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Silent Myocardial Ischemia and left Ventricular Diastolic Dysfunction in Type 2 Diabetic Patients. A Case Control study

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Abstract

Aims: People with type 2 diabetes mellitus (T2DM) have a higher cardiovascular morbidity and mortality. We sought to describe the occurrence of asymptomatic Left Ventricular Diastolic Dysfunction (LVDD) and silent Myocardial infarction (SMI) in diabetic patients in comparison with non-diabetic controls.

Methods: From March 2019 to September 2020, transthoracic 2D doppler, tissue doppler echocardiography and an exercise stress test (EST) were used to assess LVDD and SMI in diabetics (cases) and non-diabetics (controls). P values <0.05 were considered statistically significant.

Results: In total,166 participants were recruited, 95 cases and 71 controls, matched for age and sex: mean age 43 ± 7 years in cases and 40 ± 5 years in controls, p>0.05. LVDD was significantly higher in cases (n=22; 23.2%; 95%CI:15.4%-33.2%) as compared to healthy controls (n=6; 8.5%; 95% CI:3.5%-18.1%), p<0.05. Similarly, SMI was significantly higher in diabetic patients (n=13; 13.7%; 95% CI:7.8%-22.6%) as compared to the non-diabetic controls (n=2; 2.8%; 95% CI:0.5%-10.7%), p<0.05.

Conclusions: Diabetic patients have higher rates of LVDD and SMI, therefore requiring closer clinical and paraclinical follow-up for good long-term outcomes.

Keywords: Left ventricular diastolic dysfunction, Silent Myocardial Ischemia

Introduction

Type two diabetes mellitus (T2DM) remains a serious public health priority, with an estimated 8.5% global prevalence [1]. Evidence shows rising burden of this disease in many parts of the world, favored by rapid economic development and urbanization [2]. According to the International Diabetes Federation (IDF), 24 million adults aged between 20 and 70 years were living with diabetes in 2021 [3]. In Cameroon, the prevalence of diabetes is estimated at 5.7%, but with undiagnosed population of about 70% [4]. T2DM usually has multiple complications, contributing to the global health burden, with diabetes reported as the seventh leading cause of death in the United States, and responsible for 416 000 deaths in the IDF Africa region in 2021 [3, 5]. Looking at specific causes of death in diabetic patients, cardiovascular complications constitute the leading one[5, 6]. Adults with diabetes have 2–4 times increased cardiovascular risk as compared to adults without diabetes [7]. Some of these complications are usually asymptomatic

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but may be fatal if left untreated. Left ventricular diastolic dysfunction (LVDD) and silent Myocardial Infarction (SMI) are two such complications, that may be present at subclinical levels, and lead to serious complications if left untreated [8]. Evidence shows levels as high as 47%-75% of LVDD and 19%-34% for SMI in asymptomatic type II diabetic patients in the united states and Pakistan [9]. Data howevere remains sparse in resource limited settings like Cameroon on this important subject. We therefore sought in this study to describe the occurrence of LVDD and SMI in TSDM patients in comparison to healthy controls, in two reference hospitals in Cameroon.

Materials and Methods

Study Design and Participants

We did a case control study, between March 2019 and September 2020, at the Yaoundé Central Hospital (YCH) and Yaoundé General Hospital (YGH). Cases were type 2 diabetic patients attending cardiology clinic at study sites and controls were non-diabetics. The authors didn't have access to information that could identify the subjects, during data collection and after data was collected. Written consent was gotten from each of our patients before the study. Our estimated sample size was 136 participants, 68 cases and 68 controls. Were excluded participants with ischemic heart disease, a poor transthoracic echocardiographic window, myocarditis, endocarditis, cerebrovascular disease, aortic stenosis, pericarditis, obesity or other physical/mental impairment, heart rate <50 or >100 beat per minute, aortic dissection, participants with a long history of diabetes mellitus (>10 years), heart failure, renal failure, atrial fibrillation and high-grade AV blocks and patients with significant valvular heart disease.

Ethical Considerations

We obtained ethical clearance from the ethical committee of the Faculty of Medicine University of Yaoundé 1. All core ethical values were respected.

Study Procedures

Data Collection

A structured questionnaire was used and data was collected by health staff.

Biological workups

Blood was collected and analysed at a reference laboratory.

Imaging

LVDD was assessed using the criteria defined in a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology (ESC). Echocardiography and exercise stress testing were carried out as previously described by Ashour et al [10].

Data Management and Statistical Analysis

Qualitative variables were described using frequencies and 95% confidence intervals: quantitative variables with mean ± Standard deviation (SD) or median [interquartile range (IQR). Data was entered and analysed using the SPSS-22 (Statistical Packages for Social Sciences version 22). P values <0.05 considered statistically significant.

Results

Baseline clinical characteristics and Socio-demographic characteristics of study population

In total, 166 participants were retained, 95 cases, and 71 controls, both groups matched for age and sex. The mean age±SD was 43 ± 7 and 40 ± 5 years, in the case and control groups respectively (p>0.05). Most of our participants were classified under WHO grade I obesity, with a similar mean body mass index (BMI) of 28.7kg/m^2 in the cases and 26.3±31kg/m^2 in the control group, p>0.05. The mean duration of diabetes was 7±3 years, with majority of diabetic patients having poor long-term glycemic control (mean HbA1C=7.9±2.1%).

2D and doppler parameters

The E/A ratio appeared significantly lower in cases as compared to non-diabetic controls, with a mean E/A ratio of 0.83±0.4 in cases and 1.2±0.2 in controls, p<0.05. On the other hand, the mean E/e' ratio was significantly higher in diabetic patients (14.1±3) as compared to their healthy controls (6.97±1.1), p<0.05. Elsewhere, lateral e appeared significantly lower in diabetic patients (0.78±0.34 in diabetics as opposed to 1.5±0.12 in non-diabetics, p<0.05), as well as was septal e (0.62±0.2 in diabetics as opposed to 1.3±1.9 in non-diabetics, p<0.05). Lastly, the mean peak tricuspid regurgitation (TR) velocity was higher in diabetics (2.9±0.8) as compared to non-diabetics (2.3±0.6), p<0.05. Table 1 below summarizes all 2D and doppler findings in the case and control groups.

Table 1: 2D and Doppler characteristics of participants

Parameter	Diabetics, mean+SD	Controls, mean+SD	p-value
E (m/sec)	0.58 ± 0.22	0.60 ± 0.1	>0.05
A (m/sec)	1.2 ± 0.3	0.8 ± 0.12	>0.05
E/A ratio	0.89 ± 0.25	1.12 ± 0.22	**<0.05**
Lateral e (m/sec)	0.78 ± 0.34	1.5 ± 0.12	**<0.05**
Septal e (m/sec)	0.62 ± 0.2	1.3 ± 1.9	**<0.05**
E/e ratio	14.1 ± 3	6.97 ± 1.5	**<0.05**
LA size (ml/m2)	32.1 ±1.4	29.3 ±2.1	>0.05
LA volume index (ml/m2)	32 ± 3	26 ± 4	>0.05
TR velocity	31.2 ±1.6	26.8 ±3.1	>0.05
Peak TR velocity (m/sec)	2.9 ± 0.8	2.3 ± 0.6	**<0.05**
EF	63 ± 4	64 ± 5	>0.05

Legend: The table above shows the mean values of 2D and Doppler ultrasound findings. Significant p values are highlighted in bold.

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Prevalence of LVDD and SMI

Overall, LVDD was identified in 28 participants (16.9%, 95%CI: 11.7%-23.6%), with a significantly higher prevalence in diabetics (n=22; 23.2%; 95%CI:15.4%-33.2%) as compared to healthy controls (n=6; 8.5%; 95% CI:3.5%-18.1%); OR= 3.2; p<0.05. Amongst the 22 diabetic patients with diastolic dysfunction, majority (n=16; 72.8%) had grade I diastolic dysfunction while 6 (27.3%) had grade II diastolic dysfunction and no patient presented with a restrictive filling pattern (grade III). All 6 non-diabetic controls with diastolic dysfunction were classified at grade I (impaired relaxation). As concerns SMI, overall prevalence was 9.0% (95% CI: 5.3%-14.7%), with significantly higher prevalence in cases (n=13; 13.7%; 95% CI:7.8%-22.6%) as compared to non-diabetic controls (n=2; 2.8%; 95% CI:0.5%-10.7%); OR=5.5; p<0.05. Elsewhere, patients with LVDD had higher levels of SMI (29%), as compared to patients with LVDD (6.3%), p<0.05.

Discussion

In our study we found significantly higher rates of LVDD and SMI in diabetic participants as compared to healthy controls. As concerns LVDD, diabetic patients had 3-fold increased odds of having LVDD with rates as high as 23.2% as compared to non-diabetic controls (8.5%), p<0.005. These results are different from those obtained by Cosson et al, who found no evidence for a difference in LVDD in diabetic patients as compared to healthy controls [11]. The difference in our results could be explained by the smaller population in which their study was conducted and the better glycemic control in their population, as the mean HbA1c in their patients was 5.3±0.5, as opposed to 7.9±2.1 in our study. It is worth noting that variable results have been obtained on this subject in the past as our results corroborate with those obtained by several other studies [12]. In 2017, Suresh et al described as high as a 6 fold increase in LVDD in diabetic patients as compared to healthy controls [13]. Elsewhere, T2DM was reported as the strongest independent predictor of asymptomatic LVDD in patients without structural heart disease nor systemic hypertension [14]. This increase in LVDD in diabetic patients, can be explained by numerous metabolic changes in diabetic patients. Van Heerebeek et al described high levels of left ventricular stiffness in diabetic patients, irrespective of left ventricular ejection fraction (LVEF) and also showed increased fibrosis and advanced glycation end product (AGE) deposition in diabetic patients with decreased LVEF [15]. Basically, in diabetic patients, the myocardial stiffness resulting from collagen damage, interstitial fibrosis, and inflammation delays the relaxation period with negative consequences further down the chain of the diastolic and filling pressure. Persistent hyperglycemia increases glycation of myocardial interstitial proteins such as collagen by deposition of advanced nonenzymatic glycation end products (AGE) in the extracellular matrix, resulting in a further increase in myocardial stiffness [16].

As concerns SMI, T2DM patients had about six-fold increased risk of SMI as compared to healthy controls. These results are different from those obtained by Sheikh et al in 2011, who found no difference in silent myocardial ischemia between diabetics and non-diabetics [17]. This difference in findings can be explained first by the study design used in this said study (cross sectional), with a very small number of diabetic patients who were finally obtained. Our results however, corroborate with many other studies on the subject, such as those obtained by Wackers et al, who found a high prevalence of SMI in diabetics as compared to healthy controls [18]. Silent myocardial infarction in diabetic patients could be explained by the presence of autonomic neuropathy and sensory denervation. Additionally, diabetic patients have abnormal m-iodobenzylguanidine imaging, suggesting that abnormalities of pain perception may be caused by sympathetic denervation [19, 20]. Silent ischemia may delay the diagnosis of coronary artery disease, leading to more advanced disease when it is finally diagnosed.

Conclusion and Recommendation

This study suggests that left ventricular diastolic dysfunction and Silent myocardial infarction is common amongst patients with Type 2 diabetes mellitus in this resource limited setting of Cameroon, calling for closer monitoring of diabetic patients, to enable early detection and management of asymptomatic cardiovascular manifestations.

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