Right atrial strain in a normal adult African population according to age

Nyange Mushitu, Ruchika Meel

Abstract

Background: Right atrial longitudinal strain (RALS) is a useful parameter to define right atrial (RA) subclinical dysfunction prior to changes in RA dimension and volume. We sought to establish normal values for RALS in a sub-Saharan African population.

Methods: This was a retrospective, cross-sectional study from 2017 to 2019 of 100 normal individuals. All echocardiographic measurements were done as per the standard guidelines.

Results: Mean RALS was 32.7 ± 10.5%. The mean RA volume indexed to body surface area was 19.5 ± 5.7 ml/m^2. There was a negative correlation between RALS and age but it was not statistically significant (r = –0.15, p = 0.129). Males had a tendency towards higher RA volume indexed and RALS measurements compared to females (20.8 ± 6.3 and 18.7 ± 5.2 ml/m^2, p = 0.07; 34.6 ± 9.6 and 31.4 ± 10.9%, p = 0.141, respectively). Body mass index was an independent predictor of RALS (r = –0.43, p = 0.003).

Conclusion: We have provided normative data for RALS in an African population. This study provides a platform for future larger studies on RALS.

Keywords: right atrium, right atrial longitudinal strain, age, African, echocardiography

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In the last 20 years, there has been great interest in research on right atrial (RA) function, because recent data have demonstrated that assessment of RA volumetric parameters on echocardiography is an essential predictor of morbidity and mortality in various cardiovascular disorders.[1-3]

There are several imaging studies that have described RA anatomy and function. RA dimensions, volume and strain have been studied using the gold standard, cardiac magnetic resonance (CMR), computed tomography, echocardiography (two- and three-dimensional) and recently speckle-tracking echocardiography (STE). Two-dimensional echocardiography (2DE) has become the most clinically relevant non-invasive technique for evaluating the right atrium.[4-6]

It is important to define normative values of RA strain using 2DE, because RA subclinical dysfunction, as measured by strain, has been observed in several cardiovascular disorders prior to changes in the traditional indices of RA and right ventricular (RV) function such as volume, size and ejection fraction. Such cardiovascular disorders include pulmonary arterial hypertension (PAH), coronary artery disease (CAD) and heart failure with reduced ejection fraction (HFrEF). RA strain had additive prognostic value to other clinical measures, including RV strain, RA area and RA pressure in patients with PAH.[7-11] The difference between normal and abnormal RA dimension and function is therefore clinically pertinent.

Most of the available studies on the parameters of RA dimension in a normal population depend on data from North America and Europe and are in line with the guidelines of the American Society of Echocardiography (ASE) and European Society of Cardiology (ESC).[12-15] These values do not effectively represent the diverse racial and ethnic groups of the world.

The study by Soulat-Dufour *et al.* with the World Alliance Societies of Echocardiography (WASE) have suggested that there might be significant differences in normal values among different populations.[16] Currently, limited data exist regarding RA volume (RAV), size and strain in a normal black African adult population.

Age-related changes in vascular and cardiac function contribute to cardiovascular mortality. Aging is associated with abnormalities in left-sided functional parameters. However, studies on age-related changes in right-sided functional parameters are scarce.[17-19] Therefore, in this study, we sought to establish normal values for RAV and RA longitudinal strain (RALS), and its correlation with age, in a sub-Saharan black African population, using 2DE and STE.

Methods

This study was a retrospective analysis of echocardiographic findings in healthy normal controls that formed part of a study (M170389) conducted at Chris Hani Baragwanath Academic Hospital (CHBAH). It is a secondary analysis of the data collected in these healthy controls.

The study was approved by the University of the Witwatersrand ethics committee and conforms to the principles outlined in the Declaration of Helsinki. Permission to use data from the parent study was obtained. The study was approved by the Human Research Ethics Committee of the University of the Witwatersrand (clearance certificate number: M 200822).

Echocardiograms were obtained according to a standardised protocol on a Phillips iE 33 ultrasound system (Amsterdam, The Netherlands) equipped with an S5-1 transducer that transmits

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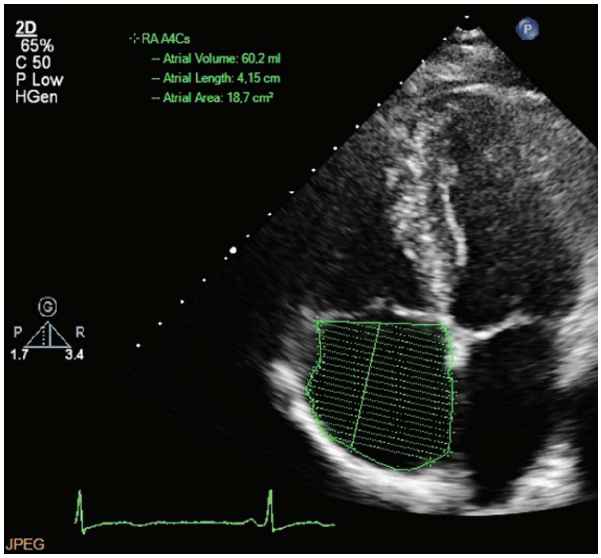

Fig. 1. Apical four-chamber view in a normal participant, showing measurement of RA volume using the discs method.

a frequency of 1.7 MHz and receives a frequency of 3.4 MHz. All data were analysed offline after being transferred to an Xcelera workstation (Philips). The RALS analysis was performed separately offline using Philips Q lab 11.0 speckle-tracking software.

Two-dimensional echocardiography was used for measurements of RA dimensions. They were performed in agreement with ASE chamber quantification guidelines of 2015 and the 2010 ASE guidelines on right heart assessment. The RA parameters (area and volume) were measured at the end of systole on an apical four-chamber view modified to optimise the RA visualisation. The RAV was measured using the single-plane method of discs by tracing an outline of the RA blood–tissue interface, ensuring that the RA appendage, superior vena cava and inferior vena cava were excluded. The tricuspid tenting area was also excluded (Fig. 1).[12,14,15]

The RALS was measured by an experienced cardiologist and clinical technologist using STE. For STE using 2D grey-scale echocardiography, apical four-chamber views were captured during breath holding at the end of the expiratory phase for a few seconds, and with an electrocardiogram recording attached. A suitable image of myocardial tissue was obtained completely separated from surrounding structures. Three successive cardiac cycles were recorded and averaged. The frame rate was set between 60 and 80 frames per second. Analysis of speckle-based strain was done using Philips Q lab 11.0 speckle-tracking software.

In four-chamber RA focused views, the endocardial surface of the RA was traced manually by a three-point-and-click approach. The system automatically generates an epicardial surface tracing. The region of interest (ROI) was therefore created, composed of seven segments. The ROI was manually adjusted as needed to allow for enough speckle tracking. The software generates the longitudinal curves for each segment with its mean value (Fig. 2).[20-22]

The number of healthy controls who were enrolled in the parent study was 100, after excluding 23 patients who did not meet the study inclusion criteria. Using the power command in Stata, we conducted a one-sample correlation test to estimate the minimum sample required to detect a correlation of at least r = 0.3 between RALS and age. The minimum sample size required was 100. All participants were subdivided into four age groups (group 1: 18–29 years, group 2: 30–39 years, group 3: 40–49 years and group 4: ≥ 50 years).

This study is a secondary data analysis, and we utilised data from an existing database. Only variables in our data collection sheet were used in this study.

Statistical analysis

Continuous variables are described using the mean and standard deviation, or median and interquartile range when variables were not normally distributed. The independent t-test was used to compare means of continuous variables by gender while the Mann–Whitney test was used for a comparison of median values by gender. One-way analysis of variance (ANOVA) was used to compare means of normally distributed continuous variables by age group or body mass index (BMI) category, while the Kruskal–Wallis test was used for comparison of medians when variables were not normally distributed. Pearson's correlation coefficients determined the association between age and RA parameters using a statistical significance threshold of 0.05.

All statistical analyses were conducted in Stata version 15. Univariate and multivariable linear regression was used to explore the association between RALS and independent

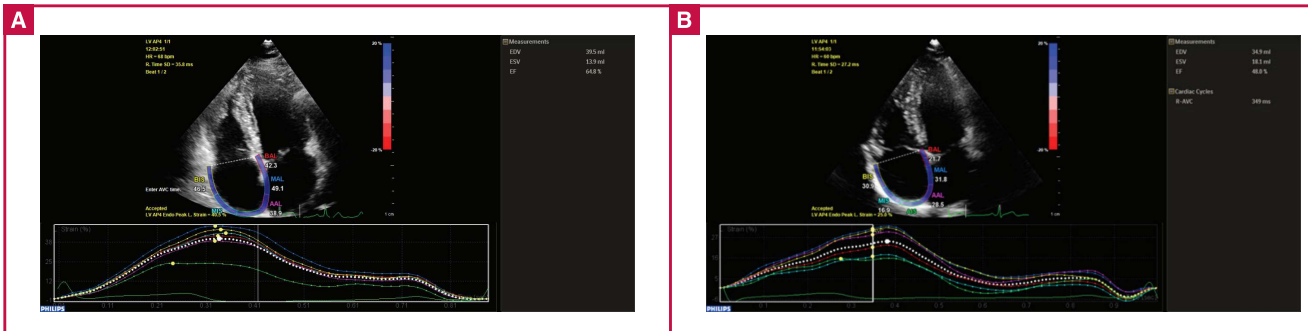

Fig. 2. STE showing decreased peak RA longitudinal strain of 25.5% in an older subject (A), compared to a younger subject of 46.5% (B).

variables at presentation [age, gender, BMI, body surface area (BSA) and RV parameters]. Independent variables were selected *a priori* for multivariate analyses. All clinically relevant and/or statistically significant variables on univariate analysis with a *p*-value ≤ 0.1 were included in the multivariate analysis.

Results

Baseline characteristics of the overall population of the study are presented in Table 1. A total of 100 participants were included, with a median age of 37.5 years [interquartile range (IQR) 26–46] with 60% female, and 24% of participants were above 50 years of age. Weight differed by age group ($p = 0.049$) and the median BMI was 28.0 (24.0–34.9) kg/m^2. A greater percentage of female participants were overweight and obese (50%). There was an age-related increase in BMI of all participants, but it was not statistically significant ($p = 0.089$).

Two-dimensional echocardiography parameters according to age groups are depicted in Table 2. There were no statistically significant differences with regard to age-related RA volumetric measurements ($p = 0.271$). RALS had a trend towards decreasing with age but did not achieve statistical significance ($p = 0.362$). RA volume indexed (RAVI) and RALS had a negative correlation with age but did not reach statistical significance ($r = –0.060$, $p = 0.526$; $r = –0.153$, $p = 0.129$, respectively) (Fig. 3).

Regarding traditional RV functional parameters such as tricuspid annular plane systolic excursion (TAPSE), RV E′, RV A′, and RV S′) there were no statistically significant differences. RV diastolic function declined with age, with RV E′/A′ showing a decrease with age ($p = 0.002$). Left ventricular (LV) diastolic function parameters showed a decrease with age but remained within ASE guideline-specified normal limits ($p < 0.001$).

Echocardiographic parameters according to gender are depicted in Table 3. Males had a tendency towards higher RAVI and RALS measurements compared to females (20.8 ± 6.3 and 18.7 ± 5.2 ml/m^2, $p = 0.07$; 34.6 ± 9.6 and 31.4 ± 10.9%, $p = 0.141$, respectively). There were no statistically significant differences in RV measurements and functional parameters between males and females. All participants had LV diastolic pulsed-wave (transmitral E and A waves) and tissue Doppler measurements within the normal accepted guideline range except for A wave and A′ lateral, which were higher in females compared to males ($p = 0.001$ and $p = 0.004$, respectively). Male participants had higher LV end-diastolic and end-systolic dimensions and volumes, as well as LA volume indexed to BSA.

Clinical and echocardiographic indices according to BMI are depicted in Table 4. Twenty-three per cent of participants were overweight and 44% were obese. Obese participants had higher heart rates than non-obese participants ($p = 0.002$) There were no statistically significant differences with regard to RA volumetric measurements, but RALS had a tendency to decrease with increasing BMI (35.7 ± 9.3%, < 25 kg/m^2; 34.6 ± 11.4%, < 30 kg/m^2; and 29.9 ± 10.1%, > 30 kg/m^2, respectively, $p = 0.571$). RV E′/A′ ratio decreased with increasing BMI ($p = 0.020$), suggestive of worsening RV diastolic dysfunction with increasing BMI. Left atrial (LA) volume and size increased with an increasing BMI ($p = 0.010$ and $p < 0.001$, respectively). Similar to RV diastolic parameters, there was worsening of LV diastolic function with an increase in BMI. Determinants of RA longitudinal strain are depicted in Table 5.

BMI was an independent predictor of RALS (BMI was a statistically significant variable on both univariate and multivariate analyses). BMI negatively correlated with RALS ($r = –0.43$, $p = 0.003$). For example, in the adjusted analyses, a unit increase in BMI resulted in a 0.72 decline in RALS. The intra-observer coefficient of variation for peak RALS was 4.6% and the inter-observer variability was 9%.

Discussion

This is the first study to provide normative age-related data for RALS in a sub-Saharan African population. Additionally, we have also provided complementary data regarding RAVI according to age and gender in this population. RALS had a tendency to decrease with age concurrent with a decline in RV diastolic function despite no alteration in RAVI, and BMI was an important independent predictor of RALS. Even though there was a tendency of RAVI to be higher in males, RAVI and RALS were not influenced significantly by gender.

Previous studies using 2DE by Wang *et al.* in 1984, and Kou *et al.* from the Normal Reference Ranges for Echocardiography (NORRE) study in 2013, were focused on Caucasians populations, and were in line with the ASE and ESC 2015 chamber quantification guideline document, which states that RAVI should be < 33 ml/m^2 (or < 35 ml/m^2 in men and < 31 ml/m^2 in women).[23,24]

In our study, we found that while the lower limits were similar to those of ASE and ESC guidelines, the upper margins were much lower (20.8 ± 6.3 ml/m^2 in male and 18.7 ± 5.2 ml/m^2 in

Table 1. Demographic and clinical characteristics of the study population according to age categories

Clinical parameters	*Total (20–62 years)* (n = *100*)	*Group 1 (18–29 years)* (n = *27*)	*Group 2 (30–39 years)* (n = *28*)	*Group 3 (40–49 years)* (n = *21*)	*Group 4 (≥ 50 years)* (n = *24*)	p-*value* (ANOVA)*#
Age (years)	37.5 (29.0–48.0)	25.0 (23.0–28.0)	34.0 (33.0–37.0)	45.0 (42.0–47.0)	54.0 (51.0–57.5)	< 0.001
Height (cm)	160.7 ± 7.3	161.6 ± 8.2	160.6 ± 6.5	162.0 ± 6.4	158.8 ± 7.9	0.499
Weight (kg)	73.0 (65.0–85.0)	67.0 (59.0–75.0)	73.0 (65.0–86.5)	80.0 (64.0–87.0)	78.3 (69.3–84.5)	0.049
Female, *n* (%)	60 (60.0)	13 (48.2)	18 (64.3)	10 (47.6)	19 (79.2)	0.078
Body mass index (kg/m^2)	28.0 (24.0–34.9)	24.0 (22.5–29.3)	29.1 (24.2–35.4)	29.0 (26.6–34.3)	30.8 (27.1–36.6)	0.089
Body surface area (m^2)	1.8 ± 0.2	1.7 ± 0.2	1.8 ± 0.2	1.8 ± 0.2	1.8 ± 0.1	0.168
Systolic blood pressure (mmHg)	126.8 ± 12.4	123 ± 11.6	126 ± 14.0	127 ± 9.1	130.8 ± 13.2	0.205
Diastolic blood pressure (mmHg)	79.3 ± 10.3	76.9 ± 10.9	79.2 ± 11.6	80.5 ± 9.3	80.9 ± 9.0	0.498
Heart rate (bpm)	72.0 (62.5–82.0)	67.0 (57.0–81.0)	75.5 (67.0–85.5)	70.0 (61.0–82.0)	71.0 (62.5–81.5)	0.217

Data reported as means ± SD or median (IQR). SD, standard deviation; IQR, interquartile range.
#Kruskall–Wallis *p*-value for non-normally distributed variables. *Statistical significance denoted by $p < 0.05$.

Table 2. Echocardiographic parameters according to the age of the study group

Variable	*Total (20–62 years) (n = 100)*	*Group 1 (18–29 years) (n = 27)*	*Group 2 (30–39 years) (n = 28)*	*Group 3 (40–49 years) (n = 21)*	*Group 4 (≥ 50 years) (n = 24)*	p-*value* (ANOVA)#*
RA parameters						
RA volume (ml)	34.8 ± 10.7	35.3 ± 11.7	33.7 ± 8.1	36.1 ± 13.8	34.3 ± 9.0	0.865
RA volume index (ml/m²)	19.5 ± 5.7	20.2 ± 5.8	19.0 ± 4.9	19.8 ± 7.2	19.1 ± 5.3	0.271
RA length (mm)	44.5 ± 5.2	44.5 ± 5.1	44.6 ± 3.9	45.3 ± 6.0	43.7 ± 6.0	0.679
RA width (mm)	36.3 ± 5.6	36.7 ± 5.9	36.9 ± 5.6	36.4 ± 6.3	34.9 ± 5.3	0.588
RALS (%)	32.7 ± 10.5	34.7 ± 10.8	32.8 ± 11.7	33.5 ± 7.3	29.6 ± 11.1	0.362
RV functional parameters						
TAPSE (mm)	19.0 (17.0–22.0)	17.0 (16.0–19.0)	19.0 (17.0–21.5)	19.0 (18.0–22.0)	19.5 (17.0–25.5)	0.099
PASP (mmHg)	15.0 (13.5–20.0)	15.0 (13.5–20.0)	17.0 (15.0–20.0)	18.0 (13.0–26.0)	15.0 (10.0–18.0)	0.465
RV base (mm)	31.0 (27.5–33.2)	32.0 (28.0–34.0)	30.0 (27.1–32.4)	31.4 (28.5–32.9)	30.0 (26.6–33.9)	0.455
RV S′ (cm/s)	11.1 ± 2.1	10.7 ± 1.9	11.3 ± 2.4	11.4 ± 2.0	11.0 ± 2.0	0.677
RV E′ (cm/s)	11.0 (8.9–13.0)	12.9 (9.5–15.9)	11.0 (9.7–12.6)	11.1 (8.0–12.5)	10.0 (7.6–11.5)	0.085
RV A′ (cm/s)	9.7 (8.4–12.1)	8.5 (7.9–10.6)	9.9 (8.7–11.6)	11.0 (9.0–13.4)	10.7 (9.0–12.8)	0.015
RV E′/A′	1.1 (0.8–1.4)	1.4 (1.1–1.9)	1.0 (0.9–1.3)	0.9 (0.8–1.3)	0.8 (0.7–1.1)	0.002
LV measurements						
LV systolic diameter (mm)	29.0 (26.0–31.5)	29.0 (26.0–32.0)	28.5 (26.0–30.0)	30.0 (28.0–32.0)	27.0 (23.5–31.0)	0.213
LV diastolic diameter (mm)	42.3 ± 5.1	42.8 ± 6.0	41.9 ± 4.2	44.0 ± 4.2	40.5 ± 5.3	0.124
End-diastolic volume index (ml/m²)	86.2 ± 23.1	89.3 ± 26.6	89.5 ± 24.2	91.0 ± 16.9	74.8 ± 19.7	0.048
End-systolic volume index (ml/m²)	18.2 (14.5–22.6)	20.1 (18.3–26.0)	18.3 (16.3–25.7)	17.4 (13.2–19.3)	14.3 (11.1–17.2)	< 0.001
LA volume (ml)	36.8 (27.7–46.8)	41.0 (23.0–50.0)	35.0 (26.0–45.9)	41.4 (29.0–44.4)	37.0 (31.5–48.0)	0.630
LA volume index (ml/m²)	21.5 (15.2–26.4)	23.8 (14.8–28.5)	19.6 (13.4–23.8)	22.7 (14.5–25.7)	20.0 (17.3–27.8)	0.574
LA size (mm)	32.0 (28.0–35.3)	30.8 (27.0–33.4)	32.0 (29.0–35.8)	33.0 (27.8–38.0)	33.0 (29.5–38.0)	0.068
Ejection fraction (%)	62.5 ± 7.1	60.5 ± 7.3	61.7 ± 6.9	65.5 ± 6.2	63.0 ± 7.5	0.104
Posterior wall diameter (mm)	8.0 (7.0–9.5)	7.0 (7.0–8.0)	8.0 (7.0–9.0)	9.0 (8.0–10.0)	9.0 (8.0–11.0)	0.001
LV diastolic parameters						
E wave (cm/s)	80.6 ± 19.7	89.1 ± 18.1	82.1 ± 17.6	76.5 ± 20.9	72.7 ± 19.7	0.017
A wave (cm/s)	56.2 ± 15.1	49.1 ± 15.3	57.3 ± 13.8	54.2 ± 13.1	64.9 ± 14.4	0.002
E/A ratio	1.4 (1.1–1.8)	1.8 (1.6–2.2)	1.4 (1.2–1.8)	1.4 (1.2–1.5)	1.1 (1.0–1.3)	< 0.001
E′ medial (cm/s)	9.5 (7.5–11.8)	11.7 (10.1–13.6)	9.1 (7.7–11.8)	9.0 (7.0–10.0)	7.7 (5.8–9.0)	< 0.001
E′ lateral (cm/s)	13.4 ± 3.3	16.0 ± 3.1	13.9 ± 2.9	12.0 ± 2.4	11.1 ± 2.6	< 0.001
A′ lateral (cm/s)	8.7 ± 2.7	7.0 ± 1.9	9.0 ± 2.4	9.6 ± 2.6	9.6 ± 2.9	< 0.001
E/E′ lateral ratio	5.9 (5.0-7.0)	5.8 (4.2-7.0)	5.8 (5.0-6.4)	5.9 (5.0-7.0)	6.2 (5.0-8.2)	0.575

Data reported as means ± SD or median (IQR). IQR, interquartile range; LA, left atrial; PASP, pulmonary artery systolic pressure; RA, right atrial; RALS. right atrium longitudinal strain; RV, right ventricle; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.
#Independent *t*-test, *p*-value or (Mann–Whitney test, *p*-value for non-normally distributed variables). *Statistical significance denoted by *p*-values < 0.05

females). Studies in African populations by Nel *et al.* and in Asian subjects by Karki *et al.* observed the same pattern.[25,26] Soulat-Dufour *et al.*, in the WASE study with 2 008 healthy adult individuals around the world, has shown that generally, Asian subjects had lower BSA compared to subjects in non-Asian countries.[16]

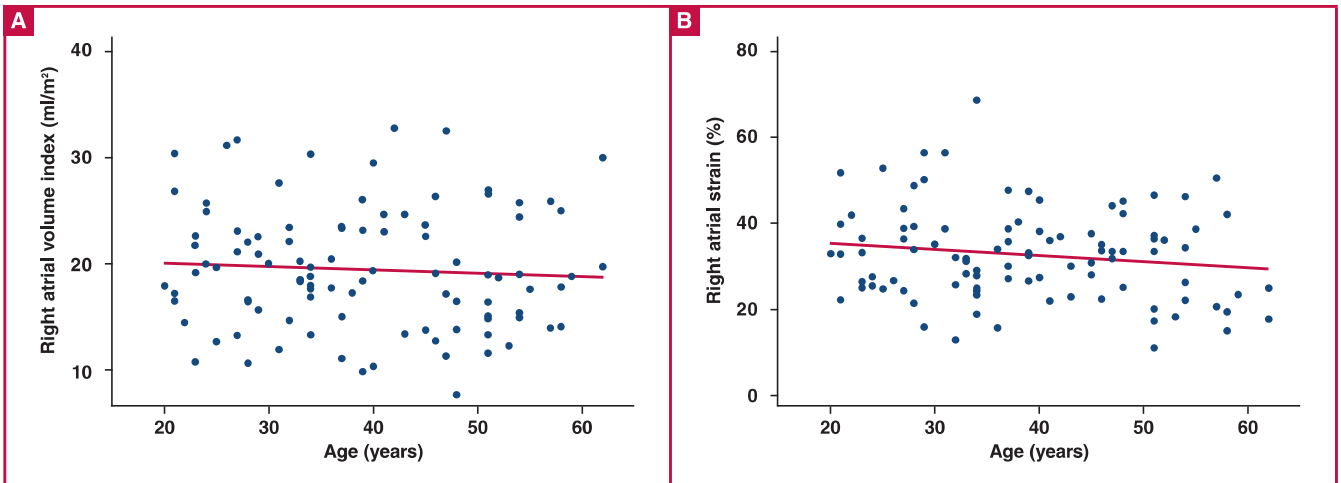

Fig. 3. (A) RA volume (ml/m²) and (B) RA longitudinal strain negatively correlated with the participants' age (r = –0.060, p = 0.526; r = –0.153, p = 0.129, respectively).

Table 3. Clinical and echocardiographic parameters of study participants according to gender

Variables	*Total (n = 100)*	*Males (n = 40)*	*Females (n = 60)*	p-*value* (ANOVA)#*
Clinical parameters				
Age (years)	37.5 (29.0–48.0)	34.0 (27.0–45.5)	39.0 (32.5–51.0)	0.055
Weight (kg)	73.0 (65.0–85.0)	68.0 (63.3–79.5)	79.0 (66.0–94.0)	0.016
Body mass index (kg/m²)	28.0 (24.0–34.9)	24.1 (22.5–29.6)	31.2 (26.6–37.8)	< 0.001
Body surface area (m²)	1.8 ± 0.2	1.8 ± 0.1	1.8 ± 0.2	0.783
Systolic blood pressure (mmHg)	126.8 ± 12.4	127.2 ± 12.2	126.3 ± 12.5	0.737
Diastolic blood pressure (mmHg)	79.3 ± 10.3	78.5 ± 11.8	79.8 ± 9.3	0.535
Heart rate (bpm)	72.0 (62.5–82.0)	65.0 (59.0–76.5)	76.0 (67.0–82.5)	0.002
RA parameters				
RA volume (ml)	34.8 ± 10.7	37.0 ± 11.8	33.3 ± 9.5	0.090
RA volume index (ml/m²)	19.5 ± 5.7	20.8 ± 6.3	18.7 ± 5.2	0.070
RA width (mm)	36.3 ± 5.6	37.9 ± 6.0	35.2 ± 5.2	0.018
RA length (mm)	44.5 ± 5.2	44.2 ± 5.6	44.7 ± 4.9	0.679
RALS (%)	32.7 ± 10.5	34.6 ± 9.6	31.4 ± 10.9	0.141
RV functional parameters				
TAPSE (mm)	19.0 (17.0–22.0)	19.0 (17.0–22.0)	18.5 (17.0–21.5)	0.659
PASP (mmHg)	15.0 (13.5–20.0)	15.0 (12.0–17.0)	17.0 (15.0–20.0)	0.056
RV E′ (cm/s)	11.0 (8.9–13.0)	11.2 (9.0–12.9)	10.9 (8.6–13.2)	0.699
RV A′ (cm/s)	9.7 (8.4–12.1)	9.1 (8.4–11.7)	10.2 (8.7–12.8)	0.155
RV S′ (cm/s)	11.1 ± 2.1	10.9 ± 2.2	11.2 ± 1.9	0.406
RV base (mm)	31.0 (27.5–33.2)	31.6 (27.8–33.2)	30.3 (27.1–33.3)	0.499
RV E/A′	1.1 (0.8–1.4)	1.0 (0.8–1.3)	1.1 (0.8–1.5)	
LV measurements				
LV systolic diameter (mm)	29.0 (26.0–31.5)	30.0 (27.5–32.0)	27.0 (25.5–30.0)	0.006
LV diastolic diameter (mm)	42.3 ± 5.1	44.2 ± 5.7	41.0 ± 4.2	0.001
End-diastolic volume index (ml/m²)	86.2 ± 23.1	94.5 ± 26.2	80.8 ± 19.2	0.003
End-systolic volume index (ml/m²)	18.2 (14.5–22.6)	16.9 (14.2–19.4)	19.8 (17.2–24.7)	0.012
LA volume index (ml/m²)	21.5 (15.2–26.4)	22.6 (16.1–28.0)	19.1 (13.3–24.6)	0.060
LA size (mm)	32.0 (28.0–35.3)	32.0 (28.3–34.0)	32.2 (27.8–36.6)	0.441
Ejection fraction (%)	62.5 ± 7.1	62.2 ± 7.8	62.7 ± 6.7	0.753
Posterior wall diameter (mm)	8.0 (7.0–9.5)	8.0 (7.0–9.5)	8.0 (7.0–9.5)	0.516
LV diastolic parameters				
E wave (cm/s)	80.6 ± 19.7	78.2 ± 16.1	82.2 ± 21.8	0.320
A wave (cm/s)	56.2 ± 15.1	50.3 ± 15.6	60.2 ± 13.5	0.001
E/A ratio	1.4 (1.1–1.8)	1.5 (1.2–1.9)	1.4 (1.1–1.4)	0.075
E′ medial (cm/s)	9.5 (7.5–11.8)	9.7 (7.9–12.0)	9.4 (7.1–11.5)	0.429
E′ lateral (cm/s)	13.4 ± 3.3	13.8 ± 3.0	13.1 ± 3.5	0.287
E/E′ lateral ratio	5.9 (5.0–7.0)	5.7 (5.0–6.8)	6.0 (5.0–7.1)	0.215

Data reported as means ± SD or median (IQR).
IQR, interquartile range; LA, left atrial; PASP, pulmonary artery systolic pressure; RA, right atrial; RALS, right atrial longitudinal strain; RV, right ventricle; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.
#Independent *t*-test, *p*-value or Mann–Whitney test, *p*-value for non-normally distributed variables. *Statistical significance denoted by *p*-values < 0.05

Ethnicity may cause variations in genetics and parameters of BSA and BMI and may directly influence echocardiographic measures. Therefore, correlation between ethnicity and RA volumetric parameters is important.

In this study, there was a trend towards higher RAVI in males compared to females but no influence of age on RAVI was noted. The aforementioned finding was akin to the recent study by Nel *et al.*[25] and the WASE study pertaining to RAVI in a normal population.[16] Grünig *et al.* and D'Ascenzi *et al.* have shown that males had a larger RA area compared to females, explaining the volume differences between genders.[27,28] D'Oronzio *et al.*, Wang *et al.* and Peluso *et al.*, using 2DE and 3DE, respectively, did not find any correlation between atrial volume and ageing, for reasons that are not fully understood.[23,29,30]

In the current study, the mean RALS was 32.7 ± 10.5%, which was lower than the value reported by Padeletti *et al.* and D'Ascenzi *et al.*[22,28] In this Italian study comprising 84 and 74 subjects, RALS was documented using the 2D STE, and the mean RALS was 49 ± 13 and 48 ± 12.68%, respectively.[22,28] These studies were done in a group of subjects with an overall lower BMI (22.4 ± 3.5 kg/m²), in contrast to our study (24–34.9 kg/m²), and this is likely the explanation for higher RALS in their cohort.

Obesity is a health problem of growing significance all over the world; its prevalence is increasing in both developed and developing countries. According to World Health Organisation data, 39% of the global population above 18 years of age are overweight and of these, 13% are obese. In Africa there is a significant trend towards obesity, with increments in BMI documented in both genders.[31] Micklesfield *et al.* studied a South Africa population from Soweto and demonstrated a significant gender difference with regard to BMI, with women being markedly more overweight and obese.[32]

In our study, 67% of normal volunteers had a BMI above 25 kg/m², which occurred more commonly in women (49%). BMI was the only independent predictor of RALS in this study. An inverse relationship was noted between BMI and RALS in the current study. A recent study by Chirinos *et al.* quantified LA strain and strain rate using STE in 1 531 middle-aged community-based participants enrolled in the Asklepios study. They demonstrated that longitudinal LA strain measured using STE decreased with elevated BMI.[33]

Obesity has been shown to have many effects on cardiovascular structure and function. Excess adiposity imposes an increased metabolic demand on the body and cardiac output. Total blood volumes are elevated in obesity, leading to a hyperdynamic circulation, which causes LV and RV structural changes, with the resultant increased ventricular mass and cavity dilatation. Obesity is the main cause of tissues fibrosis.[34]

Sokmen *et al.* and Csige *et al.* showed that uncomplicated obesity was associated with RV and RA dilatation, and increased thickness of the RV free wall. Also, these structural indices were found to be positively correlated with BMI.

Myocardial fat accumulation as a consequence of obesity may cause atrial interstitial fibrosis and subsequently atrial dilatation and stiffness.[35,36] This may be a possible mechanism explaining the inverse relationship between BMI and RALS in this study. Obesity may result in RA fibrosis, stiffness with a consequent reduction in myocardial deformation, and RALS. Furthermore, this study demonstrates that RALS tended to decrease with age and males tended to have higher values compared to females, although this finding did not reach statistical significance.

Aging is associated with the development of myocardial fibrosis. Fibrotic tissue is stiffer and less compliant, resulting in subsequent cardiac dysfunction.[37,38] We hypothesised that a combination of stiff RA and RV diastolic dysfunction associated with age-related myocardial fibrosis will have poor myocardial

Table 4. Clinical and echocardiographic indices according to body mass index

Variables	*BMI kg/m²* (n = *100*)	*BMI < 25 kg/m²* (n = *32*)	*BMI 25 to < 30 kg/m²* (n = *23*)	*BMI ≥ 30 kg/m²* (n = *44*)	p-*value** (*ANOVA*)#
Clinical parameters					
Age (years)	37.5 (29.0–48.0)	30.0 (24.5–38.5)	40.0 (30.0–48.0)	44.0 (34.0–51.0)	< 0.001
Weight (kg)	73.0 (65.0–85.0)	63.3 (57.0–65.8)	68.0 (66.0–77.6)	86.5 (82.0–99.5)	< 0.001
Female, *n* (%)	60 (60.0)	10 (31.3)	15 (65.2)	34 (77.3)	0.078
Body surface area (m²)	1.8 ± 0.2	1.7 ± 0.1	1.7 ± 0.1	1.9 ± 0.2	0.069
Systolic blood pressure (mmHg)	126.8 ± 12.4	123.6 ± 12.9	128.1 ± 10.7	128.5 ± 12.8	0.598
Diastolic blood pressure (mmHg)	79.3 ± 10.3	76.6 ± 10.8	79.3 ± 10.8	81.2 ± 9.7	0.760
Heart rate (bpm)	72.0 (62.5–82.0)	65.5 (58.0–77.0)	65.0 (57.0–81.0)	77.0 (70.5–82.5)	0.002
RA parameters					
RA volume (ml)	34.8 ± 10.7	35.1 ± 11.6	30.7 ± 9.2	36.7 ± 10.2	0.513
RA volume index (ml/m²)	19.5 ± 5.7	20.8 ± 5.9	18.0 ± 5.9	19.4 ± 5.4	0.822
RA length (mm)	44.5 ± 5.2	42.9 ± 5.7	43.4 ± 4.0	46.2 ± 5.0	0.226
RA width (mm)	36.3 ± 5.6	37.2 ± 5.5	33.2 ± 5.1	37.3 ± 5.8	0.817
RALS (%)	32.7 ± 10.5	35.7 ± 9.3	34.6 ± 11.4	29.9 ± 10.1	0.571
RV functional parameters					
TAPSE (mm)	19.0 (17.0–22.0)	19.0 (17.0–22.5)	19.0 (16.0–23.2)	18.5 (17.0–21.5)	0.898
PASP (mmHg)	15.0 (13.5–20.0)	15.0 (15.0–25.0)	17.5 (15.0–20.0)	15.0 (12.0–18.0)	0.091
RV E′ (cm/s)	11.0 (8.9–13.0)	12.0 (10.1–13.6)	11.7 (8.9–13.6)	10.2 (8.0–11.6)	0.114
RV A′ (cm/s)	9.7 (8.4–12.1)	9.0 (7.6–11.8)	10.2 (8.7–11.3)	10.3 (8.8–13.0)	0.081
RV E′/ A′	1.1 (0.8–1.4)	1.2 (0.9–1.6)	1.0 (0.8–1.5)	0.9 (0.7–1.2)	0.020
LV measurements					
LV systolic diameter (mm)	29.0 (26.0–31.5)	29.5 (25.5–32.0)	29.0 (26.0–30.0)	29.0 (26.0–32.0)	0.730
LV diastolic diameter (mm)	42.3 ± 5.1	42.1 ± 5.2	42.5 ± 4.7	42.4 ± 5.3	0.824
End-diastolic volume index (ml/m²)	86.2 ± 23.1	88.0 ± 23.3	88.6 ± 24.6	84.0 ± 22.7	0.913
End-systolic volume index (ml/m²)	18.2 (14.5–22.6)	20.0 (16.1–23.5)	18.1 (15.3–19.9)	17.1 (13.4–21.1)	0.220
LA volume index (ml/m²)	21.5 (15.2–26.4)	20.1 (13.0–23.8)	22.6 (16.7–25.8)	22.8 (16.2–30.5)	0.242
LA size (mm)	32.0 (28.0–35.3)	28.0 (25.0–32.0)	30.3 (27.0–32.0)	35.8 (33.0–38.5)	< 0.001
Ejection fraction (%)	62.5 ± 7.1	62.7 ± 5.8	64.3 ± 7.9	61.4 ± 7.6	0.199
LV diastolic parameters					
E wave (cm/s)	80.6 ± 19.7	86.2 ± 21.1	80.7 ± 21.7	76.5 ± 17.1	0.313
A wave (cm/s)	56.2 ± 15.1	52.9 ± 15.5	55.8 ± 12.7	58.5 ± 15.7	0.520
E/A ratio	1.4 (1.1–1.8)	1.7 (1.5–1.9)	1.4 (1.1–1.9)	1.3 (1.0–1.5)	0.002
E′ medial (cm/s)	9.5 (7.5–11.8)	10.7 (8.9–12.4)	9.3 (6.9–11.9)	8.7 (7.1-10.8)	0.028
E′ lateral (cm/s)	13.4 ± 3.3	14.8 ± 3.0	13.9 ± 3.1	12.2 ± 3.2	0.967
E/E′ lateral ratio	5.9 (5.0–7.0)	6.0 (5.0–7.0)	5.5 (4.9–7.0)	6.0 (5.1–7.0)	0.363

Data reported as means ± SD or median (IQR). IQR, interquartile range; LA, left atrial; PASP, pulmonary artery systolic pressure; RA, right atrial; RALS, right atrium longitudinal strain; RV, right ventricle; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.
#Independent *t*-test, *p*-value or Mann-Whitney test, *p*-value for non-normally distributed variables. *Statistical significance denoted by *p*-values < 0.05

deformation and this may result in an age-related decrease in RALS. However, we did not perform biomarkers or CMR imaging to objectively assess for the presence of fibrosis in this study.

The trend towards gender differences with RALS, although not statistically relevant, could be multifactorial in this study. In addition to a difference in biology, a higher BMI in females compared to males may explain these findings. Male participants were also younger and had higher RAVI and likely more compliant RA compared to females, which translated into higher RALS. Furthermore, males had a lower heart rate compared to females [65.0 (59.0–76.5) vs 76.0 (67.0–82.5) beats/min, p = 0.002], which allowed for a prolonged filling time of the RA chamber and therefore increased stretch of the RA wall, with the resultant higher RALS.

Padeletti *et al*. did not find differences in RALS with regard to gender and ageing.[10] This lack of association between RALS, gender and aging may be related to the limited capacity of the software in identifying all the segments of the RA due to the higher tricuspid annulus deformation compared to the mitral valve. Furthermore, this may be attributed to varying sample sizes and racial differences in the two studies.

Table 5. Multiple linear regression analysis for predictors of RA longitudinal strain

	Univariate regression			*Multivariate regression*			
Covariates	*Coef-ficient*	*Standard error*	p-*value*	*Coef-ficient*	*Standard error*	p-*value*	*Multiple* r, (p-*value*)
Age (years)				–0.06	0.10	0.558	0.40 (0.097)
Male gender	3.17	2.13	0.141	–1.15	2.80	0.683	
BMI	–0.43	0.14	0.003	–0.72	0.29	0.013	
BSA	–6.61	6.30	0.297	16.20	10.28	0.118	
RV S′	0.81	0.51	0.114	0.47	0.56	0.410	
RV base	0.0004	0.21	0.998	–0.10	0.22	0.644	
RV E′	0.49	0.33	0.149	0.98	0.73	0.186	
RV A′	–0.11	0.36	0.764	–0.65	0.75	0.387	
RV E′/A′ ratio	2.11	2.02	0.298	–5.77	5.76	0.319	
RA volume/ BSA ratio	–0.19	0.18	0.307	–0.20	0.19	0.307	

BMI, body mass index; BSA, body surface area; RA, right atrial; RV, right ventricular.

With recent advances in technology, Nemes *et al.*[39] and Qu *et al.*[40] using 3D STE and CMR, respectively, demonstrated obvious gender differences in RA strain. In contrast to our findings, they noted RA strain to be higher in females and showed an age-related decline in both genders.[39,40] The differences in analysis software and technique used in these studies may explain the discordances in results. Further studies are warranted to confirm our findings in a larger African population and also to further assess RALS.

We have confirmed the utility of RALS as a marker of subclinical disease in this population, as we did not see changes in RAVI with age but noted a trend towards lower RALS with increasing age. Therefore, RALS may anticipate RA impairment in disease prior to changes in traditional parameters such as RA size and volume. This may assist in earlier diagnosis of disease and prompt treatment strategies at a subclinical stage of the disease.

Study limitations

A minority of subjects were older than 60 years, due to the lower life expectancy in the 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).[41] RA strain measurement values vary with different vendors and software packages and this needs to be taken into consideration when defining normal values. Exercise capacity of the study subjects was not assessed to unmask subclinical diastolic dysfunction and symptoms.

Since this was a secondary data analysis, sample size was restricted to what was collected in the parent study. A larger sample size might have been able to detect finer differences. The majority of the patients were obese or overweight and this is a reflection of the current 'normal' South African population. As this was a retrospective sub-study analysis, we did not have access to blood tests to screen for diseases, as these were not performed as part of the main study.

Conclusion

We have presented the first normative values for RALS in a sub-Saharan African population. The normative data on RA strain and volumes according to age will help in differentiating normal from abnormal RA function and thus help in cardiovascular disease risk stratification in this population. Furthermore, this study provides a platform for future larger studies on RALS.

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