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ORIGINAL ARTICLE

Echocardiographic Left Ventricular Hypertrophy and Geometric Patterns in Patients with Sickle Cell Anaemia

Hypertrophie Ventriculaire Gauche et Schémas Géométriques Échocardiographiques chez les Patients Atteints de Drépanocytose

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ABSTRACT

BACKGROUND: Left ventricular hypertrophy (LVH) is a common complication in patients with sickle cell anaemia (SCA), and it has been associated with systolic and diastolic dysfunction, and sudden death. There is a wide variation in the reported prevalence of LVH in patients with SCA, partly due to the varying criteria applied, and the impact of small weight and body surface area (BSA) in SCA patients. We used four different criteria to determine echocardiographic LVH and geometric patterns in patients with steady-state SCA. Left ventricular hypertrophy was defined by LVM, LVM indexed to BSA, LVM indexed to height and LVM indexed to height$^{2.7}$ using gender-specific reference values. Left ventricular geometry was determined using LVH and relative wall thickness.

RESULTS: Eighty-two patients with steady-state SCA, aged 18years and above were studied from January 2018 to April 2018. The median [IQR] age of the patients was 23 [10] years. Forty-seven (57.3%) were females. The prevalence of LVH was highest when LVM was indexed to BSA (80.5%), followed by LVM indexed to height (73.2%). Comparable prevalences of 68.3% and 69.5% were observed using LVM and LVM indexed to height$^{2.7}$, respectively. The prevalence of LVH was similar in males and females for all the criteria.

CONCLUSION: The prevalence of LVH is high among patients with steady-state SCA irrespective of the criteria applied. The most prevalent geometric pattern was eccentric LVH. Indexing to BSA might result in over-estimation of LVH given the relatively small BSA in patients with SCA. Indexing to height$^{2.7}$ might give a more accurate estimate of LVH. **WAJM 2023; 40(2): 137–142.**

Keywords: Left ventricular hypertrophy; Left ventricular geometry; Sickle cell disease; Echocardiography.

RÉSUMÉ

CONTEXTE: L'hypertrophie ventriculaire gauche (HVG) est une complication fréquente chez les patients atteints d'anémie falciforme (ACS), et elle a été associée à un dysfonctionnement systolique et diastolique, ainsi qu'à une mort subite. La prévalence de l'HVG chez les patients atteints d'anémie falciforme varie considérablement, en partie à cause des différents critères appliqués et de l'impact du petit poids et de la surface corporelle (BSA) des patients atteints d'anémie falciforme. Nous avons utilisé quatre critères différents pour déterminer l'HVG échocardiographique et les schémas géométriques chez les patients atteints d'ACS à l'état stable. L'hypertrophie ventriculaire gauche a été définie par la MVL, la MVL indexée sur la surface corporelle, la MVL indexée sur la taille et la MVL indexée sur la taille2,7 en utilisant des valeurs de référence spécifiques au sexe. La géométrie du ventricule gauche a été déterminée en utilisant l'HVG et l'épaisseur relative de la paroi.

RÉSULTATS: Quatre-vingts deux patients atteints d'ACS à l'état stable, âgés de 18 ans et plus ont été étudiés de janvier 2018 à avril 2018. L'âge médian [IQR] des patients était de 23 [10] ans. Quarante-sept (57,3 %) étaient des femmes. La prévalence de l'HVG était la plus élevée lorsque la MVL était indexée sur la BSA (80,5 %), suivie de la MVL indexée sur la taille (73,2 %). Une prévalence comparable de 68,3 % et 69,5 % a été observée en utilisant la MVL et la MVL indexée sur la taille2,7, respectivement. La prévalence de l'HVG est similaire chez les hommes et les femmes pour tous les critères.

CONCLUSION: La prévalence de l'HVG est élevée chez les patients atteints d'ACS à l'état stable, quel que soit le critère appliqué. Le modèle géométrique le plus répandu est l'HVG excentrique. L'indexation à la BSA pourrait entraîner une surestimation de l'HVG étant donné la BSA relativement faible chez les patients atteints d'ACS. L'indexation à la taille 2,7 pourrait donner une estimation plus précise de l'HVG. **WAJM 2023; 40(2): 137–142.**

Mots clés: Hypertrophie ventriculaire gauche; Géométrie ventriculaire gauche; Drépanocytose ; Échocardiographie.

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Abbreviations: ASE, American Society of Echocardiography; **BMI,** Body Mass Index; **BSA,** Body Surface Area; **IQR,** Interquartile Range; **LV,** Left Ventricle; **LVED,** Left Ventricular End Diastolic Diameter; **LVES, Left Ventricular End Systolic; LVH,** Left Ventricular Hypertrophy; **LVM,** Left Ventricular Mass; **LVMI,** Left Ventricular Mass Index; **LVPWD,** Left Ventricular Posterior Wall in Diastole; **RWT,** Relative Wall Thickness; **SCA,** Sickle Cell Anaemia.

INTRODUCTION

Cardiac abnormalities are common in sickle cell disease (SCD), especially left ventricular hypertrophy (LVH) which is an important cause of morbidity and mortality.[1,2] The chronic anaemia associated with SCD results in increased heart rate and cardiac output, giving rise to progressive dilatation of the left ventricle (LV) and increase in left ventricular mass (LVM). Compensatory hypertrophy of the LV occurs as a response to the increased wall stress on the myocardium.[3] Left ventricular mass is a reliable and independent predictor of cardiovascular events and premature death in the general population.[4] A 40% rise in the risk of adverse cardiovascular events was associated with every 39g increase in LV mass in the Framingham study.[5] On the other hand, a low traditional cardiovascular risk factor profile in young adults has been associated with a lower LVM.[6]

Assessment of LVM has an established place in cardiovascular risk stratification and detection of subclinical disease.[7] Combination of LVM and relative wall thickness can be used to determine the different left ventricular geometry. In the non-sickle cell population, abnormal left ventricular geometric pattern confers additional prognostic information about cardiovascular risk[4,8,9] with the worst outcome associated with concentric hypertrophy followed by eccentric hypertrophy.[10] It is not clear if the same prognostic effect is applicable in the SCD population. Echocardiography is a reliable non-invasive method of measuring LVM and diagnosing LVH. It is relatively cheap and readily available even in poor resource centers.[11–13] However, several factors have been shown to impact on echocardiography-derived LVM including, age, gender, body size, exercise, and loading conditions; and this can in turn affect the assessment of LVH.[14–17]

Reports from different studies show a wide variation in the prevalence of LVH using echocardiography, due in part to the variation in the criteria and cut-off values employed in defining LVH and left ventricular geometric patterns.[18–20] In order to standardize the values, different anthropometric parameters, such as weight, BSA, height, height raised to allometric power 2.7, have been used to normalize echocardiography-derived LVM.[4,21] Given the high rate of cardiac disorders in SCD[22,23] and the clinical importance of LVM, detection of LVH is an important component of evaluating patients with SCD.[24] The aim of this study was to determine the prevalence of LVH using four criteria and cut-off values (left ventricular mass, left ventricular mass indexed to height, left ventricular mass indexed to height to the allometric power of 2.7 and left ventricular mass indexed to BSA), and the pattern of left ventricular geometry in patients with SCA.

METHODS

Study Design

The study was a cross-sectional study carried out at the haematology out-patient clinic of the University of Maiduguri Teaching Hospital over a four-month period from January to April 2018. Eighty-two patients with confirmed sickle cell anaemia in steady state, aged 18years and above and presenting for routine follow-up were enrolled following informed consent.

Clinical Evaluation

Baseline clinical and demographic data were obtained using an investigator-administered questionnaire. Weight (in light clothing) and height (without cap/ head gear/shoes) were measured using a stadiometer. Body mass index (BMI) was calculated using the formula = Weight (in kg)/ (height in m)^2. Body surface area was calculated using the formula of Dubois.[25] Complete cardiovascular examination was carried out prior to doing echocardiography.

Echocardiography

Transthoracic echocardiography was performed by a single examiner following the American Society of Echocardiography (ASE) recommendations.[26] From Mmode, the following measurements were made at end-diastole: left ventricular end-diastolic diameter (LVEDD), interventricular septal thickness and left ventricular posterior wall (LVPW) thickness. Left ventricular mass was calculated using Devereux method and left ventricular mass index (LVMI) obtained by dividing LVM by BSA.[7] Left ventricular hypertrophy was defined by LVM, LVMI, LVM indexed to height and LVM indexed to height$^{2.7}$ using gender-specific reference values (Table 1). Relative wall thickness (RWT) was defined as (LVPW × 2) / LVEDD. Four mutually exclusive left ventricular geometric patterns (Table 1) were defined in accordance with ASE guideline.

Statistical Analysis

Statistical analysis was performed with SPSS 20.0 (IBM, Chicago, Il, USA). Quantitative data were expressed as median [interquartile range] while qualitative data were expressed as counts (percentages). Categorical data were compared using Fisher's exact test. A p value of < 0.5 was considered significant.

RESULTS

Eighty-two steady-state HbSS patients, comprising 47 (57.3%) females and 35 (42.7%) males were studied. Their median age was 23. Clinical and anthropometric variables of the patients are illustrated in Table 2. The prevalence of LVH using LVM indexed to BSA and LVM indexed to height were 80.5% and 73.2%, respectively. Comparable prevalences of 68.3% and 69.5% were observed using LVM and LVM indexed to height$^{2.7}$, respectively. The prevalence of LVH was similar in males and females for all the criteria (Table 3). Abnormal LV geometry was observed in 71.95%. Eccentric and concentric LVH were observed in 37.81% and 31.70%, respectively, while 2.44% had concentric remodeling (Figure 1). Eccentric hypertrophy was significantly higher in the female gender while the two patients with concentric remodeling were both males.

DISCUSSION

This study is the first to determine prevalence of LVH in steady-state SCA patients using multiple criteria in northeastern Nigeria. Our results showed a high prevalence of LVH (69%–80%) irrespective of the criteria applied, in keeping with findings from other studies.[13,19,20,27] We observed that the highest prevalence of LVH was demon-

Table 1: Definition of Left Ventricular Hypertrophy and Geometric Pattern

Indices	Male	Females	Reference
LVM	≥225	≥163	
LVMI (g/m^2)	>115	>95	Koren *et al* (1991)
LVM/height (g/m)	≥127	≥100	Levey D *et al* (1987)
LVM/height$^{2.7}$ (g/m$^{2.7}$)	>55	>44	De Simone *et al* (1992)
LV Mass	**RWT**	**Geometric Pattern**	
Normal	<0.42	Normal	
Increased	≥0.42		Concentric LVH
Increased	≤0.42	Eccentric LVH	
Normal	≥0.42	Concentric Remodelling	

LV, Left Ventricular; LVMI, Left Ventricular Mass Index; LVM, Left Ventricular Mass; RWT, Relative Wall Thickness.

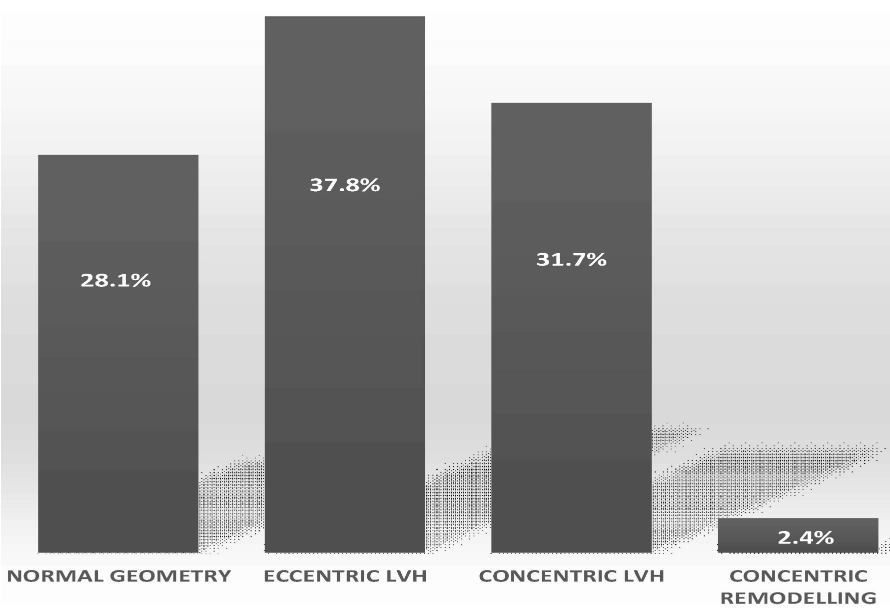

Fig. 1: Pattern of Left Ventricular Geometry. LV, Left Ventricular; LVH, Left Ventricular Hypertrophy.

strated when LVM was indexed to BSA (80.3%). Of the numerous methods for normalization of LVM, indexing to BSA is the most commonly used. This method has shown strong statistical correlation with LVM than height, and reduces variability resulting from body size and gender.[26,28] LVM indexed to BSA has been shown to minimize the effect of obesity on LVH, and therefore underestimates the prevalence of obesity-related LVH.[29,30] Body size has been shown in several reports to be an important determinant of LVM, and amongst the various measures of body size, lean body size is closely related to LVM.[31,32] Given the relatively small size and BSA in patients with SCA,[27] this method may result in over-estimation of the prevalence of LVH in this population.

Height-based indexation method may give more appropriate assessment of LVH, since this method is not influenced by body size or surface area. Using two different height indexation methods in this report, the prevalence rates for LVH were 73.6% (LVM indexed to height) and 69.5% (LVM indexed to height$^{2.7}$), respectively. Normalization of LVM to height raised to allometric power of 2.7 is associated with less variation of LVM amongst normal persons and shows better predictive value for CVD events.[14] Our result from the height-based indexation methods (i.e., 69.5% and 73.6%) was comparable to the result obtained when there was no correction for LVM (68.3%). In their study, De Simone *et al* showed that the normal variation in body size during the evaluation for LVH is reduced by normalizing LVM to height$^{2.7}$ and recommend this method.[14] Normalizing LVM to height only was less successful in reducing the variability of LVM amongst normal-weight children and adults.[14]

There is evidence that abnormal geometry is associated with systolic and diastolic dysfunction in the hypertensive population and is an independent predictor of cardiovascular outcome apart from blood pressure or other traditional cardiovascular risk factors.[8,10] However, studies exploring the correlates and prognostic significance of the various geometric patterns in SCA population are scanty. Eccentric hypertrophy was the commonest abnormal geometry encountered in our SCA population (37.4%), followed by concentric hypertrophy (31.3%). Concentric remodeling was the least common type of abnormal geometry. Abnormal geometry (predominantly eccentric hypertrophy) was more common in the female patients, contrary to what was previously reported.[20,24]

The various LV geometric patterns reflect the prevailing hemodynamic loading condition (volume or pressure overload) at the time of assessment.[33] Eccentric hypertrophy results from LVH occurring as an adaption to chronic volume overload, whereas concentric LVH and concentric remodeling occur in the setting of increased LVM due to pressure overload. Earlier studies have shown that concentric LVH pattern is commonly seen in cardiac disorders such as hypertension and aortic stenosis (AS) and is associated with increased adverse cardiovascular events.[10,21] Eccentric LVH moderately increases the risk of death compared with normal geometry, and is commonly associated with conditions such as coronary artery disease and cardiomyopathy.[9] The prevalence of concentric hypertrophy in our study was high, and differs from previous reports.[20,23] Concentric hypertrophy in patients with SCA may be attributed to a 'relative systemic hypertension' or systemic vasculopathy resulting in

Table 2: Clinical Characteristic and Echocardiographic Variables

Variables	Frequency (%)/ Median [IQR]
Clinical Parameters	
Age (years)	23 [10]
Gender	
Male	35 (42.7)
Female	47 (57.3)
Anthropometric Variables	
Height (meter)	164 [12]
Weight (kilogram)	46 [14]
BMI (Kg/m^2)	16.9 [3.5]
BSA (m^2)	1.48 [0.24]
Systolic Blood Pressure (mmHg)	100 [20]
Diastolic Blood Pressure (mmHg)	60 [17]
Haematocrit (%)	20 [7]
Echocardiographic Parameters	
LVM (g)	201 [93.3]
LVMI (g/m^2)	129 [50.2]
LVM/height (g/m)	127 [55.4]
LVM/height$^{2.7}$ ($g/m^{2.7}$)	55.7 [22.2]
LVEF (%)	68 [9]
LVEDD (mm)	54.3 [8]
LVES (mm)	33 [7]
SV (ml)	89 [36]
LVPW (mm)	10 [2]
RWT	0.37 [0.12]

Data are expressed as median and interquartile range or number (%). BMI, Body Mass Index; BSA, Body Surface Area; IQR, Inter Quartile Range; LVED, Left Ventricular End Diastolic Diameter; LVES, Left Ventricular End Systolic; LVM, Left Ventricular Mass; LVMI, Left Ventricular Mass Index; LVPWD, Left Ventricular Posterior Wall in Diastole; RWT, Relative Wall Thickness; SV, Stroke Volume.

Table 3: Prevalence of Left Ventricular Hypertrophy and Geometric Patterns in Study Population

LVH Defining Parameter	All (n=82) (%)	Male (n=35) (%)	Female (n=47) (%)	*P**
LVMI (g/m^2)	66 (80.5)	25 (37.8)	41 (62.12)	0.11
LVM/height(g/m)	60 (73.2)	25 (41.7)	35 (58.3)	0.476
LVM/height$^{2.7}$($g/m^{2.7}$)	57 (69.5)	20 (35.1)	37 (64.9)	0.052
LV mass (g)	56 (68.3)	26 (46.4)	30 (53.6)	0.347
Geometric Pattern**				
Eccentric hypertrophy	31 (37.8)	7 (22.6)	24 (77.4)	0.012*
Concentric hypertrophy	26 (31.7)	13 (50)	13 (50)	
Normal	23 (28)	13 (56.5)	10 (43.5)	
Concentric remodelling	2 (2.4)	2 (100)	0 (0)	

*LV, Left Ventricular; LVMI, Left Ventricular Mass Index; LVM, Left Ventricular Mass; *Fischer exact; **Geometric pattern determined using LVH defined by LVM/height*$^{2.7}$

increased afterload. Blood pressure values that would be considered normal for the general population may be high for SCD patients and contribute to increased risk through end-organ effects in the heart and kidney.[34]

Regression of LVH following treatment of the underlying cardiac pathology was associated with improved CVD outcomes.[35,36] Therefore, detection of LVH in patients with SCD may identify high-risk groups and allow for optimization of treatment with drugs including hydroxyurea given its favorable impact on vasculopathy and other complications of SCA.[19,37] This ultimately may result in improved quality of life and overall survival.

CONCLUSION

The prevalence of LVH is high among patients with sickle cell anaemia irrespective of the criteria applied. The most prevalent geometric pattern was eccentric LVH. The prevalence of LVH using LVMI was highest compared with the rates obtained using other methods. Indexing to BSA might result in over-estimation of LVH given the relatively small BSA in patients with sickle cell anaemia. Indexing to height$^{2.7}$ might give a more accurate estimate of LVH. Given the peculiarities in patients with SCA, there is the need to establish more uniform criteria and cut-off values for defining LVH in this population.

Limitations

This was a small-scale, single-center study. Our findings may not reflect what obtains in the general population of patients with SCA. The reference value used in defining LVH was based on normal healthy population which may not be applicable to the study population. Cardiac magnetic resonance imaging, the gold standard for assessment of cardiac structure and function, is largely unavailable in most centers in sub-Saharan Africa.

Recommendation

A large-scale prospective study is needed to determine the prognostic implications of the different LV geometric patterns in SCA patients, and to define which method of indexation is more reliable for the clinical evaluation of LVH in this population.

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