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The determinants of deleterious effects of diabetes on the myocardium

Abstract

Background and Aims: Early discovery of diabetic heart disease is a dignified mission. Classic echocardiographic method is not sensitive to detect subclinical early LV systolic dysfunction. Early deleterious effects of DM on LV systolic function appeared longitudinally by speckle tracking. We aimed to uncover the determinants of deleterious effects of DM on the myocardium using echocardiographic indices, considering the duration of DM as well as the state of DM control.

Methods and Results: 52 diabetic patients were enrolled in two groups (Group I; uncontrolled DM with HbA1c â‰¥ 6.5%) and group II; controlled DM with HbA1c5years or 5years (-15.7ï,±2.8%). (t=8.9, p=0.05).

Conclusion: The duration of DM is strongly correlated with reduction of GLS and elevation of LV filling pressure. Poor glycemic control (HbA1c>6.5%), leads to reduction in LV GLS, which is associated with preclinical LV dysfunction and elevated LV filling pressure.

Keywords: diabetes mellitus, global longitudinal strain, speckle tracking

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Introduction

Early discovery of diabetic heart disease is a tough and dignified mission as necessary steps in life style changes and efficient medical interventions can delay or even prevent the subsequent development of heart failure.[1] Diabetics with apparent normal left ventricular systolic function are frequently associated with diastolic dysfunction.[2] Classic echocardiographic method is not sensitive at all to detect subclinical early LV systolic dysfunction.[2] Early deleterious effects of DM on LV systolic function appeared longitudinally by speckle tracking because sub- endocardial fibers, which are vulnerable to ischemia, have a longitudinal course.[3]

Aim: In absence of coronary artery disease, we aimed to uncover the determinants of deleterious effects of DM on the myocardium using classic and new echocardiographic indices, considering the duration of DM as well as the state of DM control.

Methods and procedures

The study populations have been selected from patients refereed to our echocardiography lab who are known to be diabetic. We excluded any patient with systolic dysfunction (EF<50%), proved ischemic heart disease (IHD); either positive stress test or abnormal coronary angiography. In addition, we excluded any significant valvular or congenital heart diseases, arrhythmias, hypertension, and patients with heart muscle diseases or pericardial diseases. 52 patients had fulfilled these criteria and we enrolled them in two groups (Group I; uncontrolled DM with HbA1c ≥ 6.5%) and group II; controlled DM with HbA1c<6.5%. Inside each group; we divided them according to the duration of DM into >5years or <5years DM as a cut off point to chronicity of DM.

Basic investigations including fasting blood sugar level "FBS", 2-hours postprandial blood sugar "2HPPBS", HbA1c level were done to all cases. All patients had undergone TTE using General Electric VIVID 9, Echo ultrasonography machine and M4S transducer, with a frequency of 1.5-4.3MHz. The traditional indices of cardiac function were calculated: classic left ventricular systolic function by Simpson method, left ventricular end diastolic (EDD), end systolic diameter (ESD) and Ejection fraction (EF) and fractional shortening (FS). Left ventricular diastolic function using pulsed Doppler in the apical four chamber view with the following variables have been recorded: maximum velocity of early mitral filling (E), maximum velocity of late mitral filling (A), ratio of early to late velocity (E/A). Tissue Doppler imaging (TDI) Diastolic function has been calculated by measuring average of (Ea) of anterior, inferior, septal and lateral of mitral annulus, average of (Aa) of anterior, inferior, septal and lateral of mitral annulus, Ea/Aa ratio and E/Ea ratio.[4]

Assessment of 2Dglobal longitudinal strain (GLS) by speckle tracking strain analysis: LV systolic GLS was measured in 3 apical views: 2-chamber view (anterior and inferior walls), 4-chamber view (poster-septum and lateral walls) and 3-chamber view (anterior-septum and posterior wall). Each wall was divided into 3 segments (basal, mid and apical). 17 segmental strain curves were plotted. LV systolic GLS was calculated as the average value of the 3 apical strain peak values at systole. Normal value of GLS is -19.7%.

Informed written consent was collected from every patient and then the experimental protocol and informed consents were approved by the institutional review committee of the faculty of Medicine, Zagazig University.

Statistical analysis: SPSS 19 for Windows was used for statistical analysis. Continuous variables are presented as mean± standard deviation (SD), and categorical variables as percentages. Comparison of categorical and continuous variables between the two groups was performed. Correlation was performed. A "p" value <0.05 was considered statistically significant.

Results

Demographically; there was no statistically significant difference between both groups concerning the age as it was 40.4±8.9 years in group I while it was 38.3±13.8 years in group II. There were 14 males (53.8%), 12 females (46.2%) in-group I versus 12 males (46.8%) and 14 females (53.8%) in-group II; this difference was also non-significant (X=0.3, p=0.57) (Table 1).

DM: In-group I; the duration of DM was 9.19 ±3.19years while it was 5.05 ±1.50years in-group II; this difference was statistically highly significant (t=3.86, p=0.001). Concerning the type of DM; statistically, there was highly significant difference between both groups as group I has 5 cases with DM type I (19.2%) and 21 cases with type II DM (80.8%) while in group II; 14 cases have type I DM (53.8%) and 12 cases have type II DM (46.2%); (X=6.7, p=0.01) (Table 1).

Blood Sugar: Regarding fasting blood sugar (FBS); there was no statistical significant difference between both groups; in-groupI, it was 138.6±69mg/dl while it was 102.5±65mg/dl in-group II (t=1.9, p=0.06). on the other hand; there was a statistical highly significant difference between both group concerning HbA1c as it was 8.41+1.77% in group I versus 6+0.45 % in group II (t=-6.7, p=0.000). The same for the 2hours postprandial blood sugar; it was 257.19+88mg/dl in group I versus 163.0+57mg/dl in group II (t=3.09, p=0.03) (Table 1).

Table 1 Clinical parameters of both groups

	Group I	Group II	(t)	(p)
Age (years)	40±8.9	38±13.8	7.4	0.32
Duration of DM (years)	9.19 ±3.19	5.05 ±1.50	3.86	0.001
FBS¥ (mg/dl)	138±69	102±65	1.92	0.06
2HPP BS× (mg/dl)	257±88	163±57	3.09	0.003
HbA1c	8.41± 1.77	6±0.45	-6.71	0
DM Type(I/II)	%	%	X	(p)
I	19.2	53.8	6.7	0.01
II	80.8	46.2		
Gender	%	%	X	P
Male	53.8	46.2	0.3	0.57
Female	46.2	53.8		

Conventional Echocardiographic parameters: There was no statistical significant difference between both groups concerning E/A ratio, EF and FS. E/A ratio was 1.01±0.32in-group I while it was 1.09±0.27in-group II (t=0.89, p=0.773). Ejection fraction (EF); was 65.7±9.89% in-group I while it was 67.3±5.9% in-group II (t=-0.81, p=0.312). Fractional shortening (FS); it was 34±8.5%in-group I while it was 36±5.8% in-group II (t=-0.74, p= 0.362). On the other hand; there was statistically highly significant difference between both group regarding the E/é; it was 11±2.9 in-group I while it was 8.5±2.6 in-group II (t=3.5, p=0.001) (Table 2).

Table 2 Echocardiographic parameters of both Groups

	Group I	Group II	(t)	(p)
E/Aα ratio	1.01 ±323	1.09±271	0.89	0.773
EFμ (%)	65.7 ±9.8	67.3±5.9	-0.81	0.321
FS© (%)	34±8.5	36±5.8	-0.74	0.362
E/éβ ratio	11±2.9	8.5±2.6	3.5	0.001
GLS® (%)	-15.5±2.8	-19±2.35	-4.78	0

E/Aα: Ratio Early Mitral Filling Velocity (E) to Late Mitral Filling Velocity (A), EFμ: Ejection Fraction, FS©: Fractional Shortening, E/éβ: Ratio Early Mitral Filling Velocity (E) to Early Tissue Doppler Velocity (é), GLS®: Global Longitudinal Strai.

Global longitudinal strain (GLS): There was a highly significant difference between both groups; it was -15.5±2.8% in-group I while it was -19.06±2.35%in-group II (t=-4.78, p=0.000) (Table 2). When we compare the GLS according to chronicity of DM; there was significant difference between those with DM<5years duration (n=23, GLS=-19.3±2.27%) and those with DM>5 years (n=29, -15.7±2.8%). (t=8.9, p=0.05).

Correlations: GLS had significant negative correlation with diabetic duration (r=-0.785, p=0.001), HBA1C level (r=-0.728, p=0.001), E/é ratio(r=-0.517, p= 0.001), two HPP blood sugar (r=-0.515, p=0.001). However, there was no significant correlation with E/A ratio (r=0.330, p=0.017), fraction shorting (r=0.295, p=0.034), Fasting Blood Sugar "FBS" (r=-0.306, p= 0.027), EF (r=0.358, P= 0.09) (Table 3).

Table 3 Correlation of GLS versus other parameters

	Item	(r)	(P)
GLS® Vs	DM duration	-0.785	0.001
	DM control	-0.728	0.001
	E/Aα	0.33	0.017
	E/éβ	-0.517	0.001
	2HPP B.S×	-0.515	0.001
	FBS¥	-0.306	0.027
	F.S©	0.295	0.034
	E.Fμ	0.358	0.09

E/Aα: Ratio Early Mitral Filling Velocity (E) to Late Mitral Filling Velocity (A), EFμ: Ejection Fraction, FS©: Fractional Shortening, E/éβ: Ratio Early Mitral Filling Velocity (E) to Early Tissue Doppler Velocity (é), GLS®: Global Longitudinal Strain, FBS¥: Fasting Blood Sugar, 2HPP BS×: 2 Hours Post-Prandial Blood Sugar.

Interestingly; whatever the status of blood sugar control; GLS was noted to decrease gradually with the more chronicity of DM. It was -20.1±2.25% when duration of DM <5years, Decreased to -17.2±1.4% when duration of DM (5-10)years, Decreased more to -12.9±2.8% when duration of DM (11-15)years and the lowest values if the duration of DM>15 years, it was -11.8±0.91%. This difference was highly significant (f=28.3, p=0.000) (Table 4).

Table 4 Different patterns of GLS in relation to duration of DM

Duration of DM	GLS	(f)	(p)
<5 year	20.1 ± 2.25	28.3	0
5-10 year	17.2 ± 1.4		
11-15 year	12.9 ± 2.8		
>15 year	11.8 ± 0.91		

Discussion

Implementing the new technology to discover the early deleterious effects of DM on the myocardium gained popularity nowadays. In our study, we tried as much as we can to unify the variables to study the DM effects alone on the heart. We found that there is no signifiant difference between both groups regarding the Age; this looks logic as excluding the aging effect on myocardium. We agreed with Arnold et al.,[5] who stated that there is no significant difference in age between diabetic patients and healthy if they were recruited and frequency matched for age, body mass index, and body surface area. This is walking in context with Sun et al.,[6] and Cognet et al.,[7] who emphasized the important role of aging in decline of GLS; they stated that GLS deteriorates at rest with aging in a healthy population, especially in basal segments which could be partly explained by a decline in coronary flow reserve with aging.

One of the most important notes is the significant decline of GLS with more duration of DM and the significant negative correlation of GLS with duration of DM. This agrees with Nakai et al.,[8] who stated that diabetic duration is the only independent predictor for GLS reduction. Some of the discrepancy with Zhang et al.,[9] who stated that diabetic duration is not important as mean duration in controlled group was 7years while it was 8 years in uncontrolled group. This apparent contradiction may be due to the different DM duration in our

cases as it was 9.19±3.19years in-group I (longer duration) while it was 5.05±1.50years in-group II (shorter duration).

Two important findings are noticed; first; the significant difference between both groups concerning GLS; being more impaired GLS with uncontrolled DM status (Group I), second is the significant negative correlation of GLS with HBA1C. These results are in concordance with Zhang et al.,[9] who found that only GLS, not circumferential or radial strain, showed a significant difference between the controlled DM group and uncontrolled DM group. Our results agreed also with Ernande et al.,[10] who stated that GLS slightly decreased in diabetics with HbA1c<6.5% but significantly deteriorated if the blood glucose level was not tightly controlled (HbA1c>6.5). This finding is explained by the fact that the innermost sub-endocardial layer of fibers significantly contributes to LV longitudinal function, and the sub endocardium is more susceptible to myocardial fibrosis, which is the hallmark of DM deleterious effects. This implies that GLS may be a sensitive indicator of preclinical LV systolic dysfunction in patients with DM, especially if uncontrolled blood glucose levels.[11]

An apparent contradiction is noticed with Nakia et al.,[8] who stated that no correlation between reduction of GLS and HbA1c. Actually, this is not a true contradiction as they compared healthy volunteers (not diabetics) with diabetic patients.

The occurrence of diastolic dysfunction with DM will actually raise the LV filling pressure. In our work, there was significant difference as regards to E/é ratio between both groups and we found that the reduction in GLS was strongly correlated with higher E/é ratio (advanced diastolic dysfunction). This agreed with Fang et al.,[12] who stated that septal E/é was significantly higher in controlled diabetic patients than in uncontrolled cases. However, this disagree with Arnold et al.,[5] who stated that no significant difference was seen concerning septal E/é ratio between the diabetic patients and healthy controls. The same disagreement with Zhang et al.,[9] who stated that despite higher E/é ratios were observed in patients with DM than in controls, but no significant difference was observed between the two DM groups. This difference resulted from the choice of patients by Arnold et al.,[5] and Zhang et al.,[9] as they recruited control persons who are not diabetics versus diabetic cases but all of our cases were diabetics.

Conclusion

Our work confirm that LVEF measured by classic echocardiographic method is not a sensitive indicator for the early detection of subclinical systolic dysfunction. 2D STE has the potential for detecting subclinical LV systolic dysfunction, and providing useful data for the risk stratification of an asymptomatic diabetic population. The duration of DM is strongly correlated with reduction of GLS and elevation of LV filling pressure. Poor glycemic control (HbA1c>6.5%), leads to reduction in LV GLS, which is associated with preclinical LV dysfunction and elevated LV filling pressure.

Recommendation

Wide spread application of 2DSTE to calculate GLS in all diabetic patients to detect as early as possible the deleterious effects of DM on myocardium. In addition, research should be directed towards new agents that can be capable of reducing or even reverse the DM deleterious effects on the myocardium.

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Conflicts of interest

Author declares there is no conflicts opf interest.

References

1. Galderisi M. Diastolic dysfunction and diabetic cardiomyopathy evaluation by Doppler echo. *JAM COLL Cardiol.* 2006;48(8):1548–1551.
2. Sanderson JE and Fraser AG. Systolic dysfunction in heart failure with a normal ejection fraction: echo-Doppler measurements. *Prog Cardiovascular Dis*. 2006;49(3):196–206.
3. Fang ZY, Yuda S, Anderson V, et al. Echocardiographic detection of early diabetic myocardial disease. *J Am Coll Cardiol*. 2003;41(4):611–617.
4. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr.* 2015;28(1): 1–39. e14.
5. Ng AC, Delgado V, Bertini M, et al. Finding from left ventricular strain and strain rate imaging in asymptomatic patients with type 2 diabetes mellitus. *Am J Cardiol* . 2009;104(10):1398–1401.
6. Sun JP, Lee AP, Wu C, et al. Quantification of left ventricular regional myocardial function using 2-D speckle tracking echocardiography in healthy volunteers - A multi-center study. *Int J Cardiol*. 2012;167(2):495–501.
7. Cognet Thomas, Paul-Louis Vervueren, Laurent Dercle, et al. New concept of myocardial longitudinal strain reserve assessed by a dipyridamole infusion using 2D-strain echocardiography: the impact of diabetes and age, and the prognostic value. *Cardiovascular Diabetol* . 2013;12:84.
8. Nakai H, Takeuchi M, Nishikage T, et al. Subclinical left ventricular dysfunction in asymptomatic diabetic patients assessed by two-dimensional speckle tracking echocardiography: correlation with diabetic duration. *Eur J Echocardiogr*. 2009;10(8):926–932.
9. Zhang X, Wei X, Liang Y, et al. Differential change of left ventricular myocardial deformation in diabetic patients: a three-dimensional speckle tracking echo. *J Am SocEchocardiogr.* 2013;26(5):499–506.
10. Ernande L, Bergerot C, Schnell F, et al. Impaired myocardial radial function in asymptomatic patients with type 2 diabetes mellitus: a speckle-tracking imaging study. *J Am SocEchocardiogr.* 2010;23(12):1266–1272.
11. Van Hoeven K, Factor SM. A comparison of the pathological spectrum of hypertensive, diabetic, and hypertensive-diabetic heart disease. *Circulation.* 1990;82(3):848–55.
12. Fang ZY, leano R, Marwick. Relation between longitudinal and radial contractility in subclinical diabetic heart disease. *ClinSci (Lond)*. 2004;106(1):53–60.