

Original Research Article

COMPARATIVE DIAGNOSTIC UTILITY OF THE TRIGLYCERIDE-GLUCOSE (TYG) INDEX AND HBA1C IN IDENTIFYING SUBCLINICAL LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PREDIABETIC PATIENTS WITH PRESERVED EJECTION FRACTION: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Prediabetes precedes overt type 2 diabetes mellitus and is increasingly recognised as a state in which subclinical left ventricular diastolic dysfunction (LVDD) — the earliest echocardiographic manifestation of diabetic cardiomyopathy — may already be present despite preserved ejection fraction (EF). Both the triglyceride-glucose (TyG) index and glycated haemoglobin (HbA1c) have been proposed as biomarkers of this early cardiac involvement, but head-to-head comparisons of their diagnostic performance in prediabetes are limited. The objective is to compare the diagnostic utility of the TyG index and HbA1c in identifying subclinical LVDD in prediabetic patients with preserved EF, and to correlate both biomarkers with echocardiographic diastolic parameters.

Materials and Methods: This cross-sectional observational study enrolled 110 newly detected prediabetic patients (ADA criteria) with EF $\geq 50\%$ attending the Department of Cardiology, Chettinad Hospital and Research Institute. Clinical, biochemical (including TyG index and HbA1c) and comprehensive echocardiographic (E/A ratio, e' velocity, E/ e' ratio, left atrial volume index [LAVI]) data were collected. LVDD was graded per the 2016 ASE/EACVI recommendations. Diagnostic accuracy was assessed by receiver operating characteristic (ROC) curve analysis with DeLong's test to compare areas under the curve (AUC); independent predictors of LVDD were identified by multivariable logistic regression.

Results: LVDD (Grade I–III) was present in 37 of 110 patients (33.6%). Both TyG index (9.01 ± 0.32 vs 8.55 ± 0.37 , $p < 0.001$) and HbA1c ($6.15 \pm 0.12\%$ vs $5.96 \pm 0.15\%$, $p < 0.001$) were significantly higher in patients with LVDD and correlated significantly with E/A ratio, average e' , E/ e' ratio and LAVI (all $p < 0.001$). The TyG index showed an AUC of 0.834 (sensitivity 78.4%, specificity 78.1% at a cut-off of 8.88) and HbA1c an AUC of 0.827 (sensitivity

62.2%, specificity 86.3% at a cut-off of 6.12%), with no statistically significant difference between the two AUCs (DeLong's test, $p=0.933$). On multivariable logistic regression, both the TyG index (adjusted OR 3.10, 95% CI 1.45–6.64, $p=0.004$) and HbA1c (adjusted OR 3.31, 95% CI 1.58–6.95, $p=0.002$) were independent predictors of LVDD.

Conclusion: In prediabetic patients with preserved EF, the TyG index performs comparably to HbA1c in identifying subclinical LVDD, with a complementary sensitivity–specificity profile — the TyG index favouring sensitivity (screening) and HbA1c favouring specificity (confirmation). As an inexpensive index derived from routinely available fasting lipid and glucose values, the TyG index may serve as a practical adjunct, or alternative, to HbA1c for early cardiovascular risk stratification in prediabetes.

Keywords: TyG index, HbA1c, prediabetes, diastolic dysfunction, preserved ejection fraction, echocardiography, diabetic cardiomyopathy.

INTRODUCTION

Prediabetes — defined by the American Diabetes Association as an HbA1c of 5.7–6.4%, impaired fasting glucose (100–125 mg/dl), or impaired glucose tolerance on a 75 g oral glucose tolerance test — is an intermediate state of glucose dysregulation that carries a substantial risk of progression not only to overt type 2 diabetes but also to cardiovascular disease.^[1] Long before diabetes is diagnosed, chronic hyperglycaemia and insulin resistance are believed to initiate a cascade of myocardial interstitial fibrosis, impaired calcium handling, and microvascular dysfunction collectively termed diabetic cardiomyopathy, whose earliest clinically detectable manifestation is left ventricular diastolic dysfunction (LVDD) in the setting of a still-preserved ejection fraction.

HbA1c has been directly linked to subclinical diastolic impairment in prediabetes: in a cohort of 106 patients with HbA1c-defined prediabetes, Di Pino et al. demonstrated a significantly lower E/A ratio and larger left atrial volume compared with normoglycaemic controls, with HbA1c remaining an independent determinant of diastolic parameters after adjustment for confounders.^[2] Similar associations between HbA1c and impaired relaxation (reduced E/A, elevated E/e') have been reported in established type 2 diabetes.^[3,4]

The triglyceride-glucose (TyG) index — calculated as the natural logarithm of the product of fasting triglycerides and fasting plasma glucose divided by two — was first validated against the euglycaemic-hyperinsulinaemic clamp as a simple, low-cost surrogate marker of insulin resistance that does not require an insulin assay.^[5,6] Because it is derived from two tests already performed routinely in metabolic screening, the TyG index has attracted interest as a scalable alternative or adjunct to HbA1c. Elevated TyG index has since been associated with subclinical left ventricular systolic dysfunction on speckle-tracking echocardiography in patients with type 2 diabetes and in obese patients,^[7,8,9] and, more recently, with reduced tissue Doppler e' velocity and higher E/e' ratio across the spectrum of cardiovascular-kidney-metabolic syndrome.^[10]

However, direct evidence in prediabetic — as opposed to diabetic or obese — populations remains scarce, and no prior study appears to have directly compared the diagnostic accuracy of the TyG index against HbA1c for detecting LVDD in this specific group.

Given that both biomarkers are inexpensive, widely available, and reflect complementary aspects of dysglycaemia and insulin resistance, a head-to-head comparison of their diagnostic performance for subclinical LVDD in prediabetes has direct implications for early, low-cost cardiovascular risk stratification in this population. This study was therefore designed to estimate the TyG index and HbA1c in prediabetic patients with preserved EF, correlate both markers with standardised echocardiographic diastolic parameters, and formally compare their sensitivity, specificity, and area under the ROC curve for identifying LVDD, as defined by the 2016 ASE/EACVI recommendations.^[11]

MATERIALS AND METHODS

Study Design and Setting: This was a cross-sectional observational study conducted in the Department of Cardiology, in coordination with the Department of General Medicine/Endocrinology, Chettinad Hospital and Research Institute, Kelambakkam, Tamil Nadu, over a period of 12 months, inclusive of data collection, analysis, and reporting.

Study Population: Newly detected prediabetic patients (per ADA criteria) aged 30–65 years with preserved left ventricular ejection fraction (EF $\geq 50\%$ on 2D echocardiography), attending the outpatient department, were consecutively enrolled after written informed consent.

Inclusion Criteria

- Age 30–65 years, both sexes
- Newly diagnosed prediabetes per ADA criteria: HbA1c 5.7–6.4%, or fasting plasma glucose 100–125 mg/dl, or 2-hour plasma glucose 140–199 mg/dl during OGTT
- Preserved left ventricular ejection fraction (EF $\geq 50\%$) on 2D echocardiography
- Willing to provide informed consent

Exclusion Criteria

- Established type 1 or type 2 diabetes mellitus
- Known coronary artery disease, valvular heart disease, cardiomyopathy, or congenital heart disease
- Left ventricular ejection fraction <50%
- Atrial fibrillation or other significant arrhythmia precluding echocardiographic assessment
- Uncontrolled hypertension (BP >160/100 mmHg)
- Chronic kidney disease (eGFR <30 ml/min/1.73m²) or chronic liver disease
- Hypothyroidism, active malignancy, or chronic inflammatory conditions
- Pregnancy
- Poor echocardiographic window precluding adequate diastolic assessment

Sample Size: Sample size was calculated using $n = z^2(p \times q)/E^2$, with $z = 1.96$ (95% confidence interval), an expected proportion of diastolic dysfunction in prediabetes of $p = 0.386$ (based on prior South Indian data), and a precision of $E = 0.09$, yielding $n = 1.96^2 \times (0.386 \times 0.614)/0.09^2 = 112.3$, rounded to 110 patients.

Clinical and Biochemical Assessment: All patients underwent a detailed history (duration of dysglycaemia, family history of diabetes/cardiovascular disease, medication history), physical and cardiovascular examination (vitals, waist circumference, BMI), and the following laboratory investigations: fasting and post-prandial glucose with 75g OGTT where indicated; HbA1c by HPLC; fasting lipid profile; TyG index calculated as $\ln[\text{fasting triglycerides (mg/dL)} \times \text{fasting plasma glucose (mg/dL)}]/2$ ⁵; renal function tests; and thyroid-stimulating hormone.

Echocardiographic Assessment: Standard 2D, M-mode, and Doppler transthoracic echocardiography was performed by a cardiologist blinded to biochemical results. EF was measured by the modified Simpson's biplane method. Diastolic function was assessed using mitral inflow E and A wave velocities and E/A ratio, septal and lateral tissue Doppler e' velocities (averaged), E/e' ratio, left atrial volume index (LAVI), and peak tricuspid regurgitation velocity. Diastolic dysfunction was graded (Normal, Grade I, II, III) according to the 2016 ASE/EACVI recommendations.^[11] For the purpose of the present analysis, patients were dichotomised into a Normal group and an LVDD group (Grade I–III combined).

Statistical Analysis

Data were analysed using Python (SciPy, scikit-learn, statsmodels), consistent with the pre-specified plan of

entry into MS Excel and analysis with standard statistical software. Continuous variables are presented as mean $\pm$ standard deviation and compared between groups using the independent t-test; categorical variables are presented as frequencies/percentages and compared using the chi-square test. Pearson's correlation coefficients were calculated between the TyG index/HbA1c and echocardiographic diastolic parameters. ROC curve analysis was used to determine the AUC, optimal cut-off (Youden's index), sensitivity, specificity, positive predictive value, and negative predictive value of each biomarker for LVDD; DeLong's test was used to statistically compare the two AUCs. Binary logistic regression (biomarkers entered as standardised [z-score] variables, adjusted for BMI, waist circumference, and duration of dysglycaemia) was used to identify independent predictors of LVDD, with results expressed as adjusted odds ratios (OR) and 95% confidence intervals (CI). A two-tailed $p < 0.05$ was considered statistically significant throughout.

Note on data source: The results reported in Section 3 were generated from a simulated dataset ($n=110$) constructed to match the pre-specified sample size, inclusion/exclusion criteria, and variable structure of this protocol, for the purpose of demonstrating the statistical analysis and reporting format. These figures should be replaced with results from actual patient data prior to thesis submission, ethics committee reporting, or journal submission.

RESULTS

Of 110 prediabetic patients with preserved EF enrolled, 58 (52.7%) were male and 52 (47.3%) female, with a mean age of 48.2 ± 9.2 years (range 30–65 years). LVDD (Grade I or higher) was identified in 37 patients (33.6%): Grade I in 29 (26.4%), Grade II in 7 (6.4%), and Grade III in 1 (0.9%) patient; the remaining 73 patients (66.4%) had normal diastolic function.

Baseline Characteristics

Patients with LVDD had significantly higher fasting plasma glucose, 2-hour post-prandial glucose, HbA1c, triglycerides, and TyG index, and significantly lower LDL cholesterol, compared with patients with normal diastolic function. [Table 1] Age, BMI, waist circumference, blood pressure, HDL cholesterol, and eGFR did not differ significantly between groups, nor did sex distribution or family history of diabetes/cardiovascular disease.

Table 1: Baseline clinico-demographic and biochemical characteristics by diastolic function status

Variable	Normal (n=73)	LVDD (n=37)	p-value
Age (years)	47.11 $\pm$ 9.37	50.22 $\pm$ 8.65	0.088
BMI (kg/m ²)	27.66 $\pm$ 3.06	27.69 $\pm$ 3.71	0.975
Waist circumference (cm)	71.84 $\pm$ 9.35	72.31 $\pm$ 11.16	0.829
SBP (mmHg)	128.44 $\pm$ 12.95	127.22 $\pm$ 13.46	0.650
DBP (mmHg)	81.70 $\pm$ 7.29	82.59 $\pm$ 7.50	0.552
Duration of dysglycaemia (months)	5.89 $\pm$ 4.21	7.24 $\pm$ 4.07	0.111

FPG (mg/dl)	104.55 ± 4.06	114.30 ± 2.96	<0.001
2-hr PPG (mg/dl)	153.96 ± 12.98	165.41 ± 12.77	<0.001
HbA1c (%)	5.96 ± 0.15	6.15 ± 0.12	<0.001
Total cholesterol (mg/dl)	189.88 ± 28.62	179.86 ± 29.00	0.090
LDL (mg/dl)	123.23 ± 29.90	104.62 ± 31.85	0.004
HDL (mg/dl)	45.71 ± 7.74	45.41 ± 8.23	0.851
Triglycerides (mg/dl)	104.59 ± 34.53	149.00 ± 38.43	<0.001
TyG index	8.55 ± 0.37	9.01 ± 0.32	<0.001
eGFR (ml/min/1.73m ²)	97.73 ± 10.52	95.84 ± 10.12	0.365

Values are mean ± SD; p-values from independent t-test (continuous variables). Sex distribution (p=1.000) and family history of DM/CVD (p=0.139) did not differ significantly between groups (χ^2 test).

Correlation with Echocardiographic Diastolic Parameters

Both the TyG index and HbA1c showed statistically significant correlations with all four echocardiographic diastolic parameters assessed.

[Table 2] The TyG index showed a marginally stronger correlation with E/A ratio and average e' velocity, while HbA1c showed a marginally stronger correlation with LAVI.

Table 2: Correlation of TyG index and HbA1c with echocardiographic diastolic parameters (Pearson's r)

Echocardiographic Parameter	r (TyG Index)	p	r (HbA1c)	p
E/A ratio	-0.569	<0.001	-0.540	<0.001
Average e' velocity (cm/s)	-0.752	<0.001	-0.723	<0.001
E/e' ratio	0.659	<0.001	0.605	<0.001
LAVI (ml/m ²)	0.686	<0.001	0.708	<0.001

Diagnostic Accuracy: ROC Analysis and Comparison of AUCs

On ROC curve analysis, the TyG index yielded an AUC of 0.834 for identifying LVDD, with an optimal (Youden-derived) cut-off of ≥ 8.88 , giving a sensitivity of 78.4% and specificity of 78.1%. HbA1c yielded an AUC of 0.827, with an optimal cut-off of $\geq 6.12\%$, giving a sensitivity of 62.2% and specificity

of 86.3%. [Table 3] DeLong's test comparing the two AUCs showed no statistically significant difference ($z=0.085$, $p=0.933$), indicating that the TyG index performs comparably to HbA1c in overall diagnostic accuracy for LVDD in this population, with the TyG index favouring sensitivity and HbA1c favouring specificity.

Table 3: Diagnostic accuracy of TyG index versus HbA1c for identifying LV diastolic dysfunction

Parameter	AUC	Optimal Cut-off	Sensitivity	Specificity	PPV	NPV
TyG Index	0.834	≥ 8.88	78.4%	78.1%	64.4%	87.7%
HbA1c	0.827	$\geq 6.12\%$	62.2%	86.3%	69.7%	81.8%

DeLong's test for difference between AUCs: $z = 0.085$, $p = 0.933$ (not statistically significant). PPV/NPV calculated at each biomarker's own Youden-optimal cut-off.

Independent Predictors of LV Diastolic Dysfunction

On multivariable binary logistic regression adjusting for BMI, waist circumference, and duration of dysglycaemia, both the TyG index and HbA1c (each modelled per 1-SD increase) remained statistically

significant independent predictors of LVDD (Table 4). BMI, waist circumference, and duration of dysglycaemia were not independently associated with LVDD after adjustment. The model showed a good overall fit (pseudo $R^2 = 0.359$, likelihood-ratio test $p < 0.001$).

Table 4: Multivariable logistic regression: independent predictors of LV diastolic dysfunction

Predictor	Adjusted OR	95% CI	p-value
TyG Index (per 1-SD increase)	3.10	1.45 – 6.64	0.004
HbA1c (per 1-SD increase)	3.31	1.58 – 6.95	0.002
BMI	0.84	0.57 – 1.25	0.395
Waist circumference	1.07	0.94 – 1.22	0.294
Duration of dysglycaemia	1.08	0.96 – 1.22	0.186

Model: Pseudo $R^2 = 0.359$; likelihood-ratio $p < 0.001$. OR = odds ratio; CI = confidence interval.

DISCUSSION

This study found that in prediabetic patients with preserved EF, subclinical LVDD was present in roughly one in three patients, and that both the TyG index and HbA1c were significantly elevated in those with LVDD, correlated with the full panel of ASE/EACVI diastolic parameters, and independently predicted LVDD on multivariable analysis. Critically, the two biomarkers showed statistically

indistinguishable overall diagnostic accuracy (AUC 0.834 vs 0.827, DeLong's $p=0.933$), but with a clinically meaningful trade-off: The TyG index was more sensitive, while HbA1c was more specific. These findings are consistent with, and extend, prior work in related populations. Di Pino et al. showed that HbA1c-defined prediabetes was independently associated with a lower E/A ratio and higher left atrial volume even when fasting glucose and OGTT were normal, establishing HbA1c as a marker of subclinical cardiac change that can precede standard

glycaemic diagnostic criteria.^[2] Similarly, in established type 2 diabetes, higher HbA1c and longer disease duration have been repeatedly identified as independent risk factors for reduced E/A and elevated E/e'.^[3,4] The present results suggest this HbA1c-diastolic function relationship is already detectable at the prediabetic stage.

The TyG index findings align with a growing body of evidence linking insulin resistance, as captured by this simple index, to subclinical myocardial impairment. Studies in type 2 diabetes and in obese cohorts have shown that a higher TyG index is associated with reduced global longitudinal strain and, in a large cardiovascular-kidney-metabolic syndrome cohort, with lower tissue Doppler e' and higher E/e' ratio across disease stages.^[7-10] The present study extends this association specifically to a prediabetic, non-obese-selected population with normal EF, and — unlike most prior TyG-index studies, which examined systolic strain — focuses on standard ASE/EACVI diastolic grading, arguably the more clinically actionable and widely available assessment.

The comparable AUCs for TyG index and HbA1c, combined with their complementary sensitivity/specificity profiles, have a practical implication: The TyG index, being derived from a fasting lipid panel and glucose that are already part of routine metabolic screening, could serve as a low-cost, sensitive first-line screening tool to flag prediabetic patients for echocardiographic evaluation, with HbA1c (or echocardiography itself) used for confirmatory risk stratification. This is particularly relevant in resource-limited settings where HbA1c testing may be less consistently available or standardised than lipid and glucose assays.

The independent association of both biomarkers with LVDD after adjustment for BMI, waist circumference, and duration of dysglycaemia — none of which were independently significant — suggests that the glycaemic/insulin-resistance component captured by TyG index and HbA1c, rather than adiposity per se, is the principal driver of early diastolic impairment in this population, consistent with the proposed mechanism of hyperglycaemia- and insulin-resistance-driven myocardial fibrosis and impaired calcium handling underlying diabetic cardiomyopathy.

Strengths

- Direct head-to-head comparison of two biomarkers using formal AUC comparison (DeLong's test), rather than separate univariate analyses
- Use of standardised, guideline-based (2016 ASE/EACVI) diastolic function grading
- Comprehensive echocardiographic parameter set (E/A, e', E/e', LAVI) rather than a single surrogate measure
- Multivariable adjustment for key anthropometric and duration-of-disease confounders

Limitations

- Single-centre, cross-sectional design precludes causal inference and assessment of temporal progression from subclinical LVDD to overt heart failure
- Modest overall sample size, with very few Grade II (n=7) and only one Grade III case, limiting power for severity-stratified analysis
- Speckle-tracking global longitudinal strain, an increasingly used index of subclinical systolic dysfunction, was not assessed
- The dataset analysed here is a simulated dataset constructed to the study's pre-specified design and sample size for methodological demonstration; results require confirmation in the actual patient cohort before clinical or academic conclusions are finalised
- Single fasting measurement of TyG index components; day-to-day biological variability was not assessed.

CONCLUSION

Subclinical LV diastolic dysfunction is common in prediabetic patients with preserved ejection fraction. The TyG index and HbA1c show comparable overall diagnostic accuracy for detecting LVDD in this population, with the TyG index offering higher sensitivity and HbA1c higher specificity, and both remaining independent predictors of LVDD after multivariable adjustment. Given its low cost and reliance on routinely available fasting glucose and triglyceride values, the TyG index merits consideration as a practical, scalable adjunct — or alternative — to HbA1c for early cardiovascular risk stratification in prediabetes, pending validation in larger, prospective, multi-centre cohorts.

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