Article

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Prediction of Preclinical Myocardial Dysfunction among Obese Diabetics with Preserved Ejection Fraction Using Tissue Doppler Imaging and Speckle Tracking Echocardiography

Galaleldin Nagib Elkilany[1,*], Sherif A Baath Allah[2], Eric Merrell[3], Ram B Singh[4], Yomna Galal Elkilany[5], Navin C. Nanda[6], Jaipaul Singh[7], Ibrahim Kabbash[8], Mohamed Khorshid[9], Fabiola Sozzi[10], and Hani Aiash[11]

[1]Tanta University, Egypt- Gulf Medical University, Cardiovascular Departments and Al-Elaj Medical Center, Ajman, UAE
[2]RAK Medical and Health Science University and Masafi Hospital, UAE
[3]Department of Cardiovascular Perfusion, SUNY Upstate Medical University, Syracuse, NY, USA
[4]Halberg Hospital and Research Institute, Moradabad, India
[5]American University, Sharjah, UAE
[6]Alabama University at Birmingham, AL, USA
[7]School of Forensic and Applied Biology, University of Central Lancashire, Preston, UK
[8]Public Health & Community Medicine Department, Faculty of Medicine, University of Tanta, Egypt
[9]Faculty of Medicine, Zagazig University, Egypt
[10] Policlinico University Hospital IRCCS, Milan, Italy
[11] SUNY Upstate Medical University, Syracuse, NY, USA and Suez Canal University, Egypt

Abstract

Background. Obesity and type 2 diabetes mellitus (T2DM) are two interrelated and preventable disorders. However, they are responsible for significant global mortality from cardiovascular diseases (CVDs). Clinical studies have demonstrated that global longitudinal strain (GLS) using speckle tracking echocardiography (STE), can assess myocardial function accurately in apparently, healthy patients with diabetes and obesity in the settings of acute and chronic ischemia and suspected cardiomyopathy without heart failure. No such studies have been published to date regarding subclinical detection of cardiac dysfunction among obese patients with T2DM. This study aims to investigate the role of STE in the early pre-clinical diagnosis of impairment of diastolic and systolic functions in obese patients with T2DM. This study also investigated whether it is possible to detect early pre-clinical impairment of diastolic and systolic dysfunction in obese T2DM patients, via Tissue Doppler Imaging (TDI), maximum rate of left ventricular pressure development (peak dP/dt) and GLS using STE for comparison.

Subjects and Methods. After clearance from the review board of Dibba- Hospital, Alfujairah, UAE, all the available records of patients with the diagnosis of obesity and diabetes were examined. The study included 214 patients presenting with obesity in conjunction with diabetes and 93 age-matched healthy control subjects. Conventional transthoracic two dimensional echocardiography (CE), myocardial Doppler-derived early diastolic (E) and atrial pre systolic (A) velocities and GLS by STE was performed among all the patients and subjects along with tissue Doppler imaging (TDI). This study assessed maximal rate of pressure rise during ventricular contraction (peak dP/dt) in diabetes induced dilated cardiomyopathy (DCM) with mitral valve incompetence. Left ventricular ejection fraction (LVEF), GLS and TDI were also obtained, among all the subjects.

* Corresponding author: Galaleldin Nagib Elkilany, MD, FESC, FISCU. Assistant Clinical Professor and Consultant Cardiologist –SCU at Tanta University, Egypt, Gulf Medical University, Ajman , UAE & Al-Elaj Medical Center , UAE. 132 Holly Drive, LaPlace, LA, 70068, USA. Email: galal@kilany.org

Results. The results show that cardiac functions via conventional echocardiography (CE) were similar in the 2 groups. Using TDI and conventional mitral Doppler flow, obese subjects with diabetes showed an evidence of diastolic function abnormalities in the form of lower mitral annular early septal (Ea) velocity (9.5 ± 2.9 vs. 18.4 ± 3.5 cm/s, $p < 0.0001$), an increased mitral annular late (Aa) velocity (16.5 ± 2.4 vs. 14.1 ± 2.2 cm/s, $p < 0.05$), higher left ventricular filling pressure (E/Ea = 12 ± 4.4 vs 8 ± 3.1), $p < 0.05$), as well as a reduced Ea/Aa ratio (1.00 ± 0.2 vs. 1.45 ± 0.3, $p < 0.0001$, in the study group versus control group. respectively. This study also showed that severely obese subjects (BMI >35) (n = 26) had reduced left ventricular (LV) systolic and diastolic functions compared with healthy controls. Regarding, systolic function indices, the findings revealed lower average longitudinal peak systolic strain (GLS), -13.5% ±1.4 vs -19.54% ± 4.5; *in a symptomatic patients versus age matched healthy subjects respectively, ($p < 0.001$*), although, LVEF remained normal (56.48% ± 8.81). Among patients with DCM (n = 26), the findings reveal that global longitudinal systolic strain (GLS) is highly correlated with maximum rate of LV pressure development (dp/dt), although the LVEF remained normal, in comparison to GLS and dp/dt. (-9.54 ± 4.50 and 849.9 ± 277.0); respectively, $r = .790$, $*p < 0.001$). However, the frequency/grade of DCM detected by STE, among patients having obesity with T2DM, correlated closely with the degree of obesity, metabolic abnormalities and clustering of other major risk factors, especially high blood pressure. The findings also revealed that chest pain due to coronary heart disease (CAD), dyspnea and DCM were more common among female patients compared to men.

Conclusion. The results indicate that patients having obesity with T2DM should be advised to undertake early TDI and STE for early diagnosis of decreased cardiac diastolic and systolic functions and cardiomyopathy, which is likely to be missed by conventional echocardiography. Significant differences in regional and global strain were also identified between the severely obese diabetic (BMI ≥ 35) patients compared to less obese subjects.

***Keywords**:* Obesity, diabetes; diabetic cardiomyopathy; cardiac dysfunction; speckle tracking echocardiography.

Introduction

It is now well established that obesity is a major global risk factor for type 2 diabetes mellitus (T2DM) which is often referred to as diabesity [1-3]. It has also been estimated that over 80% of all obese patients will develop T2DM [1]. Previously, people over 40 years of age were diagnosed with T2DM, but now children as young as 12-15 years of age develop T2DM because of their obesity. The prevalence of the 2 disorders has reached epidemic proportion globally especially in terms of the extent of their negative impact on the health of the victims when compared to people who smoke and have hypercholesterolemia [3, 4]. In addition, T2DM and obesity are important contributors to non-ischemic heart failure (HF). Diabetic cardiomyopathy (DCM), a term coined several years ago, refers to cardio-myopathy in diabetic patients not attributable to other underlying cardiac problems, namely coronary artery disease (CAD), valvular disease, hypertension or dyslipidemia [2]. The development of DCM is most likely multifactorial. Putative mechanisms described by Xie Y and Xie Z [3] include metabolic disturbances, such as defective glycolysis and glucose oxidation, myocardial fibrosis, small vessel disease, autonomic dysfunction and abnormalities of calcium handling. It is now well established that metabolic cardiomyopathy can lead to several changes in cardiac structure and function that can be recognized by imaging in the asymptomatic phase, and these parameters can be used for monitoring either the progression of the disease or the response to therapy. This recent revelation has indicated that metabolic syndrome, obesity and diabetes are independent predictors of CAD, HF and sudden cardiac death (SCD). The Strong Heart Study demonstrated an almost 3 decades strong association between T2DM and higher left ventricular mass (LVM), wall thickness, increased arterial stiffness and systolic dysfunction compared with age -matched healthy controls [4]. It is now well established that both obesity and T2DM can lead to the devel-opment cardiovascular diseases (CVDs) if left un-treated.

Recently, novel clinical techniques, such as Tissue Doppler Imaging (TDI) and global longit-udinal strain (GLS) evaluated by speckle tracking echocardiography (STE) have been developed to detect early preclinical stage of myocardial dysfunction inpatients with obesity and T2DM [5]. Since obesity and T2DM are independent predictors of CAD, HF, stroke and SCD, it is of paramount

importance to ascertain if early diagnosis of the patients can either delay or prevent cardiac dysfunctions in these patients. Based on data reported in the literature, the main purpose of this study was to provide a guideline to clinicians with the potential benefits of early detection of preclinical myocardial abnormalities by non- invasive real time imaging techniques in obesity and T2DM. The study employed TDI and GLS using STE to detect pre-clinical impairment of diastolic and systolic functions in obese subjects with T2DM compared to cardiac function observed with conventional echocardiography (CE). Secondly, the strategy was to investigate whether echocardiographic parameters are related to metabolic abnormalities and to identify related increased risk of HF among these patients.

Subjects and Methods

The study complied with the Declaration of Helsinki and was approved by the Regional Committees for Medical and Health Research Ethics in Dibba Hospital –Al-Fujairah North Eastern Emirates, UAE. Informed consent was given by all study participants. This study recruited 214 obese patients (body mass index (BMI $\geq$ 30 kgm^2) with uncomplicated T2DM subjects (mean age = 50.2 ±12.4 years), 88 males and 126 females and 93 age-match healthy control subjects (mean age 48.5±11.6 years), 34 males and 59 females. All participants underwent both conventional echocardiography (CE) with GLS by STE and TDI. Measured Doppler parameters included isovolumic relaxation time, mitral E and A wave velocities, and deceleration time. TDI measurements included mitral annular early (Ea) and late (Aa′) diastolic velocities, calculated at the mitral annular septal velocities. To assess left atrial pressure (filling pressure of LV), the ratio of peak conventional mitral Doppler early diastolic flow velocity to mitral annular septal velocity (Ea) by TDI (E/Ea), was calculated in all patients enrolled in this study and healthy control subjects. In a subgroup of patients with DCM (n = 26) with mitral regurgitation (MR), maximal rate of pressure rise during ventricular contraction (peak dP/dt) was measured along with LVEF and GLS.

All participants underwent standard transthoracic echocardiography including TDI and STE (iE33; Philips) with a 1- to 5-MHz transducer. Chamber dimensions including left ventricle wall thickness and chamber sizes at end diastole and end systole. LVEF was estimated by the modified Simpson rule. Left atrium volumes were measured using the biplane area-length method. Left ventricular mass (LVM) in gram (g) was calculated automatically by the formula: 1.04 × [(LV end-diastole dimension + posterior wall thickness + inter ventricular septum thickness) 3 – (LV end-diastole dimension) 3] – 13.6 and indexed to height to the power of 2.7 (LV mass/h$^{2.7}$). STE analysis was performed offline using (Quantification, Philips software). GLS was calculated as the average of the negative longitudinal peak systolic strains (GLPSS) from 17 ventricular segments obtained from the apical 4-, 3-, and 2-chamber views and a line was traced along the LV endocardium. Around this line, the software selected natural acoustic markers moving with the tissues. Automatic frame by frame tracking of these markers during the heart cycle yielded a measure of contractility along the selected region of interest. Global strain values were automatically calculated by 3D-wall motion tracking for the entire length of LV myocardium in consecutive obese T2DM patients (n = 214) and controls (n = 93).

Statistical Analysis

Descriptive data are listed as mean ± standard deviation (SD) for continuous variables and as a percentage for discrete variables. Differences among the groups for baseline characteristics were compared using ANOVA. The collected data were tabulated and statistically analyzed using SPSS software statistical package version 26. Kruskal-Wallis test (1-way ANOVA) was used to compare mean values of studied groups if there were more than 2 groups. To compare 2 groups, the Mann-Whitney test was used. Wilcoxon singed rank test was used to compare mean values of ejection fraction (EF%) before and after intervention (medial ,device or surgical management). Categorical variables were represented as numbers and percentages. The Monte Carlo test was used as test of significance. The

level of significance was adopted at $p < 0.05$. In exploratory analyses, this study used forward and backward selection models to investigate the association of metabolic risk factors as continuous variables (systolic BP, waist circumference, fasting glucose, LDL cholesterol, and log-triglyceride level) with strain measures among obese- T2DM individuals.

Thirty one (14%) obese T2DM patients were studied separately and illustratively after proof of significant CAD or evidence of myocardial ischemia (>50% luminal diameter stenosis) by Rose questionnaire for functional studies and/or coronary angiography.

Results

The data in Table 1 show that females were more common and prevalent compared to males in both the groups among the 214 patients with obesity and diabetes and the 93 age-matched control subjects, As presented in Table 1, CAD and coronary risk factors including obesity, hypertension, T2DM, hypercholesterolemia and smoking tobacco were significantly ($p < 0.05$) more common among study subjects compared to controls. The results clearly reveal that women who have obesity, hypertension, diabetes and hypercholesterolemia suffered significantly ($p < 0.05$) more from chest pain compared to men. Clinical manifestations such as dyspnea and palpitation and drug therapy were also significantly ($p < 0.05$) more commonly administered in the study group compared to control group (see Table 1).

Regarding diastolic function indices, the results also show that cardiac function with CE was similar in the 2 groups (patients when compared to controls). Using TDI, diabetic obese subjects showed an evidence of diastolic function abnormalities in the form of lower Ea velocity (9.5 ± 2.9 vs. 18.4 ± 3.5 cm/s, $p < 0.0001$), an increased Aa velocity (16.5 ± 2.4 vs. 14.1 ± 2.2 cm/s, $p < 0.05$), higher left ventricular filling pressure in patients (E/Ea = 12 ± 4.4) versus control (8 ± 3.1), respectively, $p < 0.05$. and a reduced Ea/Aa ratio (1.00 ± 0.2) in patients vs. (1.45 ± 0.3, $p < 0.0001$), compared with age-matched healthy control subjects (Figure 1).

Transthoracic echocardiography- GLS were obtained in obese diabetic subjects compared to the 93 age-matched control subjects (Random blood sugar < 126 mg % and BMI < 25 kg/m^2) (Figure 2). This figure illustrates that GLS is highly correlated with maximum rate of LV pressure development (+ve dP/dt) although the LVEF is remaining normal and is of low sensitivity in detecting early intrinsic left LV myocardial contractility depression in diabetes induced dilated cardiomyopathy in comparison to systolic strain and (+ve dP/dt).

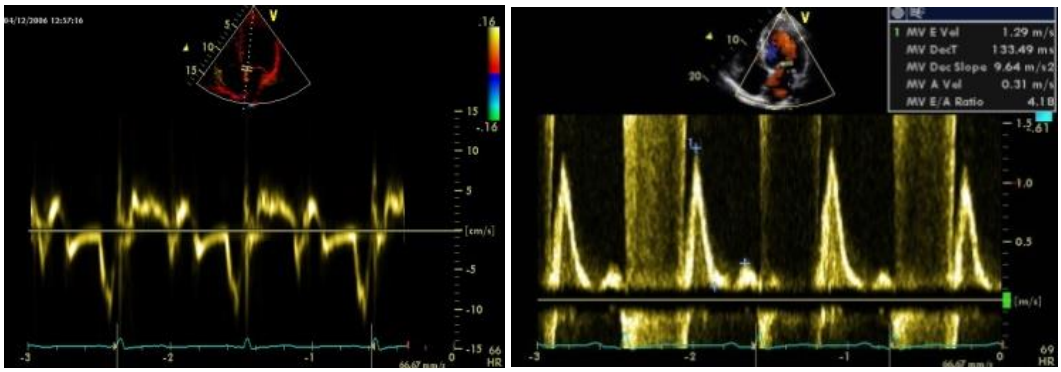
Table 1. General clinical characteristics and major risk factors for CAD in study group in comparison to control group

Risk Factors for CAD	Study group (n = 214)	Control group (n = 93)
Women, n(%)	126 (58.8)	59(63.4)
Men, n(%)	88(41.1)	34(36.55)
Mean age, years	50.2 ± 12.4	48.5 ± 11.6 years
Mean body weight, Kg	88.7 ± 7.3**	68.6 ± 4.3
BMI, Kg/m2	33.5± 3.3**	23.7 ± 2.3
Obesity, n (%)	214(100)**	10(10.7)
Hypertension	133 (62.15%)**	12 (12.9%)
Diabetes mellitus	214(100)**	0
CAD	31 (14.48%)**	0
Tobacco intake	20 (9.34 %)*	7 (7.5%)

CAD: Coronary artery disease; BMI: Basal metabolic index.
Data are expressed as mean ±SD;*p < 0.05 and **p < 0.01.

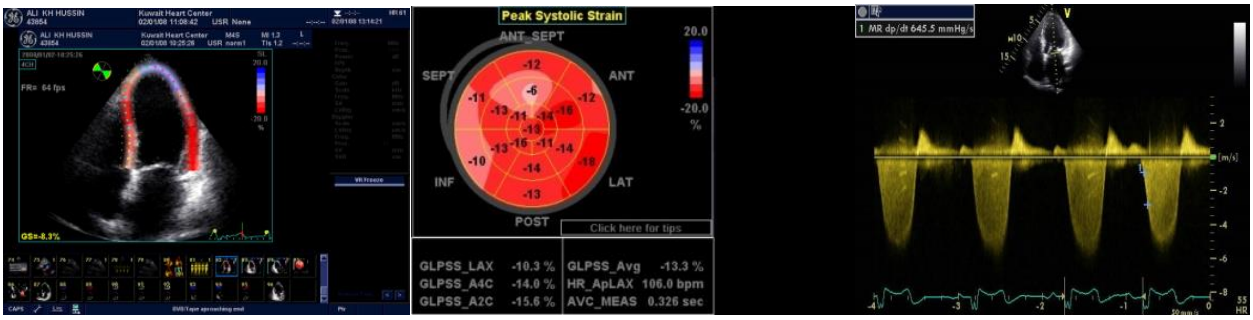
Interestingly, obesity T2DM women had increased left ventricular (LV) wall thickness (15.8 ± 2.1 mm*)* vs (11.1 ± 1.4 mm) in age-matched healthy controls, $p < 0.001$, the data also revealed that BMI correlated closely with LVM and wall thickness ($r = 0.624$, $p = 0.001$) (Figure 3).

Regarding, systolic function indices, the results from this study showed that severely obese subjects (BMI >35) had reduced LV systolic and diastolic function compared with healthy controls. This is demonstrated by lower average longitudinal peak systolic strain, and reduced (Ea), whereas LVEF remained normal (56.48% ± 8.81). Differences in regional and global strain were identified between the severely obese diabetic (BMI ≥ 35), (GLPSS (-13.5% ± 1.4)) and the age-matched healthy subjects (-19.54% ± 4.5; $p < 0.001$) (Figures 3-5).



(a) (b)

Figure 1. Tissue Doppler (left; A) shows reduced Ea (mitral annular septal velocity) in obese patient with T2DM for over 15 years, in the absence of any 2 dimensional echocardiographic or ECG abnormalities. On the right (B) Conventional mitral Doppler flow shows grade III/IV diastolic dysfunction. These images are typical for all the patients employed in this study.



(a) (b) (c)

Figure 2. Original images showing (A) longitudinal fibers responsible for long-axis contraction lie in the sub-endocardium which are particularly susceptible to the effects of fibrosis, ischemia or hypertrophy in apical 4 chamber 2-dimensional echocardiography with tracing the endocardium yielding GLS in one projection. (B) Bulls eye technique generated from apical 2,3 & 4 chamber views illustrated the impaired global longitudinal peak systolic strain (GLS) of -13% in DCM patient. (C) Rate of LV pressure development (+ve dP/dt) = 645mmhg/s. This figure illustrated that GLS is highly correlated with rate of pressure development of LV (dp/dt) although the LVEF is remaining normal and is of low sensitivity in detecting early intrinsic myocardial depression in diabetes induced cardiomyopathy (DCM) in comparison to global systolic strain and dp/dt These images are typical of several similar cases.

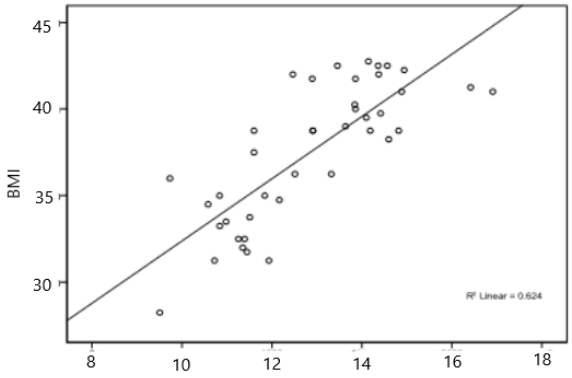
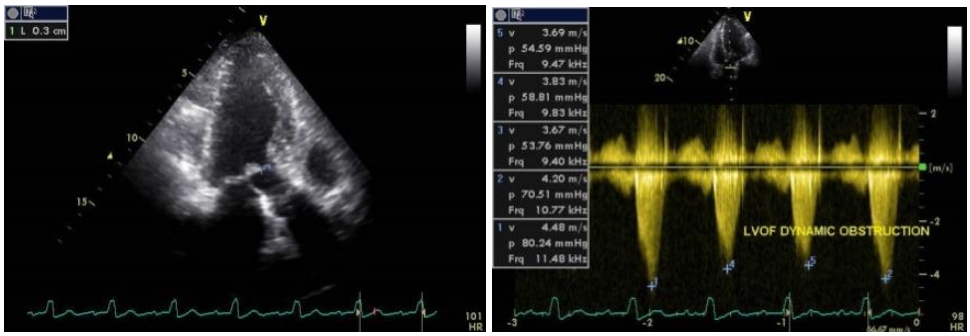
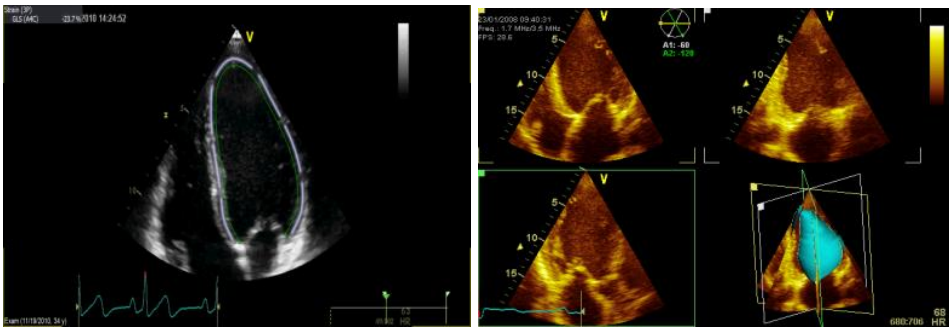


Figure 3. Correlation between body mass index (BMI) and LV wall thickness in the study group: Good positive correlation was shown between increased body weight (obesity-BMI) and left ventricular thickness, r = 0.624, p = 0.001.



(a) (b)

Figure 4. Original images of the heart of a 45 years old female patient who had T2DM (for 20 years) and arterial hypertension (last 5 years) with a BMI of 37 . The chocardiogram done immediately after admission to CCU with acute onset of progressive dyspnoea. Her echocardiography showed moderate a symmetrical septal hypertrophy and dynamic obstruction at LVOT (Max PG = 80mmHG), The mechanism is systolic anterior motion (SAM) of mitral valve. The data clearly reveal the develpment of hypertensive-induced hypertrophic obstructive cardiomyopathy in obese T2DM with LVH. The images are typical of several similar cases. .Dibba Hospital , UAE , Galal Eldin Nagib Elkilany.



(a) (b)

Figure 5. (a) Global longitudinal strain (GLS) Speckle tracking echocardiography (left) which can detect any early subtle systolic dysfunction among obese diabetic patients. (b) Three-dimensional echocardiography (right) of patient with T2DM-induced dilated cardiomyopathy. These images are typical on several similar cases. *GEN Elkilany.*

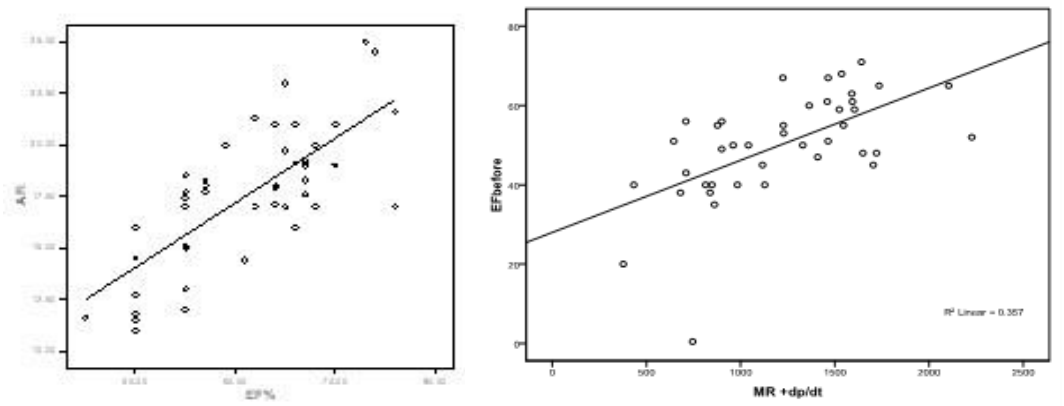
The depressed values of global longitudinal peak systolic strain (GLPSS) in apparently normal contracting hearts (EF≥50-55%) were highly suggestive of subtle LV myocardial systolic dysfunction which correlated significantly to the outcome in obese T2DM patients with LVH and impaired LV compliance, (r = .790, $p < 0.001$) compared to controls (see Tables 2).

The results presented in Table 2 showed a strong correlation ($r = .790$) and high significance of GLS ($p < 0.001$) and +ve dP/dt (<0.043) for prediction of outcomes in obese patients with diabetes induced cardiomyopathy (DCM).

Table 2. Comparison of mean and standard deviation of studied variables in relation to outcome in DCM patients before and after therapeutic intervention versus controls, *r=.790, *p< 0.001*

Subjects/outcome in relation to EF, GLPSS & dp/dt	EF% before intervention	EF% after intervention	GLPSS	dp/dt
Diabetic cardiomyopathy (n = 26) not improved	42.08 ± 13.96	35.06 ±10.10	-9.54 ± 4.50	849.9 ± 277.0
Obese diabetes (n = 214) improved	56.48 ± 8.81	61.96 ± 7.05	*-19% ± 4.5*	1504.9 ± 302.4
P value	0.010*	0.270	0.001**	0.043*

GLPSS = global longitudinal peak systolic strain, EF = ejection fraction, dp/dt = maximal rate of pressure rise during ventricular contraction. LVEF: Left ventricular ejection fraction measured by biplane technique 2 dimensional echocardiography, GLPSS: Global longitudinal systolic strain, dp/dt,: Maximum rate of LV pressure development measured from 1st and 3rd second of mitral incompetence slope by continuous Doppler flow. Data are presented as mean ±SD; * p < 0.01and *8p < 0.001.



(a) (b)

Figure 6. (A) Correlation between GLPSS and Three dimensional echocardiography (LVEF) among studied control with normal EF (r = 0.789, p < 0.05) which is indicative of strong positive significant correlation and (B) shows the correlation between EF % and MR +ve Dp/dt in DCM patients, r = 0.598, p = 0.001, which indicates good positive significant correlation).

In addition, maximal rate of LV pressure rise during isovolumic contraction phase (+ve dP/dt) and GLPSS differed significantly in a sub group of 26 symptomatic DCM and control subjects (peak dP/dt 849.9 ± 277; 0 mm Hg/s) and GLPSS (-9.54% ± 4.50) versus (1504.9 ± 302.4 mm Hg/s and -19.54 ± 4.5%), respectively, p < 0.001. These values could identify a subgroup of DCM patients (n = 26) at risk of future major cardiac events (heart failure hospitalization, depression of LVEF < 35%, cardiac arrest in need of pacing, (Table 2). Alternatively, patients who have normal values of LVEF (56.48% ± 8.81), GLPSS (-19% ± 4.5) and maximum rate of LV pressure development (+ve dP/dt = (1504.9 ± 302.4mmHg/s), showed a benign course and significant improvement of their symptoms without any cardiac intervention. These techniques had 88% sensitivity and 92% specificity for the detection of patients who may develop complications during follow up.

Discussion

The results of the present study have shown that cardiac function with conventional echocardiogram (CE) was similar in the 2 groups; (symptomatic obese T2DM patients compared to age-matched controls). However, with the help of TDI technique and GLS via STE, the results show that obese T2DM patients revealed an enlarged heart (LVH) which is correlated closely with BMI (Figure 3). Once DCM is developed, LVEF depression can be identified clearly by CE (2- and 3-dimensional echocardiography (2DE and 3DE)), +ve dp/dt and GLPSS (see Figure 6).

Similar findings have been reported by Lui et al. [8] who found that a contrast-enhanced cardiac magnetic resonance imaging can detect subclinical myocardial dysfunction in the early stages of T2DM [8]. These investigators, also reported that LV myocardial dysfunction was associated with impaired micro vascular coronary perfusion. Another study, using similar methods (TDI and GLS via STE) in obese patients, found sub-clinical differences in both systolic and diastolic functions, regardless of the presence or absence of metabolic syndrome (MS), although MS seems to be associated with worse diastolic dysfunction [9]. Compared with controls, metabolically healthy obese patients had lower GLS (−18.5 ± 2.8% in obese versus −20.8 ± 2.5% in controls), p ANOVA < 0.001, greater dyssynchrony and early diastolic dysfunction, supporting the concept that obesity per se may have adverse cardio-vascular effects regardless of MS or T2DM [9].

Furthermore, a study by Petrie [10] indicated that systolic displacement (motion of the atrioventricular plane or mitral annulus) and some myocardial velocities can be abnormal in some patients with diastolic heart failure (HF) [10]. These concordant results in the present study have been taken as evidence that heart failure is preceded by “subtle” systolic dysfunction and that “long-axis function” (GLS) can be impaired in diastolic HF. The

implication is that the HF syndrome is related to, if not, caused by these regional disturbances in long-axis function. Similar to the present study, Ringle et al. [11] reported a subclinical myocardial dysfunction in type 1 diabetes mellitus (T1DM) patients which can be detected by 2- and 3-dimensional STE (2D-STE and 3D-STE), independently of any other cardio-vascular risk factors [11]. They concluded that DCM progression was indicated by a mild decrease in longitudinal function at the follow-up, which is concordant with the present study [11]. Similar to the present study, the investigators demonstrated that diabetic patients had similar LVEF (60 vs 61%; P = NS) at base line, but impaired longitudinal function, as indicated by 2D-GLS (-18.9 ± 2 vs -20.5 ± 2; P = 0.0002) and 3D-GLS (-17.5 ± 2 vs -19 ± 2; P = 0.003). Finally, these authors concluded that diabetes induced cardiomyopathy (DCM) definitely leads to several changes in myocardial structure and function that are recognizable by STE imaging in the preclinical- asymptomatic stage and these parameters should be used for monitoring the progression of disease or the response to therapy [11].

Furthermore, clinical evaluation of symptomatic DCM patients can be supported by estimation of b-type natriuretic peptide (BNP) levels, which is of great help in distinguishing between cardiac and non-cardiac causes of acute dyspnea in the emergency department [12]. However, the guidelines emphasize that patients with high pre-test likelihood of HF may be referred directly for echocardiography [13]. This is due to the assessment that the degree of disease severity and progression among a symptomatic diabetic patients could not be assessed accurately by biomarkers as BNP [14].

Moreover, data presented in a sub-group of CAD patients in the present study have clearly demonstrated that GLS by 2D-STE can detect the acutely ischemic myocardium in diabetic patients presenting with acute chest pain which can be differentiated from DCM (Figure 7) [15].

The main imaging approaches for DCM identification have been demonstrated by Lorenzo-Almorós et al. [16]. These authors showed that several methodologies can be used for the evaluation of cardiac dysfunction in T1DM and T2DM patients. Either early, middle or late responses of DCM may be detected as outlined by Lorenzo-Almorós et al. [16].

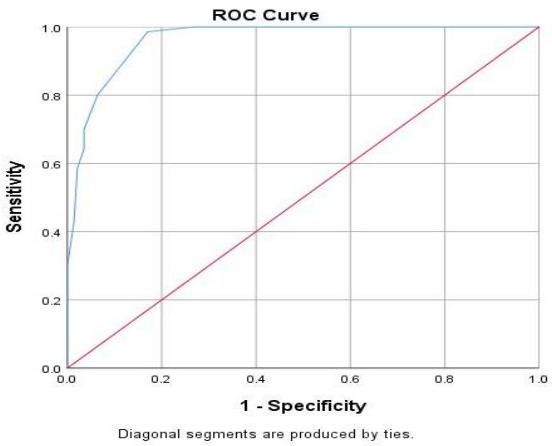


Figure 7. Recipient observer characterstic curve (ROC) showing the sensitivity and specificity of 2D Speckle Tracking Echocardiography [2DSTE] in detection of acutely ischemic myocardium in patients presenting with acute chest pain. Sensitivity & Specificity of GLS by 2D Speckle Tracking Echocardiography, showed a good sensitivity (80%) and specificity (93%). The data are mean for the recruited number of patients and controls (modified from ESC Preventive Cardiology 2020) permission from r Galal El Din Nagib El-Kilany (EUD ID: 53324); Diagnostic value of speckle-tracking 2d-echocardiogram in patients with acute chest pain and high risk of coronary artery disease.

Interestingly, in the present study it was observed that an early stage of cardiac dysfunction in either diabetes-induced cardiomyopathy or in metabolic cardiomyopathy can be quantitatively evaluated by LV myocardial deformation (GLS) and myocardial performance by dP/dt. The maximal rate of pressure rise during isovolumic LV ventricular contraction (peak +ve dP/dt) is a good index of ventricular performance as prescribed previously in the literature [17]. Peak dP/dt is sensitive to changes in contr-actility, insensitive to changes in afterload, and only mildly affected by changes in preload in comparison to LVEF which is sensitive to changes in after load and preload [17]. Moreover, both experimental and clinical studies have demonstrated that the STE method can assess myocardial function accurately in healthy subjects, in the settings of acute and chronic ischemia and diabetes–induced cardiomyopathy. Although, Edvardsen et al, reported before a systolic dysfunction in HF with normal ejection fraction by STE [18].There is no study published to date, to our knowledge, showing STE abnormal findings among obese T2DM patients.

Data from the present study indicate that GLS via STE and peak dP/dt can be used for accurate diagnosis of myocardial dysfunction in obese T2DM patients and progression to DCM, indicating its beneficial clinical use in prognosis. Interestingly, the present study revealed that a depressed value of maximum rate of LV pressure development, (+ve dP/dt) and GLS was highly correlated with depressed values of LVEF (mean value 35±10%) and major cardiovascular events in sub group of DCM patients (HF, need for pacing and cardiac death) at high sensitivity (80%) and specificity (92%), r = .790, $p < 0.001$ (see Table 2).

Recently, Mordi et al [19] did an interesting review of non-invasive imaging in diabetic cardiomyopathy. The article concluded that echocardiography is of crucial importance for clinical assessment of cardiac structure and function and moreover, it provides an excellent evaluation of subclinical LV dysfunction using systolic strain and diastolic function indices measurements, which is concordant to the present data outlined in this study. These investigators recommended a comprehensive echocardiography (CE) study with GLS and TDI which should certainly be considered as a key part in the evaluation of early DCM [19]. Finally, Wen et al [20] demonstrated a high sensitivity of area strain derived from 3D-STE (integrating longitudinal and circumferential deformation) in detecting early and subtle LV dysfunction in patients with risk factors of HF which is concordant to the present study [20].

In summary: It seems that both obesity and T2DM are major global public health problems currently affecting almost 2 billion people worldwide. Most of the patients usually die from CVDs and to a lesser extent kidney failure. As such, clinical efforts must be made to detect DCM and nephropathy as early as possible. If left, either undetected or untreated, the patients will experience a reduced quality of life and subsequently, may lead to early morbidity. Excess weight affects two-thirds of the U.S. adult population and increases the risk for the development of diabetes and subsequently CVDs and strokes. All patients should be screened for obesity and most should be screened for pre-diabetes and fully confirmed diabetes [1, 6]. The best treatment for diabetes is early identification and intervention in order to prevent the disorder. Prevention of T2DM can be accomplished through a 7% body weight loss through intensive lifestyle intervention changes that include caloric reduction via diet modification and approximately 30 min of daily moderate physical activity [7].

Conclusion

In brief, it is clear that early detection of subclinical myocardial dysfunction in obese diabetic patients can be done via STE and TDI, which may be important for early therapeutic interventions. Early diagnosis at the stage of pre-heart failure may either prevent or reverse heart failure, thereby improving the prognosis. An early stage of cardiac dysfunction and DCM or metabolic cardiomyopathy can be quantitatively evaluated via myocardial deformation (myocardial strain imaging) by STE, peak dP/dt and TDI.

In obese T2DM asymptomatic subjects either with or without MS, GLS by STE and TDI should be used as an initial screening tool for the diagnosis of subtle systolic and diastolic dysfunction, even in the presence of a normal cardiac function with CE (LVEF). Although extending non-invasive imaging by CE and GLS to all asymptomatic diabetic and obese people is currently not recommended for public, their great and valuable information on subclinical detection of early stage of LV myocardial dysfunction might preclude its limitations for the public.

Ethical Compliance

The authors have stated all possible conflicts of interest within this work. The authors have stated all sources of funding for this work. If this work involved human participants, informed consent was received from each individual. If this work involved human participants, it was conducted in accordance with the 1964 Declaration of Helsinki. If this work involved experiments with humans or animals, it was conducted in accordance with the related institutions' research ethics guidelines.

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