Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2025.364886.3859 Volume 31, Issue 5, May. 2025
ManuscriptID: ZUMJ-2503-3859
DOI:10.21608/zumj.2025.364886.3859

ORIGINAL ARTICLE

Non-invasive Markers and Left Ventricular Diastolic Dysfunction in Type II Diabetic Patients

Abdelsalam El-sayed Hussin Sherif[1], Mohamed Mostafa Al Daydamony[1], Abdelmoneam Elkilany Abdelmoneam Tantawy[2*], Mohamed Salah Abdelbasit[1]
[1] Department of Cardiology, Faculty of Medicine, Zagazig University, Egypt
[2] Department of Cardiology, Al-ahrar teaching hospital, Egypt

Corresponding author:
Abdelmoneam Elkilany Abdelmoneam Tantawy
E-Mail:
Barcamsn59@gmail.com

Submit Date: 04-03-2025
Accept Date: 24-03-2025

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is strongly associated with subclinical cardiovascular disease (CVD), often progressing undetected until advanced stages. Left ventricular diastolic dysfunction (LVDD) is a common but underrecognized complication, necessitating the identification of reliable, non-invasive predictive markers. This study aimed to evaluate non-invasive biomarkers for the early detection of LVDD in T2DM patients. **Methods:** This case-control study included 60 patients with T2DM, stratified into two groups: Group A (n=30) with LVDD grade >1 and Group B (n=30) with mild or no LVDD. Comprehensive clinical assessments were performed, including vital signs, body mass index (BMI), and cardiovascular symptoms. Electrocardiographic (ECG) parameters, such as rhythm analysis, P-wave dispersion, and QT dispersion, were evaluated. Echocardiographic and tissue-Doppler imaging were conducted to assess diastolic function, alongside laboratory investigations including serum creatinine, serum uric acid, high-sensitivity C reactive protein (Hs-CRP), and neutrophil-lymphocyte ratio (NLR). **Results:** Patients with LVDD (Group A) exhibited significantly elevated levels of serum creatinine, Hs-CRP, serum uric acid, and NLR. Urinary albumin excretion ranged from 45 to 290 mg/day (mean 168.4±7.6mg/day), and the albumin-to-creatinine ratio ranged from 3 to 16mg/mmol (mean 9.1±3.6 mg/mmol). In contrast, Group B demonstrated urinary albumin levels <30 mg/day and an albumin-to-creatinine ratio <1 mg/mmol.

Conclusion: Hs-CRP could be an independent predictor of LVDD emphasizing its potential use as a non-invasive biomarker for early screening and risk stratification in T2DM patients. Implementing Hs-CRP testing in routine clinical practice could facilitate early intervention strategies to prevent the progression of diastolic dysfunction and improve cardiovascular outcomes.**Keywords** Type 2 diabetes mellitus, Left ventricular diastolic dysfunction, Cardiovascular Disease, Echocardiography

INTRODUCTION

A common cardiac ailment known as left ventricular diastolic dysfunction (LVDD) is defined by the left ventricle's incapacity to (LV) to relax and fill adequately during diastole. This impairment compromises the heart's ability to effectively accommodate blood volume, disrupting cardiac output and potentially leading to adverse cardiovascular events [1].

Type 2 diabetes mellitus (T2DM), which is typified by insulin resistance and relative insulin insufficiency, significantly raises the incidence of LVDD. Persistent hyperglycemia in type 2 diabetic patients triggers a number of pathophysiological processes, including endothelial damage, oxidative stress, inflammation, and fibrosis, contributing to myocardial stiffness and impaired diastolic function [2].

Dapagliflozin is an example of an oral hypoglycemic drug (OHA) that inhibits sodium glucose co-transporter 2 (SGLT2), and empagliflozin has cardiovascular advantages beyond glycemic control, such as a lower risk of heart failure [3].

Echocardiography's thorough evaluation of heart function and non-invasive nature make it the gold standard for diagnosing LVDD. By analyzing specific Doppler flow parameters, echocardiography enables accurate classification of LV diastolic function into various grades [4]. Non-invasive indicators, however, include microalbuminuria, the albumin-to-creatinine ratio (ACR), uric acid, NLR, and C-reactive protein (CRP), are becoming useful instruments for LVDD risk assessment and early identification [5-7].

This study aimed to assess non-invasive laboratory markers associated with LVDD in T2DM patients, providing insights into early diagnostic and prognostic strategies.

METHODS

This case-control study was conducted at the Cardiology Department Clinic of Zagazig University Hospital and Alahrar Hospital to evaluate non-invasive markers for predicting LVDD in T2DM patients. A total of 60 patients were enrolled and categorized into two groups: Group A (30 patients with LVDD greater than grade 1) and Group B (30 patients with mild or no LVDD). The grading of LVDD was based on standardized echocardiographic criteria. Ethical approval was obtained from the Institutional Review Board (IRB# 311/23-April-2024) of Zagazig University, and the study adhered to the Declaration of Helsinki guidelines.

Inclusion criteria comprised adult patients diagnosed with T2DM, confirmed by medical records or physician diagnosis. Exclusion criteria included Type I diabetes, significant valvular or congenital heart diseases, recent myocardial infarction (within three months), severe renal impairment, dialysis-dependent end-stage renal disease (eGFR <30 mL/min/1.73 m2), immunological diseases, malignancies, severe hepatic impairment or cirrhosis, and pregnancy or lactation.

Comprehensive clinical evaluations included demographic data gathering and evaluation of risk variables, including smoking, obesity, hypertension, dyslipidemia, stroke history, peripheral arterial disease, and coronary artery disease. A systolic blood pressure of 140 mmHg or above and a diastolic blood pressure of 90 mmHg or higher were considered hypertension, under the 2018 ESH/ESC recommendations [8].

Dyslipidemia was thought to be indicated by either lower levels of high-density lipoprotein cholesterol or elevated levels of total or low-density lipoprotein cholesterol [9]. T2DM diagnosis was based on glycated hemoglobin (A1C) levels, with thresholds of <5.7% for normal, 5.7%-6.4% for prediabetes, and ≥6.5% for diabetes [10].

Among the laboratory tests were complete blood counts (CBC) to calculate the NLR, urinary albumin to evaluate microalbuminuria, ACR, serum uric acid, serum creatinine levels and Hs-CRP. These markers were assessed for their potential to indicate endothelial and diastolic dysfunction.

Electrocardiogram (ECG) assessments were performed using a 12-lead BIOCARE (ECG-300 G) system to evaluate heart rhythm, left and right ventricular hypertrophy, QT dispersion and P wave dispersion (PWD). PWD was computed as the difference

between the highest and lowest P-wave durations using both manual and computerized methods [11,12]. QT dispersion was calculated using the difference between the longest and shortest QT intervals, and it was then modified using Bazett's formula (QTc = QT/√R-R interval) [13].

A 2.5-MHz transducer-equipped Vivid 5 GE medical ultrasound equipment was used for echocardiographic exams. Data were collected and analyzed blindly to ensure objective results. Among the echocardiographic parameters measured were the following: ejection fraction (EF), left atrial diameter (LAD), left atrial volume index (LAVI), early diastolic mitral inflow velocity to early diastolic mitral annular velocity (E/e'), early to late diastolic mitral inflow velocity (E/A), tricuspid regurgitation (TR) velocity ratios, and left ventricular end-diastolic and end-systolic sizes [14,15]. The comprehensive assessment of cardiac anatomy and function provided by these measurements facilitated the identification and classification of LVDD.

RESULTS

Table 1 displays the baseline attributes of the groups under study. Group A patients were considerably older than those in Group B (mean age 58.5 ± 9.9 vs. 51.5 ± 9.4 years, p = 0.01). A significantly higher weight and BMI were noted in Group A (p < 0.001 for both), indicating a link between obesity and LVDD. Cardiovascular risk factors, including a history of coronary artery disease (CAD) and obesity, were more prevalent in Group A (p = 0.039 and p = 0.015, respectively), as shown in Table 1.

Table 1: Baseline Characteristics of the Studied Groups

Characteristic	Group A (n=30)	Group B (n=30)	Statistical Test	P Value
Age (years)	58.5 ± 9.9	51.5 ± 9.4	U = 276	0.01*
Gender (Female)	17 (56.7%)	17 (56.7%)	-	1.000
Weight (kg)	94.1 ± 11.3	85 ± 8.7	t = 3.49	<0.001*
Height (cm)	168.6 ± 9.6	172.6 ± 7.8	U = 556	0.113
BMI (kg/m²)	33.5 ± 5.8	28.4 ± 2.9	U = 196	<0.001*
Hypertension	24 (80%)	20 (66.7%)	$\chi^2 = 1.36$	0.243
Dyslipidemia	22 (73.3%)	21 (70%)	$\chi^2 = 0.08$	0.774
History of Stroke	6 (20%)	4 (13.3%)	$\chi^2 = 0.48$	0.488
Peripheral Artery Disease	4 (13.3%)	5 (16.7%)	$\chi^2 = 0.13$	0.718
Coronary Artery Disease	19 (63.3%)	11 (36.7%)	$\chi^2 = 4.27$	0.039*
Smoking	16 (53.3%)	14 (46.7%)	$\chi^2 = 0.27$	0.606
Obesity	15 (50%)	6 (20%)	$\chi^2 = 5.9$	0.015*

*Significant p-values (<0.05) are indicated by an asterisk.

Significant variations in the groups' heart function were shown by the electrocardiographic and echocardiographic results (Table 2). Higher left atrial volume index and greater P wave and QT dispersion were linked to advanced LVDD (LAVI), and elevated E/e' ratio, underscoring the importance of comprehensive cardiac assessment.

Table 2: Echocardiographic and Electrocardiographic Data of the Studied Groups

Parameter	Group A (n=30)	Group B (n=30)	Statistical Test	P Value
LVH Present (%)	12 (40%)	10 (33.3%)	$\chi^2 = 0.29$	0.592
RVH Present (%)	3 (10%)	0 (0%)	$\chi^2 = 3.16$	0.076
P Wave Dispersion (ms)	56 ± 3.1 (50-60)	33.4 ± 2.9 (29-38)	t = 29.3	<0.001*
QT Dispersion (ms)	54.6 ± 3.7 (50-60)	45.4 ± 2.8 (40-50)	t = 11.05	<0.001*
LVEDD (mm)	52.4 ± 4 (42-57)	49.2 ± 4.9 (38-58)	U = 280	0.011*
LVESD (mm)	34.5 ± 3.6 (28-41)	32 ± 3.6 (26-39)	t = 2.69	0.01*
LAD (mm)	36.7 ± 2.7 (30-41)	34.1 ± 3.1 (28-38)	U = 238	0.002*
LAVI (mL/m²)	47.5 ± 9.6 (35-68)	26.2 ± 1.7 (22-29)	t = 12.03	<0.001*
EF (%)	60.9 ± 4.5 (51-70)	62.1 ± 3.8 (56-68)	U = 512	0.357
E/A Ratio	1.6 ± 0.4 (1.1-2.4)	0.8 ± 0.1 (0.6-1)	t = 10.29	<0.001*
E/e' Ratio	12.7 ± 1.5 (10-16)	8.3 ± 0.7 (7-9)	t = 14.4	<0.001*
Late e' (cm/s)	8.8 ± 0.8 (7-10)	11.6 ± 1 (10-13)	U = 885	<0.001*
Septal e' (cm/s)	6.4 ± 0.6 (5-7)	8.4 ± 0.6 (7-9)	U = 887	<0.001*
TR Velocity (m/s)	3.2 ± 0.2 (2.9-3.6)	2.5 ± 0.2 (2.1-2.7)	t = 12.65	<0.001*

*Significant p-values (<0.05) are indicated by an asterisk.

Laboratory data (Table 3) indicated significantly higher levels of serum creatinine, Hs-CRP, uric acid, and NLR in Group A (all $p < 0.001$). The albumin-to-creatinine ratio (ACR) was also significantly elevated, suggesting that these biomarkers could aid in identifying high-risk patients.

Table 3: Laboratory Data Among the Studied Groups

Parameter	Group A (n=30)	Group B (n=30)	Statistical Test	P Value
Albumin in Urine (mg/d)	168.4 ± 7.6 (45-290)	<30 mg/d	-	-
Albumin/Creatinine Ratio (mg/mmol)	9.1 ± 3.6 (3-16)	<1 mg/mmol	-	-
Serum Creatinine (mg/dL)	1.8 ± 0.27 (1.4-2.4)	0.9 ± 0.19 (0.09-1.1)	t = 14.9	<0.001*
Hs-CRP Positive	24 (80%)	8 (26.7%)	$\chi^2 = 15.1$	<0.001*
Hs-CRP (mg/L)	3.3 ± 1.1 (2-6)	2.03 ± 0.32 (2-3)	t = 3.26	<0.001*
Uric Acid (mg/dL)	9.3 ± 1.2 (8-11)	5.3 ± 1.14 (4-7)	t = 13.3	<0.001*
NLR	2.2 ± 0.2 (1.8-2.4)	1.89 ± 0.24 (1.5-2.4)	U = 162	<0.001*

*Significant p-values (<0.05) are indicated by an asterisk.

Logistic regression analysis (Table 4) identified Hs-CRP as a significant independent predictor of LVDD (OR=17.5, 95% CI: 1.6–184.6, p=0.018). While uric acid and NLR showed strong predictive power in univariate analysis, they did not remain significant in the multivariate model, potentially due to confounding variables or multicollinearity.

Table 4: Univariate and Multivariate Logistic Regression Analysis of Predictors of LVDD

Parameter	Univariate OR (95% CI)	p Value	Multivariate OR (95% CI)	p Value
Hs-CRP	16.5 (1.7–157.5)	0.015*	17.5 (1.6–184.6)	0.018*
Uric Acid	2.59 (1.67–3.99)	<0.001*	-	-
NLR	369 (16.3–8387)	<0.001*	0.04 (0.001–2973)	0.853

*Significant p-values (<0.05) are indicated by an asterisk.

These findings emphasize that non-invasive biomarkers, particularly Hs-CRP, could enhance early diagnosis and management of LVDD in T2DM patients, supporting their inclusion in clinical practice for improved cardiovascular outcomes.

DISCUSSION

T2DM is strongly associated with subclinical CVD, often progressing undetected until advanced stages. LVDD is a common but underrecognized complication, necessitating the identification of reliable, non-invasive predictive markers.

This study identified several key predictors of LVDD in T2DM patients, including advanced age, higher BMI, elevated serum creatinine, uric acid, Hs-CRP, and NLR levels. The study found that Hs-CRP is an independent predictor of LVDD. demonstrating its potential use as an early risk stratification non-invasive biomarker. LAVI and elevated E/E′ ratio are two echocardiographic measures that further support their diagnostic use in evaluating diastolic dysfunction. These findings support the integration of non-invasive biomarkers into routine clinical assessments to facilitate early detection and targeted management of LVDD in diabetic populations.

Consistent with Wazeem et al.'s findings, which showed a favorable relationship between LVDD prevalence and advancing age, the current investigation showed that patients in Group A (with LVDD > grade 1) were substantially older than those in Group B LVDD in T2DM patients in a cross-sectional study in Kerala, India [16]. Similarly, Yadava et al. reported that diastolic dysfunction prevalence increases with age, which may be attributed to age-related myocardial stiffness, reduced compliance, and alterations in extracellular matrix composition [17]. These findings highlight age as a critical risk factor for LVDD.

Weight and BMI were also significantly higher in Group A, in agreement with Russo et al.'s study, which showed that higher BMI independently correlates with increased E/A and E/E′ ratios, indicating elevated LV filling pressures [18]. Di Bello et al. supported this by showing that diastolic dysfunction can manifest even in overweight individuals [19]. Powell et al. also found that obese patients undergoing coronary angiography exhibited higher LV end-diastolic pressures, emphasizing the link between obesity and impaired diastolic function [20].

This study identified significantly higher NLR values in Group A compared to Group

B. Supporting this, Zhang et al. showed that in hyperthyroid patients, higher NLR values were linked to higher risks of LVDD[21]. NLR, as a marker of systemic inflammation, likely contributes to myocardial fibrosis and diastolic dysfunction through the activation of pro-fibrotic pathways and myocardial remodeling, suggesting inflammation's pivotal role in LVDD pathogenesis.

Significantly higher serum creatinine levels in Group A align with Viegas et al., who found that elevated creatinine in CKD patients with diabetes correlated with advanced LVDD and worse myocardial performance indices [22]. These findings underscore the interplay between renal impairment and diastolic dysfunction, potentially mediated by fluid overload, increased myocardial fibrosis, and remodeling.

Higher serum uric acid (SUA) levels in Group A support Yang et al.'s findings, in healthy individuals, SUA was a distinct cardiometabolic risk factor for the development of LVDD [23]. Tu et al. also noted that elevated SUA correlated with LVDD criteria, such as reduced septal e′ velocity in military personnel [24]. SUA's role in promoting oxidative stress, endothelial dysfunction, and myocardial fibrosis may explain its association with LVDD [28]. Notably, clinical trials with xanthine oxidase (XO) inhibitors that reduce SUA levels have demonstrated improvements in LVDD and clinical outcomes [29].

The study also revealed significantly higher Hs-CRP levels in Group A, consistent with Shah et al., who found an association between elevated CRP levels and LV dysfunction parameters, including increased LVEDP [30]. Ghavam et al. further confirmed the strong link between high hs-CRP and diastolic dysfunction in T2DM patients [31]. These results support systemic inflammation, as indicated by hs-CRP, as a key contributor to LVDD pathophysiology.

Our findings also showed elevated albuminuria and albumin/creatinine ratios in Group A, corroborating Shogade et al.'s study, which identified a strong association relationship LVDD and microalbuminuria in individuals with type 2 diabetes [32]. Similarly, T2DM patients with albuminuria were reported to have a considerably greater risk of LVDD by Akiyama et al [34]. Since endothelial dysfunction is indicated by microalbuminuria, this suggests a potential mechanism through which impaired vascular function may contribute to myocardial relaxation abnormalities.

Echocardiographic findings in this study demonstrated higher LVEDD, LVESD, LAD, LAVI, E/A ratio, E/E′ ratio, and TR velocity in Group A. Sušić et al. reported similar results, showing that higher LVDD grades were linked to larger LV dimensions [37]. Tu et al. also linked higher LAVI and Diastolic dysfunction E/e' ratios in coronary heart disease patients[24]. Group A much higher E/E′ ratio, a reliable indicator of LV filling pressure, was consistent with research by Ayman et al., who found a similar pattern in individuals with newly diagnosed type 2 diabetes[38].

The increased E/E′ ratio observed in LVDD can be attributed to insulin resistance and hyperinsulinemia, which promote prohypertrophic myocardial changes and enhance LV stiffness[39]. This is further supported by studies suggesting that cardiomyocyte resting tension is a critical determinant of LVDD progression, particularly in diabetics with an intact left ventricular ejection fraction [40].

Clinical Implications

The identification of Hs-CRP as an independent predictor of LVDD emphasizes its potential use as a non-invasive biomarker for early screening and risk stratification in T2DM patients. Implementing Hs-CRP testing in routine clinical practice could facilitate early therapeutic techniques to enhance cardiovascular outcomes and stop diastolic dysfunction from getting worse.

Study Limitations

The study's single-center methodology and somewhat small sample size of 60 patients are among its shortcomings, which could restrict how broadly the results can be applied. Furthermore, the evaluation of the long-term course and results of LVDD in patients with type 2 diabetes was limited by the little follow-up period. It is advised that bigger, multicenter cohorts and longer follow-up times be used in future studies to confirm these results and investigate the potential clinical use of non-invasive biomarkers in LVDD prediction.

CONCLUSION

Hs-CRP could be an independent predictor of LVDD emphasizing its potential use as a non-invasive biomarker for early screening and risk stratification in T2DM patients. Implementing Hs-CRP testing in routine clinical practice could facilitate early intervention strategies to prevent the progression of diastolic dysfunction and improve cardiovascular outcomes.

REFERENCES

1- **Robinson S, Ring L, Oxborough D, Harkness A, Bennett S, Rana B et al.** The assessment of left ventricular diastolic function: guidance and recommendations from the British Society of Echocardiography. Echo Res & Practice. 2024 Jun 3;11(1):16.

2- **Grigorescu ED, Lacatusu CM, Floria M, Mihai BM, Cretu I, Sorodoc L.** Left ventricular diastolic dysfunction in type 2 diabetes-progress and perspectives. Diagnostics. 2019 Sep 17; 9(3):121.

3- **Verma S, McMurray JJ.** SGLT2 inhibitors and mechanisms of cardiovascular benefit: a state-of-the-art review. Diabetol. 2018 Oct;61:2108-17.

4- **Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T et al.** Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur J Echocardiogr. 2016 Jul 15;17(12):1321-60..

5- **Narkhede M, Pardeshi A, Bhagat R, Dharme G.** Review on Emerging Therapeutic Strategies for Managing Cardiovascular Disease. Curr Cardiol Rev. 2024 Jul 1;20(4):86-100.

6- **Amezcua-Castillo E, González-Pacheco H, Sáenz-San Martín A, Méndez-Ocampo P, Gutierrez-Moctezuma I, Massó F et al.** C-reactive protein: The quintessential marker of systemic inflammation in coronary artery disease—Advancing toward precision medicine. Biomedicines. 2023 Sep 2;11(9):2444.

7- **Wang N, Zhang C.** Recent advances in the management of diabetic kidney disease: Slowing progression. Int J Mol Sci. 2024 Mar 7;25(6): 3086.

8- **Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M et al.** 2018 Practice Guidelines for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. Blood Pressure. 2018 Nov 2; 27(6):314-40.

9- **Nikparvar M, Khaladeh M, Yousefi H, Vahidi Farashah M, Moayedi B, Kheirandish M.** Dyslipidemia and its associated factors in southern Iranian women, Bandare-Kong Cohort study, a cross-sectional survey. Scientific reports. 2021 Apr 28;11(1):9125.

10- **ElSayed NA, Aleppo G, Bannuru RR, Bruemmer D, Collins BS, Ekhlaspour L et al. (2024)** 13. Older Adults: Standards of Care in Diabetes—2024. *Diabetes Care* 47.

11- **Gomaa MM, Elsafty EE, Gomaa HM, Abdulrahim MM, Eladawy AH.** Study of P wave dispersion in patients with paroxysmal atrial fibrillation and its role in prediction of atrial fibrillation recurrence. *Egypt Heart J*. 2024 Jun 27;76(1):80.

12- **Pérez-Riera AR, de Abreu LC, Barbosa-Barros R, Grindler J, Fernandes-Cardoso A, Baranchuk A.** P-wave dispersion: an update. *Indian Pacing Electrophysiol J*. 2016 Jul 1; 16(4):126-33.

13- **Helmy H, Abdel-Galeel A, Taha Kishk Y, Sleem KM**. Correlation of corrected QT

dispersion with the severity of coronary artery disease detected by SYNTAX score in non-diabetic patients with STEMI. *Egypt Heart J*. 2017 Jun 1;69(2):111-7.

14- **Schwarzwald CC, Schober KE, Bonagura JD.** Methods and reliability of tissue Doppler imaging for assessment of left ventricular radial wall motion in horses. J Vet Intern Med. 2009 May;23(3):643-52.

15- **Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al.** Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015 Mar 1;16(3):233-71.

16- **Wazeem CM, Pillai G, Divakar A, Bhaskaran R, CM W**. Left ventricular diastolic dysfunction in type 2 diabetes mellitus: A single-centre observational study from a tertiary care hospital in south India. Cureus. 2023 Feb 6;15(2).

17- **Yadava SK, Dolma N, Lamichhane G, Poudel N, Barakoti M, Karki DB.** Prevalence of diastolic dysfunction in type 2 diabetes mellitus. Kathmandu Univ Med J (KUMJ). 2017 Jul 1; 15(59):212-6.

18- **Russo C, Jin Z, Homma S, Rundek T, Elkind MS, Sacco RL et al.** Effect of obesity and overweight on left ventricular diastolic function: a community-based study in an elderly cohort. J Am Coll Cardiol. 2011 Mar 22;57(12):1368-74.

19- **Di Bello V, Santini F, Di Cori A, Pucci A, Palagi C, Delle Donne MG et al.** Relationship between preclinical abnormalities of global and regional left ventricular function and insulin resistance in severe obesity: a Color Doppler Imaging Study. *Int J Obes (Lond*). 2006 Jun;30(6):948-56.

20- **Powell BD, Redfield MM, Bybee KA, Freeman WK, Rihal CS.** Association of obesity with left ventricular remodeling and diastolic dysfunction in patients without coronary artery disease. *Am J Cardiol*. 2006; 98(1): 116-20.

21- **Zhang H, Zhang J, Li H, Bi Y, Wang L, Li Y.** Neutrophil-to-lymphocyte Ratio is Associated with LV Diastolic Dysfunction in the Overt Hyperthyroid Patients. Front Endocrinol. 2022 Jul 14;13:906947.

22- **Viegas M, Adhyapak S, Varghese K, Patil CB.** Effect of diabetes mellitus on markers of left ventricular dysfunction in chronic kidney disease. *Indian Heart J*. **2021**;73(5): 599-604.

23- **Yang CD, Feng S, Chen JW, Aihemaiti M, Shu XY, Quan JW et al.** Serum uric acid is associated with the progression of left ventricular diastolic dysfunction in apparently healthy subjects. Dis Markers. 2022; 2022(1):9927254.

24- **Tu CM, Tseng GS, Liu CW.** Serum uric acid may be associated with left ventricular diastolic dysfunction in military individuals. *Mil Med*. 2021 Jan 1;186(1-2):e104-11.

24- **Tu Y, Liu X, Li X, Xue N.** Left atrial stiffness index–an early marker of left ventricular diastolic dysfunction in patients with coronary heart disease. BMC Cardiovascular Disorders. 2024 Jul 17;24(1):371.

25- **Cicoira M, Zanolla L, Rossi A, Golia G, Franceschini L, Brighetti G et al.** Elevated serum uric acid levels are associated with diastolic dysfunction in patients with dilated cardiomyopathy. Am Heart J. 2002 Jun 1;143(6):1107-11.

26- **Sung KT, Lo CI, Lai YH, Tsai JP, Yun CH, Hsiao CC et al.** Associations of serum uric acid level and gout with cardiac structure, function and sex differences from large scale asymptomatic Asians. PLoS One. 2020 Jul 20;15(7):e0236173.

27- **Rajesh M, Mukhopadhyay P, Bátkai S, Mukhopadhyay B, Patel V, Haskó G et al.** Xanthine oxidase inhibitor allopurinol attenuates the development of diabetic cardiomyopathy. J Cell Mol Med. 2009 Aug 2;13(8b):2330-41.

28- **Glantzounis GK, Tsimoyiannis EC, Kappas AM, Galaris DA.** Uric acid and oxidative stress. Curr Pharm Des. 2005 Dec 1;11(32):4145-51.

29- **Ogino K, Kato M, Furuse Y, Kinugasa Y, Ishida K, Osaki S et al.** Uric acid-lowering treatment with benzbromarone in patients with heart failure: a double-blind placebo-controlled crossover preliminary study. Circ Heart Fail. 2010 Jan 1;3(1):73-81.

30- **Shah SJ, Marcus GM, Gerber IL, Mckeown BH, Vessey JC, Jordan MV et al.** High-sensitivity C-reactive protein and parameters of left ventricular dysfunction. *J Card Fail*. 2006 Feb 1;12(1):61-5.

31- **Mighavam S, Hafezi Ahmadi MR, Mosavi A, Elhamdoost A, Kazeminezhad B.** The Relationship between High Sensitive C-reaction Protein (hs-CRP) and Diastolic Heart Function in Diabetes Mellitus Type II. *Asian J Pharm Clin Res*. 2016;8(S1):12-6.

32- **Shogade TT, Essien IO, Ekrikpo UE, Umoh IO, Utin CT, Unadike BC et al.** Association of microalbuminuria with left ventricular dysfunction in Nigerian normotensive type 2 diabetes patients. *Cardiovasc J Afr*. 2018 Sep 1;29(5):283-8.

33- **Mehta J, Godbole VY, Mehta KG, Lalithambigai A.** Association of

microalbuminuria with left ventricular dysfunction in type 2 diabetes mellitus. Egypt J Int Med. 2021 Dec; 33:1-6.

34- **Akiyama T, Eto Y, Matsuda H, Kimura Y, Yanagawa T.** Albuminuria and left ventricular mass index are associated with left ventricular diastolic dysfunction in type 2 diabetes mellitus patients. Diabetol int. 2014 Jun;5:129-33.

35- **Alwi I, Harun S, Soehardjono S, Nugroho N, Waspadji S, Rahman AM et al.** Left ventricular diastolic dysfunction in type 2 diabetes mellitus patient without cardiovascular disease: the association with microalbuminuria. Med J Indonesia. 2005 Aug 1;14(3):169-72.

36- **Yildirimtürk O, Kiliçgedik M, Tuğcu A, Aytekin V, Aytekin S.** The relationship of microalbuminuria with left ventricular functions and silent myocardial ischemia in asymptomatic patients with type 2 diabetes. Turk Kardiyoloji Dernegi Arsivi: *Turk Kardiyol Dern Ars*. 2009 Mar 1;37(2):91-7.

37- **Sušić L, Maričić L, Šahinović I, Kralik K, Klobučar L, Ćosić M et al.** The relationship of left ventricular diastolic dysfunction and asymmetrical dimethylarginine as a biomarker of endothelial dysfunction with cardiovascular risk assessed by systematic coronary risk Evaluation2 Algorithm and Heart Failure—A cross-sectional study. *Int J Environ Res Public Health*. 2023 Mar 1;20(5):4433.

38- **Hassan Ayman KM, Abdallah Mahmoud A, Abdel-Mageed Eman A, Marwa S, Soliman Mona M, Kishk Yehia T.** Correlation between left ventricular diastolic dysfunction and dyslipidaemia in asymptomatic patients with new-onset type 2 diabetes mellitus. Egypt J Int Med.. 2021 Dec;33:1-1.

39- **Van Heerebeek L, Hamdani N, Handoko ML, Falcao-Pires I, Musters RJ, Kupreishvili K et al.** Diastolic stiffness of the failing diabetic heart: importance of fibrosis, advanced glycation end products, and myocyte resting tension. Circulation. 2008 Jan 1;117(1):43-51.

40-**Agrawal V, Agrawal A, Dwivedi AN, Tripathi K.** Correlation between 2D echocardiography and multidetector row CT for early detection of diastolic dysfunction in normotensive diabetic patients. J Clin Diagnostic Res: JCDR. 2016 Aug 1;10(8):OC27.

Citation

Hussin Sherif, A., Al-Daydammony, M., Abdelmoneam Tantawy, A., Abdelbasit, M. Non-invasive Markers and Left Ventricular Diastolic Dysfunction in Type II Diabetic Patients. *Zagazig University Medical Journal*, 2025; (1986-1994): -. doi: 10.21608/zumj.2025.364886.3859