

Echocardiographic detection of subclinical Left Ventricular Dysfunction in Asymptomatic Type Two Diabetes Mellitus

Abstract

Background: Before systolic dysfunction and symptomatic heart, diabetic cardiomyopathy begins with left ventricular diastolic dysfunction (LVDD). Echocardiographic modalities were used to detect subclinical LV impairment in asymptomatic type 2 diabetics. This study aimed to identify subclinical left ventricular impairment in asymptomatic patients with type two diabetes using several echocardiographic techniques.

Methods: In the present prospective cohort study, 30 adults over 18 having type II diabetes mellitus (DM) (Group I) and 20 normal controls (Group II) were studied. Transthoracic echocardiography and 12-lead ECG were performed on all individuals.

Results: Pulsed wave Doppler techniques revealed significant variation in transmitral flow velocities between groups, including septal e' , lateral mitral annulus early velocity (e'), septal early diastolic peak flow velocity (E/e'), Lateral E/e' , and average E/e' . EF was significantly decreased in group I ($P < 0.001$). With a p-value of 0.001, LVESD was significantly higher in group I. The septal, lateral, and average systolic mitral annulus (S') motions in group II were significantly larger than those in group I. When comparing groups, I and II, the first showed much longer myocardial performance index (MPI) and isovolumetric contraction time (IVCT). The ET for Group I was significantly lower than that of Group II. The study group exhibited significantly greater levels of fasting blood sugar, post-prandial blood sugar, and haemoglobin A1C (HBA1C) compared to the control group ($P < 0.001$).

Conclusions: Patients having diabetes mellitus exhibited considerably greater levels of DM history fasting glucose levels, postprandial glucose levels, haemoglobin A1C (HBA1C), E/e' ratio, LVESD, IVCT, and MPI, while having significantly lower EF and ET relative to the healthy group.

Keywords: Left Ventricular Dysfunction, Asymptomatic, Diabetes Mellitus,
Echocardiography

Introduction:

Early prediction of cardiac complications among those suffering from insulin independent diabetes mellitus (DM) by using various modalities of echocardiography are of great importance to enhance the outcome of heart failure. Cardiac problems are a significant factor in the morbidity and death of diabetic individuals ^[1].

Diabetes is a risk factor in 10-30% of people who develop heart failure ^[2]. Isolated anomalies of diastolic relaxation in type two diabetes without symptoms or indicators of heart disease may indicate a diagnosis of diabetic cardiomyopathy (DCM). This is believed to be caused by microangiopathy, collagen deposition, reduced expression/activation of potassium channels and sodium pumps, and decreased sensitivity of myofilament calcium ^[3, 4].

LV diastolic dysfunction is the initial pre-clinical stage of DCM, occurring before systolic failure and progressing to symptomatic heart disease ^[5]. Diastolic dysfunction becomes more common as diabetes persists for a longer period. Diastolic dysfunction increased linearly with age ^[6]. LV diastolic dysfunction could be the initial phase of DCM, and early detection is crucial for patient care. This study aimed to identify subclinical left ventricular impairment in asymptomatic patients with type two diabetes using several echocardiographic techniques.

Patients and Methods:

A prospective cohort study was done on a sample of 30 adult patients of both genders. diagnosed with type II diabetes mellitus, along with 20 healthy adults served as the control group. This study was carried out from March 2022 to March 2023 in Tanta, Egypt, with the permission of the Ethical Committee of Tanta University Hospitals.

Included in the group of patients who did not qualify were those who had CAD, or coronary artery disease, is an inflammatory form of atherosclerosis. (Ross, 1999), Presented as Ischemic heart disease, myocardial infarction (MI), and stable angina ^[7], patients with valvular disease (congenital or rheumatic) ^[8], hypertensive patients, systemic hypertension. This condition can

occur with or without medication, and it can also affect patients with hypothyroidism, restrictive cardiomyopathy, constrictive pericarditis, or other known causes of diastolic dysfunction.

Two groups of participants were formed: **Group (I) (n=30)** Individuals with a confirmed diagnosis of type 2 diabetes mellitus according to the American Diabetes Association (ADA) [9]. Patients are considered to have diabetes if they have a history or current diagnosis of DM. According to the ADA, a patient is classified as diabetic if their haemoglobin A1C (HBA1C) is 6.5 percent or more, their fasting blood sugar is More than 126 mg/dl, and postprandial blood glucose is 200 mg/dl or more, and **Group (II) (n=20)**: normal individuals.

A clinical examination, registration of medical history, and standard laboratory testing were done to every patient. These investigations included a complete blood count (CBC), random blood sugar, fasting and postprandial blood sugar levels, haemoglobin A1C (HBA1C), liver and renal function tests, a 12-lead electrocardiogram (ECG), and transthoracic echocardiography.

12 lead Electrocardiogram:

Everyone in the study, including the control group, had a 12-lead electrocardiogram (ECG) that contained the following leads: I, II, and III for the legs; aVR, aVL, and aVF; and V1–V6 for the chest.

Transthoracic echocardiography:

Echocardiogram According to the guidelines set by the American Society of Echocardiography, parasternal long axis, short axis, and apical four-chamber imagery were analyzed quantitatively and in two dimensions using M-mode and TDE [1]. Various echocardiographic methods were used to examine the diastolic and systolic functions of the LV. Several methods were used, including transesophageal echocardiography (TDE), pulse wave (PW) echocardiography, two-dimensional (2D) echocardiography, and multi-mode

echocardiography. An M-mode echocardiogram trace in two dimensions (2D) was used to quantify the left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD). The LV ejection % was calculated using a modified version of Simpson's method. It was determined that the mitral leaflet tips were the optimal location for the pulsed Doppler sample volume. All of the following were determined: the E-wave deceleration time (DT), the early diastolic peak flow velocity (E), the late diastolic peak flow velocity (A), and the E/A ratio.

Atrial peak velocity (Am), myocardial systolic (S m) wave, myocardial early diastolic (Em) wave, myocardial ejection time (ETm), myocardial isovolumetric relaxation time (IVRTm), and myocardial isovolumetric contraction time (IVCTm) are all measurements that are collected in each area. After adding IVCTm and IVRTm, Calculating the MPI involved dividing the result by the ETm value. Additionally, the E/Em ratio was monitored as well, which is an accurate indicator of the LV filling pressures. We averaged diastolic values during three separate cardiac cycles. For data collection, three complete cardiac cycles were recorded in a cine-loop mode. The subjects were asked to lie on their left sides while they were at rest in order to gather data.

Two-dimensional (2D) echocardiography:

This two-seater This study used Simpson's method to calculate the left ventricle's ejection fraction, end-diastolic volume, and end-systolic volume. ^[10].

Assessment of diastolic function:

The implementation of pulsed-wave Doppler imaging for the assessment of mitral valve inflow was facilitated by strategically placing the Doppler sample volume inside the interstitial region between the mitral leaflets. The present research additionally examined the diastolic velocities at the early (E) and late (A) peaks, together with the E-wave deceleration time (DT) and the isovolemic relaxation time (IVRT).

The color TDI was used to evaluate the E/septal and E/lateral values of the mitral annulus in the apical 4-chamber view. The examination of these values was conducted on both the septal and lateral aspects of the annulus. The meaning of these values was then used to calculate the average ratio of E to e'. [11, 12]. **Figure 1**

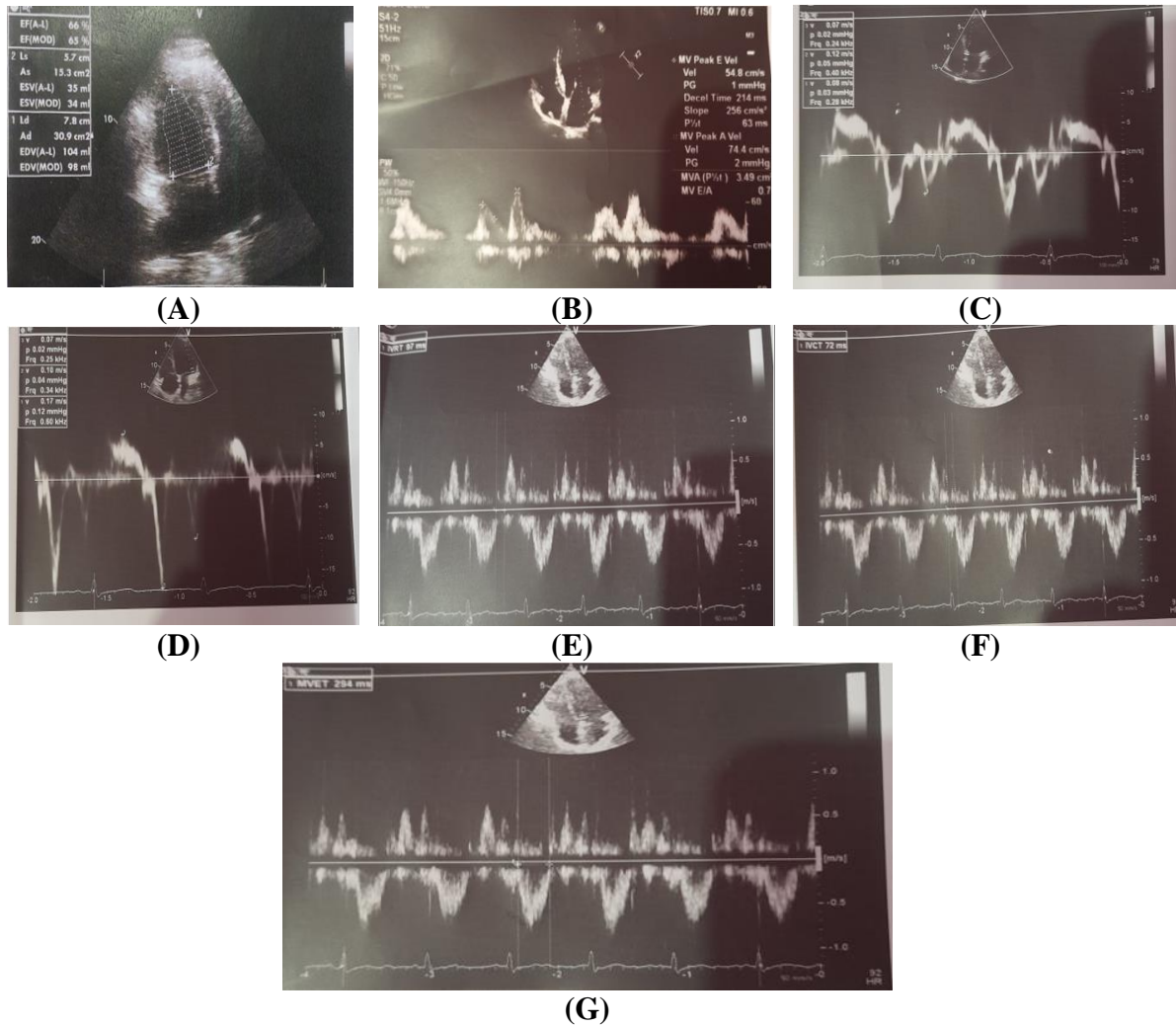


Figure 1: (A) Measurement of LVEDV, LVEDV and EF by Simpson method, (B) E/A ratio and DT, (C) S' septal and e' septal, (D) S' lateral and e' lateral, (E) IVRT, (F) IVCT, (G) ET in a case study

Statistical analysis

The statistical analysis in this study was conducted with SPSS version 26, which is developed and maintained by IBM Inc. of Chicago, Illinois, USA. Comparing the two groups regarding quantitative factors was accomplished through the utilization of an unpaired Student's t-test. To quantify the variables, we calculated their means and standard deviations (SD). We utilized

Fisher's exact test or the Chi-square test to analyze qualitative variables. The variables were presented with frequency and percentage notation. Assuming a two-tailed P value below 0.05, the statistical significance was considered acceptable.

Results:

In terms of significance, Age gaps did not exist., BMI, sex, and clinical examination within the two groups. Family history of DM was substantially greater in study group (P <0.001). The mean duration of DM was 6.47 ± 2.46 years. **Table 1**

Table 1: Demographic data and clinical examination of the studied groups

		Group I (n=30)	Group II (n=20)	P
Age (years)		48.73 \pm 12.21	51.3 \pm 8.37	0.417
BMI (kg/m²)		25.52 \pm 3.9	24.81 \pm 3.31	0.507
Sex	Male	7 (23.3%)	6 (30%)	0.844
	Female	23 (76.7%)	14 (70%)	
Family history of DM		19 (63.33%)	2 (10.0%)	<0.001*
Duration of DM (years)		6.47 \pm 2.46	---	---
Clinical examination				
Systolic blood pressure (mmHg)		127.83 \pm 5.09	126.5 \pm 3.8	0.323
Diastolic blood pressure (mmHg)		86.47 \pm 4.73	85.2 \pm 2.88	0.290
MAP (mmHg)		100.23 \pm 4.32	98.28 \pm 5.85	0.181

Data are presented as mean \pm SD or frequency (%). *Significant p value <0.05. DM: diabetes mellitus, BMI: Body mass index, MAP: mean arterial pressure.

Both groups exhibited no statistically significant variations in the levels of Hb, HCT, PLT, WBCs, AST, ALT, serum creatinine, and urea. In comparison to the control group, The study group showed significantly elevated levels of fasting blood sugar, postprandial blood sugar, and HbA1C (P <0.001). **Table 2**

Table 2: Laboratory investigations of the studied groups

	Group I (n=30)	Group II (n=20)	P
Hb (g/dL)	15.43 \pm 1.78	15.27 \pm 1.55	0.732
HCT (%)	47.12 \pm 5.54	47.07 \pm 6.24	0.976
PLT (*10³cells/μL)	258.22 \pm 82.54	244.88 \pm 65.18	0.547
WBCs (*10³cells/μL)	6.15 \pm 1.72	5.74 \pm 1.68	0.405
Fasting blood sugar (mg/dL)	173.64 \pm 23.54	87.19 \pm 5.44	<0.001*
Post-prandial blood sugar (mg/dL)	258.74 \pm 63.42	119.7 \pm 13.5	<0.001*
HbA1c (%)	7.34 \pm 0.85	4.95 \pm 0.21	<0.001*
ALT (U/L)	33.37 \pm 7.21	29.8 \pm 4.85	0.073
AST (U/L)	27.86 \pm 12.02	25.23 \pm 12.8	0.464

Serum creatinine (mg/dL)	1.04 ± 0.27	0.89 ± 0.26	0.058
Urea (mg/dL)	29.37 ± 11.89	26.79 ± 9.52	0.421

Data are presented as mean ± SD. *Significant p value <0.05. Hb: hemoglobin, HCT: hematocrit, PLT: platelet count, WBCs: white blood cells, ALT: alanine aminotransferase, AST: Aspartate aminotransferase.

There was a notable difference observed in the transmitral flow velocities between the two groups as measured by pulsed wave Doppler methods. These techniques included the following: septal e', lateral e', septal E^e', lateral E^e', and standard Ee'. The results indicated that group I had a statistically significant reduction in EF (P < 0.001). The LVESD in group I exhibited a statistically significant increase (P = 0.001). There was no notable disparity in LVEDD between both groups. **Table 3**

Table 3: The study groups' transmitral flow velocities were determined using pulsed wave doppler methods, tissue Doppler-derived E/e' ratio, EF, LVESD, and LVEDD.

	Group I (n=30)	Group II (n=20)	P
E (cm/s)	68.38 ± 20.77	58.75 ± 4.98	0.048*
E/A ratio	1.32 ± 0.38	0.86 ± 0.17	0.002*
DT (ms)	218.9 ± 39.21	189.5 ± 30.3	0.011*
IVRT (ms)	88.7 ± 17.21	185.5 ± 17.8	<0.001*
Tissue Doppler-derived E/e' ratio			
e' septal	10.04±3.69	7.56±1.49	0.008*
e' lateral	8.25±2.58	10.12±0.62	0.003*
E\ e' septal	10.31 ± 4.61	7.66 ± 1.22	0.016*
E\ e' Lateral	9.06±3.68	5.81±0.49	<0.001*
E\ e' average	9.67±3.79	7.03±0.61	0.003*
EF (%)	57.83 ± 4.23	65.15 ± 4.34	<0.001*
LVESD (cm)	3.50 ± 0.45	2.65 ± 0.46	0.001*
LVEDD (cm)	4.56 ± 0.72	4.43 ± 0.66	0.524

Data are presented as mean ± SD. *Significant p value <0.05. E/A: early and late ventricular filling velocity, DT: deceleration time, IVRT: isovolumic relaxation time, EF: Ejection fraction, LVESD: left ventricular end systolic diameter, LVEDD: left ventricular end diastolic diameter.

Group II had significantly elevated S' septal, S' lateral, and S' average. The IVCT and MPI rates in group I had much higher readings than group II did. Group I had a significantly smaller ET than group II. **Table 4**

Table 4: Pulsed wave tissue doppler of mitral annulus of the studied groups

	Group I (n=30)	Group II (n=20)	P
s` septal	7.32±1.57	8.67±1.54	0.005*
S` lateral	8.71±2.23	10.39±1.81	0.007*
S` average	8.03±1.31	9.54±0.99	<0.001*
IVCT	71.33±16.84	65.22±6.71	0.003*
ET	290.83±15.38	304.90±6.24	0.016*

MPI	0.541±0.03	0.509±0.02	<0.001*
------------	------------	------------	-------------------

Data are presented as mean ± SD. *Significant p value <0.05. IVCT: Isovolemic contraction time, ET: Ejection time, MPI: Myocardial performance index.

Discussion

Cardiovascular problems in type 2 DM patients lead to over 70% of the mortality. DM is a very prevalent form of ischemic cardiomyopathy, therefore LV dysfunction. Diabetic individuals experience cardiac damage due to macro and microvascular coronary disease, DCM, and autonomic dysfunction ^[13].

The two groups exhibited significant differences in measurements such as E (cm/s), E/A ratio, IVRT, and DT (ms). The two groups showed significant differences in septal e', lateral e', septal E\`e', lateral E\`e', and average E\`e'. If we compare Group I to group II, we find that Group I had a substantially lower EF. In group I, LVESD was considerably greater. When comparing the two groups, the LVEDD did not reveal any significant differences. S` septal, S` lateral, and S` average in group I participants had considerably lower values. In group I, the IVCT reading was significantly higher, but the ET reading was significantly lower. Additionally, It was found that group I had a significantly higher MPI.

The study did not find any statistically significant variations in MAP, systolic blood pressure, or diastolic blood pressure between the two groups. Agreeing with our findings, Magdy et al. ^[14] Groups I and II were not significantly different in terms of diastolic or systolic blood pressure. Along with our findings, Kawata et al. ^[15] demonstrated that there was no statistically significant difference in the systolic and diastolic blood pressure levels between group I and II. (p = 0.13, p = 0.075, respectively).

In the present study, it was discovered that there was no significant difference in the levels of Hb, HCT, PLT, WBCs, AST, ALT, serum creatinine, and urea between the two groups. Consistent with what we found, Ayman et al. ^[14] found that Serum creatinine and urea levels were not significantly different between the two groups. Consistent with what we found,

Mahmoud et al. ^[16] revealed that Statistical analysis did not reveal any significant difference in serum creatinine, AST, or ALT levels. among the two groups. No difference was found to be statistically significant in the levels of AST, ALT, and serum creatinine between the two groups. The present investigation discovered that the two groups had significantly different transmitral flow velocities as established using pulsed-wave Doppler techniques (E/A ratio, DT and IVRT). Consistent with what we found, Raafat et al. ^[14] highlighted that A statistically significant difference was seen between the groups that were evaluated with regard to the E/A ratio. Differing from our findings, Ayman et al. ^[14] highlighted that concerning the E/A ratio, IVRT, and DT, There was not a difference that could be considered statistically significant between the two groups.

This study found that Group (I) had a much lower EF. Consistent with what we found, Diamant et al. ^[17] conducted a prospective study that employ MR imaging techniques to evaluate the correlation between cardiac function and HEP metabolism in asymptomatic people with uncomplicated type 2 diabetes mellitus (T2DM). The study included twelve male patients with T2DM and twelve healthy controls who had their genders and ages matched. The results showed that the study group had a significantly lower EF than the control group.

Different from our findings, Ayman et al. ^[14] highlighted found the Ef values of the two groups were not significantly different ($p = 0.4$).

According to the results of this study, the E/e' ratio was much larger in group I compared to group II. Consistent with what we found, Steele et al. ^[18] showed that The research group's E/e' ratio was significantly greater than the control group's E/e' ratio. Similarly to what we found, Magdy et al. ^[14] highlighted that E/e' ratio was substantially greater in patients than in control group.

The study found that groups I and II differed significantly with respect to LVESD., with no difference in LVEDD. Consistent with what we found, Enomoto et al. ^[19] highlighted that

there was a significant difference in LVESD between the research group and the control group. Both groups showed no significant difference in LVEDD. In fact,, Saglam et al. ^[14] highlighted that When comparing the patient group to the control group, LVEDD and LVESD did not differ significantly. Their study's bigger sample size may explain why the results are contradictory with the other study.

In the present study S`medial, S` lateral and S` average was significantly lower in group I.

Consistent with what we found, Raafat et al. ^[14] highlighted S`medial and S` lateral were significantly lower in diabetic groups than control groups. Supporting our results, Zakria et al. ^[14] found that Diabetic individuals whose disease duration is more than 10 years are more likely to experience systolic dysfunction, as indicated by the statistically significant differences in the mean value of S. Similarly, Magdy et al. ^[14] demonstrated that Diabetic individuals had significantly lower values for the'septal, S' lateral, and S' average compared to the control group.

In the present study, Group I had a significantly larger IVCT, in contrast to group I, whose ET was significantly lower. In disagreement with our results, Mahmoud et al. ^[16] revealed that Neither the prediabetic nor the control group differed in terms of IVCT. This difference may be because of different sample sizes. Consistent with what we found, Mahmoud et al. ^[16] discovered that Those at risk of prediabetes had far higher MPI levels than those in the healthy control group.

The study's sample size was small, which is one of its limitations. The research was place in just one location. Exclusion of patients with cardiovascular disease, and negative exercise stress test may affect generalization of the results. Stress myocardial perfusion scintigraphy, CT angiography, and traditional coronary angiography were omitted from the imaging protocol.

Conclusions:

Patients having diabetes mellitus exhibited considerably greater levels of DM history fasting glucose levels, postprandial glucose levels, haemoglobin A1C (HBA1C), E/e' ratio, LVESD, IVCT, and MPI, while having significantly lower EF and ET relative to the healthy group.

Ethical Approval and Consent

Ethical Approval was taken from the Ethical Committee of Tanta University Hospitals. Written informed consent was obtained from the patients.

Financial support and sponsorship: Nil

Conflict of Interest: Nil

References:

1. Kazik A, Wilczek K, Poloński L. Management of diastolic heart failure. *Cardiol J*. 2010;17:558-65.
2. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertension, and cardiovascular disease: an update. *Hypertension*. 2001;37:1053-9.
3. Liu JE, Palmieri V, Roman MJ, Bella JN, Fabsitz R, Howard BV, et al. The impact of diabetes on left ventricular filling pattern in normotensive and hypertensive adults: the strong heart study. *J Am Coll Cardiol J AM* 2001;37:1943-9.
4. Poirier P, Bogaty P, Garneau C, Marois L, Dumesnil JG. Diastolic dysfunction in normotensive men with well-controlled type 2 diabetes: importance of maneuvers in echocardiographic screening for preclinical diabetic cardiomyopathy. *Diabetes Care*. 2001;24:5-10.
5. Poulsen MK, Henriksen JE, Dahl J, Johansen A, Gerke O, Vach W, et al. Left ventricular diastolic function in type 2 diabetes mellitus: prevalence and association with myocardial and vascular disease. *Circ Cardiovasc Imaging*. 2010;3:24-31.
6. Patil MB, Burji NP. Echocardiographic evaluation of diastolic dysfunction in asymptomatic type 2 diabetes mellitus. *J Assoc Physicians India*. 2012;60:23-6.

7. Álvarez-Álvarez MM, Zanetti D, Carreras-Torres R, Moral P, Athanasiadis G. A survey of sub-Saharan gene flow into the Mediterranean at risk loci for coronary artery disease. *Eur J Hum Genet.* 2017;25:472-6.
8. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens.* 2013;31:1281-357.
9. de Boer IH, Bangalore S, Benetos A, Davis AM, Michos ED, Muntner P, et al. diabetes and hypertension: a position statement by the american diabetes association. *Diabetes Care.* 2017;40:1273-84.
10. Hillis GS, Møller JE, Pellikka PA, Gersh BJ, Wright RS, Ommen SR, et al. Noninvasive estimation of left ventricular filling pressure by E/e' is a powerful predictor of survival after acute myocardial infarction. *J Am Coll Cardiol.* 2004;43:360-7.
11. Aneja A, Tang WH, Bansilal S, Garcia MJ, Farkouh ME. Diabetic cardiomyopathy: insights into pathogenesis, diagnostic challenges, and therapeutic options. *Am J Med.* 2008;121:748-57.
12. von Bibra H, St John Sutton M. Diastolic dysfunction in diabetes and the metabolic syndrome: promising potential for diagnosis and prognosis. *Diabetologia.* 2010;53:1033-45.
13. Pagano E, Konings SR, Di Cuonzo D, Rosato R, Bruno G, van Der Heijden AA, et al. Prediction of mortality and major cardiovascular complications in type 2 diabetes: External validation of UK Prospective Diabetes Study outcomes model version 2 in two European observational cohorts. *Diabetes, Obesity and Metabolism.* 2021;23:1084-91.
14. 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 Intern Med.* 2021;33:1-11.

15. Kawata T, Daimon M, Miyazaki S, Ichikawa R, Maruyama M, Chiang S-J, et al. Coronary microvascular function is independently associated with left ventricular filling pressure in patients with type 2 diabetes mellitus. *Cardiovasc Diabetol.* 2015;14:1-8.

16. Mahmoud HEM, Alsenbesy M, Sayed GOF, Ali AEM, Sabra AM. Left ventricular myocardial performance index in prediabetic patients without coronary artery disease. *Egypt J Intern Med.* 2021;33:28-33.

17. Diamant M, Lamb HJ, Groeneveld Y, Endert EL, Smit JW, Bax JJ, et al. Diastolic dysfunction is associated with altered myocardial metabolism in asymptomatic normotensive patients with well-controlled type 2 diabetes mellitus. *J Am Coll Cardiol.* 2003;42:328-35.

18. Steele JM, Urbina EM, Mazur WM, Khoury PR, Nagueh SF, Tretter JT, et al. Left atrial strain and diastolic function abnormalities in obese and type 2 diabetic adolescents and young adults. *Cardiovasc Diabetol.* 2020;19:1-9.

19. Enomoto M, Ishizu T, Seo Y, Kameda Y, Suzuki H, Shimano H, et al. Myocardial dysfunction identified by three-dimensional speckle tracking echocardiography in type 2 diabetes patients relates to complications of microangiopathy. *J Cardiol.* 2016;68:282-7.