Evaluation of Sub Clinical Myocardial Systolic Dysfunction Using 2D Global Longitudinal Strain Assessment in Type 2 Diabetes Patients in Sub-Saharan Africa

Alain Patrick Menanga[1,2], Chris Nadège Nganou-Gnindjio[1,3*], Ladé Viché[1,4], André Jules Ahinaga[1,5], Franck Ngowa[1], Guy Sadeu Wafeu[1], Donald Paulin Tchapmi Njeunje[1], Hamadou Bâ[1,3], Samuel Kingue[1,2]

[1]Internal Medicine and Specialities Department, Faculty of Medicine and Biomedical Sciences, University of Yaoundé, Yaoundé, Cameroon
[2]Internal Medicine Department, Yaoundé General Hospital, Yaoundé, Cameroon
[3]Cardiology Department, Yaoundé Central Hospital, Yaoundé, Cameroon
[4]Internal Medicine Department, Douala General Hospital, Douala, Cameroon
[5]Efoulan District Hospital, Yaoundé, Cameroon
Email: *cn_nganou@yahoo.fr

Abstract

Background: Heart failure is the commonest cardiovascular complication in type 2 diabetes mellitus. However, subclinical left ventricular dysfunction can't be detected using 2D echocardiography which is routinely used for cardiac evaluation of diabetic patients. We aimed to determine the prevalence and factors associated to left ventricular global longitudinal strain (LV GLS) impairment in type 2 diabetes Cameroonians patients. **Methods:** We conducted a cross-sectional study from January 2019 to June 2019, including type 2 diabetes patients with preserved left ventricle ejection fraction. Clinical and echocardiographic data were collected, and LV GLS was assessed using speckle tracking technique, a value ≤ −16% been considered as normal value. **Results:** We recruited 95 patients, with a mean age of 57.4 ± 11.8 years old and median diabetes duration of 5 [2 - 12] years. Echocardiographic evaluation found 56.3% of left ventricle remodelling, 51.6% of left ventricle diastolic dysfunction and mean left ventricle ejection of 63.3% ± 6.6%. LV GLS impairment was present in 43.2% (95% CI: 32.6 - 53.7) of the participants. After adjustment to all significantly associated factors, Obesity (aOR: 4; 95% CI: 1.5 - 10.6) and diastolic dysfunction (aOR: 3.1; 95% CI: 1.2 - 8.2) were independent factors associated with LV GLS. **Conclusions:** Subclinical systolic dysfunction assessed by LV GLS impairment is frequent in diabetic patients. Further

research should be carried out more extensively to integrate LV GLS in the type 2 diabetes patients' routine follow up for a better prognostic outcome, especially in low-incomes countries.

1. Introduction

Type 2 diabetes is the pathology susceptible to lead to multi organ dysfunction including the heart failure (HF) [1]. Ischemic cardiopathy, diabetic cardiomyopathy and cardiac autonomic neuropathy are the three pathophysiologic mechanisms leading to cardiac complications in diabetes [2]. Diabetic cardiomyopathy is defined as the occurrence of ventricular dysfunction in a diabetic patient and in the absence of coronary atherosclerosis or hypertension [3]. Underlying mechanisms include: altered coronary micro circulation, mitochondrial dysfunction and lipotoxicity [4] [5]. All these complications can lead to left ventricular systolic dysfunction in diabetic patients, which is found in 18% of these patients [6].

Two-dimensional (2D) echocardiography is the leading non-invasive method used routinely for cardiac imaging. However, it cannot detect early ventricular abnormalities, especially when there are no left ventricular (LV) wall motion abnormalities and no reduction in left ventricular ejection fraction. During recent years, speckle tracking echocardiography has been used to assess the global longitudinal strain (GLS) of left ventricle, to detect subclinical systolic dysfunction. Furthermore, impaired GLS is an independent predictor of adverse cardiovascular events like myocardial infarction, heart failure hospitalisations, stroke and cardiovascular mortality [7]. In addition, LV longitudinal myocardial systolic dysfunction has been shown to be the first marker of a preclinical form of diabetic cardiomyopathy in diabetic patients with preserved left ventricular ejection fraction (LVEF) without overt HF [8]. We aimed to evaluate the prevalence and factors associated to impaired LV GLS in a population of diabetic patients from a low-income country where speckle tracking echocardiography is not routinely available.

2. Methods

2.1. Study Design

We conducted a cross sectional study over a period of 6 months (January 2019 to June 2019) at Yaoundé Central Hospital, based on a consecutive sampling, included patients with type 2 diabetes mellitus (DM) and a preserved LVEF who came for outpatient consultation. Informed consent was obtained before inclu-

sion and patients with heart failure, important mitral or aortic valvulopathy, uncontrolled hypertension, atrial fibrillation, or flutter, congenital cardiopathy, anaemia or thyroid dysfunction were excluded from the study. Ethical clearance was obtained from the institutional review board of the faculty of medicine and biomedical sciences of the University of Yaoundé and administrative authorization from the hospital's directors.

2.2. Clinical Data

Clinical assessment on admission included sociodemographic characteristics, cardiovascular risk factors, and global cardiovascular risk assessment based on the WHO/ISH cardiovascular risk prediction charts for AFR D zone [9].

2.3. Echocardiography

A resting transthoracic echocardiography was carried out using an echocardiogram of brand Philips IE 33. We measured the size of the left ventricle and wall thickness in TM mode during diastole and systole using the parasternal long axis view. This enabled us to calculate the left ventricular mass. LVEF was measured using biplane disc summation method (modified Simpson's rule) obtained from apical views [10]. Diastolic dysfunction was defined as the presence of at least 50% of these criteria: 1) E/E' > 14; 2) septal E' velocity < 7 cm/s or Lateral E' velocity < 10 cm/s; 3) peak tricuspid regurgitation velocity > 2.8 m/s; 4) indexed left atrial volume > 34 ml/m^2 [11]. LVGLS was assessed using speckle tracking technique by evaluating the displacement of the endocardial border, epicardial border and myocardial midline on a 2D image [12]. From data of previous literature, we defined Normal LV GLS as ≤ −16% [13].

2.4. Statistical Analysis

Data were collected using a predesigned structured form and entered in a data entry application conceived in CsPro 7.3. Analysis was carried out using IBM SPSS Version 25. Continuous variable was described using mean ± standard deviation for normally distributed variables and Median [interquartile range] for the other quantitative parameters, while qualitative data were described with frequency and percentage. Comparisons between patient with impaired LV GLS and those with normal LV GLS were performed with t tests for normally distributed continuous variables, U MannWhitney test for non-normally distributed variables, and Chi square tests for categorical variables. Independently associated factors were identified using a multivariate logistic regression analysis including all significantly associated factors on bivariate analysis. Probability values of $p <$ 0.05 were considered statistically significant.

3. Results

3.1. General Characteristics of the Study Population

A total of 95 participants with a mean age of 57.4 ± 11.8 years were included. Fe-

males represent 62.1% and hypertension was the leading cardiovascular risk factor found in 56.8%. Table 1 summarise other characteristics of the study population.

3.2. Prevalence of LV GLS Impairment and Associated Factors

As shown in Table 2, 43.2% (95% CI: 32.6 - 53.7) of DM patients with preserved LVEF had LV GLS impairment. The mean LV GLS and LVEF were respectively −17.1% ± 3.2% and 63.3% ± 6.6%. Diastolic dysfunction was found in 49 (51.6%) patients.

Obesity and hypertension were more frequent in the group with impaired LV GLS compared to the group with normal LV GLS, with respectively 53.7% and 22.2% of participants for obesity (p = 0.002), and 70.7% and 46.3% for hypertension (p = 0.017). Diastolic dysfunction was also significantly associated to LV GLS impairment (OR: 3.4; 95% CI: 1.4 - 7.9). Patients with impaired LV GLS had a longer duration of DM compare to those with normal LV GLS (p = 0.047), the median values (IQR) of this duration were respectively 9 (3 - 15) years and 5 (1 - 10) years. After multivariate analysis, obesity (aOR: 4; 95% CI: 1.5 - 10.6) and diastolic dysfunction (aOR: 3.1; 95% CI: 1.2 - 8.2) were independently associated to LV GLS impairment, as shown in Table 3.

4. Discussion

The mean age of the participants was 57.4 ± 11.8 years. Apart from diabetes and obesity, other risk factors present were hypertension and dyslipidaemia. Because of these, more than half of our sample had at least a moderate global cardiovascular risk. The association type 2 diabetes and hypertension were found in 56.8%

Table 1. Characteristics of the study population.

Variables	Values
Gender	
Male	36 (37.9%)
Female	59 (62.1%)
Risk factors	
Obesity	34 (35.8%)
Current smoking	2 (2.1%)
Dyslipidemia	25 (26.3%)
Hypertension	54 (56.8%)
Global cardiovascular risk	
<10	36 (37.9%)
[10 - 20]	41 (43.2%)
[20 - 30]	11 (11.6%)
[30 - 40]	6 (6.3%)
>40%	1 (1.1%)
Duration of DM (Median [IQR])	5 [2 - 12] years

DM: Diabetes mellitus.

Table 2. Echocardiographic characteristics of the study population.

Variables	Values
LV GLS	
Normal	41 (43.2%)
Impaired	54 (56.8%)
Left atrial volume	
Normal	90 (94.7%)
Dilated	5 (5.3%)
Left ventricular volume	
Normal	51 (53.7%)
cLVH	12 (12.6%)
Remodelling	32 (33.7%)
Diastolic function	
Normal	46 (48.4%)
Impaired	49 (51.6%)
GLS (Mean ± SD)	−17.1% ± 3.2%
LVEF (Mean ± SD)	63.3% ± 6.6%
E/A (Mean ± SD)	0.8 ± 0.3
E/E' (Mean ± SD)	10.8 ± 4.0
Indexed left atrial volume	21.6 ± 6.4 ml/m^2

cLVH: concentric Left Ventricular Hypertrophy; LV: Left Ventricular; GLS: Global Longitudinal Strain; LVEF: Left Ventricular Ejection Fraction.

Table 3. Factors associated with impaired LV GLS.

Variables	Impaired LV GLS	Normal LV GLS	Crude OR (95% CI)	Crude p value	Adjusted OR (95% CI)$^\text{£}$	Adjusted p value$^\text{£}$
Age, years (Mean ± SD)	60.2 ± 12.0	55.2 ± 11.2	NA	0.042	NA	0.961
Female sex	26 (63.4)	33 (61.1)	1.1 (0.5 - 2.6)	0.819		
Obesity	22 (53.7)	12 (22.2)	4.1 (1.7 - 9.8)	0.002	4 (1.5 - 10.6)	0.005
Current smoking	1 (2.4)	1 (1.9)	1.3 (0.08 - 21.8)	1.000		
Dyslipidemia	13 (31.7)	12 (22.2)	1.6 (0.6 - 4.1)	0.298		
Hypertension	29 (70.7)	25 (46.3)	2.8 (1.2 - 6.6)	0.017	1.7 (0.6 - 5.2)	0.301
DM Duration*	9 [3 - 15]	5 [1 - 10]	NA	0.047	NA	0.189
Dilated left atrium	3 (7.3)	2 (3.7)	2.1 (0.3 - 12.9)	0.649		
cLVH	8 (19.5)	4 (7.4)	3.03 (0.8 - 10.9)	0.079		
LV Remodelling	19 (39)	16 (29.6)	1.5 (0.6 - 3.6)	0.337		
Diastolic dysfunction	28 (68.3)	21 (38.9)	3.4 (1.4 - 7.9)	0.005	3.1 (1.2 - 8.2)	0.021
LVEF (Mean ± SD)	62.6 ± 7.2	63.9 ± 6.2	NA	0.339		

*(Median [IQR]); $^\text{£}$Adjusted for age, obesity, hypertension, DM duration, diastolic dysfunction, NA: Not applicable.

of our study participants. A high prevalence of hypertension in patients with type 2 diabetes has been described in many studies, with a prevalence 2 to 3 times greater than in the general population [14]. This association significantly increases the cardiovascular risk through a synergistic effect, multiplying the risk by 4 in women and by 2 in men [15] [16].

A low proportion of our patients had left atrial dilation (5.3%), with a mean indexed left atrial volume of 21.6 ± 6.4 ml/m². Type 2 diabetes is not recognized as a risk factor for left atrial dilation since many studies failed to find an association between these two variables [17] [18]. We found left ventricular diastolic dysfunction in 51.6% of our participants. Diastolic dysfunction is a risk factor of heart failure with preserved ejection fraction [19] [20]. this occurs due to insulin resistance and metabolic syndrome which induce left ventricular remodelling and lead to diabetic cardiomyopathy. Diastolic dysfunction is highly associated with type 2 diabetes reaching proportions up to 60% compared to 16% in the general population [21].

Fourthy-three patients (43.2%) had a subclinical left ventricular myocardial dysfunction by alteration of the GLS. Ng *et al.* found a quasi-similar proportion of 44.8% in a similar study [22]. Wang *et al.* found a proportion of altered GLS of 50% in a similar study in patients with type 2 diabetes and preserved ejection fraction [23]. This finding can be explained by many underlying pathophysiologic mechanisms such as lipotoxicity, glucotoxicity, glycation of proteins, and altered coronary microcirculation [24] [25]. An altered GLS is also known to be an independent predictive factor of adverse cardiovascular events such as heart failure [22] [23] [26].

Obesity was significantly associated with LV GLS impairment. Conte *et al.* had the same conclusion after observing a significant difference in the mean GLS between obese and non-obese individuals [27]. This association is thought to result from insulin resistance and myocardial steatosis, leading to lipotoxicity and neuro endocrine system activation [24] [27].

Study Limitations

The cross-sectional design used does not enable us to describe the natural history and onset of the sub clinical myocardial dysfunction in our sample. The possible existence of asymptomatic and silent coronary diseases can be a confounding factor in our study.

5. Conclusion

The evaluation the left ventricular contractile function by assessing the Global Longitudinal Strain using 2D speckle tracking echocardiography is important to identify subclinical changes in myocardial function. An important proportion (43%) of the participants in our study—type 2 diabetes patients with preserved ejection fraction—had an impaired LV GLS. Factors independently associated with abnormal myocardial function are obesity and left ventricular diastolic

dysfunction. Further research is needed in our context to find additional factors associated with subclinical impaired left ventricular function. We also need to determine the short- and long-term prognosis of these patients and identify therapeutic measures to improve patient outcomes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

Authors' Contribution

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

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

LV: Data collection, data analysis/interpretation, 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;

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

FN: Data collection, critical revision of article, Approval of article;

HB: Critical revision of article, Approval of article;

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

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