ORIGINAL ARTICLE

Evaluation of Left Ventricular Diastolic Dysfunction in diabetic patients with preserved Ejection fraction and its association with myocardial performance index

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Abstract

Background: Diastolic dysfunction causes impairment of ventricular filling when the ventricle becomes stiff, relaxes slowly or incompletely. Diabetes mellitus increases the risk of diastolic dysfunction which can develop heart failure even in the absence of other co-morbidities. Tei index is an echocardiographic tool to evaluate global function of ventricle.

Objective: To determine the prevalence of Left Ventricular diastolic dysfunction (LVDD) in patients with type 2 diabetes mellitus; and its association with LV myocardial performance index (Tei Index).

Method: 100 patients with type 2 diabetes mellitus with normal left ventricular ejection fraction without overt cardiac disease were included. LVDD was determined as per using 2016 American Society of Echocardiology (ASE) guideline. LV Tei index was calculated by tissue doppler imaging method.

Results: Mean age of the patients was 58.1 ± 12.6 years with 54 percent male. Mean HbA1C was 7.45± 0.99. 23 (23%) patients met the criteria of LVDD and 46 (46%) patients did not have LVDD. Whereas 31 (31%) of patients were categorized as indeterminate. Tei index was significantly higher in patients with LVDD (0.56±0.05 and 0.43±0.06 ($p < 0.05$).

Conclusion: Prevalence of LV diastolic dysfunction in type 2 diabetes mellitus was 23% in our study. There was a significant association between LVDD and Tei index. Rising trend of prevalence of diastolic dysfunction with increasing age of patients was observed.

Key Words: *2016 ASE/EACVI guideline*, *Diastolic dysfunction, diabetes mellitus, MPI, Tei index, Tissue doppler imaging*

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Introduction:

Cardiac dysfunction is the major cause of morbidity and mortality in diabetes worldwide[1].Diabetes is a major risk factor not only for CAD, but also for left ventricular dysfunction and heart failure[2]. In the Framingham Heart Study, it was shown that HF was twice as common among men and five times as common among women with diabetes as among those without diabetes[3]. Diabetic cardiomyopathy is characterized by the development of diastolic dysfunction at the early stage, followed by systolic dysfunction in the absence of coronary artery disease, hypertension, or significant valvular heart disease[4]. Type 2 diabetes seems to be more strongly associated with the development of HFpEF than with HFrEF. In line with these findings, left ventricular diastolic dysfunction (LVDD), the preclinical stage of HFpEF, is also more prevalent among type 2 diabetes patients than in those without diabetes[5].

Although type 2 diabetes is a known risk factor of LVDD and HFpEF, the use of echocardiography is in general not considered in existing type 2 diabetes primary care disease management programs.[6] Given the large impact of both diabetes and HFpEF for

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patients and community, it is important to know the exact prevalence of LVDD in patients with type 2 diabetes as this can be helpful to target prevention and intervention strategies for both LVDD and early stages of HFpEF.

American society of echocardiography/European association for cardiovascular imaging ASE/EACVI jointly updated its complex 2009 guideline for detection of LVDD in 2016[7]. The primary goal of this update is to simplify the approach and thus increase the utility of the guidelines in daily clinical practice.

Myocardial Performance Index (MPI/Tei Index), which includes both systolic and diastolic time intervals to assess the global cardiac dysfunction was used by Tei and his co-workers in 1995[8]. The value is independent of Heart Rate and Blood Pressure. It has been evaluated in many cardiac conditions like low heart failure with reduced ejection fraction, Pulmonary Arterial Hypertension, Amyloidosis, Myocardial infarction, congenital heart disease[9]. The cut off value is different among normal and various abnormal cardiac conditions and Higher value of Tei index has been shown to correlate with poor prognosis in symptomatic HF[10]. It has also been used as a surrogate marker for diabetic cardiac dysfunctions in different studies with encouraging results. Tei index can be calculated from pulse wave doppler method and tissue doppler imaging method. Tissue Doppler Imaging (TDI) enables measurement of both relaxation and contraction time simultaneously in single cardiac cycle[11].

Current study aims to determine the prevalence of LVDD as per updated 2016 ASE/EACVI guideline in our diabetic patients having preserved EF with no evidence of overt cardiac disease and find out the association of LVDD with Tei index.

Methodology:

This is hospital based, cross sectional, prospective study conducted in Bir Hospital, Kathmandu, Nepal from 2022 February to 2022 August (6 months) with IRB clearance from the institute (NAMS). Diabetic patients with sinus rhythm, normal EF, with no gross structural heart disease (more than mild valvular disease, HCM, DCM, RCM, pericardial disease), without COPD, CKD, no ECG evidence of infarction or bundle branch block were included in the study. Informed consent was taken; Echocardiography was done, recent documents were reviewed and data were collected and recorded as per proforma by the principal investigator.

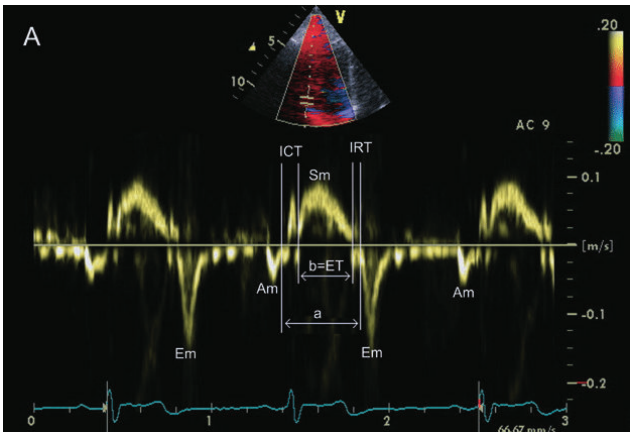
Following four variables are obtained on echocardiography (phillips affinity) as per ASE/EACVI 2016 guideline to determine whether the patient has LVDD. their abnormal cutoff values are:

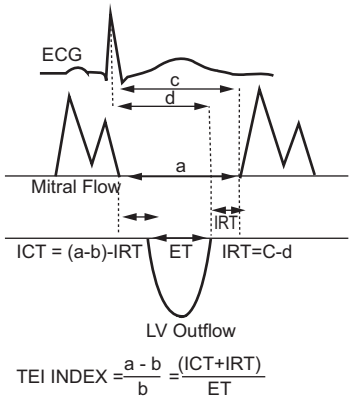
1) annular e' velocity (septal e' < 7 cm/sec, lateral e'< 10 cm/sec),
2) average E/e' ratio > 14,
3) LA maximum volume index > 34 mL/m2 calculated by biplane method and indexed with BSA,
4) Peak TR velocity > 2.8 m/sec.

LV diastolic function is considered normal if upto1 parameter is abnormal. LV diastolic dysfunction is present if at least 3 parameters are abnormal. The study is indeterminate if 2 values are abnormal.

Tei index was calculated from tissue doppler imaging method. The sample volume was placed on septal mitral annulus to get a good TDI signal as shown in figure 1 and schematic graphic representation. The interval "a" is the interval between cessation to onset of diastolic myocardial velocities. The interval "b": the ejection time (ET) is duration of systolic myocardial velocity (SMV). Tei index is calculated from following formula

MPI = (a-b)/b = (IVRT + IVCT)/ET.





Data Analysis

All data were entered into Microsoft Excel and the statistical analysis was done using the SPSS version 26 software (SPSS INC, Chicago, III). Categorical variables were analyzed as number and percentage, continuous variable with normal distribution is presented as mean ± SD. After processing of all available information, statistical analysis of their significance was done.

Age, duration of diabetes, and echo parameters were compared between different groups by performing unpaired *t*-test for normalized data. Categorical variables were compared by chi-square test. Pearson correlation test was used to correlate between MPI and LVDD association. 95% confidence interval was accepted for our study.

Results

Total 100 diabetic patients who met the inclusion and exclusion criteria were evaluated. Mean age of the patients was 58.1 ± 12:6 years with 54 percent being male. Mean duration of diabetes was 5.68 ± 5.7 years. and mean HbA1C was 7.45 ± 0.99 (available in 61 patients). (Table 1)

Table-I

Demographic and Baseline characteristics of study population

Characteristic.	Mean± SD or. Number (%)
Age(years)	58.14±12.58 years
Male (%)	46 (44.2%)
Duration of Diabetes (years)	5.68±5.7 years
HBA1C	7.45±0.992

Using the criteria of 2016 American society of echocardiography for diagnosis of LVDD, 23 (23%) patients met the criteria of LVDD and 46 (46%) patients did not have LVDD, whereas 31 (31%) of patients were categorized as indeterminate (figure 1). LVDD was more prevalent with advanced age. There was no significant difference in LVDD vs no LVDD as per sex, duration of diabetes and recent HBA1C level. (Figure 2, 3).

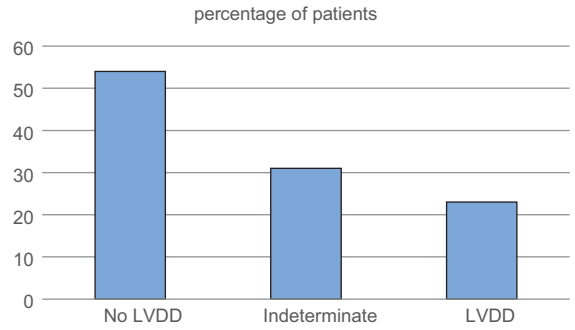


Fig.-1: *Prevalence of diastolic dysfunction*

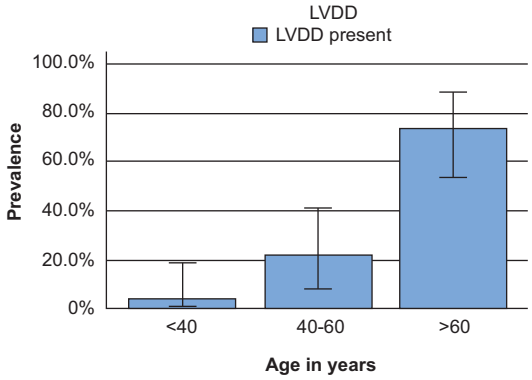


Fig.-2: *Association between age distribution and diastolic dysfunction*

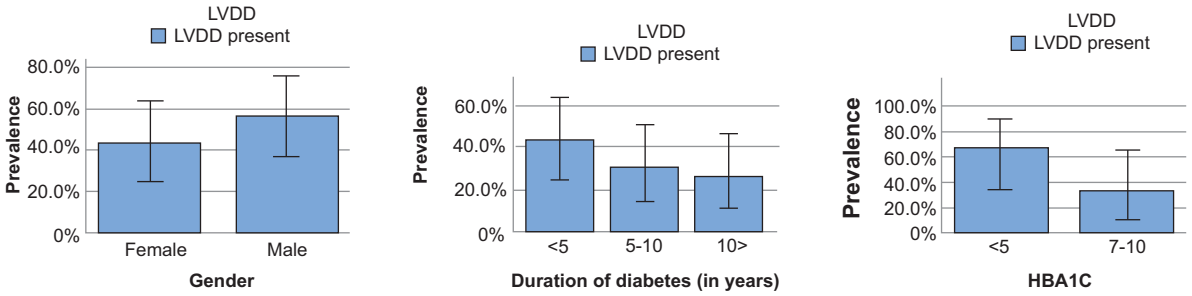


Fig.-3: *Association between sex, duration of diabetes recent HbA1C level and diastolic dysfunction.*

Tei index as calculated from the tissue Doppler imaging was 0.56± 0.05 in patients with diastolic dysfunction and 0.43±0.06 in patients with no diastolic dysfunction with significant positive correlation coefficient of 0.695 (p = 0.01). (Table 2, figure 4)

Table-II

Echocardiography parameters noted in patients Tei index mean±SD

	Tei index mean ± SD
LVDD	0.56 ±0.05
No LVDD	0.43±0.058
Indeterminate	0.5±0.053

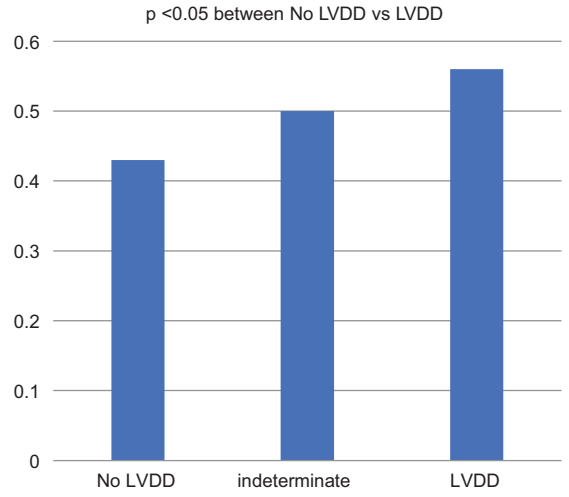


Fig.-4: comparison of tei index in between the groups

Discussion:

Prevalence of LVDD is higher diabetic patients as compared to normal individual[12]. Though inconsistently, studies have shown that older age, higher BMI, longer duration of diabetes, poor glycemic control are associated with increased risk of developing LVDD in diabetes even in the absence of hypertension and coronary artery disease[13,14]. The prevalence of LVDD in asymptomatic diabetic patients varies widely across different studies, ranging from 14% to 71% mainly because of heterogeneity of diagnostic criteria used, populations studied and associated comorbidities[15,16]. A systematic review and meta-analysis done in 2018 found the prevalence to be 46%[17].

Compared to older 2009 criteria; the updated 2016 ASE criteria detects more advanced and may be more clinically significant LVDD and is less specific to detect milder form of LVDD. Further studies are warranted to investigate the prognostic impact of these criteria.[18] Validating their accuracy is difficult. One of such attempts was done with multicentric study, where this echocardiographic assessment criteria of LVDD was compared with invasively measured LVEDP; which showed 87% accuracy to diagnose elevated filling pressure of PCWP >12 mmHg[19].

In a study conducted recently in 200 diabetic and 281 non diabetic, prevalence of LVDD was 17.5% among diabetic and 4.5% among nondiabetic respectively using 2016 ASE criteria to diagnose diastolic dysfunction.[12] These findings demonstrate similar findings of LVDD prevalence as with ourstudy which is significantly lower than other studies which has used older criteria to diagnose LVDD. More number (31%) of study patients in our study have indeterminate study in regard to LVDD assessment which is an inherent issue while using this criterion as also seen in a study by Van de *et al.* which has shown indeterminate study upto 30%[20].

As systolic and diastolic dysfunction frequently coexist, combined measurement of left ventricular chamber performance such as Tei index was thought to be more reflective. however, it does not determine the cause. The cutoff values have been different in different studies and different conditions. For example, in a study, 'cut off-points' of >0·47 identified patients with mild to moderate heart failure with a sensitivity of 86% and a specificity of 82%[21] In another study Tei index >0.63 was shown to be good predictor of both LVDP >12mmHg and LVDD[22].

One study done in India, which enrolled 100 patients with diabetes without hypertension and overt heart disease. used older criteria (E/A ratio, Valsalva, E/E') to diagnose and categorize LVDD and calculated MPI by PW doppler. Researchers found that 65% had LVDD, Mean Tei index values were significantly higher with increasing diastolic dysfunction (0.24, 0.45, 0.6 and 0.68 among normal, grade 1, grade2 and grade 3 LVDD)[23]. Lower prevalence of LVDD in our study is because of use of updated guideline to diagnose LVDD. The value of Tei index in patients without LVDD in our study is higher, probably because many of lower grade LVDD in their study population might fall in normal to indeterminate group in our study; and also, the method of measurement of Tei index is different.

Conclusion:

With updated 2016 guideline 23% of patients had LVDD in patients with diabetes with preserved ejection fraction and without obvious cardiac disease in our study. Increasing age was significantly associated with higher incidence whereas male sex, duration of diabetes and HbA1C level were not significantly different. Tei index was significantly higher in patients with LVDD than those without LVDD.

Limitations of the study : with updated guideline to assess LVDD, significant proportion of patients have indeterminate study and we did not further characterize those subset. furthermore, we have not graded LVDD. We have not taken normal subjects as control group. We have not ruled out subclinical LV systolic dysfunction with abnormal GLS.

Conflicts of interest: No conflict

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