Journal of Positive School Psychology
2022, Vol. 6, No. 4, 10500-10513

http://journalppw.com

Detection of subtle ventricular systolic dysfunction in Egyptian patients with type 2DM and Acanthosis nigricans using 2-D speckle tracking echocardiography

Eman Rashed Zaki [1], Nadia Ahmed Agiba[1], Mostafa Ismael saleh[2], Mahmoud Saeed Mahmoud[3], Marwa Said[4]

[1] Cardiology Department Faculty of Medicine for Girls Al-Azhar University, Egypt, [2] Cardiology Department Faculty of Medicine Al-Azhar University, Egypt. [3] Internal Medicine Department , Faculty of Medicine Al-Azhar University, Damietta, [4] Drmatology Department, Faculty of Medicine for Girls Al-Azhar University, Egypt.

Corresponding author: Eman Rashed

E-Mail: emanrashed791@yahoo.com

Abstract:

Background: Egyptian patients (pts) have a high prevalence of Type 2 Diabetes Mellitus (DM). A skin condition characterized by a velvety papillomatous overgrowth of the epidermis. Darkening and thickening (hyperkeratosis) of the skin occurs mainly in the flexural areas, particularly the axillae, groins, inframammary regions, and the neck. Called Acanthosis nigricans which is usually a sign of underlying diabetes. Type 2DM often presents with comorbidities & develops heart failure (HF) more frequently. Two-Dimensional Speckle Tracking Echocardiography (2D-STE) allows a precise evaluation of myocardial function. ***Aim of work***: Detection of subtle ventricular systolic dysfunction in Egyptian patients with type 2DM and Acanthosis nigricans using 2-D STE. ***Patients & methods***: The study included 80 Egyptian pts with Acanthosis nigricans and type 2 DM in addition to 40 Egyptian healthy subjects as a control group (GII) using conventional 2-D Echo-Doppler, Tissue Doppler Imaging (TDI), and 2D-STE. LV dimensions, volume, ejection fraction (EF), RV FAC, TAPSE, MV &TV velocities, were measured.***Results:*** Despite both groups showing no statistically significant differences regarding LV & RV systolic function by conventional echo (LV EF, RV FAC, and TAPSE), GI had significantly lower LV & RV GLPS compared to GII (16.73±3.4 Vs 18.5±1.1 with *P* =0.022 &-19.19 ±3.8 Vs 23±2.3 with *P* ≤0.001 respectively). LV& RV GLPS showed significant negative correlations with HbA1C, while LV GLPS showed a positive correlation with RV GLPS. ***Conclusion*** left & right ventricular systolic function were sub-clinically affected in Egyptians Type 2 diabetic patients with Acanthosis nigricans using 2D-STE

Keywords: Acanthosis nigricans, DM, NAFLD, Left ventricular function, Right ventricular function, Speckle tracking echocardiography.

Introduction:

Diabetes is a major public health problem that rapidly growing in Egypt with a large effect on morbidity and mortality. DM is around 15.6% of all adults aged 20 to 79[1] The International Diabetes Federation (IDF) registered Egypt among the world's top 10 countries in the number of patients with diabetes and this increase may be related to Obesity and Physical Inactivity which considered as major risk factors for diabetes in Egypt [1]. **Acanthosis nigricans** is a hyperpigmented, poorly defined, velvety appearance of the skin. It is usually found in flexures, such as the neck, the axilla, and the groin. Due to metabolic disorder and diabetic microangiopathy diabetics are at a higher risk of early mortality secondary to evolving macro-vascular and microvascular complications [1] diabetic cardiomyopathy may also develop and progress into congestive heart failure (HF) [8]

As no symptoms and signs appeared in the early stages of DM, it is difficult to identify the early impairment of myocardial systolic dysfunction. [9] Scientists consider having T2D may be a hazard proportionate to having a previous heart attack [1]

Right ventricular (RV) involvement in diabetic cardiomyopathy might be of importance because the right ventricle has a significant influence on overall myocardial contractility. **[10]**

Two-dimensional speckle tracking echocardiography (2D-STE) is a novel technique enabling a more reliable and comprehensive assessment of myocardial function by obtaining the myocardial strain and strain rate in longitudinal, radial, and circumferential directions based on the tracking of speckles in grayscale 2D echocardiographic images **[12],[13]**. It has been reported that speckle tracking is more sensitive than LVEF in the detection of subclinical LV systolic dysfunction. **[14]**

Aim of work:

Detection of subtle ventricular systolic dysfunction in Egyptian patients with type 2DM and Acanthosis nigricans using 2-D STE.

Patients and methods:

This study comprises 80 patients ages ranging between 35-60 years as a group I (GI) with type 2 DM in addition to sex & age-matched 40 healthy subjects as a control group as group II (GII). Patients were selected from those attending the cardiology Outpatient Clinic at Al-zharaa University Hospital during the period between August 2020 to April 2021.

Written informed consent was taken from all participants before enrollment into the study and the study was approved by the ethical committee.

Exclusion criteria:

1- Patients with LV ejection fraction (LVEF) < 50 % by conventional echocardiography.
2- Patients with significant valvular heart disease
3- Patients with ischemic heart disease.
4- Patients with serious arrhythmias.
5- Patients with congenital heart disease.
6- Patients with systemic hypertension.

All diabetic patients with a history of other major organ affection were excluded from the study. All participant was subjected to the following:

1. **Full history and clinical examination**.
2. **Twelve lead surface Electrocardiogram (ECG).**
3. **Laboratory investigations included** HbA1C, fasting and 2 hours postprandial blood glucose, Lipid profile, Hb%, and serum creatinine.
4. **Dermatology examination** both by clinical (Table-3) and dermoscopy for detection of associated Acanthosis nigricans (Table-4).
5. **Transthoracic echocardiography** was performed using Vivid-E9 GE (Vivid E9 GE, ultrasound system, Horton Norway) with tissue Doppler (TDI) & speckle tracking imaging capabilities. Standard views were obtained from all available windows using multi-frequency (1.2-3.6 MHz) matrix probeM5S.
   The examination was done while the patient was in the left lateral position, and the images and cine-loops were ECG gated. Echocardiographic measures included:

a. LV conventional measures: LV end-systolic – end-diastolic diameters (LVEDd, LVESd), posterior and septal wall thickness, ejection fraction (EF), left atrial and aortic root diameters (LA/AO). Mitral valve flow with conventional Doppler to assess the LV diastolic function (early and late diastolic velocities (MV E, MV A respectively)
b. TDI of the septal, lateral, anterior, and inferior mitral annulus was obtained from the apical 4 & 2 chamber views. Average of all early and late diastolic annular peak velocities (average e' & a'), the ratio of early diastolic mitral flow peak velocity to early diastolic annular peak velocity was measured (E/e') and average systolic S` wave peak velocity was taken.
c. RV measures include RV (basal, mid–cavitary, longitudinal, proximal RVOT, and distal RVOT diameters).
d. RV systolic function was assessed using fractional area changes (FAC) by 2D-ECHO and Tricuspid Annular Post-Systolic Excursion (TAPSE) by M-Mode on the lateral tricuspid annulus. Color-Flow Pulsed and continuous-wave Doppler were used for the assessment of TV flow (early and late TV diastolic velocities (TV E, TV A respectively). Also, Lateral tricuspid annulus systolic, early and late diastolic velocities were taken.

6. **Speckle Tracking Echocardiography:**

STE was used to measure LV longitudinal strain from apical 2, 3, and 4 chamber views using three consecutive cardiac cycles with a frame rate between 40 - 90 frames/s. (fig 1&2).

RV global longitudinal strain was measured by manual tracing of the RV wall in RV-focused apical 4-chamber view, using the same 2D-STE software applied for the LV 2D strain assessment. (fig 3).

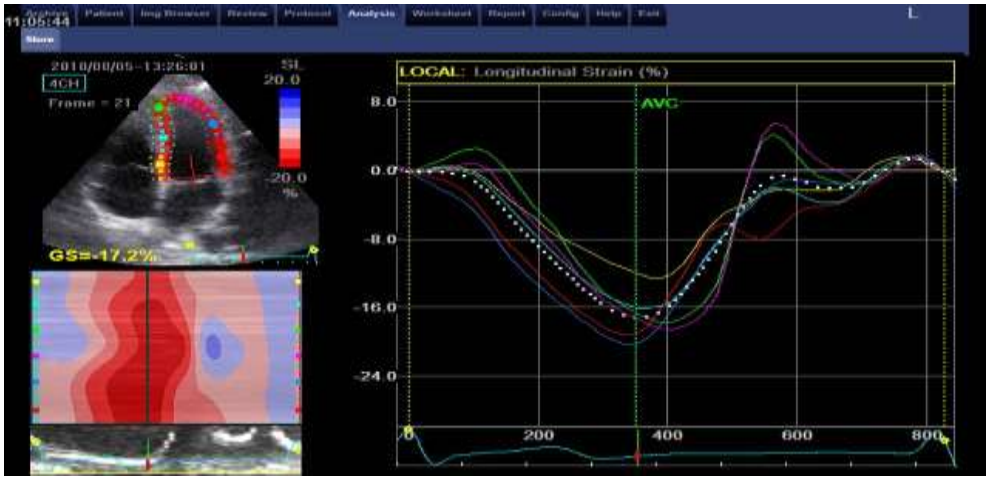

Figure (1): LV longitudinal strain by speckle tracking echo.

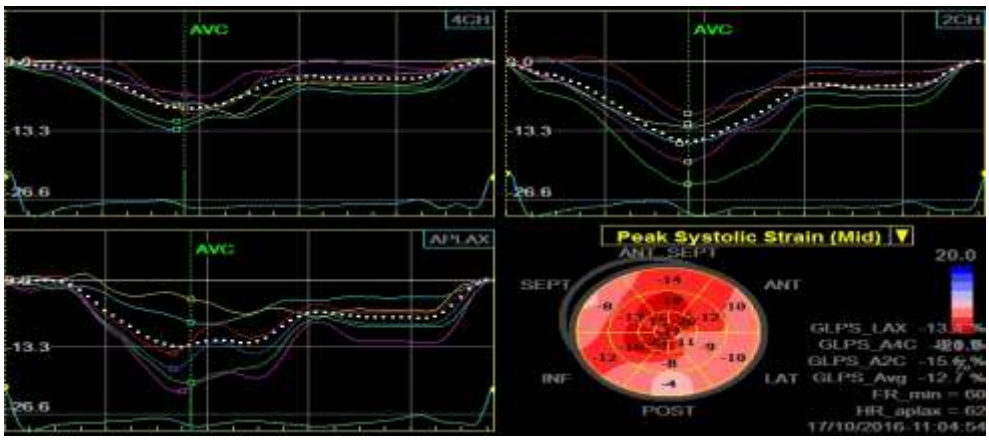

Figure (2): Curves of impaired LV longitudinal strain (LV GLPS-avg= -12.7) and Bull's eye diagram.

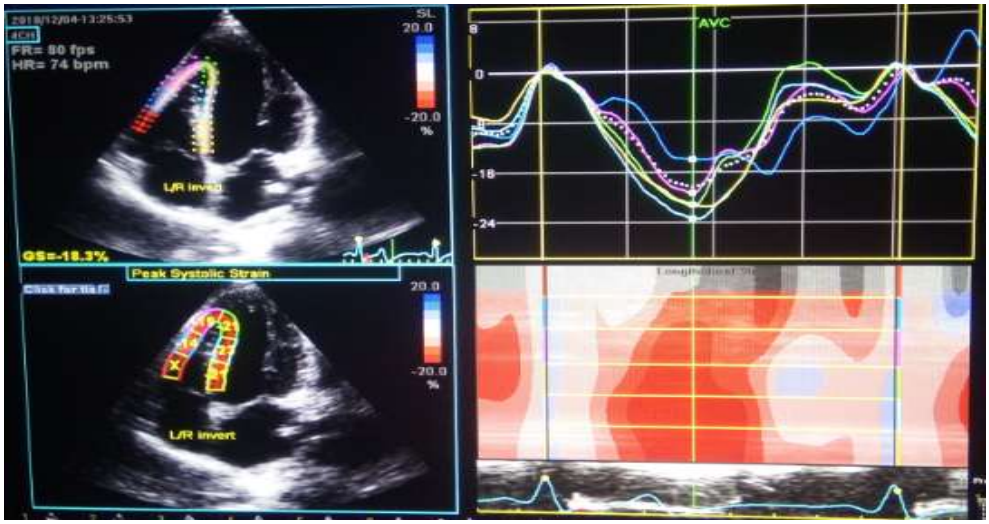

Figure (3): RV speckle tracking echo (RV GLPS-Avg= -18.3).

Statistical analysis:

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with a one-sample Kolmogorov-Smirnov test. Qualitative data were described using numbers and percentages. Association between categorical variables was tested using the Chi-square test.

Continuous variables were presented as mean ± SD (standard deviation) for parametric data and median (min-max) for non-parametric data. The two groups were compared with the Student t test for parametric data. the relation between the two studied parameters was done using a correlation coefficient. *A P*-value less than 0.05 is considered significant.

Results: This study was conducted on 120 Egyptians participates, consisting of 80 patients with type II diabetes **with Acanthosis nigricans** [group I], in addition to 40 age and sex-matched healthy Egyptian subjects as a control group [group II]. The mean age for GI was (51.17±90 years), whereas that of the control group was 48.25±10.25 years [P=0.2]. GI includes 32 [40%] Egyptian males and 48 [60%] Egyptian females while GII included 26 [65%] males and 14 [35%] females. (Table 1).

GI had significantly higher FBG, 2H PP, HbA1C, Serum creatinine, TG, LDL, and total cholesterol compared to GII. While there were no significant differences in Hb and HDL between groups (**Table 2).**

-There was a statistically significant increase in a hyperpigmented patch, and velvety-like appearance, while there is no significant difference between the two groups regarding hypopigmented patch (**Table 3).**

-There was a statistically significant increase in the percentage of (papillary projection, hyperpigmented dots, and hyperpigmented globule) dermoscopic

findings of acanthosis. While there is no significant difference between the two groups regarding the percentage of crista cutis and sulcus cutis.

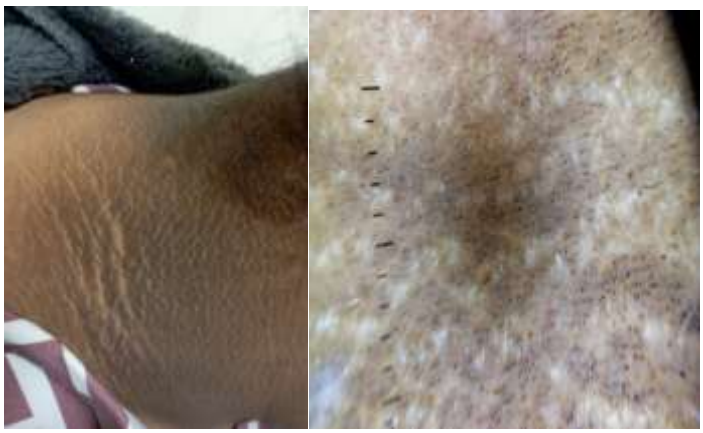

Figure 4: clinical and dermoscopic evaluation of a patient with acanthosis nigrican

Regarding the conventional echo-Doppler parameters, LVPWs, MV E Velocity, and MV E/A ratio GI was significantly lower in comparison to GII, while LA/AO ratio, MV A Velocity, and MV Deceleration Time were significantly higher in GI than GII.

Despite Aortic root and LA dimensions being in normal ranges; the Aortic root dimension was significantly lower in GI compared to GII and LA dimension was significantly higher in GI compared to GII **(Table 5)**.

-There was no significant difference between both groups regarding LV systolic mitral annular velocity (LV Sa), while the early and late diastolic mitral annulus velocities were significantly lower in GI compared to GII. E/E' ratio had a trend to be significantly higher in GI compared to GII **(Table 6).**

Regarding 2D-STE, GI had significantly lower GLPS-A4C and GLPS-Avg compared to GII **(Table 7)**

GI had significantly higher RV basal and mid diameter compared to group II, while RV longitudinal diameter was lower in GI than GII.

Concerning RV systolic and diastolic functions, GI had significantly lower RV systolic velocity (TV Sa), RV GLPS, and early TV diastolic velocity (TV Ea) in GI than GII, while the late TV diastolic velocity (TV Aa) was significantly higher in GI compared to GII **(Table 8).**

Correlation of LV and RV systolic function by speckle tracking with HbA1C:

LV GLPS-average and RV GLPS-average showed significant weak negative correlations with HbA1C **(Table 9)** and **(Figure 5&6).**

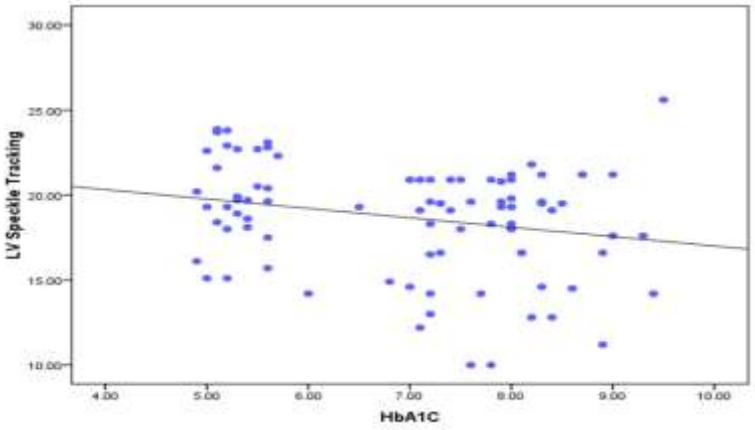

Figure (5): Scatter plot showing a reverse correlation between LV GLPS% and HBA1c% level.

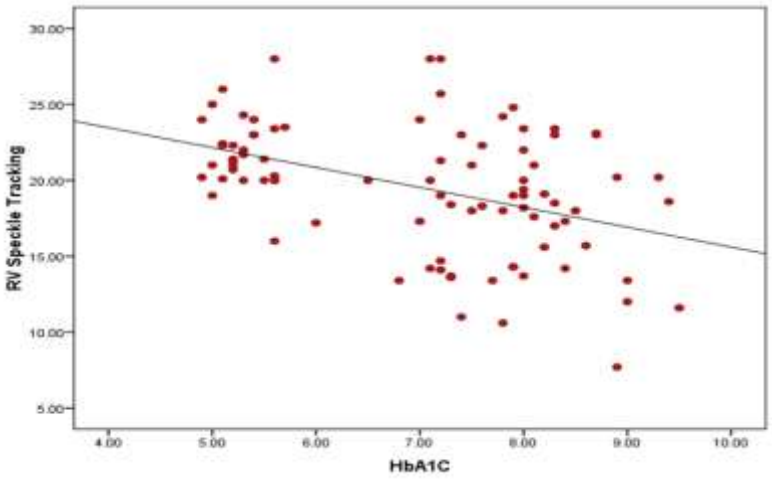

Figure (6): Scatter plot showing a reverse correlation between RV GLPS% and HBA1c% level.

Discussion:

Acanthosis nigricans is a fairly common skin pigmentation disorder characterzed by a dry, dark patches of skin that usually appear in the armpits, neck or groin. It could be a sign of an underlying as type 2 diabetes. Diabetes is a major public health problem that rapidly growing in Egypt with a large effect on morbidity and mortality. [1]. Diabetic patients often present with comorbidities such as hypertension, coronary artery disease (CAD), and heart failure. [15] Acanthosis nigricans is a substantial problem in Egypt and has a close relationship with obesity, dyslipidemia, and insulin resistance. [6]

Diabetic nephropathy is one of the main causes of end-stage renal disease which have a large impact on renal function as simply serum creatinine level [17]

The present study was designed to detect subtle ventricular systolic dysfunction in Egyptian type 2 diabetic patients with Acanthosis nigricans using 2Dspeckle tracking echocardiography. Our study showed that serum creatinine was significantly higher in Egyptian diabetic pts with Acanthosis nigricans compared to normal Egyptian subjects which were concordant with Singh, 2014 who reported that plasma creatinine was observed to be significantly higher in type-2 DM subject compared to non-diabetics [17]

This result is in disagreement with Dabla, 2010 who reported that lower serum creatinine is associated with an increased risk of type 2 diabetes. [18] and this might have been explained by the lower skeletal muscle volume in their patients.

Dyslipidemia is a common feature of diabetes There is an association between atherosclerotic cardiovascular disease and serum cholesterol and triglyceride levels in both type 1 and type 2 diabetes [19]

A significant difference was found between the two Egyptian groups in TG, LDL, and total cholesterol. These results were concordant with Ahmed et al., 2018 who found high LDL levels in diabetic patients than in the control group, [20] and Conte et al., 2013 who reported significantly higher TG levels of the diabetic especially those with BMI >30kg/m2 than the control group. [21]

myocardial steatosis was linked with LV diastolic dysfunction, independently of diabetic state, age, BMI, visceral adipose tissue, heart rate, and blood pressure [22].

MV A velocity and DT were significantly higher in our Egyptian Acanthosis nigricans diabetic patients while MV E velocity and MV E/A ratio were significantly lower compared to healthy subjects. Also, LV Tissue Doppler Imaging showed that diastolic mitral annular velocities were significantly lower in Egyptian diabetic pts compared to the healthy subject while E/E' ratio was significantly higher in DM These were concordant with Hallsworth et al have demonstrated significant changes in cardiac structure and evidence of early LV diastolic dysfunction compared with age-, sex- and BMI-matched controls, in the absence of cardiac metabolic changes or overt cardiac disease [23].

Increased liver size may affect anatomically the right ventricular function; also, the increased preload due to elevated hepatic venous pressure may contribute to the occurrence of right ventricular dysfunction [28] likewise RV dysfunction might play a significant role in diabetic cardiac involvement [29].

In Our results, a significant difference in RV basal, mid and longitudinal dimensions, despite both groups were still in normal ranges also no difference between both group were detected with systolic function using FAC or TAPSE while the systolic RV function was significantly lower in Egyptian diabetic patients compared to control group and this was concordant with Mohammed et al., 2018 who signify no statistically significant difference between his both groups regarding RV function by Fractional Area Change (FAC) and Tricuspid Annular Plane Systolic Excursion (TAPSE), but in disagreement with our result the RV inflow dimensions (basal, mid-cavity and longitudinal diameters also showed no significant difference between his groups, but his patient and control groups were with younger age, lower BMI [30].

Sunbul et al [31]. stated that there was no difference between his patient's group with Acanthosis nigricans regarding TAPSE and this was in agreement with our results. Bekler and his colleagues [32] who compared 32 individuals with NAFLD to a control group of 22 subjects without hepatosteatosis showed that tissue Doppler parameters were lower (Ea and Ea/Aa) in the patient group but they were in disagreement with our result regarding dimensions, FAC and TAPSE.

LV average GLPS- was significantly lower in the Egyptian diabetics than the healthy subjects. which was concordant with Mohammed et al., 2018 who reported that LV global longitudinal strain was lower in diabetics than normal individuals [30], and Bogdanović et al.2019[33] who found diabetics had significantly lower GLS in comparison to both euglycemic pts and healthy individuals. [33].

Regarding RV speckle tracking imaging, RV GLS was lower in Egyptian diabetics than in normal individuals, which may indicate the subclinical impairment of RV systolic function that is concordant with all studies performed on diabetics Kang et al., 2019, Mohammed et al., 2018, Kosmala et al., 2007. [34], [30]., [35] and studies on Acanthosis nigricans [31].

Diabetes usually presented with dyslipidemia weather type 1 or 2. and atherosclerotic CVD is associated with elevated serum cholesterol and triglyceride [19] in addition to Acanthosis nigricans encourage atherogenic dyslipidemia [increased small, dense low-density lipoprotein (LDL) particles, triglycerides, and decreased high-density lipoprotein (HDL) cholesterol] [37]. which explained the negative correlation of our patients between the LVGLS and TG levels ($r=-0.27$, $p = 0.036$) plus, RVGLS showed stronger negative correlation with TG and cholesterol levels (r -0.40 and-0.38 p= <0.001, <0.002 respectively).

Negative correlation between both LVGLS and RVGLS with the level of HbA1c (r=-0.32 p= 0.013 and r= -0.44, p<0.0001 respectively) in Egyptian diabetics with Acanthosis nigricans was detected in our results. This finding was concordant with Mohammed et al., 2018 who found a reverse correlation between LVGLS and RVGLS with the level of HbA1c in group I (p <0.001) [30]. Also Leung et al., 2016 evaluated the impact of improved glycemic control on cardiac function in 105 pts with type 2 DM patients assessed by 2D STE. [36]

While Jedrzejewska et al and Di Cori et al 2007. [38, 39] who did not observe any correlation between HbA1c and LVGLS in forty asymptomatic and uncomplicated patients with type 1 DM. This could be explained by the baseline characteristics of patients that were more strictly selected and more likely to represent a very early preclinical stage of the disease and good glycaemic control of them. Also Kim & Kim 2010. [40] they did not find a relationship between HbA1c and LV systolic strain or velocity. The lack of correlation between HbA1c and myocardial function may be explained by the fact that HbA1c reflects the glucose level of only 4 preceding months. As an indicator of short-term hyperglycemia, it cannot show the relationship of glycemic control with cardiac function in long-disease-duration diabetic patients likewise endothelial dysfunction induced by hyperglycemic stress is present even after glucose normalization. This means that diabetic vascular complications progress despite the restoration of normal glucose in a phenomenon known as hyperglycemic memory. [38, 39]

Conclusion:

left & right ventricular systolic function was sub-clinically affected in Egyptian Type 2 diabetic patients with Acanthosis nigricans using 2D-STE.

Recommendation: Egyptian Diabetic patients should be encouraged to optimum regular exercise and reduction of BMI to improve lipid abnormalities associated with diabetes in addition to Acanthosis nigricans. which in turn reduces the cardiovascular morbidity and mortality

The study limitation in the current study the sample size with limited Also hemoglobin A1c was done once during the study which may not accurately reflect the level of glycemic control over a long period.

References:

1. Hegazi R, El-Gamal M, Abdel-Hady, et al., Epidemiology of and Risk Factors for Type 2 Diabetes in Egypt. An n a l s of G l o b a l H e a l t h, V O L. 8 1, N O. 6, 2 0 1 5 November -December: 8 1 4 – 8 2 0.

2. Cusi K, Nonalcoholic fatty liver disease in type 2 diabetes mellitus. Curr Opin Endocrinol Diabetes Obes;2009 16:141–149.

3. McCullough A. Epidemiology of the metabolic syndrome in the USA. J. Digestive Diseases. 2011;12(5):333-340.

4. Marchesini G, Brizi M, Bianchi G, Tomassetti S, et al. Nonalcoholic fatty liver disease: A feature of the metabolic syndrome. Diabetes. 2001; 50:1844–1850.

5. Mohamed AA *, Shousha WG, Shaker O, et ale. Insulin Resistance in Egyptian Nonalcoholic Fatty Liver Disease patients. BJMMR, 2015; 6(5): 463-473.

6. Tomah S, Hamdy O, Abuelmagd, et al. Prevalence of and risk factors for non-alcoholic fatty liver disease (NAFLD) and fibrosis among young adults in Egypt. BMJ Open Gastro 2021;8: e000780. doi:10.1136/bmjgast-2021-000780

7. Tomah S, Alkhouri N, Hamdy O. Nonalcoholic fatty liver disease and type 2 diabetes: where do diabetologists stand? Clin Diabetes Endocrinol 2020;6:1–11.

8. Grundy SM, Benjamin I J, Burke G L, et al. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation, 1999; 100(10):1134-1146.

9. Hong MA, Mingxing XIE,Jing Wang, et al. Ultrasound Speckle Tracking Imaging Contributes to Early Diagnosis of Impaired Left Ventricular Systolic Function in Patients with Type 2 Diabetes Mellitus. Journal of Huazhong University of Science and Technology .2008 ; 28(6):719-23.

10. Ralph L. Widya ,Rutger W. van der Meer ,JohannesW.A.Smit, et al. Right Ventricular Involvement in Diabetic Cardiomyopathy . Diabetes Care . 2013 ; 36(2): 457–462.

11. Ballestri S , Lonardo A, Bonapace S, et al., Risk of cardiovascular, cardiac and arrhythmic complications in patients with non-alcoholic fatty liver disease. WJJ. 2014; February 21, Volume 20: Issue 7.

12. Hurlburt HM, Aurigemma GP, Hill JC, et al. Direct ultrasound measurements of longitudinal , circumferential, and radial strain using 2D strain imaging in normal adults.Echocardiography Jornal . 2007;24:723-731.

13. Ng AC, Delgado V, Bertini M, et al . Two-Dimensional Speckle Tracking Echocardiography Detects Subclinical Left Ventricular Systolic Dysfunction among Adult Survivors of Childhood, Adolescent, and Young Adult Cancer. Eur J Endocrinol .2011;32:1542-1550.

14. Abdelwahab A, Anwar M, Abdelsalam R, et al. Effect o Diabetic Duration on Left Ventricular Global Longitudinal Strain by Speckle Tracking Imaging. The American Journal of Cardiology 2017;03:051.

15. . Williams LJ, Nye BG and. Wende AR. Diabetes-Related Cardiac Dysfunction. Endocrinol Metab (Seoul). 2017;32(2):171-179.

16. Chehadeh W, Abdella N, Ben- Nakhi A, et al. Risk factors for the development of diabetes mellitus in chronic hepatitis C virus genotype 4 infection. J Gastroenterol Hepatol 2009;24:42e8

17. Singh P., Khan S., and Mittal R. K. renal function test on the basis of serum creatinine and urea in type-2 diabetics and non-diabetics. Bali Medical Journal (BMJ) 2014; 3(1): 11-14.

18. Dabla P K. Renal function in diabetic nephropathy. World J Diabetes. 2010; 1(2): 48–56.

19. Schofield JD. Liu Y. Rao-Balakrishna P.et al., Diabetes Dyslipidemia. Diabetes REVIEW Ther .(2016); 7:203–219.

20. Ahmed TA, Hassan MN, Mazen A A, et al. Detection of early left ventricular and left atrial dysfunction in type I diabetes mellitus using two dimensional speckle tracking echocardiography. The scientific journal of Al-Azhar medical faculty of girls.2018; 2(2): 106-114.

21. Conte L, Fabiani I, Barletta V, et al. Early Detection of Left Ventricular Dysfunction in Diabetes Mellitus Patients with Normal Ejection Fraction, Stratified by BMI: A Preliminary Speckle Tracking Echocardiography Study. J Cardiovasc Echogr. 2013; 23(3): 73–80.4

22. Rijzewijk LJ, Jonker JT, van der Meer RW, et al. Effects of hepatic triglyceride content on myocardial metabolism in type 2 diabetes. J Am Coll Cardiol 2010; 56: 225-233 [PMID: 20620743 DOI: 10.1016/j.jacc.2010.02.049

23. Hallsworth K, Hollingsworth KG, Thoma C, et al .Cardiac structure and function are altered in adults with non-alcoholic fatty liver disease. J Hepatol 2013; 58: 757-76[PMID: 23178979 DOI: 10.1016/j.jhep.2012.11.015].

24. Fallo F, Dalla Pozza A, Sonino N, et al. Non-alcoholic fatty liver disease is associated with left ventricular diastolic dysfunction in essential hypertension. Nutr Metab Cardiovasc Dis 2009; 19: 646-653 [PMID: 19278843 DOI:10.1016/j.numecd.2008.12.007]

25. Bonapace S, Perseghin G, Molon G, et al., Nonalcoholic fatty liver disease is associated with left ventricular diastolic dysfunction in patients with type 2 diabetes. Diabetes Care 2012; 35:389-395 [PMID: 22210573 DOI: 10.2337/dc11-1820]

26. chandran R, Meena R K, Sharma S, et al. subclinical diastolic dysfunction and its correlation with laboratory parameters in type 2 diabetes mellitus in india: a case control study. Rom J Diabetes Nutr Metab Dis. 2018; 25(2):157-164.

27. Roos C J, Scholte AJ, Kharagjitsingh AV, et al. Changes in multidirectional LV strain in asymptomatic patients with type 2 diabetes mellitus: a 2-year follow-up study. Eur Heart J Cardiovasc Imaging. 2014; 15(1):41-7.

28. Moise GC , Donoiu I and Rogoveanu. Ventricular structure and function in non-alcoholic fatty liver disease. CorSalud. 2020; Oct-Dec;12(4):425-43.

29. Widya, R., Van Der Meer, R., Smit, J.W. et al. Right ventricular function and dimensions in type 2 diabetes mellitus. J Cardiovasc Magn Reson 14, P71 (2012). https://doi.org/10.1186/1532-429X-14-S1-P71

30. . Mohammed YR, Hablas WR, Anwar AM., et al. Subclinical Right Ventricular Dysfunction in Type 2 Diabetes Mellitus: An Echocardiographic Strain/Strain Rate Study. Med. J. Cairo Univ. 2018; 86 (1): 153-162.

31. Sunbul M, Kivrak T, Durmus E, et al. Nonalcoholic steatohepatitis score is an independent predictor of right ventricular dysfunction in patients with nonalcoholic fatty liver disease. Cardiovasc Ther. 2015;33(5): 294-9.

32. Bekler A, Gazi E, Erbag G, Binnetoglu E, Barutcu A, Sen H, et al. Right ventricular function and its relationship with grade of hepatosteatosis in non-alcoholic fatty liver disease. Cardiovasc J Afr. 2015;26(3):109-13.

33. Bogdanović J, Ašanin M, Krljanac G , et al. Impact of acute hyperglycemia on layer-specific left ventricular strain in asymptomatic diabetic patients: an analysis based on two-dimensional speckle tracking echocardiography. Cardiovasc Diabetol. 2019; 18: 68.

34. Kang Y, Wang S, Huang J, et al. Right ventricular dysfunction and remodeling in diabetic cardiomyopathy. American Journal of Physiology-Heart and Circulatory Physiology, 2019; 316.

35. Kosmala W and Kosmala M. Subclinical right ventricular dysfunction in diabetes mellitus - An ultrasonic strain/strain rate study. Diabetic Medicine. 2007; 24(6):656-63.

36. Leung M, Wong VW, Hudson M, Leung DY. Impact of Improved Glycemic Control on Cardiac Function in Type 2 Diabetes Mellitus. Circ Cardiovasc Imaging. 2016 Mar;9(3): e003643. doi: 10.1161/CIRCIMAGING.115.003643. PMID: 26962125.

37. Xia M-F, Bian H and Gao X (2019) NAFLD and Diabetes: Two Sides of the Same Coin? Rationale for Gene-Based Personalized NAFLD Treatment. Front. Pharmacol. 10:877. doi: 10.3389/fphar.2019.00877

38. Jędrzejewska I , Król W, Światowiec A, et al. Left and right ventricular systolic function impairment in type 1 diabetic young adults assessed by 2D speckle tracking echocardiography. European Heart Journal - Cardiovascular Imaging, 2016; 17(4):438–446.

39. Di Cori A., Di Bello V., Miccoli R., et al. Left ventricular function in normotensive young adults with well-controlled type I diabetes mellitus. Am. J. Cardiol., 2007; 99: 84-90.

40. Kim EH and Kim YH. Left ventricular function in children and adolescents with type 1diabetes mellitus. Korean Circ J 2010;40:125–30.

Table (1): baseline demographic data of the whole study population:

Demographic data	Group I Patients group (n=80)	Group II Control group (n=40)	Test of significance	p-value
Age / years Mean ± SD	51.17±7.90	48.25±10.25	t=1.22	0.227
Sex Male Female	32 (40%) 48(60%)	26 (65%) 14 (35%)	χ^2=3.34	0.068
BMI	33.79±4.04	32.75±3.878	0.96	0.342

SD: Standard deviation, BMI: Body Mass Index., χ^2: Chi-square test, t: student t-test

Table (2): Laboratory investigations among patients and control group

Laboratory investigations	Group I Patients group (n=80)	Group II Control group (n=40)	*p*-value
FBG(mg/dl)	167.42±52.6	84.0±5.60	**≤0.001*(S)**
2H PP(mg/dl)	267.8±55.48	130.75±6.07	**≤0.001*(S)**
HbA1C(%)	7.90±0.68	5.27±0.24	**≤0.001*(S)**
Hb(%)	12.88±1.24	12.75±1.4	0.375
S. Cr(mg%)	0.93±0.16	0.82±0.14	**0.013*(S)**
TG(mg/dl)	141.98±54.94	97.60±31.13	**0.001*(S)**
HDL(mg/dl)	51.95±10.59	54.25±5.76	0.370
LDL(mg/dl)	113.80±39.01	82.85±14.22	**0.001*(S)**
Total cholesterol(mg/dl)	204.10±34.21	161.95±22.10	**≤0.001*(S)**

FBG: fasting blood glucose, 2HPP: 2hours postprandial blood glucose, HbA1C: glycosylated hemoglobin, Hb: hemoglobin, s.cr: serum creatinine, TG: triglycerides, HDL: high-density lipoprotein, LDL: low-density lipoprotein.

Table (3): Clinical findings of acanthosis nigricans in the studied groups:

Clinical finding	Group I Patients group (n=80)	Group II Control group (n=40)	x^2	p-value
Hyperpigmented patch				
Absent	10 (12.5%)	4 (10.0%)		
Mild	25 (31.25%)	8 (20.0%)		
Moderate	17 (21.25%)	20 (50.0%)	14.300	0.003*
Severe	28 (35.0%)	8 (20.0%)		
Velvety like appearance				
Absent	10 (12.5%)	0 (0.0%)		
Mild	25 (31.25%)	12 (30.0%)		
Moderate	27 (33.75%)	20 (50.0%)	10.133	0.006*
Severe	18 (22.5%)	8 (20.0%)		

Using: x^2: Chi-square test;

*p-value >0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*

Table (4): percentage of the dermoscopic finding of acanthosis nigricans in the studied groups:

Percentage of Dermoscpic Finding	Group I Patients group (n=80)	Group II Control group (n=40)	Test value	p-value
Percentage of Crista Cutis				
Mean±SD	84.25±10.29	4.00±9.28	*t*= -0.168	0.867
Range	60-95	0- 5 (%)		
Percentage of Sulcus Cutis				
Mean±SD	83.75±10.75	6.75±9.52	*t*= 0.000	1.000
Range	60-95 (%)	6 -9 (%)		
Percentage of Hyperpigmented dots				
Mean±SD	19.25±10.06	15.13±8.06	*U*= -2.176	0.025
Range	0-30 (%)	0-30 (%)		
Percentage of Hyperpigmented globule				
Mean±SD	19.75±10.04	16.50±9.26	*U*=- 2.215	.021
Range	0-50 (%)	0-50 (%)		
percentage of Papillary projection				
Mean±SD	26.25±14.59	16.00±12.02	*U*= -5.244	<0.001**
Range	5-60 (%)	0-60 (%)		

Using: t-Independent Sample t-test; U=Mann-Whitney test

*p-value >0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*

Table (5): LV conventional among patients and control groups

LV conventional	Group I Patients group (n=80)	Group II Control group (n=40)	p- value 636
IVSd (cm)	0.96±0.16	0.94±0.15	0.677
LVIDd (cm)	4.82±0.48	4.90±0.30	0.517
LVPWd (cm)	0.92±0.20	0.95±0.14	0.531
IVSs (cm)	1.32±0.24	1.31±0.31	0.841
LVIDs (cm)	2.88±0.44	2.89±0.34	0.939
LVPWs (cm)	1.39±0.22	1.52±0.23	**0.048*(s)**
2D-EF %	58.82±3.44	58.40±1.66	0.605
AO Diam (cm)	2.60±0.37	2.90±0.37	**0.006*(S)**
LA Diam (cm)	3.64±0.46	3.33±0.46	**0.016*(S)**
LA/AO	1.39±0.26	1.14±0.24	**0.001*(S)**
MV A Vel (m/s)	81.32±15.008	63.55±18.12	**≤0.001*(S)**
MV E Vel (m/s)	67.00±18.71	80.35±6.86	**0.003*(S)**
MV E/A ratio	0.84±0.26	1.32±0.32	**≤0.001*(S)**
MV Dec T (ms)	190.47±50.03	146.20±5.97	**≤0.001*(S)**

IVSd: interventricular septal thickness at end-diastole, LVIDd: left ventricular end-diastolic dimension, LVPWd: left ventricular posterior wall thickness at end-diastole, IVSs: interventricular septal thickness at end systole, LVIDs: left ventricular end-systolic dimension, LVPWs: left ventricular posterior wall thickness at end-systole, 2D-EF: two dimensional ejection fraction, AO Diam: Aortic diameter, LA Diam: left atrial diameter, , MV: Mitral valve, A Vel: late peak LV filling velocity, E Vel: early peak LV filling velocity, Dec T: deceleration time.

Table (6): ECHO LV TVI among pts and control groups.

LV TVI	Group I Patients group (n=80)	Group II Control group (n=40)	p-value
Average Sa (cm/s)	8.60±1.81	8.84±0.48	0.566
Average Ea (cm/s)	7.99±1.13	9.57±0.50	**≤0.001*(S)**
Average Aa (cm/s)	6.36±1.86	8.76±0.60	**≤0.001*(S)**
E/Ea	10.99±2.80	8.38±0.86	**≤0.001*(S)**

Sa: Systolic mitral annulus velocity, Ea: Early diastolic mitral annulus velocity, Aa: late diastolic mitral annulus velocity.

Table (7): LV Speckle Tracking among the studied groups

Speckle Tracking	Group I Patients group (n=80)	Group II Control group (n=40)	p-value
Speckle Tracking			
GLPS-LAx %	-17.46±4.14	-18.68±1.70	0.212
GLPS-A4C %	-16.22±3.36	-18.69±1.47	**0.003*(S)**
GLPS-A2C %	-16.57±3.99	-18.42±1.84	0.055
GLPS--Avg %	-16.73±3.38	-18.56±1.09	**0.022*(S)**

GLPS: Global longitudinal peak strain, LAx: Apical long-axis view, A4C: Apical four-chamber view, A2C: Apical two-chamber view, Avg: Average.

Table (8): RV conventional, TDI and 2dSTE among patients and control groups

RV conventional	Group I Patients group (n=80)	Group II Control group (n=40)	p- value
TAPSE (cm)	2.28±0.23	2.18±0.26	0.141
RV basal (cm)	3.26±0.26	3.04±0.21	**0.002*(S)**
RV mid (cm)	2.31±0.37	2.09±0.34	**0.031*(S)**
RV longitudinal (cm)	4.99±0.54	5.54±0.51	**≤0.001*(S)**
FAC %	40.87±6.35	39.50±3.23	0.368
Lateral TV Sa (cm/s)	9.48±2.63	15.27±0.92	**≤0.001*(S)**
Lateral TV Ea (cm/s)	6.68±1.78	17.48±0.69	**≤0.001*(S)**
Lateral TV Aa (cm/s)	10.97±2.48	7.22±1.18	**≤0.001*(S)**
RV GLPS %	-19.19±3.81	-23.00±2.25	**≤0.001*(S)**

TAPSE: Tricuspid annular plane systolic excursion, RV: Right ventricle, TV: tricuspid valve, Sa: Systolic tricuspid annulus velocity, Ea: Early diastolic tricuspid annulus velocity, Aa: late diastolic tricuspid annulus velocity, RV GLPS: Right Ventricular Global Peak Strain.

Table (9): Correlation of LV and RV speckle tracking with HbA1C:

		HbA1c
LV GLPS-Average	*r*	**-0.320**
	p	**0.013*(S)**
RV GLPS-Average	*r*	**-0.441**
	p	**<0.0001*(S)**

HbA1C: glycosylated hemoglobin, LV GLPS: Left ventricular global longitudinal peak strain, RV GLPS: Right Ventricular Global Peak Strain