Left atrial structural and functional remodelling study in type 2 diabetic patients in sub-saharan Africa: role of left atrial strain by 2D speckle tracking echocardiography.

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June 15, 2020

Abstract

Objective: To evaluate the role of peak atrial longitudinal strain (PALS) through speckle tracking 2D echocardiography for the assessment of structural and functional left atrial (LA) remodelling in a type 2 diabetes mellitus (T2DM) population. Methodology: We conducted a cross-sectional study during a 9-month period. Were included T2DM adults aged 18 and above. The variables assessed during the study include age and gender of participants, diabetes characteristics, cardiovascular risk factors, clinical anthropometric and haemodynamic parameters, standard echocardiographic parameters, volume-derived LA functions and 2D PALS. Results: We included a total of 102 patients. The mean age was 58±11.7 years and the M/F sex ratio was 1:1.5. Coexistent arterial hypertension (HTN) was observed in more than half (59.8%) of the population sample. Mean 2D PALS was 29.2±8.9% with 58.8% (95% CI:50.0–68.6) of subjects having a reduced LA strain (i.e.<32%). Reservoir and pump functions were the most altered LA volumetric phasic functions. Mean indexed LA maximal volume was 22.2±6.8 ml/m^2. There was a significant association between abnormal PALS and age, Body mass index (BMI), indexed LA volume, E/E' ratio, LA active ejection fraction (pump function) and LA expansion index (reservoir function). Conclusion: LA remodelling is a recurrent condition in adult T2DM Cameroonians. The Reservoir and pump LA functions were the most affected. Assessment of LA global strain allows early detection of LA remodelling with comparison to LA size standard analyses. Age, BMI, indexed LA volume, E/E' ratio, reservoir and pump LA functions were associated to 2D LA global strain impairment.

INTRODUCTION

The left atrium (LA) is not only a simple passive transport chamber but also a dynamic apparatus that plays an important role in cardiac function by adjusting left ventricular filling through its reservoir, conduit, and contractile functions. LA remodelling refers to the spectrum of pathophysiological changes in atrial structure and mechanical function, and within the electric, ionic, and molecular environments of the LA. This remodelling most often occurs in response to stresses imposed by conditions such as hypertension, heart failure, type 2 diabetes mellitus (T2DM), and obesity [1]. Remodelling constitutes the basis of atrial cardiomyopathy. It has been recently defined by an expert consensus as a complex of structural, architectural, contractile or electrophysiological modifications affecting the atria with the potential of inducing significant clinical manifestations [2]. It has also been identified as an independent predictor of adverse cardiovascular event in T2DM, a pathology whose prevalence is constantly increasing in sub-Saharan Africa [3,4]

Analysis of LA size through standard echocardiographic methods is commonly used but has proven to be inaccurate in the assessment of LA remodelling [5]. They are subjective, depend on the level of expertise of the operator, lack sensibility in detecting early abnormalities and do not apprehend all the components of myocardial function [6]. Bidimensional speckle tracking echocardiography allow a direct and angle-independent analysis of myocardial deformation, thus giving sensitive and reproductible myocardial dysfunction indices which overcome the limits of Doppler-derived measurements [7]. Evaluation of LA deformation mechanics could help in detecting LA dysfunction earlier than the standard measurement methods [8].

This study aims to evaluate the role of peak atrial longitudinal strain through speckle tracking 2D echocardiography for the assessment of structural and functional LA remodelling in a T2DM adult population in Cameroon.

METHODS

Study design and population

A cross-sectional study was conducted during a 9-month period (from January 2019 to September 2019). Patients were recruited at National Obesity Centre and the Centre for treatment of Diabetes and Hypertension of the Yaoundé Central Hospital. We included in the study, T2DM adults aged 18 and above, no matter the duration of diabetes follow up, with no history of a proven cardiac disease caused by a condition other than hypertension (HTN) or T2DM such as coronary artery disease, significant valvular heart disease, obstructive hypertrophic cardiomyopathy, atrial fibrillation or flutter.

Data collection

A thorough clinical examination was carried out at inclusion. The variables assessed at this point of the study included, the age and gender of participants, diabetes characteristics, cardiovascular risk factors, clinical, anthropometric and haemodynamic parameters. The clinical examination was followed by a resting electrocardiographic recording.

Echocardiography

Transthoracic echocardiography was performed in all patients using a machine equipped with a 5 MHz X5-1 probe (Plilips iE33) and the QLAB Ultrasound cardiac analysis software for strain measurement. Standard echocardiographic parameters were obtained, these included LV ejection fraction through Simpson's Biplane method, LV mass index and LV diastolic function through Tissue Doppler imaging derived E and E' peak velocities at the lateral mitral annulus. The biplane Simpson's method was used for calculation of LA volumes. Left atrial volume was planimetered in the four-chamber and two-chamber views by tracing the endocardial border (pulmonary vein confluence and LA appendage were excluded)[9].

Maximum LA volume (LA max) was obtained at left ventricular (LV) end-systole, from the 2D frame, just before the mitral valve opened. Pre-atrial volume (Vpre-A) was obtained from the diastolic frame, just before the mitral valve reopened as the result of atrial contraction. Left atrial minimum volume (LA min) was assessed at LV end-diastole, from the smallest volume seen after LA contraction.

Left atrial phasic function assessment was done using the following formulas [10]:

Reservoir function: LA emptying fraction total = ((LA max – LA min)/LA max) × 100%; expansion index = ((LA max – LA min)/LA min) × 100%

Conduit function: Passive emptying volume = LA max - Vpre-A; passive LA emptying fraction = ((LA max - Vpre-A)/LA max) × 100%;

Contractile function: LA active emptying fraction = ((LA pre-A – LA min)/LA pre-A) × 100%; LA active emptying volume = V pre-A – LA min.

The echocardiographic evaluation was concluded by peak atrial longitudinal strain (PALS) measurement by 2D speckle tracking echocardiography. Apical four- and two-chamber views were obtained using 2D greyscale echocardiography for speckle-tracking analysis. This was performed during end-expiratory breath-hold and stable ECG recording. An adequate greyscale image that allowed separation of myocardial tissue and surrounding structures was obtained. Three consecutive cardiac cycles were recorded and averaged. The QLAB software allowed offline semi-automated analysis of speckle-based strain. The endocardial surface of the LA was traced manually in both four- and two-chamber views by a three-point-and-click approach. The system then automatically generates an epicardial surface tracing (Figure 1). The region of interest was thus created, and this was then manually adjusted as needed to allow for adequate speckle tracking [11]. A PALS value less than 32% was considered abnormal.

Statistical analysis

Statistical analysis was performed with SPSS version 25.0 software. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were described with number of subjects (percentages). Means and proportions were respectively compared with the Student t test and Chi square or Fisher exact test. Multivariate linear regression analysis was used to identify possible independent determinants of abnormal PALS. Independent variables with a p-value less than 0.05 on bivariate analysis were included in the multivariate model. A p value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

Of the 102 individuals, 61 were female (59.8%) with a male to female sex ratio of 1:1.5 and the mean age was 58 ± 11.7 years. More than half of the population had hypertension associated to T2DM, precisely 59.8% of the subjects. The mean duration of diabetes was 7.4 ± 6.2 years and 29 patients (28.4%) presented micro vascular complications of diabetes. About $\frac{3}{4}$ of the study population (77.9%) had a treatment regimen including at least one oral antidiabetic drugs and slightly more than $\frac{1}{4}$ (28%) had insulin in their treatment. The study population was globally in overweight with a mean body mass index (BMI) of 28.9 ± 5.6 kg/m^2 (Table I).

LA volumetric parameters and LA global strain

The mean maximum indexed LA volume (LAVi) was 22.2 ± 6.8 ml/m^2. The reservoir and contractile LA functions were the most altered with respect to normal population values. The mean peak atrial longitudinal strain at the reservoir phase for the total population was 29.2 ± 8.9%, with a prevalence of abnormal PALS of 58.8% (95% CI : 50.0 – 68.6).

Variation of clinical and echocardiographic parameters with PALS

Individuals with a reduced PALS were significantly older (60.4 ± 11.1 vs 54.6 ± 11.9 years, p = 0.013), had a greater BMI (30.1 ± 6.0 vs 27,1 ± 4.4 kg/m^2, p = 0.007), higher systolic blood pressure (SBP) (p = 0.034) and greater E/E' ratio (12.1 ± 4.6 vs 8.9 ± 2.3, p < 0.001). Furthermore, LAVi (p = 0.006), LA expansion index (p < 0.001), LA global (p < 0.001) and active (p = 0.002) ejection fractions were significantly higher in subjects with abnormal PALS (Table II).

On multivariate analysis, E/E' ratio (adjusted p = 0.032) and BMI (adjusted p = 0.022) were independently associated to abnormal PALS after adjustment for all the significant variables.

DISCUSSION

We assessed the role of LA global longitudinal strain by evaluating the LA remodeling in a Cameroonian T2DM adults. We included a group of diabetic patients, predominantly females, with more than half of them having coexistent hypertension. Given that global cardiovascular risk is very high in diabetic patients, its reduction constitutes a major treatment objective [12]. Despite the high proportion of hypertensive patients in the population, we found only à third of them with a renin-angiotensin-aldosterone system blocker in their treatment regimen. Thus, reflecting the difficulties in applying ESC/ESH treatment recommendations [13] in Africa, especially in Cameroon, which could be linked to the relative high cost of these medications in our context, making them less available to the majority of hypertensive patients. Mean LVEF was 63.1%, corresponding to the classical presentation of patients with cardiac disease related to diabetes, where diastolic dysfunction is the main abnormality at the early stage[14].

LA structural remodelling is classically expressed by the measurement of the LAVi by 2D (or 3D) echocardiography [1]. Increased LAVi is a surrogate marker of increased and chronic pressure overload and is a key measurement used in clinical practice to assess diastolic dysfunction of the LV [15]. The mean value of LAVi (22 ± 6 ml/m^2) in the study was within the normal reference range of the American society of Echocardiography [16]. However, we observed greater alterations of the reservoir function (LA global ejection fraction) and the contractile function.

PALS was significantly reduced in the study population compared to a non-diabetic black African population in South Africa (29.2 ± 9 vs 39 ± 8.3, $p < 0{,}001$)[11]. Meanwhile this results is similar to those found by Markman and al. in a diabetic population with a mean PALS of $28.5 \pm 11.7\%$ [17]. Concerning the role of PALS in early detection diastolic and LA dysfunction, it is important to highlight that LA strain was markedly reduced in many patients with normal LAVi. In 2016, Bassam and al, had similar results in a group of hypertensive subjects in whom LA strain measured by speckle tracking echocardiography allowed early detection of LA dysfunction even before LA dilatation [7].

Finally, univariate linear regression allowed to highlight a significative negative association of PALS with age, BMI, SBP, E/E' ratio and LAVi. The reservoir (LA expansion index and LA global ejection fraction) and the contractile functions were positively correlated to PALS. Cardiac disease during diabetes leads to atrial fibrosis with consequent reduced atrial compliance [18]. Muranaka and al, also suggested that LA fibrotic modifications during T2DM are responsible for reduced phasic functions determined by LA strain[19].

This study had several limitations: (i) LA strain measurement lacks a criterion standard - strain values vary with different software packages; (ii) the quantitative values defined for LA strain are vendor-specific; (iii) the software used for assessing strain does not have a specific mode for LA strain study; and (iv) coronarography which is the gold standard to exclude coronary artery disease could not be performed.

CONCLUSION

LA remodeling is a recurrent condition in the adult T2DM population. The reservoir and pump LA functions were the most affected. Assessment of LA global strain allows early detection of LA remodeling and dysfunction with comparison to LA size standard analyses and LV filling pressures determined by E/E' ratio respectively. Age, BMI, indexed LA volume, E/E' ratio, reservoir and pump LA functions were associated to 2D LA global strain impairment.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge all the volunteers who accepted to participate to this study, the National centre for Obesity and The Centre for treatment of Diabetes and Hypertension of the Yaounde Central

Hospital.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

APM: Concept/design, Data analysis/interpretation, Critical revision of article, Approval of article;

CNNG: Concept/design, Data collection, Data analysis/interpretation, Drafting article, Critical revision of article, Approval of article;

AJA: Data collection, data analysis/interpretation, critical revision of article, approval of article;

GSW: Statistics, drafting article, critical revision of article, Approval of article;

LV: Data collection, data analysis/interpretation, critical revision of article, Approval of article,

DNT**:** Statistics, drafting article, critical revision of article, Approval of article;

JB: Critical revision of article, Approval of article,

SK: Concept/design, Critical revision of article, Approval of article.

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Table I: Baseline characteristics, diabetes and cardiovascular risk factors' characteristics

Variables	Abnormal PALS (n = 60)	Normal PALS (n = 42)	Total (n = 102)	Crude p value	Adjusted p value[£]
Age (years)	60.4 ± 11.05	54.6 ± 11.9	58 ± 11.7	0.013	0.533
Male, n (%)	20 (33.3)	21 (50)	41 (40.2)	0.091	
Duration of diabetes (years)	8.1 ± 6.9	6.5 ± 4.8	7.4 ± 6.2	0.175	
Glycated haemoglobin (%)	7.8 ± 2.6	6.6 ± 2.2	7.3 ± 2.5	0.063	
Microvascular complications, n (%)	18 (30)	11 (26.2)	29 (28.4)	0.824	
Macrovascular complications n (%)	3 (5)	2 (4.8)	5 (4.9)	0.956	
Hypertension, n (%)	40 (66.7)	21 (50)	61 (59.8)	0.091	
Chronic kidney disease, n (%)	3 (5)	0 (0)	3 (2.9)	0.266	
Dyslipidemia, n (%)	13 (21.7)	4 (9.5)	17 (16.7)	0.105	

Variables	Abnormal PALS (n = 60)	Normal PALS (n = 42)	Total (n = 102)	Crude p value	Adjusted p value[£]
Total cholesterol level (g/l)	1.8 ± 0.5	1.6 ± 0.3	1.7 ± 0.5	0.208	
Duration of HTN, (years)	7.4 ± 5.7	8.6 ± 6.4	7.8 ± 5.9	0.430	
Oral antidiabetics, n (%)	47 (78.3)	32 (76.2)	79 (77.5)	0.799	
Insulin, n (%)	17 (28.3)	12 (28.6)	29 (28.4)	0.979	
ACEi/ARA, n (%)	24 (40)	11 (26.2)	35 (34.3)	0.148	
Statin, n (%)	11 (18.3)	5 (11.9)	16 (15.7)	0.380	
SBP (mmHg)	144.5 ± 21.8	135.2 ± 21.1	140.6 ± 21.9	0.034	0.937
DBP (mmHg)	88.3 ± 12.2	85.2 ± 11.5	87 ± 11.9	0.211	
Heart rate (bpm)	75.2 ± 12.5	79.2 ± 12.4	76.9 ± 12.6	0.111	
BMI (Kg/m^2)	30.1 ± 6.04	27.1 ± 4.4	28.9 ± 5.6	0.007	0.022

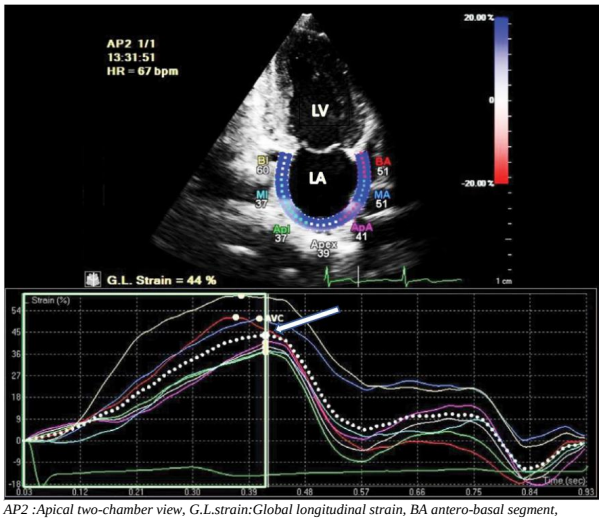
Values are mean ± standard deviation, number of subjects (%); HTN = Hypertension; ACEi angiotensin-converting enzyme inhibitors; ARA = angiotensin receptors antagonists; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index [£]: Adjusted for all significant variables on bivariate analysis ($p<0.05$).

Table II: Echocardiographic parameters, LA phasic volumetric functions and peak atrial longitudinal strain.

Variables	Abnormal PALS (n = 60)	Normal PALS (n = 42)	Total (n = 102)	Crude p value	Adjusted p value[£]
LVEF – Biplane (%)	62.7 ± 7.1	63.6 ± 6.2	63.1 ± 6.7	0.482	
LV mass index (g/m^2)	78.9 ± 20.8	74.2 ± 22.4	77 ± 21.5	0.282	
E/A ratio	0.8 ± 0.3	0.8 ± 0.3	0.8 ± 0.3	0.546	
E/E' ratio	12.1 ± 4.6	8.9 ± 2.3	10.8 ± 4.1	< 0.001	0.032
LAVi (ml/m^2)	23.7 ± 7.1	19.9 ± 5.7	22.2 ± 6.8	0.006	0.419
LA total éjection volume (ml)	24.4 ± 7.7	23.5 ± 9.4	24.1 ± 8 .4	0.584	
LA passive éjection volume (ml)	12.6 ± 7.1	12.4 ± 7.1	12.6 ± 7	0.893	
LA global éjection fraction	55.4 ± 12.5	65.0 ± 10.3	59.4 ± 12.6	< 0.001	0.511
LA expansion index (%)	149.2 ± 74.3	210.4 ± 93.01	174.4 ± 87.5	< 0.001	0.879
LA active éjection volume (ml)	12.53 ± 5.4	12.07 ± 5.4	12.3 ± 5.4	0.674	

Variables	Abnormal PALS (n = 60)	Normal PALS (n = 42)	Total (n = 102)	Crude p value	Adjusted p value[£]
LA active éjection fraction	40.6 ± 14.5	49.3 ± 10.8	44.2 ± 13.7	0.002	0.069

Values are mean ± standard deviation; LVEF = left ventricular ejection fraction; LV = left ventricular; E = early diastolic velocity of mitral flow; A = atrial velocity of mitral flow; E' = early diastolic velocity of mitral annulus; LAVi = left atrial volume index; LA = left atrial;[£]: Adjusted for all significant variables on bivariate analysis ($p<0.05$).



AP2 :Apical two-chamber view, G.L.strain:Global longitudinal strain, BA antero-basal segment, AM:Antero-medial segment, ApA:Antero-apical segment, BI:Infero-basal segment, MI:infero-medial segment, ApI:Infero-apical, HR:Heart rate, LA:Left atrium, LV:Left ventricle.

Figure 1: Two-chamber view depicting peak systolic strain in the reservoir phase. Six segmental longitudinal strain curves are visible, and the dashed curve represents the average value of strain. The peak systolic left atrial strain is indicated by the white arrow. Y-axis represents the strain value in %, X-axis the duration of a cardiac cycle from R to R ECG in seconds. At the top, we have the corresponding M-mode display.