Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.journals.elsevier.com/ijc-heart-and-vasculature

Prevalence and significance of isolated left ventricular non-compaction phenotype in normal black Africans using echocardiography ☆

Samantha Nel [a], Bijoy K. Khandheria [b,*], Elena Libhaber [a], Ferande Peters [a,c], Claudia Ferreira dos Santos [a,c], Hiral Matioda [a], Sacha Grinter [a], Nirvathi Maharaj [a,c], Mohammed R. Essop [a]

[a] Division of Cardiology, Chris Hani Baragwanath Academic Hospital and University of the Witwatersrand, R68 Old Potchefstroom Road, PO Bertsham, Johannesburg 2013, South Africa
[b] Aurora Cardiovascular and Thoracic Services, Aurora Sinai/Aurora St. Luke's Medical Centers, University of Wisconsin School of Medicine and Public Health, Marcus Family Fund for Echocardiography (ECHO) Research and Education, 2801 W. Kinnickinnic River Parkway, Ste. 880, Milwaukee, WI, 53215, USA
[c] Cardiovascular Pathophysiology and Genomics unit, University of the Witwatersrand, 7 York Road, Parktown 2193, Johannesburg, South Africa

ABSTRACT

Background: Several large, prospective screening studies of predominantly Caucasian patients have suggested that hypertrabeculation may not necessarily be pathologic unless there is concomitant left ventricular (LV) dysfunction, LV dilatation, history of arrhythmia, family history, or characteristic gene mutations. This conundrum may be magnified in blacks, in whom hypertrabeculation and LV hypertrophy is more common. We therefore investigated the frequency of hypertrabeculation/isolated LV non-compaction (ILVNC) phenotype in normal black Africans and evaluated LV function using sensitive measures of deformation and twist.
Methods: Two hundred and fifty-three volunteers were recruited and evaluated according to strict inclusion and exclusion criteria. Their mean age was 36.3 ± 12.2 years.
Results: Trabeculations were found in 12 (4.74%) participants. Three (1.2%) subjects had ≥ 4 LV trabeculations. The LV apex was the most common anatomical site for the location of trabeculations. Subjects with trabeculations were more likely to be males of a younger age, and had greater LV end-diastolic and end-systolic parameters and lateral e'. However, 0.8% of the population fulfilled the Stollberger criteria, and none fulfilled the Jenni, Milwaukee, or Baragwanath criteria. All subjects in this study had normal rotation patterns with no differences in rotational parameters or net twist.
Conclusions: Trabeculations may be found as a normal variant in black Africans. Assessing trabeculations alone may infer ILVNC; however, utilizing the more comprehensive ILVNC criteria enables differentiation of a possible LVNC phenotype. Normal individuals with hypertrabeculation have normal LV function and normal rotation patterns, with no differences in rotational parameters or net twist.

1. Introduction

Two-dimensional (2D) echocardiography is the basis for identifying isolated left ventricular noncompaction (ILVNC). Currently there are several echocardiographic criteria used to diagnose ILVNC [1]. The major problems with utilising echocardiography for the diagnosis relate to the lack of a gold standard to compare these criteria, the poor reproducibility when applying these criteria, and that in some instances the phenotype of ILVNC has been observed in clinical scenarios that may not imply disease, such as in athletes and pregnant women [2–4]. In patients with normal ejection fraction (EF), the differentiation of ILVNC from a normal variant can be challenging.

The potential impact of race on ILVNC diagnosis has been highlighted in several studies that suggest that trabeculations may be more common in individuals of African ancestry [1,2,5–7]. Among African individuals, it is possible to differentiate normal individuals from patients with ILVNC with a low EF by using a more comprehensive set of echocardiographic criteria (Baragwanath criteria),

which we have utilised, that incorporates aspects of both the Jenni and Stollberger criteria [8]. In the real world, however, it can be challenging to separate ILVNC phenotype from normality when confronted with individuals with a normal EF if not systematically studied. In clinical practice at Chris Hani Baragwanath Hospital (CHBH), we have utilised functional parameters such as tissue Doppler e' and left ventricular (LV) twist patterns (presence/absence of rigid body rotation) in conjunction with previously proposed comprehensive CHBH criteria to aid in this differentiation. This approach is feasible but remains untested.

A recent analysis of normal individuals suggested that racial differences were important reasons for variability in echocardiographic parameters of the LV [9–12]. Thus, there is the possibility that the previously observed frequency of trabeculations in individuals of African origin may represent racial variability. Hence, we undertook this study to determine what percentage of individuals satisfied the conventional echocardiographic criteria in current clinical use. A second aim was to determine whether individuals with a possible ILVNC phenotype have functional abnormality such as abnormal relaxation and abnormal LV twist patterns.

2. Methods

This prospective cross-sectional study was conducted at CHBH. Subjects were recruited from unrelated hospital staff and volunteers following an advertisement about this study. A total of 300 subjects were screened by clinical evaluation, electrocardiography (ECG), and echocardiography. Subjects were included in the study based on 1) absence of cardiac-related symptoms, 2) normal blood pressure ($\leq$140/90 mmHg), 3) absence of cardiovascular/systemic disease based on clinical evaluation, and 4) presence of sinus rhythm (heart rate between 50 and 90 beats/min). Subjects were excluded based on 1) use of any chronic medication, 2) abnormal 12-lead ECG, 3) abnormal findings on echocardiogram, or 4) suboptimal image quality on the echocardiogram. All subjects who fulfilled the inclusion and exclusion criteria were enrolled in the study after providing informed consent. The final sample comprised 253 individuals, who then underwent comprehensive echocardiography according to a standardised protocol. The study was approved by the University of the Witwatersrand ethics committee (M110204) and is in accordance with the principles outlined in the Declaration of Helsinki.

2.1. Echocardiography

All echocardiograms were obtained according to a standardised protocol on a Philips iE33 machine (Amsterdam, The Netherlands) equipped with an S5-1 transducer that transmits a frequency of 1.7 MHz and receives a frequency of 3.4 MHz. All data were transferred to an Xcelera workstation (Philips) and analysed offline.

All echocardiographic measurements were averaged from three heartbeats. Measurements relating to chamber size and function were performed in accordance with the American Society of Echocardiography (ASE) chamber quantification guidelines of 2015 [13]. Parameters relating to LV diastolic function were measured using pulsed-wave Doppler and tissue Doppler and interpreted according to the consensus ASE/European Association of Echocardiography (EAE) guidelines for the evaluation of LV diastolic function by echocardiography [14]. LVEF was calculated using the modified Simpson's method [13]. LV mass was calculated using the formula:

$$\text{LVmass} = 0.8 \times \{1.04[([\text{LVEDD} + \text{IVSd} + \text{PWd}]^3 - \text{LVEDD}^3)]\} + 0.6.$$

Relative wall thickness was calculated using the formula:

$(2 \times \text{PWd}) \div \text{LVEDD}$.

(LVEDD, LV end-diastolic diameter; IVSd, interventricular septal wall thickness in diastole; PWd, posterior wall thickness in diastole.)

2.2. Speckle-tracking analysis

The 2D speckle-tracking images were acquired at a frame rate of 50–80 frames per second, during sinus rhythm, with < 10% variability in heart rate. Parasternal short-axis images at the level of the LV base, showing the tips of the mitral valve leaflets, and a short-axis image at the apical LV level were used to assess LV rotation. The tracking points were placed on an end-diastolic frame in each parasternal short-axis image. In areas of hypertrabeculation, the tracking points were placed in the compacted part of the muscle. Tracking points were separated about 60 degrees from one another to fit the total LV circumference. After positioning these points, the program tracked them. In keeping with the standard ASE/EAE consensus document on myocardial deformation, counter-clockwise rotation was assigned a positive value and clockwise rotation a negative value [13]. The peak systolic rotation was measured at the apex. Thereafter, the basal rotation at a time isochronous to that of the peak apical rotation was measured. Net instantaneous twist was then calculated as peak apical rotation minus basal rotation [1]. In addition to quantifying apical and basal rotation, we analysed the direction of rotation during the ejection phase of systole and identified rotation as either normal or having evidence of rigid body rotation, which was either entirely counter-clockwise or clockwise at both the base and apex during the ejection phase of systole.

2.3. Echocardiographic assessment for established ILVNC criteria in the normal population

The presence or absence of trabeculations was documented by analysing the short-axis and apical long-axis views of the LV. An abnormal trabeculation was identified if it occurred distal to the papillary muscles, did not have any attachment to the interventricular septum, and was seen in both apical and short-axis views. Thereafter, the presence of bilayered myocardium was documented and the noncompacted dimension and compacted dimension were measured in systole and diastole using short-axis images. The ratio of noncompacted to compacted (NC/C) endocardium was then calculated in systole and diastole. An analysis using the Jenni, Stollberger, and Milwaukee criteria was performed [1]. In addition, we applied the comprehensive published criteria used previously at CHBH, which has been named the Baragwanath criteria, to differentiate ILVNC from normal individuals [8].

Baragwanath criteria

(1) Ratio of NC/C measured at end systole > 2.
(2) Presence of $\geq$ 3 prominent trabeculations in the LV apex that did not originate from the septum.
(3) Deep intertrabecular recesses that filled with blood from the ventricular cavity as visualised on colour Doppler ultrasound [8].

Jenni criteria

(1) Bilayered myocardium consisting of NC/C > 2.
(2) Predominant location of the pathology is midlateral, midinferior, and apex.
(3) Evidence of intertrabecular recesses filled with blood from the LV cavity.

(4) Acquisition of short-axis image, with a measurement of the NC/C ratio performed at end-systole [1].

Stollberger criteria

(1) Four or more trabeculations seen protruding from the LV wall, located apically to the papillary muscles and visible in one imaging plane.
(2) Trabeculations with the same echogenicity as the myocardium and synchronous movement with ventricular contractions.
(3) Perfusion of the intertrabecular recesses from the LV cavity.
(4) Differentiation between false chords, aberrant bands, and trabeculations in the apical four-chamber view, as well as atypical views to obtain the best image quality [1,15].

Milwaukee criteria

(1) Evaluation of the trabeculation sizes in multiple imaging windows, at different ventricular levels, throughout the cardiac cycle.
(2) Identification of the bilayered myocardium (C and NC) in the short-axis views, the mid and apical levels, the apical two- and four-chamber views, and the apical long-axis view.
(3) Measurement of NC/C > 2 in diastole in the short-axis view [1].

Intertrabecular spaces were defined as deep myocardial recesses that communicate with the ventricular cavity only, and not with the coronary circulation [16]. False tendons were defined as linear fibromuscular structures, <3 mm, seen across the LV cavity, usually inserting into a papillary muscle and without attachment to the mitral valve (Supplementary Figure 1) [17,18]. LV membranes or LV bands were identified as discrete fibromuscular structures, also seen across the LV cavity without insertion into a papillary muscle (Supplementary Figures 2, 3) [19].

2.4. Statistics

Statistical analyses were performed using a Dell statistical program, Statistica 13.0. Results are presented as mean ± standard deviation for continuous variables or frequency and percentage for categorical variables. Differences between the two groups were assessed using the independent *t*-test or Mann-Whitney test if variables were not normally distributed. Categorical data were compared with a Fisher's exact test. Probability (P) value < 0.05 was considered statistically significant.

3. Results

The clinical and echocardiographic characteristics of the study population, as well as a comparison by sex, are presented in Table 1. The mean age of the 253 participants was 36.3 ± 12.2 years, with 150 (59.3%) female participants. All patients had diastolic pulsed-wave and tissue Doppler measurements within the normal accepted guideline range. Males had higher systolic blood pressure, body surface area, end-diastolic and end-systolic dimensions and volumes, LV mass, left atrial volumes, and lateral e'.

3.1. LV trabeculations

Trabeculations were found in 12 (4.74%) participants (Table 2). Ten of the 12 participants with trabeculations were male. Three

Table 1
Clinical and echocardiographic characteristics of the overall population, and males vs. female.

Variables	Overall (n = 253)	Females (n = 150)	Males (n = 103)	P values
Clinical parameters				
Age, years	36.3 ± 12.2	37.1 ± 12.5	35.0 ± 11.6	0.23
Systolic blood pressure, mm Hg	121 ± 12	119 ± 12	124 ± 11	**0.001**
Diastolic blood pressure, mm Hg	76 ± 10	75 ± 10	77 ± 9	0.17
Pulse, bpm	76 ± 12	79 ± 11	72 ± 12	**<0.0001**
BSA, m^2	1.8 ± 0.2	1.8 ± 0.2	1.9 ± 0.2	**0.0002**
Body mass index, kg/m^2	27.9 ± 6.2	29.6 ± 6.4	25.5 ± 5.0	**<0.0001**
Two-dimensional LV measurements				
LV end-diastolic diameter, mm	43.0 ± 4.5	41.9 ± 4.4	44.5 ± 4.3	**<0.0001**
LV end-systolic diameter, mm	28.2 ± 3.9	27.2 ± 3.4	29.1 ± 3.7	**0.0001**
Septal wall thickness, mm	8.9 ± 1.5	8.8 ± 1.5	9.1 ± 1.5	0.06
Posterior wall thickness, mm	8.7 ± 1.3	8.6 ± 1.4	9.0 ± 1.3	**0.008**
Relative wall thickness, ratio	0.40 ± 0.83	0.37 ± 0.09	0.37 ± 0.81	0.83
End-diastolic volume, mL	88.5 ± 23.6	85.0 ± 21.9	93.6 ± 25.2	**0.002**
End-diastolic volume indexed to BSA, m^2	48.6 ± 12.2	47.7 ± 11.8	50.7 ± 12.1	**0.03**
End-systolic volume, mL	33.8 ± 9.9	31.9 ± 9.9	36.6 ± 10.8	**0.0002**
End-systolic volume indexed to BSA, m^2	18.6 ± 5.1	17.9 ± 4.6	19.7 ± 5.5	**0.0049**
Ejection fraction, %	62.3 ± 5.7	62.7 ± 5.7	61.7 ± 5.6	0.13
Left atrial volume indexed to BSA, m^2	18.1 ± 5.5	18.8 ± 5.4	17.1 ± 5.5	**0.01**
LV mass, grams	124.3 ± 32.5	117.1 ± 30.7	134.8 ± 32.3	**<0.0001**
LV mass/BSA index, kg/m^2	68.2 ± 15.9	65.5 ± 15.4	72.1 ± 15.9	**0.002**
LV diastolic parameters				
E peak, m/s	80.5 ± 16.9	81.9 ± 17.9	78.6 ± 15.3	0.09
A peak, m/s	57.4 ± 14.5	59.6 ± 15.5	54.2 ± 12.3	**0.003**
E/A, ratio	1.5 ± 0.4	1.4 ± 0.4	1.5 ± 0.44	0.49
Deceleration time, ms	155.7 ± 80.5	160.6 ± 92.9	148.7 ± 57.6	0.70
Medial e', m/s	10.0 ± 6.6	10.1 ± 8.3	9.9 ± 2.4	0.44
Medial a', m/s	8.0 ± 1.9	8.0 ± 1.9	8.1 ± 1.9	0.73
Lateral e', m/s	14.2 ± 3.4	13.8 ± 3.6	14.7 ± 3.1	**0.04**
Lateral a', m/s	7.8 ± 2.2	7.9 ± 2.4	7.7 ± 2.0	0.47

Data presented as mean ± standard deviation or number (percentage).
Bold represents statistical significance.
*LV diastolic parameters were measurable in only 149 females and 102 males.
BSA, body surface area; LV, left ventricular; e', late diastolic velocity; a', early diastolic velocity.

Table 2
Subjects with left ventricular trabeculations.

Trabeculations (n = 12)	n (%)
≥4	3 (1.18%)
3	6 (2.37%)
2	2 (0.79%)
1	1 (0.39%)
Predominant location of trabeculations	
Apex only	9 (3.56%)
Mid-lateral wall only	1 (0.39%)
Mid-inferior wall only	0 (0%)
Dual segments	
Apex/mid-lateral walls	1 (0.39%)
Apex/mid-inferior walls	1 (0.39%)

(1.2%) subjects had ≥ 4 LV trabeculations. The LV apex was the most common anatomical site for the location of trabeculations. False tendons were identified in 22 (8.7%) subjects (Supplementary Figure 1), and a further 19 (7.5%) subjects had LV membranes/ bands (Supplementary Figures 2, 3). A comparison between subjects with trabeculations and those without trabeculations revealed that the subjects with trabeculations were of a younger age and had greater LV end-diastolic and end-systolic diameters and lateral e'. LV mass indexed to body surface area and LV volumes indexed to body surface area were no different between the two groups (Table 3).

3.2. ILVNC criteria

No subjects fulfilled the Jenni, Milwaukee, or Baragwanath criteria, and only 2 (0.8%) fulfilled the Stollberger criteria. The two participants satisfying the Stollberger criteria had ≥ 4 trabeculations identified in the apical three-chamber view. Nine of the 12 individuals with trabeculations had a systolic compacta thickness ≤ 8 mm. The two participants satisfying the Stollberger criteria had compacta thicknesses of 8.1 mm and 8.6 mm. From the group of participants with trabeculations, the overall mean NC/C systolic ratio was 1.5 ± 0.4 and the mean NC/C diastolic ratio was 2.7 ± 0.1.

3.3. LV rotation patterns

Of the 253 subjects, 37 could not be analysed for rotation patterns due to technical difficulties such as suboptimal images and off-axis imaging. All remaining subjects in this study whose images could be analysed had normal twist patterns in systole with the base moving clockwise and the apex counterclockwise. The LV apical and basal rotation and net twist were not different between those with trabeculations and those without trabeculations (Table 4).

4. Discussion

The main findings of this study were as follows: 1) trabeculations were found in 4.74% of participants, 2) no subjects fulfilled the Jenni, Milwaukee, or Baragwanath criteria, and only 2 (0.8%) fulfilled the Stollberger criteria, and 3) there were no differences in rotation patterns, quantitative LV rotation parameters, or LV twist between subjects with and without trabeculations.

In this normal cohort of African patients, almost 20% had a combination of trabeculations, false tendons, and LV bands. However, true trabeculations as defined in this study occurred in only 4.74% of patients. Gati et al. found that in their control group, which comprised both Caucasian and Afro-Caribbean subjects, 7% of subjects had trabeculations [2]. In contrast, Tamborini et al. used echocardiography in a Caucasian population and found in their

Table 3
Clinical and echocardiographic characteristics of participants with LV trabeculations vs. non-trabeculation LV.

Variables	Trabeculations (n = 12)	Non-trabeculation (n = 241)	P value
Clinical parameters			
Age, years	25.1 ± 8.5	36.8 ± 12.1	**<0.001**
Males	10 (83.3%)	93 (38.6%)	0.02
Systolic blood pressure, mm Hg	123 ± 11	121 ± 13	0.66
Diastolic blood pressure, mm Hg	71 ± 10	76 ± 10	0.05
Pulse, bpm	71 ± 12	77 ± 12	0.08
BSA, m²	1.7 ± 0.14	1.8 ± 0.2	0.23
Body mass index, kg/m²	25.3 ± 5.2	28.1 ± 6.2	0.09
Two-dimensional LV parameters			
LV end-diastolic diameter, mm	45.6 ± 4.0	42.8 ± 4.5	**0.04**
LV end-systolic diameter, mm	30.6 ± 3.4	27.9 ± 3.9	**0.02**
Septal wall thickness, mm	9.2 ± 1.4	8.9 ± 1.4	0.43
Posterior wall thickness, mm	8.8 ± 1.4	8.8 ± 1.3	0.99
Relative wall thickness, ratio	0.4 ± 0.1	0.4 ± 0.1	0.15
End-diastolic volume, mL	92.5 ± 14.4	88.3 ± 24.0	0.38
End-diastolic volume indexed to BSA, m²	53.2 ± 8.9	48.7 ± 12.1	0.11
End-systolic volume, mL	34.2 ± 8.3	33.8 ± 10.1	0.78
End-systolic volume indexed to BSA, m²	19.7 ± 4.9	18.5 ± 5.1	0.43
Ejection fraction, %	63.6 ± 6.8	62.2 ± 5.6	0.54
Left atrial volume, mL	35.6 ± 9.5	32.6 ± 10.3	0.33
Left atrial volume indexed to BSA, m²	20.4 ± 5.3	17.9 ± 5.5	0.13
LV mass, grams	141.2 ± 32.2	123.4 ± 32.3	**0.002**
LV mass indexed to BSA, m²	75.0 ± 20.1	65.4 ± 16.4	0.12
LV diastolic parameters			
E peak, m/s	87.9 ± 13.0	80.1 ± 17.0	0.08
A peak, m/s	54.2 ± 14.9	57.6 ± 14.4	0.39
E/A, ratio	1.7 ± 0.44	1.5 ± 0.44	0.05
Deceleration time, ms	178.4 ± 106.7	153.9 ± 79.6	0.27
Medial e', m/s	10.8 ± 1.7	9.9 ± 6.7	0.08
Medial a', m/s	7.2 ± 1.9	8.1 ± 1.9	0.16
Lateral e', m/s	16.9 ± 2.7	14.0 ± 3.4	**<0.01**
Lateral a', m/s	8.0 ± 2.5	7.8 ± 2.2	0.79

Data presented as mean ± standard deviation or number (percentage).
Bold indicates statistical significance.
BSA, body surface area; LV, left ventricular.

Table 4
Rotation patterns.

Variables	Overall * (n = 216)	Trabeculated (n = 12)	Non-trabeculated (n = 204)	P value
Apical rotation	5.99°±3.12°	5.55°±2.17°	6.02°±3.17°	0.61
Basal rotation	−5.19°±3.14°	−5.91°±2.97°	−5.15°±3.15°	0.41
Net twist	11.24°±4.25°	11.45°±3.46°	11.23°±4.30°	0.86

*Of the 253 patients recruited, rotation patterns were measurable in only 216 patients.

normals that 40.8% with abnormal images had a combination of false tendons and trabeculation [19]. Our finding of 4.74% having ≥ 4 trabeculations is concordant with the findings of Boyd et al., who at pathology found that 4% of normal individuals had ≥ 4 trabeculations [20]. At autopsy in hearts free of cardiac disease, Boyd et al. found prominent LV trabeculations in 323 of 474 (68%) specimens. "Prominent trabeculation" was defined as "discrete muscle bundles>2 mm in diameter [20]."

In this study, all observed differences in LV and LA parameters can be attributed to the relative predominance of the male sex,

as shown in Table 1. Subjects with trabeculations appeared to have a trend suggesting greater LV dilation (trend toward larger LVEDD and LVEDV) and higher LV mass. This may suggest that some degree of difference in LV volume overload was present in the group with trabeculation. However, all subjects with trabeculation had normal systolic function and LV rotation patterns. Thus, subjects with a potentially abnormal or variant phenotype in this study had no functional abnormality. This implies that trabeculations may represent a normal anatomical variant and should be interpreted as a normal finding on echocardiography when associated with normal LV function.

We previously showed that in 54 normal controls no individuals satisfied the Baragwanath criteria for ILVNC [8]. A major finding of that study of normal African individuals was that some individuals may have morphological features very suggestive of LVNC phenotype if the Stollberger criteria are used whereas no individuals satisfied the other criteria tested. Gati et al. found that none of their controls of African descent had LVNC [2]. In contradistinction, Kohli et al. showed that more black individuals in their control groups fulfilled echocardiographic criteria for noncompaction than Caucasian individuals (13.3% vs. 3.3%) [7]. There are several factors that may relate to these diverse findings. Firstly, the study of individuals of African descent may differ because the African population is not a homogenous population and may vary with regard to genetics, body surface area, and even variability of echocardiographic parameters [10]. The latter was demonstrated in the Echocardiographic Normal Ranges Meta-Analysis of the Left Heart (EchoNoRMAL) study, in which left atrial diameters were greater in Afro-Caribbean and lesser in African subjects [10].

A second reason for the variability of results is the non-uniformity of LVNC criteria used. Not only do the studies mentioned vary with regard to the criteria used, but, since the publication of Kohli et al. in 2008, the individual criterion themselves have been modified—including those utilised by Jenni et al. and Stollberger et al [5,16–18,21]. Thus, the current criteria are more similar, more encompassing, and stricter. A third reason for the discrepancy relates to echocardiography technique, which may differ with regard to protocols and imaging. In this study, all short-axis imaging was performed on axis using x-plane imaging, whereas, as acknowledged by the authors, Kohli et al., in their retrospective analysis, collected all echocardiographic data without a focus on LVNC [7]. As a result, there was the potential for short-axis views to be more oblique, increasing the likelihood of a diagnosis of LVNC. Finally, there are several other well-recognised impediments to accurate LVNC echocardiographic diagnosis, including analysis in varying imaging planes and different phases in the cardiac cycle as well as the lack of reproducibility of criteria [22].

From the aforementioned discussion it is evident that abnormal LV phenotype with either increased trabeculation or even a phenotypic mimicker of LVNC cardiomyopathy exists in normal individuals. We propose the following approach to the diagnosis of possible LVNC in Africans using echocardiography [2,11,13,23–25]. Firstly, exclude adaptive (athletes and pregnancy) and pathological states (bicuspid aortic valve and sickle cell anaemia) in which LVEF may be normal. Secondly, establish that the patient truly is normal using ASE reference values for LV size, geometry, and systolic and diastolic function. In this manner cardiomyopathy associated with LVNC phenotype, such as hypertrophic cardiomyopathy or Fabry disease, can be excluded. Thereafter, critical echocardiographic analysis of images in long- and short-axis views should be performed employing simultaneous biplane imaging to ensure that the short axis is minimally oblique. If trabeculations do exist, ensure that they are not mimickers such as false tendons and then apply either the Jenni or CHBH criteria. If the technology is available, ensure that the LV twist pattern is normal. Normality may be proposed if the individual has some phenotypic features

consistent with LVNC but does not fulfill the proposed echocardiographic criteria and has normal functional parameters. In those who do fulfill the echocardiographic criteria but have normal functional parameters and no family history of LVNC, serial observation is required even though this probably represents normality.

4.1. Limitations

There are several limitations to our study that may be overcome in future studies. Firstly, older individuals (>65) were underrepresented owing to difficulty recruiting normal healthy older individuals in a peri-urban African environment; therefore, the results may only pertain to individuals between the ages of 20 and 60. Furthermore, recruitment was on an ad hoc basis and thus resulted in an uneven age and sex distribution. A second important limitation is that subclinical disease was not excluded because haemoglobin, thyroid hormone, glucose, and lipid levels were not assessed. A third limitation was that demographic data that may be associated with being overweight or obese, such as smoking, education level, and degree of physical activity, were not systematically recorded. No systematic data were collected about the degree of exercise performed by individuals, but there were no elite/competitive athletes. Lastly, absolute LV rotation and twist values may vary between vendors, and as a result, the quantitative values used in this study may not be applicable to other vendors' technology.

5. Conclusion

The results of this study suggest that although hypertrabeculation is common, all current diagnostic criteria are useful in excluding the diagnosis of ILVNC. The presence of normal measures of systolic and diastolic function also indicate that hypertrabeculation itself is unlikely to represent a pathologic state.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100585.

References

[1] T.E. Paterick, M.M. Umland, M.F. Jan, et al., Left ventricular noncompaction: a 25-year odyssey, J. Am. Soc. Echocardiogr. 25 (2012) 363–375.
[2] S. Gati, N. Chandra, R.L. Bennett, et al., Increased left ventricular trabeculation in highly trained athletes: do we need more stringent criteria for the diagnosis of left ventricular non-compaction in athletes?, Heart 99 (2013) 401–408.
[3] F. Andre, A. Burger, D. Lossnitzer, et al., Reference values for left and right ventricular trabeculation and non-compacted myocardium, Int. J. Cardiol. 185 (2015) 240–247.
[4] N. Kawel, M. Nacif, A.E. Arai, et al., Trabeculated (noncompacted) and compact myocardium in adults: the multi-ethnic study of atherosclerosis, Circ. Cardiovasc. Imaging 5 (2012) 357–366.
[5] F. Zemrak, M.A. Ahlman, G. Captur, et al., The relationship of left ventricular trabeculation to ventricular function and structure over a 9.5-year follow-up: the MESA study, J. Am. Coll. Cardiol. 64 (2014) 1971–1980.
[6] D. Andreini, G. Pontone, J. Bogaert, et al., Long-term prognostic value of cardiac magnetic resonance in left ventricle noncompaction: a prospective multicenter study, J. Am. Coll. Cardiol. 68 (2016) 2166–2181.

[7] S.K. Kohli, A.A. Pantazis, J.S. Shah, et al., Diagnosis of left-ventricular non-compaction in patients with left-ventricular systolic dysfunction: time for a reappraisal of diagnostic criteria?, Eur. Heart J. 29 (2008) 89–95.

[8] F. Peters, B.K. Khandheria, C. dos Santos, et al., Isolated left ventricular noncompaction in sub-Saharan Africa: a clinical and echocardiographic perspective, Circ. Cardiovasc. Imaging 5 (2012) 187–193.

[9] P. Lancellotti, L.P. Badano, R.M. Lang, et al., Normal Reference Ranges for Echocardiography: rationale, study design, and methodology (NORRE Study), Eur. Heart J. Cardiovasc. Imaging 14 (2013) 303–308.

[10] Echocardiographic Normal Ranges Meta-Analysis of the Left Heart Collaboration. Ethnic-specific normative reference values for echocardiographic LA and LV size, LV mass, and systolic function: The EchoNoRMAL Study, JACC Cardiovasc. Imaging 8 (2015) 656–665.

[11] N.S. Chahal, T.K. Lim, P. Jain, J.C. Chambers, J.S. Kooner, R. Senior, Ethnicity-related differences in left ventricular function, structure and geometry: a population study of UK Indian Asian and European white subjects, Heart 96 (2010) 466–471.

[12] E. Oechslin, R. Jenni, Nosology of noncompaction cardiomyopathy: The emperor still wears clothes!, Can. J. Cardiol. 33 (2017) 701–704.

[13] R.M. Lang, L.P. Badano, V. Mor-Avi, et al., Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, J. Am. Soc. Echocardiogr. 28 (2015) 1–39.e14.

[14] S.F. Nagueh, O.A. Smiseth, C.P. Appleton, et al., Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, J. Am. Soc. Echocardiogr. 29 (2016) 277–314.

[15] P. Luke, C. Eggett, I. Spyridopoulos, T. Irvine, A comparative analysis of British and American Society of Echocardiography recommendations for the assessment of left ventricular diastolic function, Echo. Res. Pract. 5 (2018) 139–147.

[16] C. Stollberger, J. Finsterer, Left ventricular hypertrabeculation/noncompaction, J. Am. Soc. Echocardiogr. 17 (2004) 91–100.

[17] C. Stollberger, B. Gerecke, R. Engberding, et al., Interobserver agreement of the echocardiographic diagnosis of LV hypertrabeculation/noncompaction, JACC Cardiovasc. Imaging 8 (2015) 1252–1257.

[18] C. Gebhard, B.E. Stahli, M. Greutmann, P. Biaggi, R. Jenni, F.C. Tanner, Reduced left ventricular compacta thickness: a novel echocardiographic criterion for non-compaction cardiomyopathy, J. Am. Soc. Echocardiogr. 25 (2012) 1050–1057.

[19] G. Tamborini, M. Pepi, F. Celeste, et al., Incidence and characteristics of left ventricular false tendons and trabeculations in the normal and pathologic heart by second harmonic echocardiography, J. Am. Soc. Echocardiogr. 17 (2004) 367–374.

[20] M.T. Boyd, J.B. Seward, A.J. Tajik, W.D. Edwards, Frequency and location of prominent left ventricular trabeculations at autopsy in 474 normal human hearts: implications for evaluation of mural thrombi by two-dimensional echocardiography, J. Am. Coll. Cardiol. 9 (1987) 323–326.

[21] N. Maharaj, B.K. Khandheria, F. Peters, E. Libhaber, M.R. Essop, Time to twist: marker of systolic dysfunction in Africans with hypertension, Eur. Heart J. Cardiovasc. Imaging 14 (2013) 358–365.

[22] H. Geyer, G. Caracciolo, H. Abe, S. Wilansky, S. Carerj, F. Gentile, H.-J. Nesser, B. Khandheria, J. Narula, P.P. Sengupta, Assessment of Myocardial Mechanics Using Speckle Tracking Echocardiography: Fundamentals and Clinical Applications, J. Am. Soc. Echocardiogr. 23 (4) (2010) 351–369, quiz 453-355.

[23] S.F. Saleeb, R. Margossian, C.T. Spencer, et al., Reproducibility of echocardiographic diagnosis of left ventricular noncompaction, J. Am. Soc. Echocardiogr. 25 (2012) 194–202.

[24] B.E. Stahli, C. Gebhard, P. Biaggi, et al., Left ventricular non-compaction: prevalence in congenital heart disease, Int. J. Cardiol. 167 (2013) 2477–2481.

[25] F. Peters, B.K. Khandheria, E. Libhaber, N. Maharaj, C. dos Santos, H. Matioda, M.R. Essop, Left ventricular twist in left ventricular noncompaction, Eur. Heart J.Cardiovasc. Imaging. 15 (2014) 48–55.