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Non Invasive Assessment of Left Ventricular Structure and Functions in Nigerians with Keloids

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Abstract

Background: Keloid formation is an old phenomenon and it is almost exclusive to blacks. Nigeria is the most populous black nation in the world. Greater propensity to cardiac hypertrophy and higher prevalence and severity of hypertension in blacks compared with whites are well documented in literature.

Objective: To assess the influence of keloid on left ventricular size and functions.

Methods: Ninety (90) subjects with keloid were age, sex, body mass index and body surface area matched with 90 controls without keloid. All had echocardiographic examination done.

Results: Subjects with keloid had statistically significant left ventricular end diastolic diameter in diastole (P<0.011), left ventricular posterior wall thickness in diastole (P<0.0001), interventricular septal wall thickness in diastole (P<0.0001), left ventricular mass (P< 0.048), left ventricular mass index (P<0.044) and relative wall thickness (P<0.0001) compared with controls. Keloid subjects have significant abnormal left ventricular geometric patterns compared to controls but no statistical difference was observed in diastolic and systolic functions.

Conclusion: Keloid is associated with increased left ventricular end diastolic diameter, interventricular septal thickness in diastole, posterior wall thickness in diastole, relative wall thickness, left ventricular mass, left ventricular mass index and abnormal left ventricular geometric patterns but has no influence on the systolic and diastolic function. However, there is need for more longitudinal studies to establish the prognostic implications of these findings.

Keywords: Keloid, Left ventricular mass and Left ventricular hypertrophy

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1. Introduction

As early as 13th Century, the work of Art of facial marks on terracotta sculptures among the Yoruba of Western Nigeria is memorable and suggestive of the presence of keloids[1]. In a survey of 4,877 people in a rural African community, incidence of 6.2% was found by Oluwasanmi[2]. The male to female ratio within the same age group is the same[2]. The average age at onset is 10-30years. Persons older than 65years rarely develop keloid for the first time[3].

Keloid is a benign hard skin growth resulting from excessive collagen production. It occurs following skin injury, trauma or sometimes trivial injury. It is itchy and painful but unlike hypertrophic scar which fade within 12 months, keloid are persistent and may continue to enlarge[4].

Left ventricular hypertrophy (LVH) is increase in cardiac muscle mass of the left ventricle. It is a significant independent cardiovascular risk for heart failure, renal failure and cerebrovascular disease[5]. LVH has been described in various clinical conditions such as hypertension, obesity and diabetes mellitus. Racial differences, age, gender and environmental factors such as; diet, body size and physical activity were demonstrated in various studies to play important role in left ventricular mass[5]. Studies have revealed that blacks have greater propensity to cardiac hypertrophy and vascular smooth muscle cell hyperplasia and hypertrophy when age, sex and height of arterial blood pressure matched with whites[6,7,8].

The concurrence of increased predisposition to keloid and greater propensity of cardiac hypertrophy in blacks prompted this study. It is well documented in literature that blacks have higher keloid predisposition, greater propensity to cardiac hypertrophy but there are few reports exploring the possible clinical link between keloid and LVH. Is this a mere coincidence in blacks or is there any clinical relevance? This study was conducted to evaluate any clinical evidence of possible link between keloid and LVH.

2. Methods

This is a prospective, case-controlled study of non-invasive assessment of 90 Nigerians with keloid and 90 controls. This study was conducted in 2008 at the Cardiology Unit of Obafemi Awolowo University Teaching Hospital Complex(OAUTHC), Ile-Ife.

Inclusion criteria are; ages between 18 years to 65 years and keloid score of 10 and above while exclusion criteria are; clinical and echocardiographic evidence of hypertension, heart failure, valvular heart diseases, congenital heart diseases cardiomyopathy, cor pulmonale, pericardial effusion or thickening, renal failure, diabetes mellitus, chest deformity, obesity BMI >30, significant history of alcohol intake (80g/day for male and 60g/day for female for a period of 10 years) and smoking of at least 10 pack years, pregnancy, abnormal hematological or biochemical profile such as anaemia of any cause, azotemia, electrolytes imbalance, impaired or elevated blood sugar and total cholesterol > 5.0mmol/l.

Subjects with keloid were volunteers from dermatology and plastic surgical outpatient clinics who had predetermined minimum keloid score (Appendix 1) of 10 and between age range of 18 years and 65 years[3]. Controls were volunteers from among the staffs and students of affiliated institutions with OAUTHC Ile Ife, who have no keloid. Ethical clearance was duly obtained from the Ethical and research committee of OAUTHC Ile- Ife. Written consents were equally obtained from participants before they were interviewed, clinically examined and echocardiography examination.

Echocardiography performed using Siemens ultrasound machine, Sonoline G60s, GM-56400ADOE, model-7474922 in an air conditioned room. Measurements were obtained in multiple cross-sectional planes with the use of standard transducer positions-the parasternal long and short axis views, and the apical four and five chamber views. The echocardiographic studies were done with the patient lying on their left side and at end expiration. Our echocardiographic machine had an inbuilt ECG mode, which helps in accurate measurement of diastolic and systolic time(s).

2D/M-mode measurements were done according to the American Society of Echocardiography convention of border limit of leading edges to leading edges for both septum and posterior wall[9]. Measurements were averaged over

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3 readings. The following measurements were obtained; chamber dimensions; left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), left atrial diameter (LAD), aortic root diameter (AOD), Wall sizes such as; interventricular septal thickness in diastole (IVSTD), posterior wall thickness in diastole (PWTD) and Left ventricular mass (LVM) and left ventricular mass index (LVMI), indexed to body surface area (BSA) were calculated using the ASE[10] formula.

LVM (g) (ASE) = $0.8(1.04(LVEDD+IVSTD+PWTD)^3 - (LVEDD)^3) + 0.6g$.

LVMI (g/m^2) = LVM/BSA.

Relative wall thickness (RWT) was calculated using the formula. RWT = IVSTD + PWTD /LVEDD.

There are 4 different geometric patterns of LVH; concentric hypertrophy with high RWT and LVMI, concentric remodeling with normal LVMI with high RWT, eccentric hypertrophy with normal or low RWT and high LVMI and normal geometry with normal LVMI and RWT. Cutoff values[10,11] for LVMI and RWT are as follows; > $114.8g/m^2$, > 0.45.

Stroke volume, stroke index, cardiac output, cardiac index, fractional shortening and ejection fraction were obtained. Total peripheral resistance (TPR) was calculated using the formula.

TPR = Mean arterial pressure/cardiac output

Using Pulsed wave / Continuous wave Doppler echo the following measurements were made: systolic function; Doppler derived maximal aortic flow velocity (AVV max) and the aortic flow velocity time integral (AVVTI). The pulse-wave Doppler indices of left ventricular diastolic filling[12,13] were taken; Peak early filling flow velocity of mitral valve (E) in cm/s, Peak late (atrial) filling flow velocity of mitral valve (A) in cm/s, ratio of peak early filling to late filling flow velocities of mitral valve (E/A), isovolumic relaxation time (IVRT), deceleration time of early diastolic mitral inflow (DT). Pulmonary venous flow parameter were taken; systolic pulmonary venous flow velocity (S), diastolic pulmonary venous flow velocity (D), ratio of systolic and diastolic pulmonary venous flow velocity (S/D) and pulmonary venous peak atrial contraction reversed velocity (A^r)

Colour flow Doppler[14] was used to assess presence of valvular stenosis, regurgitation across valves and inter-atrial and interventricular shunts which duly excluded from the study.

All demographic and echocardiographic measurements were recorded in standard data format and data analysis was done on computer using the Statistical Package for Social Sciences (SPSS) standard version 11.0. Results were expressed as means ± standard deviation for continuous variables and proportions and percentages for categorical variables. Comparisons of continuous data between subjects with keloid and age and sex matched controls were made with 2-tailed t-test for independent groups. Categorical variables of subjects with keloid were compared with controls by chi-square. Level of statistical significance was set at $P<0.05$.

3. Results

Ninety subjects with keloid (38 males and 52 females) and ninety controls (38 males and 52 females) aged between 18 and 65 years participated in the study. There was no significant difference in the age, weight, height, body surface area and body mass index.

Subjects with keloid had higher end diastolic dimensions such as; left ventricular end diastolic diameter, interventricular septal thickness in diastole, posterior wall thickness in diastole when compared with controls but there is no difference in left ventricular end systolic diameter, left atrial diameter and aortic root diameter. Relative wall thickness, left ventricular mass, and left ventricular mass indexed to body surface area were significantly higher in subjects with keloid than controls. Fractional shortening and ejection fraction showed no difference between the two groups. Stroke volume, cardiac output, stroke index and cardiac index of subjects with keloid were significantly lower while calculated total peripheral resistance was significantly higher compared with controls.

Fifty one (56.7%) subjects with keloid had normal geometry compared to seventy three (81.1%) controls, twenty two (24.4%) had concentric

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remodelling compared to eleven (12.2%) controls, nine (10.0%) had concentric hypertrophy compared to one (1.1%) control and eight (8.9%) had eccentric hypertrophy compared to five (5.6%) controls.

In the doppler echocardiographic data of studied population. There is no significant difference in mitral E and A velocities, E/A ratio, IVRT, deceleration time, ratio of systolic and diastolic velocities of pulmonary venous flow, retrograde atrial velocity of pulmonary vein, maximal aortic valve flow velocity and aortic valve flow velocity time integral. Although diastolic dysfunction occurred more frequently in subjects with keloid compared with controls however, this did not reach statistical significance. Systolic dysfunction was not observed in either of the two groups.

Table 1: Clinical characteristic of the study population

Parameter	Keloids Mean(SD)	Control Mean (S.D)	P value
Age (years)	33.60(12.63)	33.70(12.45)	0.934
Sex: Male	No (%) 38 (42.2)	No (%) 38 (42.2)	
Female	52 (57.8)	52 (57.8)	
Weight (kg)	64.48(8.30)	64.72(8.20)	0.843
Height (m)	1.65(0.09)	1.66(0.08)	0.543
Body mass index (kg/m2)	23.59(2.87)	23.44(2.68)	0.709
Body surface area (1.75)	1.71(0.14)	1.71(0.15)	0.925

Table 2: 2D /M mode Echocardiography of study population

Parameter	Keloid Mean (S.D)	Control Mean (S.D)	P value
IVSTD (cm)	0.96(0.16)	0.86(0.13)	<0.0001*
PWTD (cm)	0.93 (0.14)	0.86(0.13)	<0.0001*
LVEDD (cm)	4.39(0.46)	4.57(0.46)	<0.011*
LVESD (cm)	2.98(0.32)	2.97(0.46)	0.867
Left atrial diameter (cm)	3.32 (2.23)	3.12 (0.47)	0.381
Aortic root diameter(cm)	2.82(0.31)	2.72 (0.46)	0.078
Relative wall thickness	0.43 (0.07)	0.38 (0.05)	0.0001*
Left ventricular mass(g)	139.5 (37.1)	130.9 (38.4)	0.048*
Left ventricular mass index (g/m^2	80.9 (20.0)	75.1 (18.7)	0.044*

Table 3: 2D/M mode Echocardiographic Derived values

Parameter	Keloids Mean (SD)	Controls Mean (SD)	P value
CO (L/min)	5.18 (1.13)	5.79 (1.23)	0001*
CI ($L/min/m^3$)	3.03 (0.66)	3.40 (0.70)	0.0001*
SV (ml)	69.47 (16.83)	76.47 (20.74)	0.005*
SI (ml/m^3)	40.17 (10.29)	44.79 (11.58)	0.005*
TPR	18.14 (4.5)	15.77 (3.5)	0.0001*
FS (%)	31.92(5.53)	33.18(5.94)	0.144
EF (%)	67.78(7.59)	69.37(7.27)	0.155

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Table 4: Left ventricular Geometric patterns of Study Population

Geometric pattern	Keloids No (%)	Controls No (%)	P value
Normal	51(56.7)	73(81.1)	0.03*
Concentric remodelling	22(24.4)	11(12.2)	0.013*
Concentric hypertrophy	9(10.0)	1(1.1)	0.003*
Eccentric hypertrophy	8(8.9)	5(5.6)	0.03*

Table 5: Doppler Echocardiographic Data of study population

Parameter	Keloids Mean (S.D)	Controls Mean (S.D)	P value
Mitral E- Velocity (m/s)	0.73(0.15)	0.73(0.15)	0.940
Mitral A- Velocity (m/s)	0.53(0.11)	0.56(0.10)	0.407
Mitral E/A ratio	1.42 (0.40)	1.37(0.30)	0.317
IVRT (ms)	84.20(14.34)	84.43(4.98)	0.915
Deceleration time (ms)	199.21(40.76)	196.46(37.49)	0.637
Pulm.venous Systolic velocity	0.563 (0.126)	0.553 (0.131)	0.595
Pulm. Venous Diastolic velocity	0.485 (0.129)	0.450 (0.109)	0.051
Pulm. venous S/D ratio	1.19(0.21)	1.24(0.17)	0.081
Pulm. Vein retrograde a-velocity (m/s)	0.32(0.07)	0.32 (0.05)	0.569
AVVTi	19.75(3.92)	19.70(4.04)	0.935
AVVmax(m/s)	0.99(0.19)	0.99(0.24)	0.96

Table 6: Diastolic and systolic function of study population

Diastolic function	Keloids No (%)	Controls No (%)	P- value
Normal	77(85.7)	84(93.4)	0.07
Impaired relaxation	6(6.6)	3(3.3)	0.058
Pseudo normalization	4(4.4)	3(3.3)	0.08
Restrictive	3(3.3)	0 (0)	0.053
Systolic function Normal Dysfunction	100 (100%) 0(0%)	100 (100%) 0(0%)	0.10 0.10

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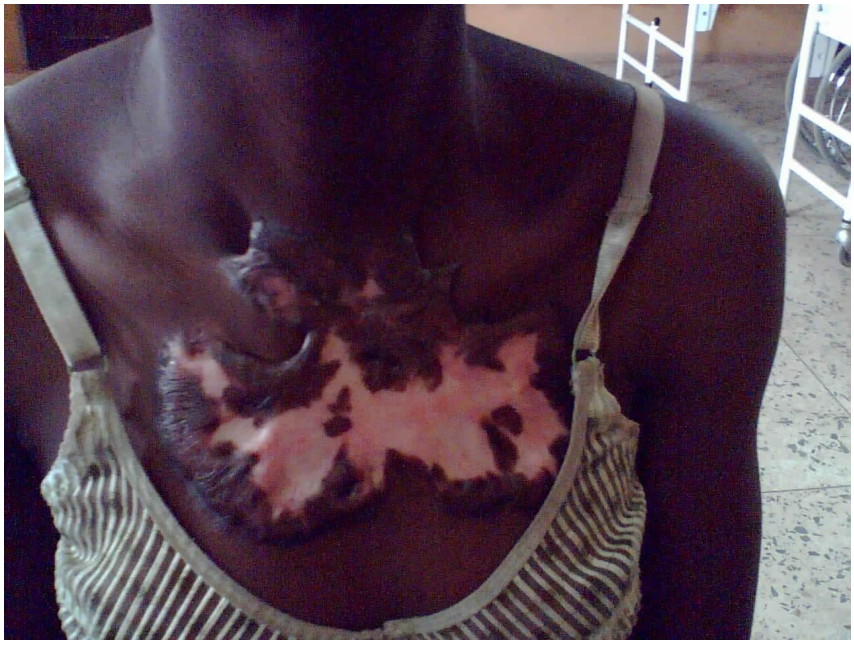

Figure 1: A Keloid Patient

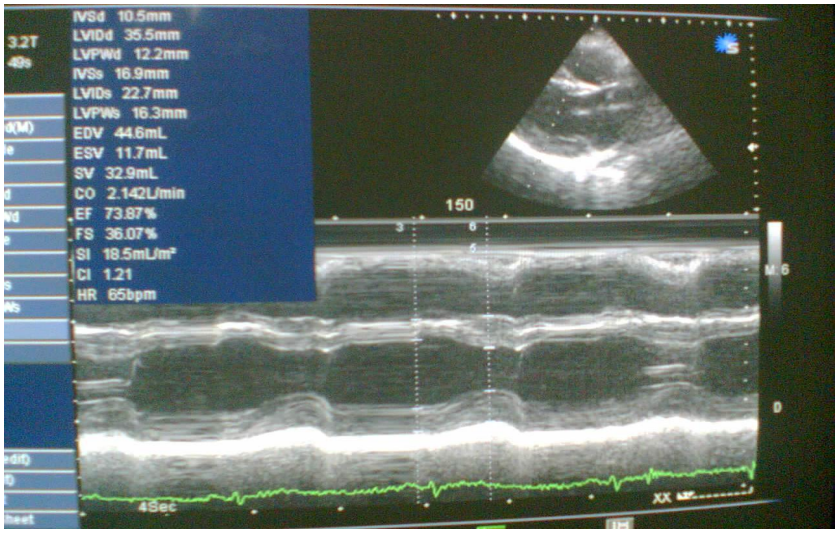

Figure 2: 2D/M echocardiogram of 39 year old female subject with keloid

4. Discussion

This is the first study assessing the left ventricular size and function in keloid. Subjects and controls selection were carefully done to obviate all possible confounding variables of left ventricular hypertrophy. 70.6% of studied populations were aged 18 to 40years, this represent the economic productive class of our national population whose health indices are paramount.

Significant differences between the subjects with keloid and the controls in the end-diastolic dimensions; LVEDD, (P<0.01) IVSTD (<P10.0001) PWTD (P<0.001), RWT (P<0.0001), LVM (P<0.048) and LVMI (P<0.044) when subjects with keloid were compared with controls seen in this study is significant evidence of increased left ventricular size in keloid, having excluded possible cofounding variables of LVH.

Subjects with keloid had significantly higher than the controls concentric remodelling (P<0.013), concentric hypertrophy (P<0.003) and eccentric hypertrophy (P<0.03). Subjects with keloid were equally found to have significantly reduced stroke volume (p<0.005), cardiac output (p<0.001), stroke index (p<0.005), cardiac index (p<0.0001) compared to control. There is characteristic higher total peripheral resistance in subjects with keloid

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compared with controls ($p<0.0001$). Koibuchi et al have shown that angiotensin 11 induced vascular smooth muscle cell (VSMC) hyperplasia and hypertrophy is dependent on transforming growth factor beta (TGFb), a notable cytokine implicated in the pathogenesis of keloids. Higher peripheral resistance seen in this study may be due to increased VSMC hyperplasia/hypertrophy described in keloids[15].

There was no significant difference in the mean ejection fraction and fractional shortening and left ventricular end systolic dimension of subjects with keloid compared with controls. Doppler echocardiographic data of mitral E, A and E/A ratio, IVRT, deceleration time, systolic and diastolic pulmonary venous flow velocities and ratio of systolic and diastolic pulmonary venous flow velocities and pulmonary vein retrograde a-wave velocity, aortic flow velocity time integral and peak aortic flow velocity of the subjects with keloid were not statistically different from those of controls. Keloid therefore is not an independent risk factor for left ventricular systolic or diastolic dysfunction.

Recommendation and limitation

Our findings in this study revealed that subjects with keloid had increased left ventricular size and abnormal geometric pattern with characteristic reduced stroke volume and cardiac output and higher peripheral resistance compared to those without keloid but has no significant influence on the left ventricular systolic and diastolic functions. However, there is need for more longitudinal studies to establish the prognostic implications of these findings. There is equally need for genetic studies and gene typing that may correlate left ventricular hypertrophy and keloid formation.

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Appendix I: Keloid Score

Location	**Surface area (horizontal × vertical dimension) cm^2**	
	L	R
Face & neck		
Chest		
Back		
Abdomen		
Upper limbs		
Lower limbs		

Total surface area ……

Surface area: 1-10cm^2 = 1, 11-20cm^2 =2, 21-30cm^2 =3, 31-40cm^2 =4, ≥ 41cm^2 =5.

Shape: Pedunculated =1 Flat =2 Combined = 3

Pain/ Tenderness: Present =2 absent = 0

Activity/Itching: Present =2 absent =0

Type of injury: Trivial/unknown =1, Trauma/surgical =2, Skin sepsis =3, Combined = 4

Psychological trait: Unaffected=1Anxiety =2Anxiety/Depression=3

Previous therapy: none =0, Topical only =1, Intralesional injection =2, Surgical =3

Outcome of therapy: Successful =1, Partially successful =2, Unsuccessful =3, Repeated failure = 4.

Total Score = /26

Appendix ii：subject entry data

Serial No …….

Hospital No ……... Age …….. Sex: M [ ] F [ ]

Past medical history: HT [ ] DM [ ] Renal Dx [ ] Heart failure [ ]

Family history: HT [ ] DM [ ] Sudden cardiac death [ ] Keloids [ ]

Alcohol intake: yes [ ] no [ ]. If yes, quantity ……

Smoking: yes [ ] no [ ]. If yes, No of pack/year ……..

Examination: Weight …….. Height ……..

BMI …… BSA …… Pulse rate …….....

DBP……ii……. SBP……..ii…….MAP ……

JVP ……Precordium…….

Heart sounds..... Murmur……..

Keloid score ……..

Lab: PCV …… WBC ……N……L……E……B……ESR ……[WG]

Na+ ……K ……HCo3- …… Urea …… Creatinine …… FBS ……

Total Cholesterol ……. Urinalysis: Protein [ ] Glucose [ ]

Urine microscopy ……..

CXR: CTR …… Aortic unfolding [ ] Lung fields ……

ECG: HR …….. Rhythm ……...LAE [ ] LVH [ ]

ECHO: LVEDD ……. LVESD ……. LAD …….AOD……..

PWTD ……IVSTD……RWT……..

LVM ……. LVMI ……. Geometric pattern……..

LVEDV ……. LVESV …….

Comment …….

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