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Role of Mitral Annular Plane Systolic Excursion in Prediction of Left Ventricular Subclinical Systolic Dysfunction in Patients with Type 2 Diabetes: A Speckle Tracking Echocardiography Study

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Abstract

Background: Diabetes mellitus (DM) is a major risk factor for the occurrence of heart failure even in patients with preserved left ventricular ejection fraction (LVEF), we aimed to assess the usefulness of mitral annular plane systolic excursion (MAPSE) to predict subclinical left ventricular systolic dysfunction in patient with type II diabetes mellitus in comparison to global longitudinal strain (GLS) derived from speckle tracking echocardiography (STE).

Patients and methods: The study included 80 asymptomatic patients with type II DM, all of them had preserved LVEF > 50%, and 30 healthy subjects as a control group, echocardiography was performed to all patients and control group with measurement of the following parameters, MAPSE was measured using M-mode imaging in the apical four chamber view, GLS was measured using 2 dimensional STE, the ECG-gated images were obtained in apical long-axis, four- and two-chamber views

Results: The study included 80 patients, 42 of them were males, their mean age is 47.55 ± 5.54 years, MAPSE were significantly lower in patients (14.51 ± 2.13 mm) compared to control group (16.60 ± 1.67 mm) $p < 0.001$, the GLS was significantly lower in patients ($-15.85 \pm 2.79\%$) compared to control ($-21.95 \pm 2.84\%$), p value < 0.001 . MAPSE was linearly and strongly correlated to the GLS, and MAPSE value of 16.4 mm had (a sensitivity of 100% but its specificity is 73.2, AUC=0.887, PPP=48, NPP=100, P value < 0.001) when compared to the GLS in prediction of subclinical dysfunction.

Conclusions: MAPSE is a simple and rapid diagnostic tool in prediction of left ventricular subclinical systolic dysfunction in asymptomatic type II diabetic patients, and its strongly correlated to the gold standard STE derived global longitudinal strain.

Keywords: Mitral Plane Excursion, Speckle Tracking Echocardiography, Subclinical Dysfunction, Diabetes Mellitus

Introduction

Diabetes mellitus (DM) is a major risk factor for the occurrence of heart failure even in patients with preserved left ventricular ejection fraction (LVEF). This is known as diabetic cardiomyopathy. (1-3) Diabetic cardiomyopathy is currently defined as a diastolic dysfunction, however recent investigations have found that left ventricular (LV) longitudinal myocardial systolic dysfunction is the first marker of a preclinical form of diabetic cardiomyopathy in DM patients with preserved LVEF. (4-6) Two-dimensional speckle tracking echocardiography (STE) is an angle independent method that enables measurements of the global longitudinal strain (GLS), however STE requires a special software that is not available in every echocardiographic laboratory. (7-9) Thus, we aimed to compare usefulness of a more simple, rapid and available echocardiographic method in detecting early LV systolic dysfunction which is

the mitral annular plane systolic excursion (MAPSE) (10-11) to the GLS in patient with type II diabetes mellitus and with preserved LVEF.

Study population

The study is a prospective case control study, it included 80 asymptomatic patients with type II DM, all of them had preserved LVEF 50%, excluding those with hypertension, left bundle branch block, or conduction delay, atrial fibrillation, and paced rhythm, 30 healthy subjects were included as a control group.

Methods

An informed consent was obtained from all patients and control group. And the study was approved by the ethical committee. The study was carried between January 2017 to June 2017.

Baseline clinical and laboratory investigation

All patients and control group were subjected to full history taking including age ,gender, duration of diabetes , laboratory investigations including HbA1c, lipid profile.

Echocardiographic evaluation

Echocardiography was performed to all patients and control group using (Philips iE33) and the followings were measured:

- The LV end-diastolic dimensions(LVEDD), LV end systolic dimensions (LVESD), and LV EF (12)
- Pulsed wave Doppler of mitral inflow velocities were obtained to measure diastolic early filling velocity (E)wave and late diastolic velocity(A) wave, E/A ratio, and E wave. (12)
- Pulsed wave tissue Doppler imaging was obtained after placement of the sample volume at the level of the septal and lateral mitral annuli. From these recordings, myocardial systolic (Sa), early diastolic (Ea), and E/Ea ratio were measured and averaged. (12)
- MAPSE was measured using M-mode imaging in the apical four chamber view. The M-mode cursor was placed on the septal and lateral mitral annulus parallel to the LV walls , then both values were averaged(13).
- GLS was measured using 2 dimensional STE , the ECG-gated images were obtained in apical long-axis, four- and two- chamber views at the frame rate of 50–70 per second and stored digitally.

The endocardial border of the myocardium was traced automatically and corrected manually, if needed. Segmental strain was presented as a bull- eye map and GLS was automatically calculated(14).

Statistical analysis

Statistical analyses were performed by using SPSS system for Windows(version 20 Chicago, IL, USA), Continuous variables were presented as mean ± SD and were compared by Student’s t-test or Mann-Whitney U test for variables with or without normal distribution, respectively. Categorical variables were expressed as percentages and evaluated with a Chi square test or Fisher’s exact test . Correlations between variables were tested by using the Spearman’s correlation test. ROC analyses was performed and best cut off value was determined and at that point sensitivity and specificity were determined .The results were considered significant when the p value was less than 0.05.

Results

Baseline clinical and laboratory data

The study included 80 patients, 42 of them were males, their mean age is 47.55 ± 5.54years which was statistically non significant from the age of the 30 control subjects 47.55 ± 5.54years(p=0.825), the remaining baseline clinical and laboratory data is seen in **table 1**.

Table 1: baseline clinical and laboratory data of the studied groups

Parameter Mean ±SD	Cases (No= 80)	Control (No=30)	P
Age (years)	47.88 ± 5.93	47.55 ± 5.54	0.825
Gender (male)(No,%)	42(52.5)	14(46.6)	0.548
DM duration (years)	6.96 ± 4.18	-	-
Heart rate(bpm)	73.75 ± 7.50	72.25 ± 7.12	0.569
Systolic BP(mmHg)	118.12 ± 10.09	116.67 ± 10.73	0.691
Diastolic BP(mmHg)	73.33 ± 7.61	71.67 ± 8.35	0.553
Urea(mg/dl)	30.76 ± 3.26	29.20 ± 4.99	0.246
Creatinine (mg/dl)	0.85 ± 0.09	0.80 ± 0.10	0.128
HbA1C%	8.46 ± 1.85	5.53 ± 0.34	<0.001*
FBS(mg/dl)	157.71 ± 45.73	91.60 ± 6.48	<0.001*
PPG(mg/dl)	215.02 ± 58.04	121.05 ± 4.71	<0.001*
Total cholesterol(mg/dl)	199.91 ± 34.43	178.65 ± 11.92	<0.001*
LDL cholesterol(mg/dl)	99.26 ± 18.84	87.30 ± 7.09	<0.001*
HDL cholesterol(mg/dl)	44.79 ± 7.75	56.70 ± 4.13	<0.001*
TG(mg/dl)	175.60 ± 47.82	117.30 ± 12.35	<0.001*

BP: blood pressure;DM: diabetes mellitus; FBS:fasting blood sugar; HDL:high density lipoprotein; LDL:low density lipoprotein PPS:post pandial sugar;TG:triglycerides. *: Statistically significant at p ≤ 0.05

Echocardiographic data

The LVEF showed non significant difference between patients and control , however the E, Ea ,Sa, septal , lateral and average MAPSE were significantly lower in patients compared to control , the average MAPSE was (14.51 ± 2.13mm) in patients compared to control group (16.60 ± 1.67mm) p value <0.001, the A,Aa, E/

Ea was significantly higher in patients compared to control group as seen in **table 2**. Regarding STE the GLS was significantly lower in patients (-15.85 ± 2.79%)compared to control (-21.95 ± 2.84),p value <0.001as seen in **table 2, figure1**.

Table 2: echocardiographic data of the studied groups

	Cases (No= 80)	Control (No=30)	P
LVEDD(mm)	48.74 ± 1.51	48.85 ± 1.90	0.979
LVESD(mm)	30.11 ± 2.30	29.90 ± 2.47	0.724
LVEFEF(%)	67.16 ± 5.29	66.35 ± 5.30	0.601
E (cm/s)	70.28 ± 15.51	76.68 ± 9.14	0.021*
A (cm/s)	77.31 ± 14.60	65.96 ± 5.97	<0.001*
E/A	0.94 ± 0.41	1.16 ± 0.15	<0.001*
Sa(cm/s)	8.16 ± 1.47	9.85 ± 0.69	<0.001*
Ea(cm/s)	8.14 ± 2.01	14.48 ± 1.19	<0.001*
Aa(cm/s)	9.66 ± 2.37	7.35 ± 0.94	<0.001*
E/Ea	9.06 ± 2.45	5.29 ± 0.61	<0.001*
Septal MAPSE(mm)	13.70 ± 2.09	15.70 ± 1.72	<0.001*
Lateral MAPSE(mm)	15.39 ± 2.34	17.50 ± 1.79	<0.001*
Average MAPSE(mm)	14.51 ± 2.13	16.60 ± 1.67	<0.001*
GLS(%)	-15.85 ± 2.79	-21.95 ± 2.84	<0.001*

A: late diastolic velocity, Aa: late diastolic annular velocity, E: early diastolic velocity, Ea: early diastolic annular velocity, EF:ejection fraction, GLS: global longitudinal strain ,LVEDD:left ventricular end diastolic dimensions, LVESD: left ventricular end systolic dimensions ,MAPSE: mitral annular plane systolic excursion , Sa: systolic annular velocity. *: Statistically significant at p ≤ 0.05

Figure 1: 2D-speckle tracking echocardiography images for one of the diabetic patients, showing longitudinal strain in different segments of LV in apical 4,2,3 chamber views (image A,B,C respectively) and the Bull's eye showing the reduced global longitudinal strain (image D), the last image E shows MAPSE of the same patient at the lateral mitral annulus.

On correlation analysis we found that MAPSE was different parameters in the patient group, it was linearly and significantly correlated to, the LVEF($r=0.388$, $p<0.001$), Sa($r=0.715$, $p<0.001$), and GLS($r=0.789$, $p<0.001$) and negatively and significantly correlated to the duration of diabetes ($r=-0.713$, $p<0.001$), and to HbA1c ($r=-$

0.295 , $p=0.008$) in patients with type II DM. And by applying the multivariate analysis for the previous parameters we found that MAPSE was the strongest predictor of GLS in diabetic patients ($B=0.719$, 95% CI LL=0.384, UL=1.055, $P<0.001$). (figure2)

Figure 2: correlation between MAPSE and different parameters in patients group

To measure the sensitivity and specificity of MAPSE to predict subclinical left ventricular systolic dysfunction in type II diabetic patients the ROC curve was applied, and we found that MAPSE cutoff 16.4mm had(a sensitivity of 100% but its specificity is

73.2, AUC=0.887, PPP=48, NPP=100, P value <0.001) when compared to the GLS in prediction of subclinical dysfunction in type II diabetic patients. (figure3)

Figure 3: ROC curve showing the sensitivity and specificity of MAPSE to predict subclinical systolic dysfunction in comparison to GLS.

Discussion

In our study we found that MAPSE and GLS which are parameters for assessment of global longitudinal systolic function were reduced in diabetic patients with preserved LVEF, and MAPSE was strongly linearly correlated to the GLS, and MAPSE was the best predictor of GLS on multi regression analysis. Many studies evaluated the role of STE derived GLS in assessment of LV subclinical systolic dysfunction in diabetic patients, however a limited number of researches in literature were discussing the role of MAPSE in assessment of subclinical systolic dysfunction in diabetics.

Subclinical LV longitudinal systolic dysfunction in asymptomatic DM patients(role of GLS).

Causes of LV subclinical dysfunction in DM patients are microvasculopathy, myocardial hypertrophy and cardiac fibrosis(1). Abnormal calcium currents and reduced sensitivity of intracellular proteins to calcium result in impaired excitation-contraction coupling contribute to subclinical and clinical myocardial systolic dysfunction(15-17).

Many studies concluded that there is a sort of subclinical systolic dysfunction in diabetic patients with normal LVEF. Decrease in GLS has been consistently described as an early marker of myocardial involvement in diabetic patients and is considered as a gold standard technique for detection of subclinical systolic dysfunction. Ernande et al. prospectively studied 154 asymptomatic DM patients with preserved LVEF of $\geq 50\%$ without overt heart disease to evaluate the association of LV longitudinal function with LV remodeling, and showed that 23% of DM patients with preserved LVEF had LV longitudinal systolic dysfunction determined as $GLS < 18\%$ (18). diabetic cardiomyopathy is currently defined in terms of diastolic dysfunction, which is the earliest functional alteration in the course of diabetic cardiomyopathy(19,20), however Ernande et al. in another study proved the presence of LV longitudinal dysfunction in DM patients with preserved LVEF of $\geq 55\%$, as assessed by GLS, despite these patients' normal diastolic function. This indicates that diastolic dysfunction should not be considered the first marker of a preclinical form of diabetic cardiomyopathy(21). Nakai et al. studied 60 asymptomatic diabetic patients with normal LV ejection fraction (EF) and 25 age-matched healthy volunteers. They reported that GLS was reduced in DM patients when compared to normal subjects in presence of preserved LVEF, and showed LV longitudinal systolic dysfunction determined as $GLS < 17.2\%$, and concluded that In addition to diastolic dysfunction, subclinical LV longitudinal dysfunction is preferentially and frequently observed in asymptomatic diabetes patients with normal LVEF. The decrease in LS correlated with duration of diabetes. 2DSTE has the potential for detecting subclinical LV systolic dysfunction and might provide useful information of the risk stratification in an asymptomatic diabetic population(22).

Subclinical LV longitudinal systolic dysfunction in asymptomatic DM patients(role of MAPSE).

Left ventricular longitudinal shortening plays an important role in cardiac pump function and can be evaluated by measuring long axis, M-mode-derived technique which is MAPSE.(23,24)

MAPSE has been proposed as a well-established clinically useful echocardiographic parameter for the assessment of LV longitudinal function and correlates with global systolic function of the LV. (25,26) Although good imaging quality is required for most of echocardiographic techniques for good interpretation of LV systolic function, MAPSE in the majority of patients is quiet independent of imaging quality.

Regarding its linear correlation with the EF, MAPSE represents the amount of displacement of the mitral annular plane towards the apex and thus assesses the global change in size of the LV cavity (in the long-axis direction). Thus, it can be interpreted as the volume change during ejection and therefore a close association between the long-axis shortening and ejection fraction (EF) has been suggested in different patient groups with normal or reduced LV function.(27-31)

Regarding its linear correlation with the Sa, tissue Doppler systolic annular velocity provides a sensitive tool for detection of the global longitudinal LV function, Wenzelburger FW et al,(32) studied 62 with heart failure with preserved EF at rest and after cardiopulmonary exercises and found that at rest MAPSE correlated with peak systolic myocardial velocity ($r = 0.545$, $P < 0.001$), and on exercise with myocardial tissue velocities ($P < 0.001$), and concluded that MAPSE is a simple diagnostic tool for heart failure with preserved ejection fraction.

Regarding its linear correlation with the GLS, a good correlation between MAPSE and longitudinal strain at rest has also been shown in heart failure patients with normal or preserved LVEF as studied by Wenzelburger FW et al, (32) they found that at rest MAPSE correlated with longitudinal strain ($r = 0.432$, $P = 0.001$) and on exercise with LV apical rotation ($r = 0.582$, $P < 0.001$), longitudinal strain ($r = 0.589$, $P < 0.001$), in addition, Tsang et al. (33) recently propose that speckle-tracking-derived mitral annular displacement is a clinically useful tool for rapid, accurate, and robust estimates of LVEF irrespective of LV endocardial definition.

Loncarevic et al(34), studied 210 DM patients (group I: 70 asymptomatic DM patients without hypertension (HTA) and coronary artery disease(CAD)+; group II: 70 DM patients with HTA and no CAD; group III: 70 DM patients with CAD and no HTA) and 80 healthy individuals, comprehensive echocardiography including MAPSE and speckle tracking strain analysis, was done, MAPSE were significantly lower in all patients with DM compared to control, and further deteriorated in DM patients with concomitant CAD or HTA, peak global longitudinal strain was impaired in DM patients without HTA and CAD, compared to control. And concluded that DM has strong and independent influence on LV function that can be detected by conventional and speckle tracking echocardiography in everyday clinical practice, even in asymptomatic patients.

Conflicts of interest

The authors have no conflicts of interest to declare.

Conclusions

MAPSE is a simple and rapid diagnostic tool in prediction of left ventricular subclinical systolic dysfunction in asymptomatic type II diabetic patients, and its strongly correlated to the gold standard

STE derived global longitudinal strain .

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