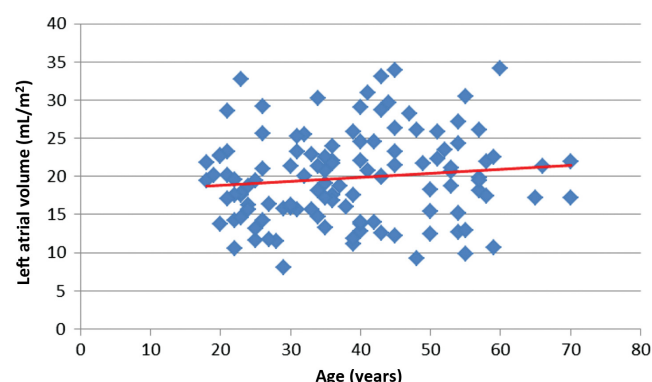
<sup>a</sup>Group 1 vs Group 3  $P < 0.05$ , <sup>b</sup>Group 2 vs Group 3  $P < 0.05$ , <sup>c</sup>Group 1 vs Group 4  $P < 0.05$ , <sup>d</sup>Group 2 vs Group 4  $P < 0.05$ , <sup>e</sup>Group 3 vs Group 4  $P < 0.05$ .

LA AEVi, left atrial active emptying volume index; LAEF, left atrial emptying fraction; LA exp index, left atrial expansion index; Max-LAVi, maximum left atrial volume index; Min-LAVi, minimum left atrial volume index; PEF, passive emptying fraction; PEV, passive emptying volume; Pre-A LAVi, pre-atrial contraction left atrial volume index;  $\mathcal{E}_R$ , peak left atrial strain in the reservoir phase;  $\mathcal{E}_{CT}$ , peak left atrial strain in the contractile phase.

in the reservoir phase ( $\mathcal{E}_R$ ) and contractile phase ( $\mathcal{E}_{CT}$ ) were calculated (3). The QRS onset was used as the first reference frame. The LA stiffness index was calculated non-invasively as the ratio of  $E/E'$  lateral and  $\mathcal{E}_R$  (9, 18).

## Statistical analysis

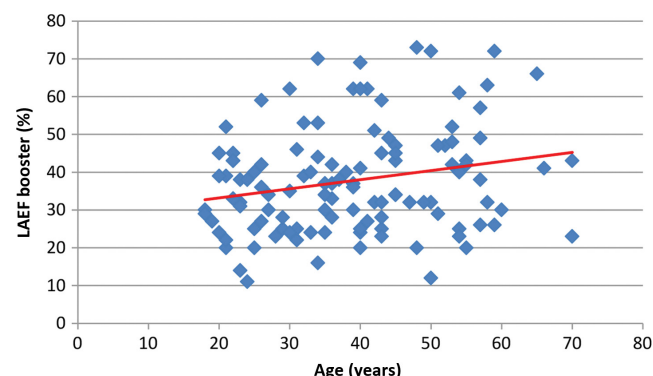
Statistical analysis was performed with Statistica (version 12.5, series 0414 for Windows). Continuous variables are



**Figure 1**  
Correlation between left atrial volume indexed and age ( $r = 0.14$ ,  $P = 0.08$ ).

expressed as mean ± standard deviation (s.d.) or median (interquartile range). One-way analysis of variance (ANOVA) or Kruskal–Wallis test was used to compare continuous variables according to age categories when the distribution was non-normal. *Post hoc* comparisons were performed with the Scheffé test.

Univariate and multivariate linear regression analyses were used to identify possible independent determinants



**Figure 2**  
Correlation between left atrial emptying fraction (LAEF) and age ( $r = 0.2$ ,  $P = 0.02$ ).

of LA  $\mathcal{E}_R$ ,  $\mathcal{E}_{CT}$  and maximum LA volume indexed (LAVi). Multivariate models to predict LA  $\mathcal{E}_R$  and maximum LAVi were selected in a multiple linear regression analysis. Univariate variables with Pearson's correlation coefficient  $\geq 0.8$  were not included in the multivariate models. The aforementioned models were further analyzed using the forward and backward multiple linear regression methods. The assumptions were verified by performing residual analysis and advanced Durbin–Watson statistics.

Intra-observer and inter-observer variabilities were assessed for peak positive LA  $\mathcal{E}_R$ , peak negative LA  $\mathcal{E}_{CT}$ , maximum LAVi and minimum LAVi. Measurements were done in 20 randomly selected subjects. To assess inter-observer variability, two independent observers measured LA volumetric and strain parameters. Intra-observer variability was calculated from an analysis by the same observer one month after the first measurement. Inter-observer and intra-observer reproducibility were assessed by calculating coefficients of variation. These were calculated as the standard deviation of the differences divided by the mean (14). The *t*-test for dependent variables was used to compare the mean and standard deviation of the values derived for strain and volume and calculate the significance value. A *P* value  $< 0.05$  was considered statistically significant.

## Results

### Baseline characteristics and echocardiographic findings

Of the 120 individuals, 60 were men and the mean age was  $38.7 \pm 12.8$  years. Comparisons among the four preselected age groups (Table 1) revealed that although all parameters remained within normal defined ranges, there were age-related differences. An increment in LV wall thickness ( $P < 0.001$ ), the *A* wave ( $P < 0.001$ ) and *E/E'* ( $P < 0.001$ ) was noted with aging, whereas a concomitant

decrement in LV volumes ( $P = 0.001$ ), *E* wave ( $P < 0.001$ ) and *E'* ( $P < 0.001$ ) was observed. No significant changes in LV ejection fraction ( $P = 0.7$ ) or LV mass occurred ( $P = 0.4$ ).

### LA volumetric parameters for the total sample

All normative data are presented in Table 2. No significant differences in the maximum and minimum LAVi were noted among the four age categories ( $P = 0.1$ ,  $P = 0.2$ ). Furthermore, even though there was a trend of increasing  $LA_{max}$  with older age, it did not reach statistical significance ( $P = 0.08$ ) (Fig. 1). Analysis of the parameters relating to the various phases of LA function revealed that there was no change in reservoir function parameters with age ( $P > 0.05$ ). The conduit function parameters decreased with older age, whereas parameters indicative of booster function displayed either a significant increase with age (LA active emptying volume index,  $P = 0.001$ ) or a trend suggestive of increasing function as measured by LA active emptying fraction (Fig. 2 and Table 2).

### Determinants of maximum LAVi

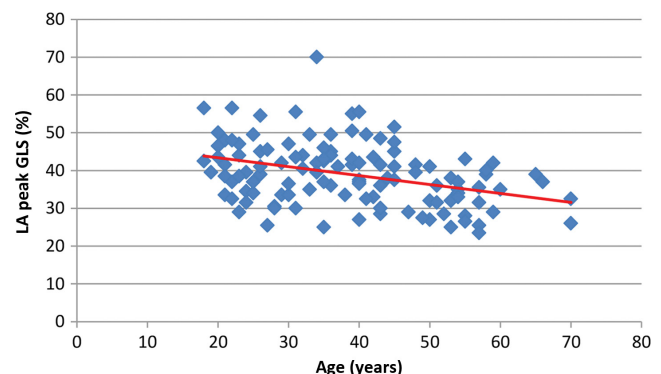
On univariate analysis, the main determinants of maximum LAVi were sex ( $P = 0.03$ ), body mass index ( $P = 0.009$ ), heart rate ( $P = 0.0002$ ), end-diastolic volume index ( $P = 0.001$ ), end-systolic volume index ( $P = 0.002$ ), *E* wave ( $P = 0.01$ ), *A* wave ( $P = 0.02$ ), *E/E'* medial ( $P = 0.008$ ), *S'* lateral ( $P = 0.004$ ), *E/E'* lateral ( $P < 0.001$ ), average *E/E'* ( $P < 0.001$ ), minimum LAVi ( $P < 0.001$ ), LA emptying fraction total ( $P = 0.03$ ), pre-*A* LAVi ( $P < 0.001$ ) and LV mass indexed ( $P = 0.015$ ). Age was not a determinant of maximum LAVi ( $P = 0.2$ ).

On multivariate linear regression analysis, the main predictors of maximum LAVi were male sex, heart rate,

**Table 3** Multivariate linear regression analysis for maximum left atrial volume indexed.

Variables	$\beta$ Coefficient $\pm$ standard error	Partial coefficient	$R^2$	<i>P</i> Value
Model $r = 0.54$ , $P < 0.0001$				
Age (years)	$-0.04 \pm 0.04$	$-0.09$	0.11	0.32
Men	$-3.2 \pm 1.16$	$-0.25$	0.15	0.006
Heart rate (beats/min)	$-0.13 \pm 0.04$	$-0.27$	0.09	0.003
<i>E/E'</i> lateral (ratio)	$1.5 \pm 0.39$	0.35	0.14	0.0001
LVMi ( $g/m^2$ )	$0.08 \pm 0.03$	0.26	0.08	0.004

LVMi, left ventricular mass index.



**Figure 3**

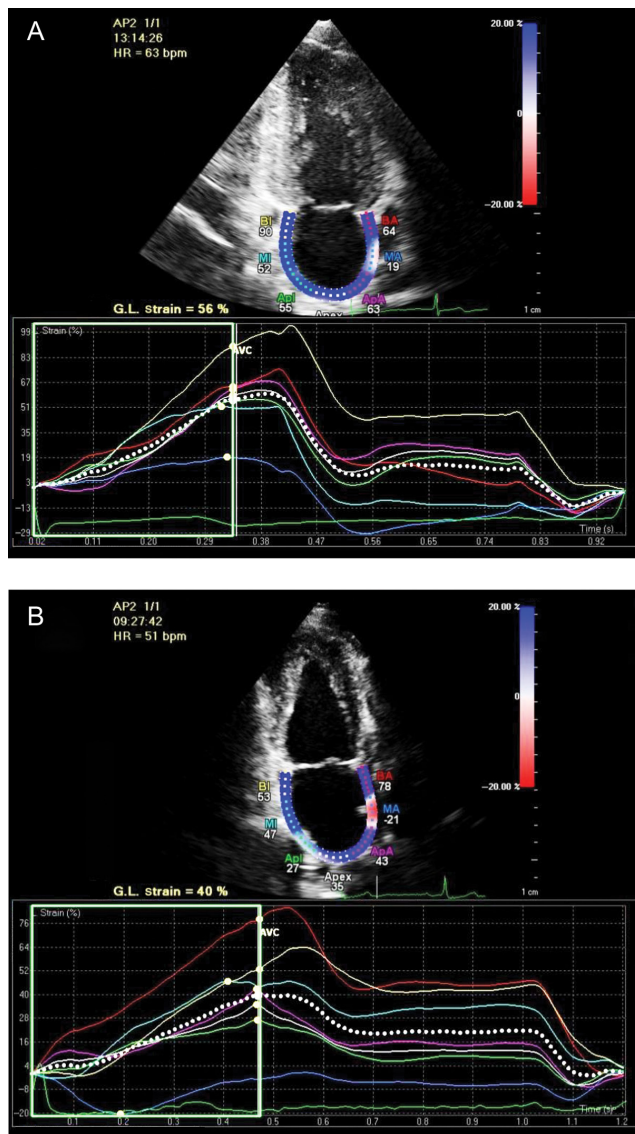
Correlation between left atrial (LA) peak global longitudinal strain (GLS) and age ( $r = -0.36$ ,  $P < 0.001$ ).



$E/E'$  lateral and LV mass indexed after adjustment for age (Table 3).

### LA strain indices

All normative data are presented in Table 2. There was a significant decrease in the LA  $\epsilon_R$  ( $P<0.0001$ ) with advancing age (Figs 3 and 4). No significant difference was noted in the LA  $\epsilon_{CT}$  among the age groups ( $P=0.27$ ). The LA stiffness index increased in the older age groups ( $P<0.001$ ) (Table 2).



**Figure 4**  
Two-chamber view depicting peak left atrial strain in the reservoir phase ( $\epsilon_R$ ) in a 21-year-old man (A) and a 51-year-old man (B).

### Factors determining LA strain

On univariate analysis, factors such as age ( $P<0.001$ ), body surface area ( $P=0.002$ ), LV mass ( $P=0.01$ ),  $E$  wave ( $P<0.001$ ),  $E/A$  ratio ( $P=0.04$ ),  $E'$  medial ( $P<0.001$ ),  $E'$  lateral ( $P<0.001$ ),  $E/E'$  medial ( $P=0.002$ ),  $S'$  medial ( $P<0.001$ ),  $S'$  lateral ( $P<0.001$ ), average  $E/E'$  ( $P=0.006$ ), LA emptying fraction total ( $P<0.001$ ), pre-atrial LAVi ( $P=0.005$ ), minimum LAVi ( $P<0.001$ ), LA expansion index ( $P<0.001$ ), passive emptying volume ( $P=0.003$ ) and passive emptying fraction ( $P<0.001$ ) were independently associated with LA  $\epsilon_R$ .

On multivariate linear regression analysis, age,  $E/E'$  medial,  $E'$  medial and reservoir phase indices (LA expansion index and LA emptying fraction total) were independently associated with LA  $\epsilon_R$  after adjustment for sex (Table 4). Age was no longer a significant determinant when  $S'$  lateral and  $E'$  medial were added to the model after adjusting for sex (Table 4).

### Reproducibility of LA volumetric and strain parameters

The intra-observer coefficient of variation for LA<sub>max</sub> was 3% with a mean difference  $\pm$  S.D. of  $0.23 \pm 0.61$  ( $P=0.10$ ). The inter-observer variability for LA<sub>max</sub> was 0.9% with a mean difference  $\pm$  S.D. of  $2.7 \pm 2.6$  ( $P=0.0001$ ). The intra-observer coefficient of variation for LA  $\epsilon_R$  was 4.8% with a mean difference  $\pm$  S.D. of  $3.2 \pm 0.67$  ( $P=0.3$ ) and for LA  $\epsilon_{CT}$  was 4.6% with a mean difference  $\pm$  S.D. of  $1.43 \pm 0.31$  ( $P=0.3$ ). The inter-observer variability coefficient was

**Table 4** Multivariate linear regression analysis for left atrial strain in the reservoir phase ( $\epsilon_R$ ).

Variables	$\beta$ Coefficient $\pm$ standard error	Partial coefficient	$R^2$	P value
Model 1 $r=0.57$ , $P<0.0001$				
Age (years)	$-0.17 \pm 0.05$	-0.29	0.16	0.001
Men	$-0.8 \pm 1.34$	-0.05	0.05	0.53
Left atrial emptying fraction total (%)	$0.24 \pm 0.04$	0.44	0.03	<0.001
$E/E'$ medial (ratio)	$-0.79 \pm 0.26$	-0.25	0.21	0.006
Model 2 $r=0.58$ , $P<0.0001$				
Age (years)	$-0.17 \pm 0.05$	-0.29	0.16	0.001
Men	$-1.0 \pm 1.33$	-0.07	0.05	0.40
Left atrial expansion index (%)	$0.02 \pm 0.004$	0.46	0.03	<0.001
$E/E'$ medial (ratio)	$-0.79 \pm 0.26$	-0.27	0.22	0.003
Model 3 $r=0.53$ , $P<0.0001$				
Age (years)	$-0.09 \pm 0.07$	-0.13	0.45	0.16
Men	$-1.0 \pm 1.34$	-0.06	0.03	0.45
$S'$ lateral (cm/s)	$0.97 \pm 0.27$	0.31	0.11	<0.001
$E'$ medial (cm/s)	$0.74 \pm 0.33$	0.2	0.48	0.02

9% for both LA  $\mathcal{E}_R$  ( $P=0.6$ ) and  $\mathcal{E}_{CT}$  ( $P=0.6$ ) with a mean difference  $\pm$  s.d. of  $3.2 \pm 0.35$  and  $1.2 \pm 0.13$ , respectively.

## Discussion

### Main findings

This study provides normative age-related data for LA volumetric parameters and LA strain in a black African population. Normal aging is associated with key physiological changes such as increasing systolic blood pressure and declining LV diastolic function with abnormal relaxation and increased LA stiffness. Volumetric analysis of LA function reveals that global measures of LA function remain normal with advancing age, but conduit function declines and booster function increases. Furthermore, normal aging is associated with an absolute decline in global LA reservoir strain, whereas contractile LA strain remains unchanged.

Aging is a key factor that may influence LA volumetric measurements. Maximum LAVi did not change with increasing age in our study. Additionally, age was not an independent predictor of maximum LAVi in our study. There are discrepant findings from a number of studies relating to the effect of aging on LA volume (1, 6, 7, 10, 11, 12). This may be attributed to varying sample sizes, racial differences and different methods used for assessing maximum LA volumes. However, the impact of advancing age on LA volumetric measurements that are surrogates of conduit and booster function appears to be more consistent. Our findings suggest that with aging, a decrement in conduit volumes occurs, whereas simultaneously an increase in booster function volumes occurs, which is consistent with other studies (2, 7). This may be explained by an age-associated decrease in early relaxation, thus resulting in a relative decrease in the conduit function and greater reliance on the booster function for LV filling (2, 7). The evidence for a decrease in early relaxation was based on declining  $E'$  on tissue Doppler imaging and  $E$  wave on pulsed-wave Doppler in this study. However, it is to be noted that the aforementioned parameters still fall within the normal reference ranges defined in guidelines (16).

The major factors determining LA  $\mathcal{E}_R$  are initial and final length of the longitudinal fibers. Initial length is determined by atrial contraction and  $LA_{min}$  (19). Final length is determined by atrial relaxation, the atrial longitudinal compliance in response to the volume of blood entering the atrium from the pulmonary veins during ventricular systole and the descent of the mitral

annulus during systole (9, 19, 20). The latter may be affected by factors governing LV systolic function and end-systolic volume (19).

The age-related decline in LA  $\mathcal{E}_R$  in our study conforms with earlier studies by Sun *et al.* and Saraiva *et al.* (21, 22). In this study, factors that may determine the initial length (namely  $LA_{min}$  and LA  $\mathcal{E}_{CT}$ , a surrogate of LA contraction) do not differ among age groups. The effect of aging on factors determining final length is more intriguing. There are no validated echocardiographic parameters that can be used as a surrogate of atrial relaxation (18). In this study, LA stiffness increased with aging, whereas  $S'$  decreased with age despite the LA volume maximum not changing with aging. This may infer that with aging in normal individuals the decrement we observed in peak reservoir strain most likely occurs because of abnormalities determining final length rather than initial length. The  $S'$  at both annuli decreases with age, whereas atrial stiffness increases in this study. Although age appears to be a predictor of LA  $\mathcal{E}_R$ , it appears that  $S'$  and indices of diastolic function such as  $E'$  are more consistent predictors. The link between decreasing efficient early relaxation and LA strain is difficult to elucidate in normal individuals with normal LA pressures. One postulate may be that the same process predisposing to diminishing abnormal early relaxation may also affect the LA reservoir function, for example, fibrosis of the subendocardium and atria with aging or subendocardial ischemia (9).

A final observation from our data is the disconnect between volumetric indices and LA strain with aging. As outlined earlier, volumetric techniques indicate that  $LA_{max}$  and  $LA_{min}$  do not change with aging, implying that volumetric filling during the reservoir phase is maintained, whereas conduit function declines, prompting greater reliance on booster function for LV filling. Although the absolute volumetric values may differ among populations, this trend is consistent. Similarly, studies using speckle-tracking have indicated that decline in peak reservoir longitudinal strain with aging is a consistent trend despite different populations studied and different vendors used. In our study, strain in the atrial contractile phase was relatively preserved with increasing age. Previous studies have reported variable findings with regard to change in LA contraction with age (9, 21). Boyd *et al.* and Sun *et al.* reported an increase in atrial contractile strain with increasing age, whereas a few smaller studies reported no change in this parameter with advanced age (9, 21). Thus, larger studies are needed to confirm the relation between atrial contractile strain

and age. However, the above findings imply that strain is decreased absolutely or relatively to LA volume during the reservoir and contractile phases of LA function with aging. This may imply that strain is a more sensitive marker of subclinical change in atrial function with aging (9). The effect of radial compliance or contraction on LA volume was not studied and may represent a compensatory means of maintaining the observed changes in LA volume with age despite the relative or absolute decrement in atrial longitudinal strain.

## Study limitations

This study had several limitations: (1) A minority of subjects were older than age 60, due to a lower life expectancy in a South African population (the average life expectancy of an adult in 2014 was estimated at 59.1 years for males and 63.1 years for females, according to Statistics South Africa), (2) LA strain measurement lacks a criterion standard—strain values vary with different software packages and (3) exercise capacity of the study subjects was not assessed to unmask subclinical diastolic dysfunction and symptoms.

## Conclusions

Volumetric analysis confirms that age-related trends in the changes of LA reservoir, conduit and contractile function in an African population are similar to that observed in other populations. Similarly, the trend of declining reservoir strain with advanced age also is a consistent finding while the preservation of atrial contractile strain with increasing age requires analysis in larger studies.

## Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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