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ORIGINAL RESEARCH

Risk Factors of Subclinical Left Ventricular Systolic Dysfunction in Older Adults with Type 2 Diabetes and Preserved LVEF

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Objective: This study evaluates cardiac function in older adults with T2DM and preserved LVEF using two-dimensional speckle-tracking echocardiography to explore the risk factors associated with subclinical left ventricular systolic dysfunction (GLS <18%) in this population.

Methods: All patients (n = 87, aged 60 years and above) and controls (n = 20) underwent clinical assessment and echocardiography, including GLS assessment.

Results: Univariate analysis identified gender (OR 3.368, p=0.008), proteinuria (OR 5.918, p=0.003), eGFR (OR 0.971, p=0.003), HDL (OR 0.201, p=0.013), triglycerides (OR 3.379, p=0.005), and HOMA-IR (OR 1.173, p=0.049) as potential risk factors for subclinical LV systolic insufficiency in older T2DM patients with preserved LVEF. Following adjustment for age and clinical covariates, multivariate logistic regression confirmed proteinuria (OR 4.063, p=0.030), eGFR (OR 0.974, p=0.049), hypertriglyceridemia (OR 3.069, p=0.050), and HOMA-IR (OR 1.249, p=0.026) as independent predictors.

Conclusion: Despite normal global LVEF, proteinuria, hypertriglyceridemia, reduced eGFR, and insulin resistance are closely associated with the development of subclinical left ventricular systolic insufficiency in asymptomatic older adults with T2DM.

Trial Registration: This study adheres to the principles outlined in the Declaration of Helsinki and received approval from the Ethics Review Committee of Huadong Hospital, affiliated with Fudan University (Approval No. 2022K150). Written informed consent was obtained from all participants. The registration number of this study at the Chinese Clinical Trial Center is ChiCTR2200062070.

Keywords: type 2 diabetes, subclinical left ventricular systolic insufficiency, diabetic kidney disease, older adults

Diabetes mellitus (DM) is established as a risk factor for alterations in cardiac function, including subclinical left ventricular systolic dysfunction. Diabetic cardiomyopathy (DCM), a prevalent cardiac impairment associated with diabetes, is defined as cardiac abnormalities that are not fully explained by other cardiovascular causes and are potentially induced by DM.[1] Some studies suggest that left ventricular diastolic dysfunction constituted the earliest dysfunction in the course of DCM;[2] however, recent research has demonstrated that left ventricular systolic dysfunction may represent the initial manifestation of subclinical DCM in patients with DM, preserved left ventricular ejection fraction (LVEF), and no overt signs of heart failure.[3]

Diabetic kidney disease (DKD), a prevalent microvascular complication of diabetes mellitus (DM), affects approximately 40% of patients with Type 2 diabetes mellitus (T2DM) globally.[4] Multivariate logistic regression analysis indicated that both T2DM and kidney disease serve as independent risk factors for a global longitudinal strain (GLS) < 18%.[5] Certain clinical guidelines advocate for the intensive prophylactic use of cardiac medications in patients with

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DM and persistent microalbuminuria; however, the diagnostic threshold for microalbuminuria varies across these guidelines.[6]

Compared with conventional echocardiography, two-dimensional speckle-tracking echocardiography constitutes a novel ultrasound imaging modality developed to objectively quantify myocardial function and provide insights into myocardial strain.[7] This technique permits the evaluation of global longitudinal strain (GLS) and facilitates the identification of subtle, discrete alterations in ventricular systolic function that conventional echocardiography cannot discern. In patients with T2DM, preserved ejection fraction, and no ischemic heart disease, impaired GLS has been demonstrated to be independently associated with adverse events.[8,9] Providing incremental prognostic value beyond conventional echocardiography, this technique has been further validated. Mochizuki et al compared the clinical characteristics of patients with diabetes mellitus (DM) and preserved LVEF. Their findings indicated that left ventricular posterior wall thickness, left ventricular mass index, and left ventricular volume were significantly greater in the GLS <18% group compared to the GLS ≥18% group, and that proteinuria exhibited a considerable correlation with GLS.[5] Ernande et al conducted a prospective study investigating the relationship between GLS and left ventricular remodeling, involving 154 asymptomatic patients with DM, LVEF ≥ 50%, and no significant heart disease. Over a 3-year follow-up period, progression was observed in patients with GLS < 18% but not in those with GLS ≥ 18%.[10] Consequently, in our study, we adopted GLS < 18% as the reference standard for subclinical left ventricular systolic dysfunction, a threshold that has also been utilized in numerous recent studies addressing this topic.

Age is an independent risk factor for the development of complications in patients with T2DM. In the context of global aging, the prevalence of type 2 diabetes among older adults continues to rise, with cardiovascular event risks significantly higher than those of younger patients. The pathophysiological changes in this population exhibit notable distinctiveness compared to other age groups, often accompanied by multiple metabolic disorders, impaired renal function, and vascular endothelial dysfunction, further accelerating the progression of diabetic cardiomyopathy (DCM). However, due to the reduced cardiac reserve function and strong symptom concealment in older adults with type 2 diabetes, traditional echocardiographic indicators (such as LVEF) may mask early myocardial damage, often leading to delayed diagnosis of DCM. In this context, given the unique pathophysiological changes and complex etiology of this population, it has become increasingly necessary to explore targeted health management strategies tailored to their specific needs through research. The pathogenesis of DCM is considered to be multifactorial.[2] However, the characteristics of older adults with T2DM that are associated with impaired left ventricular longitudinal myocardial systolic function remain unclear. Research on older adults with type 2 diabetes mellitus (T2DM) who are asymptomatic for cardiac dysfunction and exhibit preserved LVEF on conventional echocardiography remains limited. Therefore, this study employed a novel imaging modality, two-dimensional speckle-tracking echocardiography, using a more sensitive parameter, GLS, to detect early changes in cardiac function in this population. In addition, we incorporated emerging clinical indicators, including HOMA-IR, NLR, and systemic SII, to comprehensively explore the risk factors associated with impaired longitudinal systolic function of the left ventricle in asymptomatic older adults with T2DM and preserved LVEF. Our findings may aid in the early identification of older adults at risk for DCM, enabling timely intervention and potentially reducing the incidence of adverse cardiovascular events.

Research Content and Methods

Subjects and Groups

A total of 87 older adults (aged ≥60 years) with T2DM, diagnosed at Huadong Hospital Affiliated with Fudan University between November 2021 and August 2024, were included in this study. This cohort comprised 50 patients with uncomplicated DM and 37 patients with diabetic kidney disease. Additionally, 20 age-matched individuals (aged ≥60 years) who visited the hospital for routine health check-ups during the same period were selected as healthy controls. These controls had no history of cardiac disease, as confirmed by medical history inquiry and echocardiography. The sample size for the control group was determined based on previous similar studies.

All enrolled patients were between 60 and 80 years of age. The diagnoses of T2DM and diabetic kidney disease (DKD) were established by the hospital in accordance with the Chinese Guidelines for Clinical Diagnosis and Treatment of Diabetic Kidney Disease[11] and the American Diabetes Association (ADA) 2021 Guidelines.[12] The exclusion criteria were as follows: (1) end-stage renal disease requiring maintenance hemodialysis, peritoneal dialysis, or renal transplantation; (2) non-diabetic kidney diseases, including primary or secondary glomerular diseases, systemic diseases, hereditary kidney diseases, or normoalbuminuric DKD; (3) known cardiac diseases, such as heart failure, coronary artery disease, stable angina, prior myocardial infarction, history of percutaneous coronary intervention or coronary artery bypass grafting, atrial flutter or fibrillation, left or right bundle branch block, congenital heart disease, or the presence of an implanted pacemaker or implantable cardioverter-defibrillator; (4) left ventricular ejection fraction (LVEF) < 50%; (5) a history of or active malignant tumor.

The study complied with the Declaration of Helsinki and was approved by the Ethics Review Committee of Huadong Hospital, affiliated with Fudan University (No. 2022K150). Written informed consent was obtained from all participants.

Clinical Data Collection

All participants underwent a comprehensive health assessment, including a physical examination and a structured interview. Basic demographic and anthropometric data, including age, sex, height, and weight, were collected. Body mass index (BMI) and body surface area (BSA) were subsequently calculated using standard formulae. Obesity was defined as a BMI of 24 kg/m² or greater.

Following hospital admission, fasting blood samples were collected from all patients for a complete blood count, biochemical assays, routine urinalysis, glucose metabolism assessment, and other relevant indicators. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. A positive smoking history was defined as current or former smoking. Hypertension was diagnosed based on a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg, measured on at least three separate occasions in a calm state and without the use of antihypertensive medication.

Imaging Parameter Acquisition

Data acquisition and analysis were performed using a GE Vivid E95 diagnostic ultrasound machine equipped with an M5S 2D probe (frequency range: 1–5 MHz). Synchronized limb lead electrocardiography and EchoPAC quantitative analysis software were also utilized.

Acquisition of Conventional Echocardiographic Parameters

Prior to echocardiography, all patients underwent resting blood pressure measurement and electrocardiographic recording in the supine position. All participants were in normal sinus rhythm throughout the examination. Conventional echocardiography was initially performed to exclude any previously undetected structural heart disease. Standard measurements were obtained for the left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDd), left ventricular end-systolic diameter (LVESd), left ventricular ejection fraction (LVEF), interventricular septal thickness (IVST), and left ventricular posterior wall thickness (LVPWT). Pulsed-wave Doppler echocardiography was used to measure the early (E) and late (A) diastolic filling velocities at the mitral valve orifice. Subsequently, from the apical four-chamber view, the early diastolic mitral annular velocities (e') were measured at the septal and lateral walls of the mitral annulus. The E/A and E/e' ratios were then calculated. Furthermore, the left ventricular mass index (LVMI) was calculated using a standardized formula.

Acquisition of Two-Dimensional Speckle-Tracking Echocardiographic Parameters

Images of three consecutive cardiac cycles were acquired from the apical two-chamber, three-chamber, and four-chamber views using the M5S 2D probe. For speckle tracking analysis, the region of interest was defined as the myocardium between the epicardial and endocardial borders, thereby encompassing the entire left ventricular myocardium. Subsequently, strain values were calculated for each of the three apical views. The GLS was then determined by averaging the peak systolic strain values from all 17 segments across the three standard views and was reported as an absolute value. In this study, left ventricular myocardial segmentation was performed using a 17-segment model.

Specifically, the left ventricle was divided into three levels (basal, mid-cavity, and apical). The basal and mid-cavity levels were each subdivided into six equal segments (60° each) in the short-axis orientation, while the apical level was divided into four equal segments (90° each). The most distal portion of the apex, beyond the end of the ventricular cavity, was defined as the apical cap, completing the 17-segment model.

The population flow chart in this study is shown in Figure 1.

Diagnostic Criteria and Calculation Formulae

Relevant Diagnostic Criteria

The threshold for subclinical left ventricular systolic dysfunction in patients with DM and preserved LVEF was set at GLS < 18%.[10] The threshold for left ventricular diastolic dysfunction was set at E/e' > 14.[13]

All patients with DM were divided into three groups based on the urine albumin/creatinine ratio (UACR):

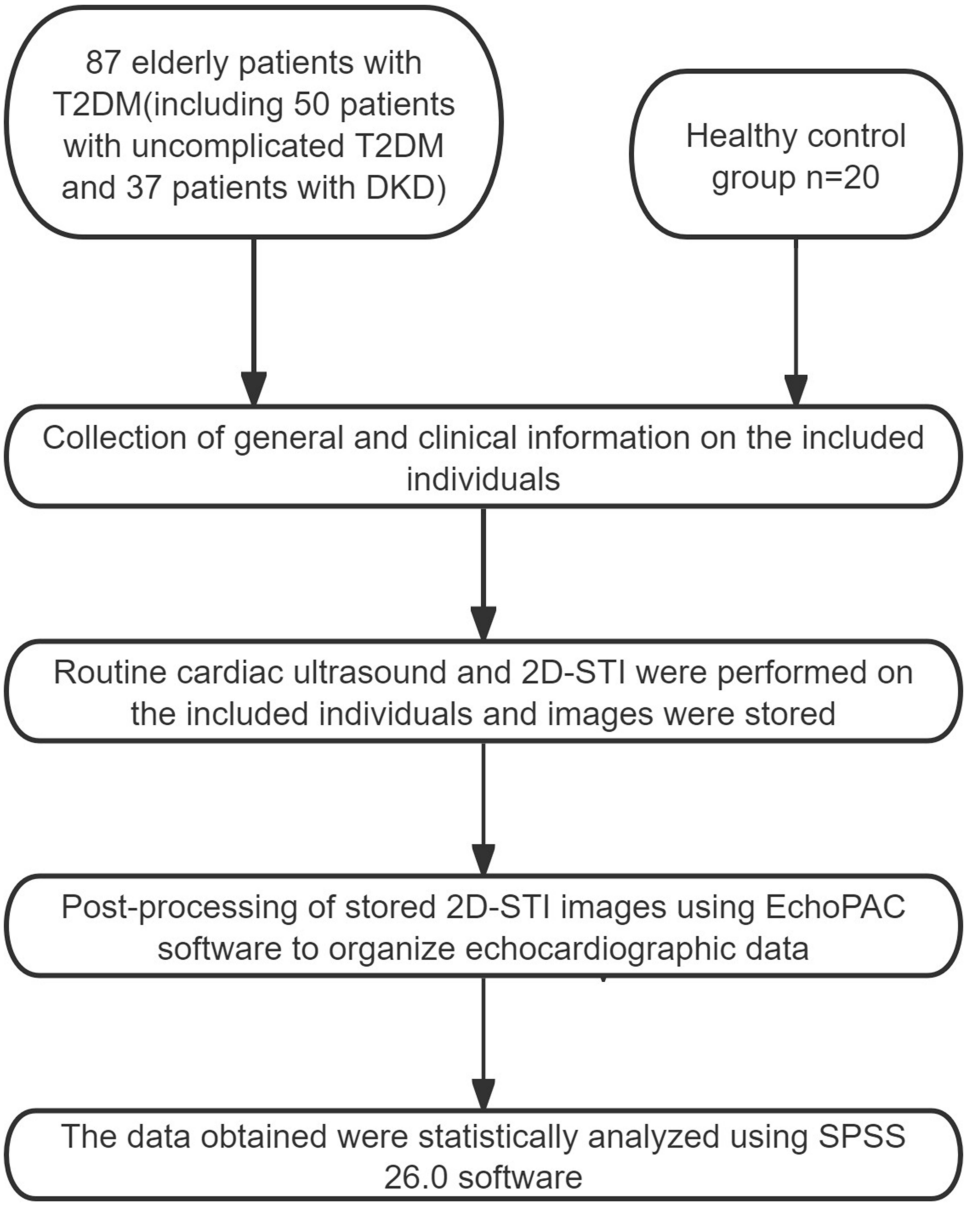

Figure 1 Flow chart of the population in this study.
Abbreviations: T2DM, type 2 diabetes mellitus; DKD, Diabetic kidney disease.

1. Normoalbuminuria group (UACR < 30 mg/g, n = 50).
2. Microalbuminuria group (UACR = 30–300 mg/g, n = 25).
3. Macroalbuminuria group (UACR ≥ 300 mg/g, n = 12).

Calculation Formulae

HOMA-IR = fasting blood glucose × fasting insulin/22.5; TYG = ln [fasting triglycerides (TG, mg/dl) × fasting blood glucose (FBG, mg/dl)]/2; NLR (neutrophil/lymphocyte ratio) = neutrophil count/lymphocyte count; SII (Systemic Immunoinflammatory Index) = platelet count × neutrophil count/lymphocyte count; SIRI (Systemic Inflammatory Response Index) = monocyte count × neutrophil count/lymphocyte count.

Statistical Analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Normally distributed continuous variables are presented as mean ± standard deviation (SD). Comparisons between two groups were made using the independent samples *t*-test, while comparisons among multiple groups were conducted using one-way analysis of variance (ANOVA). Non-normally distributed continuous variables are expressed as median (interquartile range, IQR), and were analyzed using the Mann–Whitney U (M-W) test for two-group comparisons and the Kruskal–Wallis (K-W) test for multiple-group comparisons. Categorical data are reported as frequencies (percentages) and were compared using the chi-squared (χ^2) test. Logistic regression analysis was employed to identify factors independently associated with subclinical left ventricular systolic and diastolic insufficiency, to calculate the odds ratios (ORs) and their 95% confidence intervals (CIs). A two-tailed P-value of less than 0.05 was considered statistically significant.

Results

Comparison of General Information and Echocardiographic Indicators of All Subjects

Comparison of General Information

The baseline characteristics of the study participants are presented in Table 1. The healthy control group (n=20) had a median age of 68.50 (66.00, 73.00) years and comprised 55% males, with 25% being former or current smokers. The

Table 1 Baseline Characteristics of All Subjects

	Patients with DKD n=37	**Patients with DM n=50**	**Control n=20**	**P value**
Age, years	68.00(64.00,71.50)	69.00(62.75,73.00)	68.50(66.00,73.00)	0.595
Male, n%	26(70.3%)[b]	18(36.0%)	11(55.0%)	0.006
Body Mass Index, kg/m^2	24.01±2.55	23.81±2.58	23.05±2.14	0.369
Obesity, n%	17(45.9%)	24(48.0%)	5(25.0%)	0.193
SBP, mmHg	139.35±16.32[ab]	131.20±14.73	125.40±9.48	0.002
DBP, mmHg	80.00(69.00,84.50)	76.00(68.00,82.50)	78.00(74.00,83.75)	0.603
Smoking, n%	10(27.0%)	5(10.0%)	5(25.0%)	0.095
CRP, mg/L	1.73(00.80,3.06)[b]	0.90(00.80,1.89)[a]	3.52(1.34,4.70)	0.001
White blood cell count, 10^9/L	6.40(05.05,7.10)	5.85(04.98,7.20)	5.25(4.03,6.85)	0.148
Platelet count, 10^{12}/L	195.95±51.38	203.00±49.82	210.20±43.93	0.570
Percentage of lymphocytes, %	26.73±7.91[ab]	31.18±10.54	34.22±12.30	0.021
Percentage of monocytes, %	64.27±8.02[ab]	59.36±10.69	56.66±13.70	0.021
Hemoglobin, g/L	122.14±17.76[ab]	130.56±15.25	135.70±14.85	0.006
RDW, %	12.90(12.50,13.55)	13.00(12.68,13.50)	12.95(12.63,13.20)	0.552
Glycated hemoglobin, %	7.70(6.70,8.85)[a]	7.85(6.80,9.23)[a]	5.76(5.63,5.76)	<0.001
Seralbumin, g/L	38.60±4.73[b]	41.77±2.79	41.01±3.00	0.003
Urea nitrogen, mmol/L	7.40(5.35,10.25)[ab]	5.65(4.50,8.10)	5.70(4.95,6.10)	0.005

(*Continued*)

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Table 1 (Continued).

	Patients with DKD n=37	Patients with DM n=50	Control n=20	P value
eGFR, mL/min/1.73m^2	59.00(34.00,89.50)[ab]	90.00(67.00,96.25)	86.50(76.25,91.00)	0.002
Serum creatinine, umol/L	107.00(74.45,158.05)[ab]	64.55(52.23,90.10)	74.85(58.68,84.73)	<0.001
Uric acid, umol/L	348.43±93.09[b]	292.02±69.61	319.81±64.87	0.005
HDL, mmol/L	1.07(0.93,1.35)[ab]	1.29(1.02,1.61)	1.39(1.34,1.39)	0.006
LDL, mmol/L	2.49(1.61,2.82)[a]	2.53(2.01,3.04)[a]	3.20(2.96,3.20)	<0.001
Fasting blood glucose, mmol/L	6.10(4.80,8.15)[a]	6.25(5.28,7.83)[a]	4.90(4.70,5.78)	0.047
Triglyceride, mmol/L	1.50(1.00,2.15)	1.28(1.01,1.52)	1.48(1.28,1.68)	0.311
Cholesterol, mmol/L	4.25(3.52,4.68)[a]	4.38(3.77,5.01)[a]	5.17(4.76,5.22)	0.001
Tyg	8.89±0.67	8.77±0.63	8.71±0.41	0.486
PLR	131.13(84.98,155.41)	116.19(88.49,151.99)	134.28(88.77,145.61)	0.822
NLR	2.47(01.86,2.95)[ab]	1.89(01.41,2.56)	1.78(01.03,2.12)	0.007
SII	457.84(343.54,591.43)	364.68(245.49,631.35)	348.22(229.39,452.64)	0.084
SIRI	0.83(0.59,1.24)[a]	0.63(0.41,1.27)	0.50(0.35,0.79)	0.022
RPP	10125.00(8559.00,11,508.50)[a]	9553.50(8563.50,11,523.50)[a]	8544.00(8046.00,9940.50)	0.012

Note: a. compared with the normoalbuminuria group, P < 0.05; b. compared with the macroalbuminuria group, P < 0.05. Data are presented as mean ± standard deviation for normally distributed data and median (interquartile range) for non-normally distributed data, or n (%).

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; CRP, C-reactive protein; RDW, Red blood cell distribution width; eGFR, Estimated glomerular filtration rate; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; Tyg, triglyceride glucose index; PLR, platelet-lymphocyte ratio; NLR, neutrophil-lymphocyte ratio; SII, Systemic Immunoinflammatory Index; SIRI, Systemic Inflammatory Response Index; RPP, rate-pressure product.

mean body mass index (BMI) was 23.05 ± 2.14 kg/m², the mean systolic blood pressure (SBP) was 125.40 ± 9.48 mmHg, and the median diastolic blood pressure (DBP) was 78.00 (74.00, 83.75) mmHg.

For the uncomplicated DM group (n=50), the median age was 69.00 (62.75, 73.00) years, with 48% males and 10% former or current smokers. The mean BMI was 23.81 ± 2.58 kg/m², the mean SBP was 131.20 ± 14.73 mmHg, and the median DBP was 76.00 (68.00, 82.50) mmHg.

In the DKD group (n=37), the median age was 68.00 (64.00, 71.50) years, and 27% were male. The mean BMI was 24.01 ± 2.55 kg/m², mean SBP was 139.35 ± 16.32 mmHg, and median DBP was 80.00 (69.00, 84.50) mmHg.

No statistically significant differences were observed among the three groups regarding age, BMI, smoking history, white blood cell count, platelet count, erythrocyte distribution width (RDW), or triglycerides.

Uncomplicated DM Group Vs Control Group

No statistically significant differences (P > 0.05) were observed among the three groups for age, BMI, systolic blood pressure, diastolic blood pressure, smoking history, white blood cell count, or platelet count. However, compared with the control group, the uncomplicated DM group exhibited statistically significant differences (P < 0.05) in several parameters. Specifically, levels of C-reactive protein (CRP), free triiodothyronine (T3), low-density lipoprotein (LDL), and cholesterol were significantly lower in the uncomplicated DM group, whereas glycated hemoglobin, fasting blood glucose, and the rate-pressure product (RPP) were significantly higher.

DKD Group Vs Control Group

Compared with the control group, the DKD group exhibited significantly higher levels of systolic blood pressure, percentage of neutrophils, glycated hemoglobin, fasting blood glucose, urea nitrogen, serum creatinine, NLR, SIRI, and RPP (all P < 0.05). Conversely, the DKD group had significantly lower levels of lymphocyte percentage, hemoglobin, high-density lipoprotein (HDL), LDL, cholesterol, and eGFR (all P < 0.05).

DKD Group Vs Uncomplicated DM Group

Compared with the uncomplicated DM group, the DKD group demonstrated significantly higher levels of systolic blood pressure, CRP, neutrophil percentage, urea nitrogen, serum creatinine, uric acid, and NLR (all P < 0.05). Conversely, the

DKD group had significantly lower levels of lymphocyte percentage, hemoglobin, eGFR, and HDL (all $P < 0.05$). There were no statistically significant differences between the two groups regarding white blood cell count, platelet count, monocyte percentage, RDW, glycated hemoglobin, fasting blood glucose, triglycerides, or cholesterol (all $P > 0.05$).

Comparison of Ultrasound Indicators

Conventional Echocardiographic Indicators

No significant differences were observed in conventional echocardiographic indicators—including LAD, LVEDd, LVESd, IVST, LVPWT, LVEF, SV, LVEDV, HR, E, A, E/A, and E/e'—between the uncomplicated DM group and the control group, or between the DKD group and the uncomplicated DM group (Table 2). However, when comparing the DKD group with the control group, the A-value was significantly higher in the DKD group ($P < 0.05$). All other conventional echocardiographic indicators showed no statistically significant differences between these two groups.

Comparison of Two-Dimensional Speckle-Tracking Echocardiographic Indicators

Two-dimensional speckle-tracking echocardiography revealed that the global longitudinal strain (GLS) was significantly lower in the DKD group (mean = 15.86 ± 2.12%) compared to both the uncomplicated DM group and the control group ($P < 0.05$) (Table 2). Furthermore, subclinical left ventricular systolic insufficiency, defined as GLS < 18%, was identified in 56 of the 107 study participants. Notably, this condition was present in 30 patients (81.08%) in the DKD group, a proportion significantly higher than that observed in the uncomplicated DM group and the control group ($P < 0.05$).

In the comparison between the uncomplicated DM group and the control group, no statistically significant differences were observed ($P > 0.05$). However, the mean GLS (%) in the DM group was slightly lower than that in the control group (18.18 ± 2.29 vs 19.21 ± 1.83). Within the uncomplicated DM group, 21 individuals exhibited subclinical left ventricular systolic insufficiency (GLS < 18%), accounting for 42.00% of the group, which was higher than the 25.00% observed in

Table 2 Comparison of Echocardiographic Indicators in All Subjects

	Patients with DKD n=37	**Patients with DM n=50**	**Control n=20**	**P value**
LAD, mm	37.00(34.00,42.00)	36.00(33.75,40.00)	35.50(32.25,39.75)	0.332
LVEDd, mm	45.41±5.00	44.46±4.09	43.60±3.03	0.247
LVESd, mm	28.00(25.50,31.00)	28.00(25.00,30.25)	27.00(25.00,29.00)	0.500
IVST, mm	9.00(9.00,10.00)	9.00(8.00,10.00)	9.00(9.00,9.75)	0.448
LVPWT, mm	9.00(8.50,10.00)	9.00(8.00,9.00)	9.00(8.00,9.00)	0.244
LVEF, %	63.00(61.00,66.50)	65.00(63.00,68.00)	66.50(61.00,68.00)	0.146
LVMI, g/m^2	81.41±21.03	78.00±16.29	76.90±15.10	0.578
SV, mL	55.00(43.50,72.50)	52.00(37.75,61.50)	50.00(39.25,61.00)	0.352
LVEDV, mL	86.00(69.50,115.00)	78.50(58.00,93.75)	73.00(63.50,95.75)	0.191
HR, bpm	75.38±13.87	75.26±12.58	69.30±8.52	0.154
E	67.00(57.50,79.00)	65.00(54.75,78.00)	63.50(49.50,69.75)	0.482
A	99.35±20.11[a]	93.32±16.26	84.85±18.51	0.018
E/A	0.69(0.57,0.85)	0.67(0.59,0.84)	0.73(0.65,0.81)	0.353
E/A≤0.8	26 (70.27%)	36 (72.00%)	15 (75.00%)	0.931
IVRT, ms	90.24±19.39	87.68±16.78	89.40±13.39	0.781
E/e'	10.13(8.26,11.48)	9.71(7.66,11.43)	8.45(7.53,9.98)	0.170
E/e'>14	4 (10.81%)	4 (8.00%)	1 (5.00%)	0.745
Fractional shortening, %	0.37(0.35,0.40)	0.36(0.34,0.40)	0.37(0.36,0.42)	0.551
GLS (%)	15.86±2.12[ab]	18.18±2.29	19.21±1.83	<0.001
Patients with GLS < 18%, n%	30 (81.08%) [ab]	21 (42.00%)	5 (25.00%)	<0.001

Note: a. compared with the normoalbuminuria group, $P < 0.05$; b. compared with the macroalbuminuria group, $P < 0.05$.
Abbreviations: LAD, Left atrial diameter; LVEDdm, Left ventricular end-diastolic diameter; LVESd, Left ventricular end-stage systole diameter; IVST, Interventricular septum thickness; LVPWT, Left ventricular posterior wall thickness; LVEF, Left ventricular ejection fraction; LVMI, Left ventricular mass index; SV, Stroke volume; LVEDV, Left ventricular end-diastolic volume; HR, heart rate; E, peak early diastolic mitral flow velocity; A, peak late diastolic mitral flow velocity; e', spectral pulsed-wave Doppler-derived early diastolic; IVRT, Isovolumic relaxation time; GLS, global longitudinal strain.

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the control group (5 individuals). Nevertheless, these differences between the groups did not reach statistical significance ($P > 0.05$).

Comparison of Baseline Characteristics and Ultrasound Indicators of Patients with DM at Different Albuminuria Levels

A total of 87 patients from the uncomplicated DM and DKD groups were stratified into three subgroups based on their Urinary Albumin-to-Creatinine Ratio (UACR). Statistically significant differences across these subgroups were observed for gender and the percentage of smokers (Supplementary Table 1). In contrast, no significant differences were found in age, BMI, the prevalence of hypertension, or the duration of DM.

Comparisons of baseline characteristics among the three groups revealed the following. Relative to the control group, the microalbuminuria group exhibited significantly higher levels of blood urea nitrogen, serum creatinine, and a higher percentage of subjects with significantly impaired renal function (eGFR < 60 mL/min/1.73 m²). Conversely, this group had significantly lower levels of 25-(OH)D, serum albumin, and eGFR.

Similarly, the macroalbuminuria group demonstrated significantly higher values than the control group for the percentage of smokers, percentage of neutrophils, blood urea nitrogen, serum creatinine, percentage of significantly impaired renal function (eGFR < 60 mL/min/1.73 m²), blood uric acid, fasting C-peptide, and NLR. In contrast, the macroalbuminuria group had significantly lower percentages of lymphocytes, and lower levels of 25-(OH)D, serum albumin, and eGFR.

In the direct comparison between the macroalbuminuria and microalbuminuria groups, glycated hemoglobin was the only parameter that was significantly lower in the macroalbuminuria group. No other significant differences were observed in the remaining baseline characteristics or laboratory indices.

The comparison of conventional echocardiographic indicators among the three groups revealed that SV (stroke volume, mL) and LVEDV (left ventricular end-diastolic volume, mL) in the macroalbuminuria group were significantly higher than those in both the microalbuminuria and normoalbuminuria groups (Supplementary Table 2). Although the means of SV and LVEDV in the microalbuminuria group were slightly elevated compared to the normoalbuminuria group, these differences did not reach statistical significance. No statistically significant differences were observed among the three groups in terms of LAD, LVEDd, LVESd, IVST, LVPWT, LVEF, LVMI, HR, E, E/A, IVRT, and E/e'. Furthermore, the prevalence of left ventricular diastolic insufficiency, defined as E/A < 0.8 or E/e' > 14, did not differ significantly among the groups ($P > 0.05$).

Two-dimensional speckle-tracking echocardiography revealed that the left ventricular global longitudinal strain (GLS) was significantly worse (ie, higher values) in both the microalbuminuria and macroalbuminuria groups compared to the normoalbuminuria group ($P < 0.001$; Supplementary Table 3). Among all 87 patients with diabetes mellitus (DM), subclinical left ventricular systolic dysfunction, defined as GLS < 18%, was identified in 51 cases (58.62%). When stratified by group, the proportion of patients with subclinical dysfunction was significantly higher in the macroalbuminuria group (91.70%) than in the normoalbuminuria group (42.00%, $P < 0.05$). Similarly, the microalbuminuria group also exhibited a higher proportion (76.00%) compared to the normoalbuminuria group ($P < 0.05$). Although the prevalence of subclinical dysfunction was greater in the macroalbuminuria group than in the microalbuminuria group (91.70% vs 76.00%), this difference did not reach statistical significance ($P > 0.05$).

Comparison of Baseline Characteristics and Echocardiographic Indicators of Patients with DM Grouped According to GLS < 18%

The 87 subjects were stratified into two groups based on the presence of subclinical left ventricular systolic dysfunction, defined as GLS < 18%: the GLS < 18% group (n = 51) and the GLS ≥ 18% group (n = 36).

As presented in Table 3, patients in the GLS < 18% group exhibited significantly higher levels of UACR, proteinuria prevalence, leukocyte count, neutrophil percentage, blood urea nitrogen, prevalence of eGFR < 60 (mL/min/1.73 m²), serum creatinine, uric acid, fasting insulin, fasting C-peptide, triglycerides, HOMA-IR, triglyceride-glucose index (TyG),

NLR, SIRI, and RPP compared to the GLS ≥ 18% group ($P < 0.05$). Conversely, the same group had significantly lower levels of lymphocyte percentage, eGFR, and HDL ($P < 0.05$).

No statistically significant differences were observed between the two groups regarding age, BMI, systolic and diastolic blood pressure, hypertension prevalence, smoking history, DM duration, glycated hemoglobin, or fasting blood glucose ($P > 0.05$).

Table 3 Baseline Characteristics of Patients with T2DM Grouped According to GLS < 18%

	Patients with GLS≥18% n=36	**Patients with GLS<18% n=51**	**P value**
Age, years	68.50(64.00, 72.00)	68.00(63.00, 73.00)	0.802
Male, n%	33.30%	62.70%	0.007
BMI, kg/m^2	23.54±2.75	24.14±2.40	0.284
Obesity, n%	47.20%	47.10%	0.988
SBP, mmHg	131.00(122.25, 149.50)	136.00(125.00, 143.00)	0.451
DBP, mmHg	75.50(68.25, 84.75)	77.00(70.00, 83.00)	0.430
Hypertension, n%	72.20%	84.30%	0.170
Smoking, n%	8.30%	23.50%	0.065
UACR	3.36(0.46, 12.84)	51.83(7.34, 282.30)	<0.001
Albuminuria, n%	19.40%	58.80%	<0.001
CRP, mg/L	0.89(0.80, 1.73)	1.28(0.80, 2.99)	0.270
DM duration, years	14.00(10.00, 20.00)	17.00(10.00, 20.00)	0.441
White blood cell count, 109/L	5.30(4.68, 6.90)	6.50(5.50, 7.30)	0.016
Platelet count, $10^{12}/L$	208.97±47.17	193.67±51.94	0.164
Percentage of lymphocytes, %	32.90(26.65, 40.35)	26.10(20.90, 32.20)	0.003
Percentage of monocytes, %	57.80±9.84	64.02±9.20	0.003
Hemoglobin, g/L	127.22±14.13	126.80±18.58	0.910
RDW, %	12.90(12.60, 13.48)	13.00(12.60, 13.50)	0.890
Glycated hemoglobin, %	7.55(6.73, 8.75)	8.00(6.80, 9.10)	0.641
25-(OH)D, ng/mL	16.50(11.85, 24.48)	14.40(10.20, 19.59)	0.089
Seralbumin, g/L	40.50 (38.53, 42.95)	40.90(37.90, 42.90)	0.935
Urea nitrogen, mmol/L	5.65(4.50, 7.05)	7.30(5.30, 10.10)	0.005
eGFR, $mL/min/1.73m^2$	90.00(72.50, 94.00)	68.00(35.00, 92.00)	0.005
eGFR<60, n%	13.90%	43.10%	0.004
Serum creatinine, umol/L	63.25(51.18, 82.20)	90.90(64.40, 154.60)	<0.001
Uric acid, umol/L	285.25±82.08	337.72±80.39	0.004
HDL, mmol/L	1.32(1.04, 1.74)	1.07(0.93, 1.37)	0.012
LDL, mmol/L	2.56±0.81	2.34±0.76	0.218
Fasting insulin, uIU/L	7.95(5.30, 13.38)	13.50(9.40, 17.60)	0.004
Fasting C-peptide, ng/mL	1.90(1.15, 2.72)	2.70(1.40, 3.10)	0.037
Fasting blood glucose, mmol/L	5.80(4.90, 6.98)	6.50(4.80, 8.40)	0.100
Triglyceride, mmol/L	1.18(0.91, 1.45)	1.43(1.07, 2.16)	0.004
Cholesterol, mmol/L	4.43±1.06	4.20±0.99	0.298
HOMA-IR	2.08(1.36,3.17)	3.77(2.29,6.19)	0.001
Tyg	8.54±0.55	9.02±0.64	<0.001
NLR	1.71(1.28,2.47)	2.47(1.80,3.49)	0.002
SII	364.68(246.83,558.96)	438.67(338.80,702.83)	0.057
SIRI	0.60(0.42,1.13)	0.83(0.57,1.42)	0.017
RPP	9345.50 (8116.50,10,464.00)	10,332.00 (8814.00,11,696.00)	0.029

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; UACR, Urinary albumin-creatinine ratio; CRP, C-reactive protein; RDW, Red blood cell distribution width; eGFR, Estimated glomerular filtration rate; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; Tyg, triglyceride glucose index; PLR, platelet-lymphocyte ratio; NLR, neutrophil-lymphocyte ratio; SII, Systemic Immunoinflammatory Index; SIRI, Systemic Inflammatory Response Index; RPP, rate-pressure product.

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E and E/A values in the group with GLS < 18% were significantly lower, and the percentage of E/A <0.8 was significantly higher than that in the group with GLS ≥ 18%, suggesting that subjects who developed subclinical left ventricular systolic insufficiency might have concomitant left ventricular diastolic dysfunction (Table 4).

Analysis of Risk Factors for Subclinical Left Ventricular Systolic Insufficiency in Patients with DM

All 87 older adults with DM were included, and GLS < 18% was set as the dependent variable (Table 5). A univariate logistic regression analysis was performed on clinical data that were statistically different from those analyzed above or considered traditional risk factors for cardiovascular disease (CVD). Variables included general information (age, gender, BMI, DM duration, and smoking history), UACR, blood indicators related to renal function (eGFR, blood urea nitrogen, serum creatinine, and blood uric acid), serum albumin and lipid indicators (triglycerides, cholesterol, HDL, and LDL), glucose metabolism indicators (fasting blood glucose, fasting insulin, fasting C-peptide, glycated hemoglobin, and HOMA-IR) and inflammation-related serological indicators (white blood cell count, percentage of neutrophils, SIRI, SII, etc).

Statistically significant indicators in the univariate analysis, including gender, proteinuria, white blood cell count, percentage of neutrophils, blood urea nitrogen, eGFR, serum creatinine, uric acid, HDL, fasting C-peptide, HOMA, fasting blood glucose, triglycerides (combined as Tyg), and RPP, traditional risk factors for CVD, including age, obesity, and hypertension, DM duration, and smoking history, as well as the development of subclinical left ventricular systolic insufficiency (GLS < 18%) were included as dependent variables to perform a multivariate logistic stepwise regression analysis among the 87 DM patients and the 37 DKD patients respectively, with the results shown below (Table 5, Figure 2):

The multivariate logistic regression analysis showed that proteinuria, eGFR, triglycerides, and HOMA were significant risk factors for subclinical left ventricular systolic insufficiency in older adults with T2DM. In regression model 1, as the eGFR decreased, the risk of developing subclinical left ventricular systolic insufficiency in the subjects gradually increased. eGFR was an independent risk factor for GLS < 18% (OR = 0.974, 95% CI = 0.949–1.000, P <

Table 4 Characteristics of Cardiac Ultrasound Indicators in Patients with T2DM Grouped According to GLS < 18%

	Patients with GLS≥18% n=36	**Patients with GLS<18% n=51**	**p**
LAD, mm	36.00(33.25, 40.00)	38.00(34.00, 42.00)	0.263
LVEDd, mm	44.86±4.70	44.86±4.40	0.999
LVESd, mm	28.03±4.05	28.14±3.48	0.893
IVST, mm	9.00(8.00, 10.00)	10.00(9.00, 10.00)	0.106
LVPWT, mm	9.00(8.00, 9.00)	9.00(8.00, 10.00)	0.063
LVMI, g/m^2	77.59±17.13	80.77±19.33	0.431
SV, mL	53.00(40.25, 64.75)	52.00(41.00, 64.00)	0.866
LVEDV, mL	78.50(61.25, 98.75)	86.00(65.00, 99.00)	0.599
HR, bpm	71.00(63.50, 81.75)	78.00(69.00, 86.00)	0.055
E	72.50(64.00, 84.25)	61.00(51.00, 75.00)	0.001
A	93.00(76.75, 101.75)	98.00(89.00, 105.00)	0.180
IVRT, ms	88.42±17.13	89.02±18.54	0.878
E/e'	10.00(8.03, 11.48)	9.90(8.00, 11.07)	0.617
E/e'>14, n%	13.90%	5.90%	0.203
Fractional shortening, %	0.36(0.34,0.39)	0.37(0.35,0.40)	0.685

Abbreviations: LAD, Left atrial diameter; LVEDdm, Left ventricular end-diastolic diameter; LVESd, Left ventricular end-stage systole diameter; IVST, Interventricular septum thickness; LVPWT, Left ventricular posterior wall thickness; LVEF, Left ventricular ejection fraction; LVMI, Left ventricular mass index; SV, Stroke volume; LVEDV, Left ventricular end-diastolic volume; HR, heart rate; E, peak early diastolic mitral flow velocity; A, peak late diastolic mitral flow velocity; e', spectral pulsed-wave Doppler-derived early diastolic; IVRT, Isovolumic relaxation time; GLS, global longitudinal strain.

Table 5 Univariate Logistic Regression Analysis for the Development of Subclinical Left Ventricular Systolic Insufficiency in Patients with T2DM

GLS<18%	Univariate OR (95% CI)	p	Multivariate(model 1)	p
Age, years	0.990(0.914–1.072)	0.799	0.913(0.811–1.028)	0.134
Male, n%	3.368(1.375–8.250)	0.008	2.117(0.519–8.632)	0.296
Obesity, n%	0.993(0.423–2.335)	0.988	1.117(0.339–3.683)	0.856
Hypertension, n%	2.067(0.724–5.905)	0.175		
Smoking, n%	3.385(0.880–13.022)	0.076	2.197(0.335–14.387)	0.412
Albuminuria, n%	5.918(2.186–16.025)	0.003	4.063(1.149–14.369)	0.030
CRP, mg/L	1.204(0.930–1.559)	0.160		
DM duration, years	1.019(0.965–1.076)	0.493	1.058(0.978–1.145)	0.162
Glycated hemoglobin, %	0.993(0.788–1.252)	0.952		
25-(OH)D, ng/mL	0.966(0.920–1.014)	0.159		
eGFR, mL/min/1.73m^2	0.971(0.953–0.990)	0.003	0.974(0.949–1.000)	0.049
HDL, mmol/L	0.201(0.057–0.715)	0.013	0.655(0.102–4.214)	0.656
LDL, mmol/L	0.703(0.402–1.230)	0.217		
Triglyceride, mmol/L	3.379(1.434–7.963)	0.005	3.069(1.002–9.395)	0.050
Cholesterol, mmol/L	0.795(0.517–1.223)	0.297		
HOMA-IR	1.173(1.001–1.375)	0.049	1.249(1.027–1.521)	0.026
PLR	1.000(0.992–1.008)	0.987		
NLR	1.357(0.962–1.913)	0.082		
SII	1.001(1.000–1.002)	0.183		
SIRI	1.511(0.863–2.645)	0.149		

Abbreviations: CRP, C-reactive protein; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; PLR, platelet-lymphocyte ratio; SII, Systemic Immunoinflammatory Index; SIRI, Systemic Inflammatory Response Index; OR, odds ratio; CI, confidence interval.

0.05). Triglycerides were also a risk factor for the development of subclinical left ventricular systolic insufficiency, and with the elevation of triglycerides, the risk was progressively higher (OR = 3.069, 95% CI = 1.002–9.395, P < 0.05). The HOMA-IR was calculated to quantify insulin resistance.[14] With the increase in insulin resistance, the probability of subclinical left ventricular systolic insufficiency in older adults with T2DM progressively increased (OR = 1.249, 95% CI = 1.027–1.521, P < 0.05). In model 1, the risk of subclinical left ventricular systolic function in the DKD group with positive proteinuria was 4.063 times that in the uncomplicated DM group with negative proteinuria (P < 0.05). However,

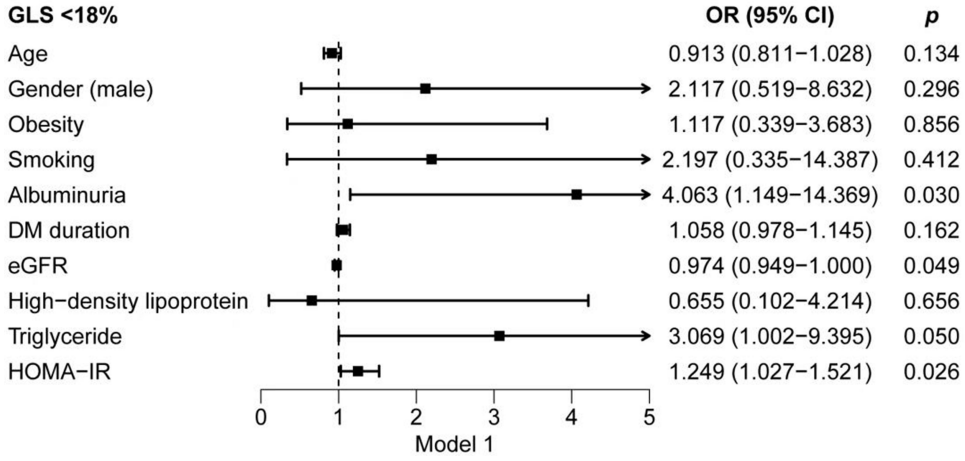

Figure 2 vForest plot.Multivariate Logistic Regression Analysis of the Development of Subclinical Left Ventricular Systolic Insufficiency in Patients with T2DM.
Abbreviations: OR, odds ratio; CI, confidence interval; GLS, global longitudinal strain.eGFR, Estimated glomerular filtration rate.

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unfortunately, after including only patients in the DKD group, none of the above risk factors remained statistically significant in model 2 (Supplementary Table 4).

Discussion

This study aims to explore the risk factors associated with impaired left ventricular longitudinal myocardial systolic function in asymptomatic older adults with T2DM and preserved LVEF. Our data analysis identified proteinuria, insulin resistance, reduced eGFR, and hypertriglyceridemia as independent risk factors for early subclinical left ventricular systolic dysfunction in asymptomatic older adults with T2DM and preserved LVEF.

Proteinuria is recognized as a marker of microvascular dysfunction. The Urinary Albumin-to-Creatinine Ratio (UACR), a robust indicator for screening proteinuria, is now incorporated into numerous clinical guidelines. Its primary role is to identify patients with type 2 diabetes mellitus (T2DM) who have persistent microalbuminuria, thereby guiding the initiation of intensive prophylactic therapy with cardioprotective medications.[15.] According to our results, the proteinuria is a risk factor for subclinical left ventricular systolic insufficiency in older adults with T2DM in both univariate and multivariate logistic regression models, which is in line with the conclusions made by Peter P[6] and Yasuhide[5] et al, suggesting that albuminuria could be used as a biomarker to screen DM patients for increased cardiovascular risk. An earlier study at our hospital showed that, in older adults with DKD, patients with macroalbuminuria had a significantly higher risk of developing subclinical left ventricular systolic insufficiency than those with microalbuminuria. However, this difference was not statistically significant in this study, although the subjects showed a gradual decrease in GLS and a gradual increase in the percentage of GLS < 18% as the albuminuria became more severe, which may be related to the small sample size of the macroalbuminuria group.

Elevated glucose or altered insulin sensitivity has been found to affect cardiac function by altering the cardiac extracellular matrix (ECM).[16,17] It has been suggested that both fasting glucose, which reflects instantaneous glucose levels, and glycosylated hemoglobin, which reflects long-term glycemic control, can be used as markers to screen DM patients who are at an increased risk of CVD.[18] However, in many studies, controlling glycosylated hemoglobin or fasting blood glucose alone cannot alleviate the burden of left ventricular dysfunction in mouse models or prevent cardiovascular complications in diabetic patients.[19–21] Our results correspond to it. Another researcher suggests reversing the adverse effects of acute hyperglycemia on left ventricular systolic myocardial mechanics by increasing blood glucose variability.[22,23] In the field of prevention and management of DCM in older adults, effective glycemic management remains to be further investigated and guided. Insulin resistance might be an important trigger for systolic dysfunction in T2DM patients.[24] Among the subjects included in this study, we quantified insulin resistance by HOMA-IR and Tyg.[25] These indicators were significantly different between the two groups, demonstrated to be risk factors for GLS < 18% in the univariate or multivariate logistic regression analysis, once again proving the promoting effect of insulin resistance on the onset of DCM.

Studies that examined endocardial myocardial biopsy samples have shown significant interstitial fibrosis with infiltration of inflammatory leukocytes in patients with HFpEF.[26] Inflammatory indicators such as white blood cell count, NLR, as well as SII and SIRI, reflect systemic inflammation and immune balance in the body. High SIRI is an independent risk factor for DKD, while elevated SII is associated with an increased risk of kidney disease progression in biopsy-confirmed DKD cases.[27] In this experiment, we found that the white blood cell count, NLR, and SIRI in the group with GLS < 18% were significantly higher than those in the group with GLS ≥ 18%, validating the role of inflammation in mediating the pathogenesis of DCM in the older population. Biomarkers reflecting inflammation, as cost-effective and readily available indicators of inflammation, may be applied to the early screening of subclinical left ventricular systolic dysfunction in older T2DM patients.

Hypertriglyceridemia is implicated in myocardial steatosis, leading to subclinical left ventricular systolic and diastolic dysfunction.[28,29] In the geriatric DM cohort of this study, high triglycerides, as a risk factor for GLS < 18%, remained statistically significant in the multivariate logistic regression analysis, which was consistent with previous findings.[5] Triglyceride overload in the myocardium of patients with DM is reversible[30] and can be intervened therapeutically by caloric restriction (CR). A more scientific and detailed incorporation of lifestyle intervention therapies, including diet and

exercise, into the health management of patients with DM at high risk of cardiovascular events may help reduce the risk of CVD in older adults with T2DM.[31]

In this study, eGFR was also found to be an independent risk factor for the development of subclinical left ventricular systolic insufficiency in older adults with T2DM, which was consistent with previous findings.[32] But this result was not statistically significant in the model that included only DKD patients likely due to the limited number of macroalbuminuria samples.

Many studies considered left ventricular diastolic dysfunction to be the earliest dysfunction in the course of DCM.[33] However, with the increasing use of 2D and 3D STE parameters in clinical and research settings, new cardiac ultrasound indicators, represented by GLS, have shown tremendous value in the screening of subclinical myocardial dysfunction. Recent research has included GLS in its analyses, demonstrating that systolic dysfunction, instead of diastolic dysfunction, is the first manifestation of DCM.[7,24] Among the subjects included in this study, when e/e' was considered as a criterion, we found that in different levels of proteinuria grouping, the proportion of patients with subclinical left ventricular systolic dysfunction was much higher than that of patients with diastolic dysfunction, suggesting that, at least in the older population we studied, significant diastolic dysfunction might not be developed in early DM, with subclinical systolic dysfunction being the predominant issue. Meanwhile, in the group with GLS < 18%, the proportion of patients with E/E' > 14 was more limited, suggesting that subclinical systolic insufficiency preceded or coexisted with diastolic insufficiency in a significant proportion of DM patients. The application of abnormal systolic strain as a marker to evaluate myocardial function and screen older adults with T2DM with high cardiovascular risks may yield more sensitive results.

This study focuses on subclinical cardiac dysfunction in older adults (≥60 years old) with type 2 diabetes mellitus (T2DM), a population distinguished by unique pathophysiological characteristics and clinical management challenges. The aging process contributes to the development of cardiovascular complications in these patients through mechanisms such as impaired mitochondrial function in cardiomyocytes. Concurrently, aging introduces confounding factors, including limited physical activity, that can mask the early symptoms of myocardial dysfunction. The cardiac reserve function of older adults is limited, meaning that once they enter the stage of overt heart failure, the prognosis is extremely poor. According to data from the World Health Organization, the global population aged ≥60 years is projected to increase from 12% in 2015 to 22% by 2050. In China, for instance, the prevalence of diabetes among individuals aged 60 and older is 20.2%, approximately twice that of the general adult population. These trends underscore the critical need for a paradigm shift in prevention and control strategies, moving from a "symptom-driven" to a "subclinical damage-driven" approach. Such a shift is essential not only for improving individual patient outcomes but also for mitigating the overall cardiovascular disease burden in an aging society. The pathogenesis of diabetic cardiomyopathy (DCM) is recognized as multifactorial. Consequently, identifying risk factors linking diabetic kidney disease (DKD) to cardiovascular disease (CVD) represents a crucial first step toward developing targeted prevention and treatment. This study, therefore, aimed to analyze the risk factors for subclinical left ventricular systolic insufficiency in older patients with type 2 diabetes mellitus (T2DM). We employed global longitudinal strain (GLS) in lieu of left ventricular ejection fraction (LVEF) to assess ventricular function, seeking to detect subtle, early impairments in systolic function that are not discernible through conventional echocardiography. The study is technically innovative and fills a research gap in an older subgroup. Based on these results, we suggest that the risk factors identified in this experiment—high triglycerides, low eGFR, and insulin resistance—be considered as modifiable factors, providing a critical window of opportunity for early intervention to prevent cardiac function decline in older adults with type 2 diabetes. Besides, we recommend that GLS assessments be incorporated into routine screening protocols for older adults with T2DM who present with these risk factors, even in the absence of heart failure symptoms or a reduction in LVEF. This approach could facilitate the early detection of incipient DCM, enabling earlier clinical intervention and thereby improving patient outcomes and quality of life. However, this study has certain limitations. It is a single-center, cross-sectional study with a relatively small sample size. Moreover, some variables in the logistic regression analysis had wide confidence intervals, indicating a degree of statistical uncertainty. As an exploratory investigation, our findings are preliminary and should be interpreted with caution. Future multicenter studies with larger cohorts and longitudinal designs are warranted to validate and extend our findings. A notable limitation of this study is that coronary artery disease (CAD) was excluded based on medical history,

electrocardiogram, and echocardiogram alone. As coronary angiography—the gold standard for CAD diagnosis—was not routinely performed, the possibility of asymptomatic CAD cannot be entirely ruled out. Furthermore, the selection of confounders for our logistic regression and sequential models was based on prior literature. This underscores the necessity for more comprehensive analyses, incorporating a broader range of potential variables, in future research.

In conclusion, this study demonstrates that proteinuria, reduced eGFR, hypertriglyceridemia, and insulin resistance are independent risk factors for early subclinical left ventricular systolic insufficiency in asymptomatic older patients with type 2 diabetes mellitus (T2DM) and preserved left ventricular ejection fraction (LVEF). Our findings suggest that routine GLS assessment should be considered for patients in this demographic who present with these risk factors, even before the onset of heart failure symptoms or a measurable decline in LVEF.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author (Xiaoli Zhang, xiaolizhang@fudan.edu.cn) on reasonable request.

Ethics Approval and Consent to Participate

The study complies with the Declaration of Helsinki and was approved by the Ethics Review Committee of Huadong Hospital, affiliated with Fudan University (No. 2022K150). All participants have signed a written informed consent form.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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