

The prevalence of Sub-Clinical Left Ventricle Dysfunction and Relevant Intensifying Factors in Type 2 DM Patients using Strain Echocardiography Indices

Mehdi Pishgahi¹, Rama Bozorgmehr^{2*}, Fatemeh Farahani³, Faezeh Soltani³, Minoo Haghshenas⁴

¹Interventional Cardiologist, Clinical Research Development Unit, Shohadaye Tajrish Hospital, Shahid Beheshti University of Medical Science, Tehran, Iran, ²Internist, Pulmonology Fellow Clinical Research Development Unit, Shohadaye Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran, ³Students Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, ⁴Internist, Shahid Beheshti University.

Correspondence: Rama Bozorgmehr, Internist, Pulmonology Fellow Clinical Research Development Unit, Shohadaye Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. E-mail: r.bozorgmehr@sbm.ac.ir

ABSTRACT

Background and objective: Diabetes Mellitus is the most prevalent metabolic disease in the worlds so that according to the World Health Organization (WHO), it is the latent epidemic disease. Type 2 DM patients are susceptible to left ventricle (LV) dysfunction and heart failure. The symptoms associated with LV dysfunction, especially in early stages, may be at the minimum level so that they can be attributed to other non-heart factors. The aim of this study is to evaluate sub-clinical LV dysfunction and relevant intensifying factors in type 2 DM patients. **Method of study:** This is a descriptive-analytical study (cross-sectional) study conducted on 107 type 2 DM patients with normal heart function according to previous echocardiography and electrocardiography reports. The demographic information of cases was first recorded and paraclinical evaluation results were collected. Then, LV function was measured using strain echocardiography with speckle method and the correlation of global longitudinal strain (GLS) results with demographic information and paraclinical test results was assessed. **Results:** The evaluation of the correlation of demographic features as well as paraclinical test results with the prevalence of sub-clinical LV dysfunction and global longitudinal strain in type 2 DM patients revealed that, the correlation of HbA1c>8% (p=0.004) and systolic blood pressure >160mmhg (p=0.007) with the prevalence of sub-clinical LV dysfunction is significant. This study show some relation but without significance between years of diabetes (in group of more than 10 years), BMI>35 and chronic alcohol user with GLS. **Conclusion:** The results of this study revealed that researchers should pay more attention to cardiovascular disorders in the process of treating type 2 DM patients with and inappropriate blood sugar control and blood pressure control. They should pay more attention to echocardiography with newer methods such as speckle strain echocardiography in order to early diagnose of heart disorders in this group of patients.

Keywords: Diabetes mellitus, echocardiography, global longitudinal strain, sub-clinical LV dysfunction.

Introduction

Diabetes mellitus is the most prevalent metabolic disease in the world so that according to the World Health Organization

(WHO), it is the latent epidemic disease. Type 2 diabetes accounts for 90% of total diabetes diseases in the world, which is originated from aging, obesity, lack of physical activity and prolonged age of diabetic patients. According to studies, diabetes increases the risk of heart failure and LV dysfunction, which may be associated with hypertension, obesity and coronary diseases ^[1]. Inappropriate blood sugar control is associated with abnormal LV relaxation, increased filling pressure and systolic retraction disorder ^[2]. In addition, it is observed that coronary micro-vascular disorder is prevalent in diabetic patients, in the absence of epicardial coronary stenosis ^[3]. The symptoms of LV dysfunction may be at the minimum level, especially in early stages, and they may be attributed to other non-heart factors. Inappropriate blood sugar control is

Access this article online

Website: www.japer.in

E-ISSN: 2249-3379

How to cite this article: Mehdi Pishgahi, Rama Bozorgmehr, Fatemeh Farahani, Faezeh Soltani, Minoo Haghshenas. The prevalence of Sub-Clinical Left Ventricle Dysfunction and Relevant Intensifying Factors in Type 2 DM Patients using Strain Echocardiography Indices. *J Adv Pharm Edu Res* 2018;8(S2):116-120.

Source of Support: Nil, Conflict of Interest: None declared.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

associated with LV dysfunction and improved blood sugar control can improve LV function.

Echocardiography is a non-invasive scanning tool that comprehensively evaluates the heart structure and functions. It is frequently used in the diagnosis of LV dysfunction. The appropriate use of the diagnostic value of echocardiography in managing LV dysfunction in type 2 DM patients can mitigate cardiovascular effects of this disease [4]. Strain echocardiography makes it possible to conduct a precious, angle-independent and systolic function location-specific assessment in LV. It is a superior technique by far for evaluating longitudinal strain of LV for diagnosing diabetes-related heart diseases [5]. Karagöz et al conducted a study to evaluate sub-clinical LV dysfunction with two-dimensional STE and to compare the prevalence of LV dysfunction in diabetic patients with and without retinopathy. They concluded that STE could serve as a new beneficial technique for determining sub-clinical LV dysfunction in DM patients [6]. Anderson et al conducted a study in 2010 using strain and tissue doppler imaging techniques and revealed that non-complicated type 2 DM patients suffer LV longitudinal systolic disorder and global diastolic disorders [7]. They used strain echocardiography with speckle and GLS index measurement to evaluate the heart function in order to diagnose the probable sub-clinical LV dysfunction and relevant factors in DM patients.

Method of Study

This is a descriptive-analytical (cross-sectional) study. The target population consisted of type 2 DM patients with no apparent cardiovascular disease and with normal heart function, according to previous test reports and their medical records. Samples were collected using conventional sampling method. Assuming a prevalence level of 10%, according to available references, confidence level of 95% and error level of 4.5%, the total number of samples was calculated to be 171. If the prevalence and error levels are considered 0.5 and 0.1, respectively, the number of sample size will be reduced to 97. This study evaluated 150 cases. Inclusion criteria were LVEF \geq 50, no record or symptom of heart diseases including coronary diseases, congenital or significant valve diseases, atrial fibrillation and apparent wall motion abnormality during echocardiography. When cases were selected, they were explained with the study objectives. The written consent of the cases who were interested in participating in the study was collected. The demographic, clinical and paraclinical information were collected and recorded using a researcher-made questionnaire. The questionnaire included different information including age, sex, years with diabetes (type and symptom intensity), and cardiovascular risk factors such as diabetes, hypertension, family history, hyperlipidemia, smoking, alcohol use, in-hospitalization diagnosis, and electrocardiogram, echocardiography and laboratory test findings. This study evaluated LV function using strain echocardiography with speckle method. Considering the

importance of echocardiography results, all cases underwent strain echocardiography with speckle test by a single cardiologist expert in echocardiography. Then, based on echocardiography report form, ejection fraction, GLS and GLSR were recorded in 6 intermediate segments of LV and their mean value was recorded. The data was introduced to SPSS to analyze the relationship of demographic and paraclinical information with GLS indexes and the sub-clinical LV dysfunction in DM patients.

Results

This descriptive-analytical study evaluated 107 type 2 DM patients (44.1% male and 55.9% female) who referred to Shohadaie Tajrish heart clinic from 2016 to 2017. Table 1 shows the demographic information of the cases:

Table 1: age, number of children and duration of hospitalization

variable	mean	STD	Min.	Max.
Age (year)	59.72	1.1	25	86
BMI	27.53	4.4	19.33	37.70
Years with diabetes (year)	11.61	9.8	1	34

In addition, this study evaluated the risk factors of cardiovascular diseases as well as factors affecting echocardiography results including smoking, addiction, alcohol, hypertension and family background in cardiovascular diseases.

Table 2: smoking, addiction, alcohol use, hypertension and family background in cardiovascular diseases

variable	(%)	
Smoking	+	23.4
	-	76.6
Addiction	+	2.9
	-	97.1
Alcohol use	+	19.7
	-	80.3
Hypertension	+	30.8
	-	69.2
Family background in cardiovascular diseases	+	26.5
	-	73.5

Moreover, the prevalence of long-term effects of diabetes was studied. Of the cases, 33.6%, 19% and 12.1% suffered diabetic neuropathy, nephropathy and retinopathy, respectively. The systolic and diastolic blood pressures of the studied cases were 143.26 ± 25.4 and 14.4 ± 85.63 , respectively.

In this study According to specified cut off in the measurement of GLS, 38.1% of patient have $GLS < 18$, others have $GLS > 18$.

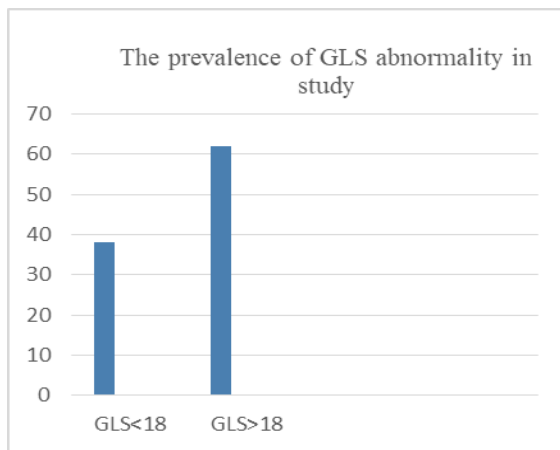


Chart 1:

Table 3 shows echocardiographic and laboratory test results.

Table 3: echocardiographic and laboratory test results

variable	Mean	STD
Ejection Fraction	57%	4.1
FBS	178.95	66.6
HbA1c	8.56	2.02
HDL	36.5	2.3
LDL	165.3	7.1
TG	175.5	8.7
Tchol	205	5.1

The main aim of this study was to evaluate the relationship of sub-clinical LV dysfunction with probable risk factors including BMI>35, systolic blood pressure>160, diastolic blood pressure>90, HbA1c>8 and years with diabetes>10.

Table 4 shows the relationship of GLS and demographic information of the cases including BMI, years with diabetes, systolic and diastolic blood pressure.

Table 4: relationship of GLS and demographic information of diabetic patients including BMI, years with diabetes, systolic and diastolic blood pressure

Variable	r	p-value
Age	-0.164	0.10
BMI	≥35	-0.479
	<35	-0.046
Years with diabetes	≥10	-0.177
	<10	-0.056
Systolic blood pressure	160<	-0.379
	160≥	-0.052
Diastolic blood pressure	90<	-0.144
	90≥	-0.075

Significance is shown by *

In addition, the correlation of smoking and alcohol consumption with GLS was assessed. Alcohol users were grouped to chronic and normal users (table 5).

Table 5: correlation of smoking and alcohol consumption with GLS

Variable	N	r	P value
smoking	Normal smoker	15	-0.046
	Heavy smoker	10	-0.127
Alcohol use	Normal user	14	-0.030
	Chronic user	7	-.673

Heavy smoker: a smoker who reports consuming 20 pack/year or more per day.

Chronic user was defined by using alcohol more than 5days a week in men and 3days a week in women.

Discussion

Today, diabetic cardiomyopathy is defined based on the diastolic function of the heart because according to observations, the diastolic disorder of the heart is the first functional change of diabetic observations and LV diastolic disorder is considered as an important diagnostic parameter [8].

The results of this study showed that GLS index shows the sub-clinical disorders of the heart. In DM patients, it has a significant correlation with systolic blood pressure>160mmHg (p=0.007), and poor control DM (Hb A_{1c}>8%) (P=0.008). This correlation implies that in type 2 DM patients, inappropriate blood sugar control, hypertension can increase the incidence of the sub-clinical disorders of the heart and prone the patients to clinically events and poor prognosis in future. Although BMI>35, chronic alcohol use and years with diabetes>10 didn't show any significant relation with GLS, but this study revealed some important relation of these factors with GLS in DM patients that may be other studies with more samples will show significant correlation between them. In DM patients, cardiovascular probable risks can be reduced by controlling the above-mentioned factors. Nakai et al reported that in DM patients GLS is significantly lower than that of normal people with the same age, despite having similar LVEF. In addition, 43% (60.26) of DM patients showed longitudinal systolic disorder in LV defined as GLS<17.2% [9]. Moreover, Ernande et al showed that 23% (154.36) of type 2 DM patients with fixed LVEF had longitudinal systolic disorder with GLS<18% [10].

Different factors have been introduced for the pathophysiology of LV longitudinal disorders in DM patients of which it can be referred to micro-vasculopathy, myocardial hypertrophy, and the heart fibrosis [11]. It has been recently stated that growth transforming beta factor, the differentiation of fibroblast cells due to hyper insulinemia and hyperglycemia-induced out-cell matrix adjustment disorder are causes generating the mechanisms of kidney and heart fibrosis and the incidence of the heart sub-clinical disorders in DM patients [12]. Ernande et al studied 154 type 2 DM patients with no symptom, with LVEF>50% and without chronic heart disease in order to evaluate the relationship of LV longitudinal function with LV remodeling. They reported that LV remodeling in patients with GLS<18% showed an increasing trend in a three-year follow-up while this trend was not observed in patients with GLS>18%. In addition, GLS has a direct relationship with diastolic and systolic volume changes in a three-year period [10].

LV diastolic function is influenced by many factors including age, blood pressure and LV hypertrophy. Ernande et al stated that LV longitudinal disorder is significantly observed in DM patients, despite having normal diastolic function and

LVEF>55%. Considering this finding, the researchers introduced a theory saying that diastolic disorder should not be considered as the first cardiographic marker of the heart sub-clinical disorders in DM patients ^[13]. There have been few studies on the relationship of the influential factors of the incidence and advance of the heart sub-clinical disorders in type 2 DM patients. Furthermore, other studies on the effect of high blood sugar and inappropriate control of diabetes on the heart disorders are in concordance with the results of this study where high blood sugar is accompanied by increased myocardial steatosis, and consequently by sub-clinical LV dysfunction ^[14]. Mochizuki et al obtained the same results and showed that high blood sugar imposes negative effects on LV function and decreases GLS. Other studies have obtained almost the same results ^[15]. For example, Vinereanu et al observed that the increased level of HbA1c in type 2 DM patients goes with the heart sub-clinical disorders ^[16].

Blood pressure was another factor showed a significant correlation with sub-clinical LV dysfunction in this study. The study of Ballo et al observed that patients who suffer diabetes and hypertension at the same time, show higher prevalence of sub-clinical disorders in 2D echocardiography compared to DM patients with no hypertension and their GLS level is significantly lower than DM patients with no hypertension ^[17].

Considering the above-mentioned results, it seems that inappropriate control of blood pressure in DM patients and suffering hypertension at the same time is an independent factor of decreased GLS level. It serves as a long-term prognosis of the heart functional disorders in the patients so that the prognosis of DM patients can be improved by controlling this factor.

In general, it can be concluded from the results of different studies that the pathogenesis of diabetic cardiomyopathy has no precise cause and is considered as a multi-factor cause. Defining that which demographic, clinical or laboratory attributes of DM patients are associated with LV longitudinal systolic myocardial disorder needs further investigations.

In this study has revealed some important relationship with Chronic alcohol user, long standing DM(>10y) and BMI>35 and GLS in diabetic patients. Although this factor didn't show any significant relationship with GLS but maybe other studies with more sample will show significant correlation between this factor.

References

- Fang ZY, Prins JB, Marwick TH. Diabetic cardiomyopathy: evidence, mechanisms, and therapeutic implications. *Endocr Rev.* 2004; 25:543-567.
- Fang ZY, Schull-Meade R, Downey M, Prins J, Marwick TH. Determinants of subclinical diabetic heart disease. *Diabetologia.* 2005; 48:394-402.
- Leung M, Leung DY. Coronary microvascular function in patients with type 2 diabetes mellitus. *EuroIntervention.* 2016; 11:1111-1117.
- Ng AC, Delgado V, Bertini M, et al. Findings from left ventricular strain and strain rate imaging in asymptomatic patients with type 2 diabetes mellitus. *Am J Cardiol.* 2009; 104:1398-1401.
- Leung M, Phan V, Whatmough M, Heritier S, Wong VW, Leung DY. Left ventricular diastolic reserve in patients with type 2 diabetes mellitus. *Open Heart.* 2015;2: e000214.
- Karagöz, T. Bezin, I. Kutlutürk, S. Külahçoğlu, I. H. Tanboğa, A. Güler, C. Y. Karabay, et al. Subclinical left ventricular systolic dysfunction in diabetic patients and its association with retinopathy: A 2D speckle tracking echocardiography study. 2015 May; 40 (Suppl 3): 240–246. Published online 2014 Sep 11. doi: 10.1007/s00059-014-4138-6
- Andersson Ch, Gislason GH, Weeke P, Hoffmann S, Hansen PR, Torp-Pedersen Ch, Peter Søgaard P. Diabetes is associated with impaired myocardial performance in patients without significant coronary artery disease. *Cardiovascular Diabetology* 2010, 9-3.
- From AM, Scott CG, Chen HH. The development of heart failure in patients with diabetes mellitus and pre-clinical diastolic dysfunction a population-based study. *J Am Coll Cardiol.* 2010;55(4):300–5.
- Nakai H, Takeuchi M, Nishikage T, Roberto M. Lang3, and Otsuji Y. Subclinical left ventricular dysfunction in asymptomatic diabetic patients assessed by two-dimensional speckle tracking echocardiography: correlation with diabetic duration. *European Journal of Echocardiography* (2009) 10, 926–932 doi:10.1093/ejehocard/jep097
- Ernande L, Bergerot C, Girerd N, Thibault H, Davidsen ES, Gautier Pignon-Blanc P, et al. Longitudinal myocardial strain alteration is associated with left ventricular remodeling in asymptomatic patients with type 2 diabetes mellitus. *J Am Soc Echocardiogr.* 2014;27(5):479–88.
- Bando YK, Murohara T. Diabetes-related heart failure. *Circ J.* 2014;78(3):576–83.27. Lan HY. Transforming growth factor-beta/Smad signalling in diabetic nephropathy. *Clin Exp Pharmacol Physiol.* 2012;39(8):731–8.
- Lan HY. Transforming growth factor-beta/Smad signalling in diabetic nephropathy. *Clin Exp Pharmacol Physiol.* 2012;39(8):731–8.
- Ernande L, Bergerot C, Rietzschel ER, De Buyzere ML, Thibault H, Pignonblanc PG, et al. Diastolic dysfunction in patients with type 2 diabetes mellitus: is it really the first marker of diabetic cardiomyopathy? *J Am Soc Echocardiogr.* 2011;24(11):1268–75. e1261.
- Rijzewijk LJ, van der Meer RW, Smit JW, Diamant M, Bax JJ, Hammer S, et al. Myocardial steatosis is an independent predictor of diastolic dysfunction in type 2 diabetes mellitus. *J Am Coll Cardiol.* 2008;52(22):1793–9.

15. Mochizuki Y, Tanaka H, Matsumoto K, Sano H, Toki H, Shimoura H, Ooka J, et al. Clinical features of subclinical left ventricular systolic dysfunction in patients with diabetes mellitus. *Cardiovascular Diabetology* (2015) 14:37 DOI 10.1186/s12933-015-0201-8
16. Vinereanu D, NICOLAIDES E, TWEDDEL AC, Christoph F. M^{ADLER*}, Ben HOLST*, Lucy E. BODEN et al. Subclinical left ventricular dysfunction in asymptomatic patients with Type II diabetes mellitus, related to serum lipids and glycated haemoglobin. *Clinical Science* (2003) 105, 591–599 (Printed in Great Britain)
17. Ballo P, Cameli M, Mondillo S, Giacomini E, Lisi M, Padeletti M, Bocelli A, Galderisi M. Impact of diabetes and hypertension on left ventricular longitudinal systolic function. *Diabetes Res Clin Pract.* 2010 Nov; 90(2): 209–215. Published online 2010 Sep 6. doi: 10.1016/j.diabres.2010.08.004.
18. Zieman SJ, Kass DA. Advanced glycation endproduct crosslinking in the cardiovascular system: potential therapeutic target for cardiovascular disease. *Drugs.* 2004;64(5):459–70.