A Study on Biochemical Predictors of Left Ventricular Diastolic Dysfunction in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: The prevalence of coronary artery disease (CAD) is nearly 3 times more common in diabetes mellitus (DM) patients than in non-DM patients. Impaired glucose tolerance can be considered as a major risk factor of CAD. Hyperinsulinemia is one of the conditions of abnormal glucose metabolism significantly affects atherosclerosis development.

Aim of the Study: This study aims to determine the risk factors in the onset of the left ventricular diastolic dysfunction (LVDD) within 4 years of follow-up of patients with Type 2 DM (T2DM).

Materials and Methods: A total of 48 patients with T2DM were subjected to baseline fasting blood samples for fasting blood sugar (FBS), high sensitive C-reactive protein (hsCRP), hemoglobin A1c (HbA1c), and triglycerides (TG) levels. Resting transthoracic two-dimensional echocardiography and Doppler imaging to assess LVDD, left ventricular myocardial index (LVMI), and left ventricular mass at baseline and annually for 24 months was done in all the patients. Diastolic function was categorized based on mitral inflow and Doppler tissue imaging parameters. All the data were analyzed using standard statistical methods.

Observations and Results: Among 48 patients with T2DM aged 45–70 years, the mean age was 56.34 ± 35; 26 males and 22 females with a male-to-female ratio of 1.8:1. Baseline body mass index was 28.97 ± 3.60, mean FBS was 128 ± 6.21, and mean HbA1c was 7.5 ± 1.21. The mean duration of T2DM in the patients was 7.23 ± 3.10 years.

Conclusions: The baseline hsCRP and TG levels can predict the presence of LVDD within 24 months in Type 2 diabetes patients with previously normal systolic and diastolic cardiac function, whereas angiotensin receptor blocker therapy might have a protective role.

Key words: Diabetes mellitus, Left ventricular diastolic dysfunction, Coronary artery disease, Type 2 diabetes

INTRODUCTION

Review of literature shows that Type 2 diabetes mellitus (T2DM) patients are at a risk to develop cardiomyopathy (diabetic cardiomyopathy) clinically characterized by the left ventricular diastolic dysfunction (LVDD).[^1] Even in patients with good glycemic control, the incidence of LVDD is 47%.[^2] High levels of high-sensitivity C-reactive protein (hsCRP) have been found to be associated with subclinical LVDD in patients with cardiovascular (CV) risk factors.[^3] Therefore, the aim of the present study was to determine possible risk factors that could predict the new onset of LVDD within 48 months of follow-up in a T2DM patient cohort. DM is the most common cause of CAD in young people. Similarly, nearly, 50% of patients with recently diagnosed as T2DM have CAD at the time that DM is diagnosed.[^4] Developing acute myocardial infarction (AMI) in patients with T2DM is 50% and 150% greater in men and women with DM, respectively.[^5] The prevalence of sudden death due to CAD is 150% and 300% more frequent in men and women with DM, respectively, than in the non-diabetic population.[^6] The frequency of developing AMI and silent ischemia is more common with a greater morbidity and mortality; after AMI in these patients, there would be slower reperfusion speeds following thrombolytic treatment; a larger number of vessels involved; more diffuse distribution and more

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severe narrowing of the left coronary artery; and a higher rate of restenosis after coronary angioplasty.\[^8\] In spite of this evidence, it is noteworthy that less than one-third of diabetic patients are aware of their greater cardiovascular risk.\[^9\] In this context, the present study was conducted to determine the risk factors in the onset of LVDD within 4 years of follow-up of patients with T2DM.

**Aim of the Study**
This study aims to determine the risk factors in the onset of LVDD within 4 years of follow-up of patients with T2DM.

**Study Period**
The study period was from July 2015 to June 2017.

**Institute of Study**
The study was conducted at Kannur Medical College, Anjarakandy, Kannur, Kerala.

**MATERIALS AND METHODS**
Totally, 48 patients were included in the study. They were aged between 45 and 70 years. There were 26 males and 22 female patients. They were diagnosed as T2DM and attending the Department of Medicine of a tertiary teaching hospital. An ethical committee clearance was obtained before the commencement of the study. An Ethical Committee cleared consent letter was used in the study.

**Inclusions Criteria**
1. Patients with diagnosed T2DM and aged between 45 and 70 years were included.
2. Patients with no history of Angina, AMI were included.

**Exclusion Criteria**
1. Patients with coronary artery disease, inflammatory states, and active malignancy were excluded.

All the patients were elicited of clinical history, collection of demographic data. All the patients were estimated of body mass index (BMI). The laboratory investigations included were fasting blood samples for fasting blood sugar (FBS), hsCRP, hemoglobin A1c (HbA1c), and triglycerides (TG) levels at the baseline visit. Resting transthoracic two-dimensional echocardiography and Doppler imaging to assess LVDD, left ventricular myocardial index (LVMI), and left ventricular mass at baseline and annually for 24 months was done in all the patients. The LV ejection fraction was estimated using the Simpson biplane method. The E- and A-wave peak velocities and deceleration time (DT) were measured using the mitral inflow profile. The E’ velocity from the septal and lateral mitral valve annulus and the mean value were determined, and the respective E/E’ ratios were derived. An E/E’ septal ratio >15 was considered to be indicative of elevated LV filling pressure. Diastolic function was categorized based on mitral inflow and Doppler tissue imaging parameters. All the data were analyzed using standard statistical methods.

**OBSERVATIONS AND RESULTS**
A total of 48 patients included in the present study with T2DM were aged 45–70 years with a mean age of 56.34 ± 35. There were 26 males and 22 females with a male-to-female ratio of 1.8:1. At the beginning of the study, the mean BMI was 28.97 ± 3.60, mean FBS was 128 ± 6.21, and mean HbA1c was 7.5 ± 1.21. The mean duration of T2DM in the patients was 7.23 ± 3.10 years. All the patients had normal both systolic and diastolic cardiac function that were followed up for 48 months. At the beginning of the study, 21/48 (43.75%) had arterial hypertension, 23 patients (47.91%) had dyslipidemia [Table 1].

Among the 48 patients, 45 (93.75%) were taking oral antihyperglycemic agents; 44 (91.66%) were on metformin, 12 (25%) were on sulfonylurea, 9 (18.75%) were on dipeptidyl peptidase-4 (DPP-4) inhibitors, and 5 (10.41%) were on glinides [Table 2].

Among 48 patients, 14 were on angiotensin-converting enzyme (ACE) inhibitors, 08 (16.66%) were on angiotensin receptor blockers (ARBs), 3 (6.25%) were on diuretics, and 4 (8.33%) were on beta-blockers [Table 3].

At the end of the study, 2 years (24 months) 15/48 (31.25%) patients were found with diagnosis of LVDD. Univariate logistic regression analysis showed that LVDD was associated with BMI (odds ratio [OR]: 1.16, 95% confidence interval [CI]: 0.79–1.49, \(P < 0.05\)), ARBs (OR: 0.19, 95% CI: 0.05–1.04, \(P < 0.05\)), hsCRP (OR: 1.12, 95% CI: 1.08–1.51, \(P < 0.05\)), TG (OR: 12.07, 95% CI: 3.01–6.04, \(P < 0.05\)), and LVMI (OR: 1.0, 95% CI: 1.00–1.09, \(P < 0.05\)), [Table 4].

In the present study, there was no statistically significant correlation between LVDD and sex, age, diabetes duration, history of hypertension, dyslipidemia, and TG levels. Univariate logistic regression analysis controlling for the above factors showed that LVDD was most likely associated with BMI, hsCRP, TG, and LVMI. The study also showed that the ARBs usage was negatively associated with LVDD [Table 4].

**DISCUSSION**
In the present study, the Univariate analysis of laboratory values obtained shows that higher hsCRP and TG levels
might predict the new onset of LVDD, whereas ARB therapy might have a protective role in T2DM patients. Earlier studies have shown that CRP is a marker of the left ventricular dysfunction. In patients with heart failure, CRP is increased and positively associated with parameters of the left ventricular dysfunction. A previous study on diabetic complications indicated that hypertriglyceridemia was closely associated with early stages of LV systolic longitudinal myocardial dysfunction in asymptomatic DM patients with preserved left ventricular ejection fraction. Elevated fasting TG are thought to be a cause of myocardial steatosis, resulting in subclinical LV systolic and diastolic dysfunction. Another study demonstrated that efficient modification of risk factor profile and, especially, of dyslipidemia, can be achieved by Proprotein convertase subtilisin/kexin Type 9 inhibitors, reducing low-density lipoprotein levels substantially and eventually reducing the incidence of cardiovascular events and ischemic left ventricle dysfunction. In this study, usage of ARBs might have a protective role in the establishment of LVDD in T2DM patients. The same pattern was observed in other studies in which ARBs and ACE inhibitors inhibited ventricular fibrosis in hypertensive diastolic heart failure. In this study, this type of protection was not found with ACE inhibitors. However, the limitation of the present study is that it is a small sample size. The favorable effects of DPP-4 inhibitors and pioglitazone on the left ventricular function were not observed in this study.

**CONCLUSIONS**

The baseline hsCRP and TG levels can predict the presence of LVDD within 24 months in Type 2 diabetes patients with previously normal systolic and diastolic cardiac function, whereas ARB therapy might have a protective role. FBS and HbA1c levels did not show any predictive potential in this Type 2 diabetes patient cohort.

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