Scientific Research Publishing

World Journal of Cardiovascular Diseases, 2022, 12, 374-381
https://www.scirp.org/journal/wjcd
ISSN Online: 2164-5337
ISSN Print: 2164-5329

Left Ventricular Diastolic Dysfunction and Silent Myocardial Ischemia amongst Asymptomatic Type 2 Diabetic Patients in Two Referral Hospitals in Cameroon

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How to cite this paper: Walinjom, J.N., Boombhi, J., Etoa, M., Ambe, C.C., Eho, E., Menanga, A. and Kingue, S. (2022) Left Ventricular Diastolic Dysfunction and Silent Myocardial Ischemia amongst Asymptomatic Type 2 Diabetic Patients in Two Referral Hospitals in Cameroon. *World Journal of Cardiovascular Diseases*, **12**, 374-381.
https://doi.org/10.4236/wjcd.2022.127037

Received: June 7, 2022
Accepted: July 15, 2022
Published: July 18, 2022

Abstract

Background: Cardiovascular events, the leading cause of death among diabetic patients, are usually under-diagnosed due to subclinical presentation. **Methods:** We conducted a cross-sectional study from March-2019 to September-2020, in two reference hospitals in Yaoundé, Cameroon, to assess the prevalence of asymptomatic Left Ventricular Diastolic Dysfunction (LVDD) and Silent Myocardial Infarction (SMI) and potentially associated factors. **Results:** Out of 95 participants (mean age ± SD: 43 ± 7 years; M/F sex-ratio 1.6), 22 (23.1%; 95% CI: 15.8% - 32.6%) had LVDD and fewer (n = 13, 13.6%; 95% CI: 8.2% - 22.0%) had SMI, p = 0.86. Though not statistically significant, patients with ≥5 years diabetes duration, as well as patients with HbA1C ≥ 7.5% had two-fold increased risk of LVDD (p = 0.22 and p = 0.15 respectively). LVDD was significantly higher in patients with SMI (29% vs 6.3%, p < 0.05). **Conclusion**: The significant presence of asymptomatic cardiovascular manifestations in this population entails mandatory preventive screening, especially, in patients with long standing diabetes and poor glycemic control, to allow timely detection and management.

Keywords

Asymptomatic Cardiovascular Manifestations, Left ventricular Diastolic Dysfunction, Silent Myocardial Ischemia, Type 2 Diabetes, Cameroon

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1. Introduction

Cardiovascular diseases represent the principal causes of mortality and morbidity among people with type 2 diabetes. Adults with diabetes have 2 - 4 times increased cardiovascular risk as compared to those without diabetes. Despite therapeutic advances made, high morbidity and mortality remains associated with this chronic illness [1]. Left ventricular diastolic dysfunction (LVDD) represents the earliest preclinical manifestation of diabetic cardiomyopathy, and has fatal complications amongst which, is, rapid progression to symptomatic heart failure. Silent Myocardial Infarction (SMI) is another significant cardiovascular disease, occurring 2 to 6 times more frequently in diabetic population [2]. It is a transitory impairment of myocardial flow, without angina, pain nor other symptoms. Though these events are often asymptomatic and unrecognized, conventional echocardiography or recent echocardiographic models such as tissue Doppler imaging (TDI) and exercise stress testing are goal standards for their early diagnosis [2] [3]. The implications of these events are enormous, both in terms of increased risk of developing major or even fatal cardiovascular complications and cost to health-care systems which are increasingly faced with treating these serious complications.

Several studies have demonstrated high frequencies of LVDD and SMI amongst asymptomatic type 2 diabetic patients with frequencies of 47-75% for LVDD and 34% and 19% for SMI in the United States and Pakistan respectively [4] [5] [6] [7] [8]. In Nigeria, 58% of type 2 diabetic patients presented impaired relaxation [9]. However, in Cameroon where diabetes burden is significant, there is paucity of data on the subject. We sought to determine the prevalence of asymptomatic LVDD and SMI as well as to assess the relation of LVDD with age, duration of diabetes mellitus (DM), Glycosylated hemoglobin levels (HbA1c), and SMI in type 2 diabetic subjects in two hospitals in Cameroon.

2. Materials and Methods

2.1. Study Design and Participants

We carried out a hospital based, cross sectional and analytical study, between March 2019 and September 2020, at two tertiary level hospitals in Yaoundé, Cameron; the Yaoundé Central Hospital (YCH) and Yaoundé General Hospital (YGH). Following consecutive sampling, all consenting type 2 diabetic patients presenting for cardiology consultation or follow-up were recruited. With an expected prevalence of asymptomatic manifestations of (17.3%) and 95% confidence interval, our minimal sample size was estimated at 86 participants [10]. Excluded were participants with ischemic heart disease, hypertension, cerebrovascular disease, aortic stenosis, pericarditis, myocarditis or endocarditis, acute aortic dissection, high-grade AV blocks, obesity or other physical/mental impairment, heart failure, significant valvular heart disease, heart rate < 50 or >100 beats per minute, atrial fibrillation and other arrhythmias that may interfere with Doppler studies, patients with long history of diabetes mellitus (>10 years)

or advanced diabetic complications (e.g. renal failure, severe peripheral arterial disease) and subjects with very poor transthoracic echocardiographic window.

2.2. Ethical Considerations

Ethical approval was obtained from the institutional review board of the Faculty of Medicine and Biomedical Sciences University of the University of Yaoundé I, and approvals from the directors of YCH and YGH as well as the heads of Cardiology units. All core ethical values were respected.

2.3. Study procedures

2.3.1. Data Collection

Data was collected using structured questionnaires by health staff. It consisted of demographic data (age, sex, religion, region of origin, occupation, level of education and residence) and clinical history (history of hypertension, associated complications such as stroke, treatment modality of hypertension, history of T2DM, presence of associated complications and modality of treatment, history of kidney disease and modality of treatment, social history; that is smoking habits, alcohol and sports).

2.3.2. Biological Workups

To evaluate the effect of long term glycemic control on the occurrence of asymptomatic cardiovascular events, we conducted HbA1C measurement in all study participants. 10 mL of whole blood was collected from each participant and all HbA1C measurements carried out at the analysis laboratory of the Yaoundé Central Hospital.

2.3.3. Assessment of Cardiovascular Events

Echocardiography and exercise stress testing were carried out as previously described by Ashour *et al.* [10]. 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) [11].

2.4. Data Management and Statistical Analyses

Data was entered and analyzed using the SPSS-22 (Statistical Packages for Social Sciences version 22). Qualitative variables were described using frequencies and 95% confidence intervals, while quantitative variables with mean ± Standard deviation (SD) or median [interquartile range (IQR)]. The Pearson chi-square test was used to compare categorical variables with p values < 0.05 considered statistically significant.

3. Results

A total of 107 participants were enrolled. Twelve were excluded amongst which; ischemic heart disease (4), atrial fibrillation (3), renal failure (2), heart failure

(1), cerebrovascular disease (1) or poor transthoracic echocardiographic window (1). Hence, a total of 95 (88.8%) participants were retained.

3.1. Baseline Characteristics of Study Population

Define the mean age of the participants was 43 ± 7 years with a male predominance (M/F sex ratio: 1.6). Table 1 below summarizes the baseline characteristics of the study population.

3.2. Prevalence of LVDD and SMI

Of the 95 asymptomatic type 2 diabetic patients, 22 had LVDD, giving a prevalence of 23.1% (15.8% - 32.6%) and 13 had SMI, giving a prevalence of 13.6% (8.2% - 22.0%).

3.3. Factors Associated to LVDD

Patients with age ≥ 45 years had no significant increased risk of LVDD (OR: 0.4; p = 0.6). Though not statistically significant, patients with long standing diabetes melitus (≥5 years duration) appeared to have higher chances of presenting with LVDD as compared to those with shorter diabetes duration (OR: 1.5; p = 0.2). To add, patients with poor glycemic control (HbA1c >7.5%) appeared to have a two-fold increased risk of LVDD (OR: 2; p = 0.2). Lastly, LVDD was significantly higher in participants with SMI (29% as compared to 6.3% in participants without SMI, p < 0.05).

4. Discussion

This study sought to determine the prevalence of asymptomatic LVDD and SMI; as well as assess the relation of LVDD with age, duration of diabetes, HbA1c levels and SMI among type 2 diabetic patients in two hospitals in Cameroon.

Table 1. Baseline characteristics of asymptomatic type 2 diabetic patients.

Variable	Overall (N = 95)
Mean age, years	43 ± 7
Mean Duration of type 2 diabetes, years	7 ± 3
Mean BMI, kg/m^2	28.7 ± 3
Mean HbA1C, %	7.9 ± 2.1
E/A ratio	0.83 ± 0.4
E/e' ratio	14.1 ± 3
LA size (ml/m^2)	32.1 ± 1.4
TR velocity	31.2 ± 1.6
Mean EF	63 ± 4

BMI: Body Mass Index, LA: left Atrium, HbA1C: Glycated haemoglobin.

In total, 23.1% of our participants had diastolic dysfunction. This is high compared to that reported by Sohail *et al.* (15%) and could be explained by the diagnostic tool used [12]. Conventional echocardiography was used to make the diagnosis of diastolic dysfunction in their study where as we used tissue Doppler echocardiography which is a more sensitive diagnostic tool. As such, Yadava *et al.* in 2017 using a similar diagnostic method described similar levels of LVDD (27%) [13]. Elsewhere, other studies have described higher levels of LVDD [2] [14] [15] [16]. Ojji *et al.* in Nigeria reported diastolic dysfunction of 58% amongst normotensive diabetic patients [17]. This could be attributed to the fact that their population was older that ours, their mean age being 55 ± 8 years compared to 43 ± 7 years in our study. It is worthy of note that in healthy individuals with no cardiovascular diseases, early diastolic filling decreases with age [18].

As concerns potential factors associated to LVDD, contrary to findings by Ojji *et al.* and Boyer *et al.*, we found no significant association between age and LVDD [7] [9]. This could be explained by the relatively young study population and limited sample size in our study. Even in healthy individuals without cardiovascular disease, early diastolic filling decreases with age, coupled with alteration in active relaxation and passive electric the left ventricle, therefore making age a potential determinant of LVDD [19] [20]. Though not statistically significant, patients with duration of diabetes > 5 years had almost 2-fold increased risks of LVDD, while those with poor glycemic control (HbA1c > 7.5) had 2-fold increased risks of having LVDD. These results are similar to previous findings [6] [21] [22]. To add, hyperglycemia per se can lead to alteration in substrate supply and utilization by cardiac myocytes that represent the primary injury in the pathogenesis of diastolic function impairment and subsequently diabetic cardiomyopathy [10].

As concerns SMI, we obtained a 13.6% prevalence in our study. This is lower compared to that reported by Deluca *et al.* (34%) and Sheikh *et al.* (19%), and could be explained by an older population by Deluca *et al.*, and the non-exclusion of hypertensive patients by Sheik *et al.* [5] [14]. The pathophysiology of silent ischemia remains controversial, and several factors may play a role, including differences in plasma opioid receptors, ischemic damage to nerve endings, and psychological factors [23]. Regardless of the cause, silent ischemia may delay or mask the diagnosis of Coronary Artery Disease (CAD), contributing to more advanced disease when it is finally discovered. Lastly, patients with SMI had significantly occurrence of LVDD. These results therefore highlight the importance of systematic preventive screening of SMI in asymptomatic diabetic patients.

Limitations

Other tests such as coronary angiography to exclude coronary artery disease (CAD) as the underlying cause of myocardial dysfunction rather than diabetic cardiomyopathy were not performed. Nevertheless; the patients included in the study are relatively young and asymptomatic, so the possibility of CAD would

possible be low.

5. Conclusion

Asymptomatic cardiovascular manifestations are common in patients with type 2 diabetes with LVDD diagnosed in 23.1% asymptomatic diabetic patients and SMI in 13.6% of asymptomatic diabetic patients. Interestingly, LVDD appears higher in patients with long diabetes duration (≥5 years), poor glycemic control (HbA1c levels > 7.5%), and in those with SMI. This suggests that, early diagnosis of LVDD and SMI in diabetic patients should be done using tissue doppler echography and exercise stress test respectively especially in older patients with long standing history of DM and those with poor glycemic control, so as to allow for timely detection of these asymptomatic cardiovascular events, for prompt management, hence improving outcome and survival.

Acknowledgements

I earnestly thank my supervisor Professor Samuel Kingue a Great Mentor and an outstanding teacher; my co-supervisor; Dr Jerôme BOOMBHI and Dr Martine ETOA for the meticulous guidance and immense support which they gave me during this study. I also give special thanks to my wife Dr, Mrs Emerentia Walinjom my destiny sustainer. Special thanks to all the cardiologists I worked with, but most especially, the head of the Cardiology department of the Faculty of Medicine and Biomedical Sciences, Yaounde I and of the General Hospital of Yaounde, Professor Alain Menanga for his availability, coaching and selfless support during all my years in specialisation. Above all, to God Almighty, giver of life, health and wisdom, I wish to express unending gratitude. His faithfulness is the main pedestal for this accomplishment.

Conflicts of Interest

The authors declare no conflicts of interest.

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