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Original Research Article

LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN ASYMPTOMATIC PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is linked to left ventricular diastolic dysfunction (LVDD), a heart failure precursor, even without cardiovascular comorbidities. This study assessed LVDD prevalence and predictors in asymptomatic T2DM patients.

Materials and Methods: In a cross-sectional study, we enrolled 104 adults (aged 18–64 years) with T2DM per American Diabetes Association criteria, excluding those with hypertension or cardiovascular disease. Assessments included anthropometric measurements (height, weight, BMI), biochemical tests (fasting plasma glucose, 2-hour postprandial glucose, HbA1c, lipid profile, urea, creatinine, urinary albumin-to-creatinine ratio), fundoscopy, electrocardiography, and echocardiography with tissue Doppler imaging. LVDD was classified into grades I–III using E/A and E/e' ratios. Statistical significance was set at $P<0.05$, with multinomial logistic regression identifying LVDD predictors.

Results: Of 104 patients, 61 (58.7%) had LVDD: 42 (40.3%) grade I, 14 (13.5%) grade II, 5 (4.8%) grade III. LVDD patients had higher mean HbA1c (8.23 ± 0.97 vs. 7.26 ± 0.54, $P<0.001$), higher BMI (24.3 ± 3.18 vs. 22.7 ± 1.94, $P=0.002$), and lower median HDL-C (35 vs. 46 mg/dL, $P=0.001$) than those with normal LV function. Logistic regression identified HbA1c (OR, 7.226; 95% CI, 2.162–24.149; $P<0.001$), BMI (OR, 1.207; 95% CI, 1.071–1.501; $P=0.041$), and HDL-C (OR, 0.930; 95% CI, 0.854–0.989; $P=0.048$) as independent predictors.

Conclusions: LVDD is prevalent (58.7%) in asymptomatic T2DM patients. Elevated HbA1c, increased BMI, and reduced HDL-C predict LVDD, emphasizing glycemic control, weight management, and lipid optimization to reduce cardiovascular risk.

Keywords: Type 2 diabetes mellitus, left ventricular diastolic dysfunction, glycated hemoglobin, body mass index, high-density lipoprotein cholesterol.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a global health challenge, affecting millions and significantly increasing the risk of cardiovascular complications, including heart failure, even in the absence of overt microvascular or macrovascular diseases such as coronary artery disease or hypertension.[1]This heightened risk is partly attributed to diabetic cardiomyopathy, a condition characterized by left ventricular diastolic dysfunction (LVDD), which manifests as impaired left ventricular relaxation,

increased passive diastolic stiffness, and contractile dysfunction.[1-4]These functional abnormalities arise from complex pathophysiological mechanisms, including impaired endothelium-dependent and endothelium-independent vasodilation, oxidative stress, advanced glycation end-product accumulation, and myocardial fibrosis, all of which compromise cardiac performance and predispose patients to heart failure.[1]

LVDD is a critical early marker of diabetic cardiomyopathy, detectable through advanced echocardiographic techniques, and has been demonstrated even in asymptomatic, normotensive patients with T2DM.[5]The subclinical nature of LVDD in these patients underscores the importance of early detection to prevent progression to symptomatic heart failure, a condition associated with significant morbidity and mortality.[6-9]Prior studies have reported a high prevalence of LVDD in T2DM, ranging from 54% to 63%, but the specific predictors and their relative contributions remain incompletely understood, particularly in asymptomatic populations without confounding comorbidities.[4,10-12] Identifying these predictors could guide targeted interventions to mitigate cardiovascular risk.

This study aimed to evaluate the prevalence of LVDD in asymptomatic T2DM patients, characterize its echocardiographic features, classify its grades (I–III), and identify associated risk factors. By focusing on a well-defined cohort free of hypertension and cardiovascular disease, we sought to isolate the direct effects of T2DM on diastolic function and provide insights into potential preventive strategies.

MATERIALS AND METHODS

Study Design and Population

This cross-sectional study was conducted at a tertiary care centre from January 2022 to December 2022, targeting adults aged 18 to 64 years with T2DM, diagnosed according to American Diabetes Association (ADA) guidelines: glycated hemoglobin (HbA1c) ≥6.5%, fasting plasma glucose (FPG) ≥126 mg/dL, 2-hour postprandial glucose (PPG) ≥200 mg/dL during a 75-g oral glucose tolerance test (OGTT), or symptoms of hyperglycemia with random plasma glucose ≥200 mg/dL.[7]To ensure a homogenous cohort and isolate the effects of T2DM, we excluded patients with type 1 diabetes, pregnancy, hypertension (defined as blood pressure ≥140/90 mmHg or use of antihypertensive medications), pre-existing cardiovascular disease (e.g., coronary artery disease, heart failure, arrhythmias, or valvular heart disease), or those unwilling to provide consent.

The sample size was calculated using the formula $4pq/L^2$, where p = 63% (estimated LVDD prevalence based on prior studies [9], q = 100 - p, and L = 10% (absolute precision), with an additional 10% for non-response, yielding a minimum sample of 104. We initially screened 180 patients, of whom 104 met the inclusion criteria. Exclusions were due to hypertension (n=45), cardiovascular disease (n=20), or non-consent (n=11). The study was approved by the institutional ethics committee, and all participants provided written informed consent, with assurances of anonymity and confidentiality.

Data Collection

Demographic data, including age, sex, and duration of diabetes, were recorded via structured interviews. Anthropometric measurements were conducted using standardized protocols to ensure accuracy. Height was measured to the nearest 0.1 cm using a calibrated stadiometer, and weight was measured to the nearest 0.1 kg using a digital scale, with body mass index (BMI) calculated as weight (kg) divided by height squared (m^2). Blood pressure was measured twice in the seated position after a 5-minute rest using a calibrated sphygmomanometer, with the average of two readings recorded to minimize variability.

Biochemical assessments were comprehensive to evaluate metabolic and renal status. Fasting plasma glucose (FPG) and 2-hour PPG were measured during a standardized 75-g OGTT, adhering to World Health Organization protocols. HbA1c was quantified using high-performance liquid chromatography, a gold-standard method for assessing long-term glycemic control. Lipid profile analysis included total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), measured via enzymatic assays. Renal function was assessed through serum urea and creatinine levels, with urinary albumin-to-creatinine ratio (UACR) determined from spot urine samples to detect microalbuminuria (defined as UACR 30–300 mg/g).[10]Fundoscopy was performed by a trained ophthalmologist to evaluate diabetic retinopathy, classified as non-proliferative (NPDR) or proliferative based on established criteria.

Electrocardiography (ECG) was conducted using a 12-lead system to exclude arrhythmias or ischemic changes. In patients with abnormal ECG findings, stress testing (treadmill or dobutamine stress echocardiography) was performed to rule out asymptomatic coronary artery disease, ensuring that only patients without significant cardiovascular pathology were included.

Echocardiographic Assessment

Echocardiography was performed by a cardiologist blinded to clinical data using a Philips X7-2 imaging system, a high-resolution platform suitable for detailed cardiac assessment. Examinations included M-mode, two-dimensional imaging, pulsed-wave Doppler, and color-flow Doppler, adhering to American Society of Echocardiography guidelines.[4]Structural parameters measured included left atrial (LA) diameter, left ventricular internal diameters at end-diastole (LVIDd) and end-systole (LVIDs), interventricular septum diameter at

end-systole (IVSs), and ejection fraction (EF), calculated using the modified Simpson's rule to assess systolic function.

Diastolic function was evaluated using trans-mitral pulsed-wave Doppler and tissue Doppler imaging, which provide complementary insights into left ventricular filling dynamics. Key parameters included:

1. E/A ratio: The ratio of early (E) to late (A) diastolic trans-mitral flow velocities, measured at the mitral valve leaflet tips, reflecting the balance between passive and active ventricular filling.
2. E/e' ratio: The ratio of E velocity to early diastolic mitral annular velocity (e'), averaged from septal and lateral annulus measurements using tissue Doppler, indicating left ventricular filling pressures.
3. Isovolumetric relaxation time (IVRT): The time interval between aortic valve closure and mitral valve opening, measured in milliseconds, assessing the relaxation phase of diastole.
4. Deceleration time (DT): The time from peak E wave to baseline, measured in milliseconds, reflecting the time required for left atrial and ventricular pressure equalization.

LVDD was classified into three grades based on established criteria,[10]

1. Grade I (impaired relaxation): E/A ratio <0.8, E/e' ratio <8, indicating early diastolic dysfunction with slowed relaxation.
2. Grade II (pseudo-normal filling): E/A ratio 0.8–1.5, E/e' ratio 8–12, reflecting compensated dysfunction with elevated filling pressures.
3. Grade III (restrictive-like filling): E/A ratio >1.5, E/e' ratio >12, indicating advanced dysfunction with high filling pressures and reduced compliance.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 27.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or median (range) for non-normally distributed data, as determined by the Shapiro-Wilk test. Categorical variables were reported as numbers and percentages. Group comparisons used the Student's t-test for normally distributed continuous variables, the Mann-Whitney U test for non-normally distributed variables, and the chi-square test for categorical variables. One-way analysis of variance (ANOVA) with Games-Howell post hoc tests was used to assess differences in echocardiographic parameters (e.g., IVRT, DT) across LVDD grades, accounting for unequal variances. Pearson's correlation coefficients were calculated to evaluate relationships between HbA1c and echocardiographic parameters (E/A and E/e' ratios), providing insights into glycemic control's impact on diastolic function. Multinomial logistic regression was performed to identify independent predictors of LVDD, including variables with univariate significance (P<0.05). The regression model adjusted for potential confounders, such as age, duration of diabetes, and lipid parameters, to isolate the effects of significant predictors. Normality and homogeneity of variance were confirmed using Shapiro-Wilk and Levene's tests, respectively. A P-value <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the institutional ethics committee (IEC/SFTMC/2018/3/002). Participants provided written informed consent, and anonymity and confidentiality were assured through secure data storage and de-identification protocols, in compliance with local data protection regulations. Patients were informed about their right to withdraw from the study at any time without affecting their clinical care.

RESULTS

Among the 104 patients with T2DM (mean age, 45.52 ± 9.85 years; 55.8% male, 44.2% female), 61 (58.7%) had LVDD: 42 (40.3%) with grade I, 14 (13.5%) with grade II, and 5 (4.8%) with grade III. The majority (46.2%) were aged 41–50 years, with a mean diabetes duration of 8.12 ± 4.96 years. Baseline characteristics are presented in Table 1. Patients with LVDD had significantly higher mean HbA1c (8.23 ± 0.97 vs. 7.26 ± 0.54, P<0.001), higher mean BMI (24.3 ± 3.18 vs. 22.7 ± 1.94, P=0.002), and lower median HDL-C (35 vs. 46 mg/dL, P=0.001) compared to those with normal left ventricular function. Other significant differences included higher PPG (262 ± 66.8 vs. 238 ± 38.3 mg/dL, P=0.024), higher median TC (210 vs. 190 mg/dL, P<0.05), higher mean TG (245 ± 68.5 vs. 199 ± 35.3 mg/dL, P<0.05), and higher median LDL-C (123 vs. 107 mg/dL, P<0.05). Fasting plasma glucose showed no significant difference (170 ± 39.2 vs. 175 ± 25.9 mg/dL, P=0.435). UACR distribution revealed 53 (51%) patients with UACR <30 mg/g, 47 (45.2%) with UACR 30–300 mg/g, and 4 (3.8%) with UACR >300 mg/g, with a significant association between UACR and LVDD (P=0.001). Among 47 patients with NPDR, 38 (80.9%) had LVDD, compared to 9 (19.1%) with normal LV function (P=0.001).

Echocardiographic parameters (Table 2) showed that patients with LVDD had a lower median E/A ratio (0.80 vs. 1.20, P=0.001), higher mean E/e' ratio (8.48 ± 2.20 vs. 6.79 ± 0.55, P=0.001), longer median DT (248 vs. 198 msec, P=0.001), and larger mean LA diameter (35.2 ± 3.40 vs. 31.7 ± 2.73 mm, P=0.001). Mean EF was lower in patients with LVDD (63 ± 5.64 vs. 65.9 ± 5.99, P=0.009). ANOVA revealed significant differences in IVRT (P=0.001) and DT (P=0.001) across LVDD grades, with post hoc Games-Howell tests confirming differences between grades 0 vs. I (P=0.001), grades 0 vs. III (P=0.002), grades I vs. II (P=0.001), grades

I vs. III (P=0.002), and grades II vs. III (P=0.001) for DT, indicating progressive worsening with higher grades. Mean LA diameter varied significantly across grades (P=0.001): 31.7 ± 2.73 mm (normal), 35.2 ± 3.40 mm (grade I), 31.9 ± 8.64 mm (grade II), and 39.4 ± 0.54 mm (grade III). IVSs was higher in LVDD patients (10.8 ± 2.71 vs. 9.74 ± 1.36 mm, P=0.001), while LVIDd (42.2 ± 6.44 vs. 42.1 ± 5.58 mm, P=0.908) and LVIDs (25.4 ± 5.74 vs. 27.2 ± 4.56 mm, P=0.170) showed no significant differences. (Table 2)

Among 89 patients with moderate-to-poor glycemic control (HbA1c >7%), 57 (64.0%) had LVDD, compared to 32 (36.0%) with normal LV function (P=0.02). Multinomial logistic regression (Table 3) identified HbA1c (OR, 7.226; 95% CI, 2.162–24.149; P<0.001), BMI (OR, 1.207; 95% CI, 1.071–1.501; P=0.041), and HDL-C (OR, 0.930; 95% CI, 0.854–0.989; P=0.048) as independent predictors of LVDD. Pearson's correlation coefficients (Table 4) showed a mild negative correlation between HbA1c and E/A ratio (r = -0.18, P=0.07) and a significant positive correlation with E/e' ratio (r = 0.32, P=0.001), as illustrated in Figure 1.

Table1:Baseline Characteristics of the Study Population

Characteristic	Overall (N=104)
Age (years), mean (SD)	45.52 (9.85)
Duration of diabetes (years), mean (SD)	8.12 (4.96)
BMI (kg/m²), mean (SD)	23.65 (2.83)
FPG (mg/dL), mean (SD)	172.12 (34.25)
PPG (mg/dL), mean (SD)	252 (57.73)
HbA1c (%), mean (SD)	7.83 (0.95)
TC (mg/dL), mean (SD)	204.95 (44.93)
TG (mg/dL), mean (SD)	226.27 (61.31)
LDL-C (mg/dL), mean (SD)	117.33 (28.09)
HDL-C (mg/dL), mean (SD)	40.5 (8.6)
UACR (mg/g), mean (SD)	70.40 (86.03)
Urea (mg/dL), mean (SD)	32.87 (7.10)
Creatinine (mg/dL), mean (SD)	0.83 (0.19)
SBP (mmHg), mean (SD)	118 (9.23)
DBP (mmHg), mean (SD)	71.2 (7.48)
E/A ratio, mean (SD)	1.03 (0.35)
E/e' ratio, mean (SD)	7.78 (1.91)
IVRT (msec), mean (SD)	99.92 (15.88)
DT (msec), mean (SD)	220.13 (35.77)
EF (%), mean (SD)	64.22 (5.63)
LA (mm), mean (SD)	33.59 (4.66)
IVSs (mm), mean (SD)	10.38 (2.30)
LVIDd (mm), mean (SD)	42.15 (6.07)
LVIDs (mm), mean (SD)	26.18 (5.33)

(BMI: body mass index; FPG: fasting plasma glucose; PPG: post prandial plasma glucose; HbA1C: glycosylated hemoglobin; TC: total cholesterol; TG: triglyceride; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; UACR: urinary albumin to creatinine ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; E/A: ratio of E wave and A wave; E/é: ratio of E wave and é wave; IVRT: isovolumetric relaxation time; DT: deceleration time; EF: ejection fraction; LA: left atrial diameter; IVSs: interventricular septum diameter at end systole; LVIDd: left ventricular internal diameter end diastole; LVIDs: left ventricular internal diameter end systole).

Table 2: Echocardiographic Parameters by LVDD Status

Parameter	LVDD Present (n=61)	LVDD Absent (n=43)	P Value
E/A ratio, median (range)	0.80 (1.60)	1.20 (0.50)	0.001*
E/e' ratio, mean (SD)	8.48 (2.20)	6.79 (0.55)	0.001†
DT (msec), median (range)	248 (178)	198 (54)	0.001*
EF (%), median (range)	35 (39.9)	31 (14)	0.001*
IVSs (mm), mean (SD)	10.8 (2.71)	9.74 (1.36)	0.001†
LVIDd (mm), mean (SD)	42.2 (6.44)	42.1 (5.58)	0.908†
LVIDs (mm), mean (SD)	25.4 (5.74)	27.2 (4.56)	0.170†

Mann-Whitney U test; †Student's t-test

(LVDD: left ventricular diastolic dysfunction; SD: standard deviation E/A: ratio of E wave and A wave; E/é: ratio of E wave and é wave; DT: deceleration time; EF: ejection fraction; IVSs: interventricular septum diameter at end systole; LVIDd: left ventricular internal diameter end diastole; LVIDs: left ventricular internal diameter end systole).

Table 3: Multinomial Logistic Regression Analysis for LVDD Predictors

Variable	β	S.E.	Wald	P Value	OR	95% CI
Age	0.010	0.039	0.061	0.806	1.010	0.936–1.089
Duration of Diabetes	-0.044	0.088	0.244	0.621	0.957	0.805–1.138
BMI	0.211	0.111	2.875	0.041	1.207	1.071–1.501
PPG	-0.007	0.006	1.328	0.249	0.993	0.981–1.005
HbA1c	1.978	0.616	10.320	<0.001	7.226	2.162–24.149
DBP	0.007	0.001	0.578	0.887	1.119	0.785–1.163
TC	0.009	0.012	0.521	0.471	1.009	0.985–1.033
TG	0.008	0.007	1.233	0.267	1.008	0.994–1.023
LDL-C	-0.011	0.017	0.379	0.538	0.990	0.957–1.023
HDL-C	-0.072	0.044	2.736	0.048	0.930	0.854–0.989
UACR	-0.006	0.006	1.223	0.269	0.994	0.983–1.005
Urea	-0.038	0.056	0.468	0.494	0.963	0.863–1.074
Creatinine	0.738	2.104	0.123	0.726	2.091	0.034–129.150
Constant	-15.890	5.282	9.049	0.003	0.000	—

(LVDD: left ventricular diastolic dysfunction; BMI: body mass index; PPG; post prandial plasma glucose; HbA1C: glycosylated hemoglobin; DBP: diastolic blood pressure; TC; total cholesterol; TG; triglyceride; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; UACR; urinary albumin to creatinine ratio; β: regression coefficient; S.E: standard error; Wald: chi- square test value; df: degree of freedom; OR: odds ratio; C.I: confidence interval).

Table 4: Pearson's Correlation Coefficients for HbA1c and Echocardiographic Parameters

Parameter	Correlation Coefficient (r)	P Value
E/A ratio	-0.18	0.07
E/e' ratio	0.32	0.001

(Pearson's correlation coefficients (r) and corresponding P-values for the relationships between glycated hemoglobin (HbA1c) and two echocardiographic parameters: the E/A ratio and the E/e' ratio, in patients with type 2 diabetes mellitus.)

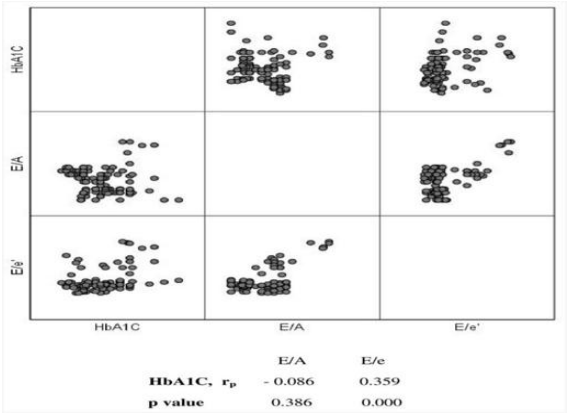

Figure 1: Association between Glycated Hemoglobin (HbA1c) and Echocardiographic Parameters

[Scatter plot showing the relationship between HbA1c and E/A ratio (left panel) and E/e' ratio (right panel) in patients with type 2 diabetes mellitus. The left panel illustrates a mild negative correlation (r = -0.18, P=0.07), and the right panel shows a significant positive correlation (r = 0.32, P=0.001)].

DISCUSSION

This study confirms a high prevalence of LVDD (58.7%) in asymptomatic T2DM patients, aligning with prior reports of 54.3–55.0%.[11,13-15]The predominance of grade I LVDD (40.3%) indicates that early diastolic impairment is common, potentially serving as a precursor to symptomatic heart failure. The identification of HbA1c, BMI, and HDL-C as independent predictors underscores the critical roles of glycemic control, obesity, and dyslipidemia in LVDD pathogenesis, offering actionable targets for intervention.

Glycemic Control and LVDD

Elevated HbA1c was the strongest predictor, with a 7.22-fold increased odds of LVDD per 1% increase, reflecting the impact of chronic hyperglycemia on myocardial stiffness and fibrosis.[16-18]This finding is consistent with studies reporting a linear increase in LVDD prevalence with rising HbA1c levels.[9] Chronic hyperglycemia promotes advanced glycation end-products, oxidative stress, and inflammation, which impair myocardial relaxation and increase diastolic stiffness.[2]The significant correlation between HbA1c and E/e' ratio (r = 0.32, P=0.001) and the near-significant negative correlation with E/A ratio (r = -0.18, P=0.07) highlight the sensitivity of these echocardiographic parameters in detecting glycemic-related diastolic dysfunction.[12,14,16]The lack of association with FPG, unlike PPG (P=0.024), suggests that postprandial hyperglycemia may contribute more significantly to LVDD, possibly due to acute glycemic excursions that exacerbate oxidative stress and endothelial dysfunction.[17]This distinction has clinical implications, emphasizing the need for postprandial glucose monitoring and control in T2DM management.

Obesity and LVDD

The association between higher BMI and LVDD (OR, 1.207; P=0.041) aligns with evidence linking obesity to diastolic dysfunction through increased

cardiac workload, systemic inflammation, and altered myocardial metabolism.[5,19]Our study found a mean BMI of 24.3 ± 3.18 kg/m² in LVDD patients compared to 22.7 ± 1.94 kg/m² in those with normal LV function (P=0.002), consistent with a prior study reporting a mean BMI of 27.6 ± 2.2 kg/m² in LVDD cases.[12]Obesity contributes to LVDD by increasing left ventricular mass, promoting myocardial lipid accumulation, and inducing insulin resistance, all of which impair diastolic relaxation.[20]The absence of waist circumference or insulin resistance markers (e.g., HOMA-IR) in this study limits further exploration of role of visceral adiposity, but the BMI association suggests that weight management is a critical strategy for LVDD prevention.

Lipid Profile and LVDD

Low HDL-C emerged as an independent predictor of LVDD (OR, 0.930; P=0.048), with a median of 35 mg/dL in LVDD patients compared to 46 mg/dL in those with normal LV function (P=0.001). This finding is notable, as HDL-C is inversely associated with arterial stiffness, a key contributor to diastolic dysfunction.[6,21-23]The protective effects of HDL may stem from its anti-inflammatory and antioxidant properties, which mitigate endothelial dysfunction and myocardial stress.[21,24]While TC, TG, and LDL-C were higher in LVDD patients, only HDL-C remained significant in multivariate analysis, suggesting a unique role in LVDD pathogenesis. This aligns with studies showing that HDL-C, but not TC or TG, is inversely associated with pulse wave velocity, a marker of arterial stiffness linked to LVDD.[22,25]

Microvascular Complications

The significant associations between LVDD and microalbuminuria (P=0.001) and NPDR (P=0.001) highlight the interplay between microvascular complications and diastolic dysfunction. Of 47 patients with microalbuminuria, 38 (80.9%) had LVDD, and among 47 with NPDR, 38 (80.9%) had LVDD, suggesting shared pathophysiological pathways, such as endothelial dysfunction and oxidative stress.[9,12,26]These findings underscore the importance of screening for microvascular complications in T2DM patients with LVDD, as they may indicate a higher cardiovascular risk profile.

Echocardiographic Insights

Echocardiographic parameters provided robust evidence of diastolic impairment. The lower E/A ratio (0.80 vs. 1.20, P=0.001) and higher E/e' ratio (8.48 ± 2.20 vs. 6.79 ± 0.55, P=0.001) in LVDD patients indicate impaired relaxation and elevated filling pressures, respectively.[14,17,27-29]Prolonged DT (248 vs. 198 msec, P=0.001) and increased LA diameter (35.2 ± 3.40 vs. 31.7 ± 2.73 mm, P=0.001) further confirm progressive diastolic dysfunction, with the highest LA diameter in grade III LVDD (39.4 ± 0.54 mm) [4,10]. The significant difference in IVRT across grades (P=0.001) and the lower EF in LVDD patients (63 ± 5.64 vs. 65.9 ± 5.99, P=0.009) suggest that subclinical systolic dysfunction may coexist, though EF remained within normal limits.[24]These parameters (E/A, E/e', DT, IVRT) are sensitive and reliable markers for detecting and grading LVDD, with potential for routine clinical use.[30]

Therapeutic Implications

The identification of HbA1c, BMI, and HDL-C as predictors suggests multiple therapeutic targets. Tight glycemic control is paramount, as each 1% increase in HbA1c increases LVDD odds by 7.22 times.[9,14]Sodium-glucose cotransporter-2 (SGLT2) inhibitors (e.g., empagliflozin, canagliflozin) and glucagon-like peptide-1 (GLP-1) receptor agonists (e.g., liraglutide, semaglutide) have shown promise in reducing heart failure risk and improving diastolic function, potentially through weight reduction, anti-inflammatory effects, and improved glycemic control.[17,21,23,31]For example, the EMPA-REG, CANVAS, and DAPA-HF trials demonstrated reduced heart failure events with SGLT2 inhibitors, while liraglutide and semaglutide improved diastolic function in weight-dependent and substrate-utilization pathways, respectively.[17,21,23,31]Lifestyle interventions, including exercise, medical nutrition therapy, and weight loss, are critical for addressing BMI and may enhance HDL-C levels.[17]The protective effect of HDL-C (OR, 0.930) suggests that strategies to increase HDL-C, such as aerobic exercise or niacin therapy, could mitigate LVDD risk, though further research is needed to confirm efficacy.[21]

Limitations and Future Directions

This single-centred study design and moderate sample size (n=104) may limit generalizability, necessitating multicentre studies with larger cohorts. The absence of waist circumference, neck circumference, waist-to-hip ratio, fasting insulin, or HOMA-IR measurements restricts insights into visceral adiposity and insulin resistance, which are likely relevant to LVDD. Future research should include these markers to better characterize obesity-related mechanisms. Longitudinal studies are needed to assess the progression of LVDD and the impact of interventions, such as SGLT2 inhibitors or GLP-1 analogues, compared to lifestyle modifications. Cost-effectiveness analyses could guide resource allocation for early LVDD screening and management in T2DM patients. Additionally, exploring genetic or biomarker profiles (e.g., B-type natriuretic peptide) could enhance risk stratification and personalize therapeutic approaches.

CONCLUSION

This study demonstrates that LVDD is highly prevalent (58.7%) in asymptomatic T2DM patients, even in the absence of hypertension or cardiovascular disease. HbA1c, BMI, and HDL-C are significant, independent predictors, with each 1% increase in HbA1c increasing LVDD odds by 7.22 times, each 1-unit increase in BMI increasing

odds by 1.207 times, and each 1 mg/dL increase in HDL-C reducing odds by 0.17%. These findings highlight the importance of early echocardiographic screening to detect LVDD and targeted interventions to optimize glycemic control, reduce body weight, and enhance HDL-C levels. Such strategies, combining lifestyle modifications and pharmacological therapies like SGLT2 inhibitors or GLP-1 analogues, may prevent progression to heart failure and other cardiovascular complications in this high-risk population.

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