Journal of Diabetes & Metabolism - Open Access

Research Article
OPEN ACCESS Freely available online
doi:10.4172/2155-6156.1000108

Left Ventricular Remodeling in Diabetic Patients with and without Hypertension

Ashraf M. Anwar[1,2*], Mansour M Mostafa[1] and Youssef F. M. Nosir[1,2]

[1]*Department of Cardiology, Al-Azhar University, Cairo, Egypt*
[2]*Department of Cardiology, King Fahd Armed Forces Hospital, Jeddah, Saudi Arabia*

Abstract

Aim: The current study was designed to assess left ventricular (LV) mass in patients with diabetes mellitus (DM) using 2-dimensional echocardiography (2DE).

Subjects and methods: The study included 165 patients (mean age 56.5 ± 12.5 years, 69.7% males) divided into 3 equal groups. I: included patients with DM only, II: included patients with hypertension only and III: included patients with both. Additional 35 normal subjects were added as control group. LV dimensions, wall thickness, systolic function and mass were assessed by 2DE.

Results: Compared to normal's, Group I and Group III patients showed significant increase of LV dimensions, wall thickness and mass (all p<0.0001). Comparison between Group I and Group III showed no significant difference in all values except for LV wall thickness which was significantly higher in Group III than Group I (1.3 ± 0.2 cm vs 1.4 ± 0.2 cm; p<0.006). In Group II patients, LV wall thickness, mass and mass index were significantly higher than in Group I (p<0.001) while LV dimensions showed no significant difference between both patient groups. All patients in Group I, II and III showed significant reduction in LV fractional shortening than normal's (28.6 ± 7.0 vs 35.7 ± 7.1; p<0.0001) with no significant difference between the three groups.

Conclusion: DM is an independent risk factor for the increased LV mass and impaired systolic function regardless of association with hypertension or not.

Keywords: Diabetes mellitus; Left ventricular mass; Left ventricular hypertrophy

Introduction

Left ventricular (LV) hypertrophy either defined by echocardiographic or electrocardiographic criteria has been shown to be a strongly independent risk factor for cardiovascular morbidity and mortality [1-3]. Hypertension and obesity have been regarded as the most common cause of increased LV mass in general population [4,5]. Diabetes Mellitus (DM) is a well known and important risk factor for cardiovascular mortality and morbidity. Several epidemiological investigators described the association between LV hypertrophy and impaired glucose tolerance [6,7]. The results of the studies that evaluated the relation between DM and LV mass are inconsistent [8-11]. 2-dimensional echocardiography (2DE) is the primary non-invasive diagnostic modality for the calculation of LV mass because it is cost-effective and offers real-time, high spatial and temporal resolution imaging for initial evaluation and follows up [12].

The aim of our study was to evaluate the effect of DM on LV dimensions, wall thickness and mass in both normotensive and hypertensive patients.

Subjects and Methods

Two hundred consecutive patients (mean age 56.5 ± 12.5 years, 69.7% males) (Table 1) were referred to cardiology clinic for the first time for cardiac assessment. Depending on the history, the patients were divided into 4 groups:

Group I: included 55 patients with DM only (25 males and 30 females).

Group II: included 55 patients with hypertension only (35 males and 20 females).

Group III: included 55 patients with DM and hypertension (22 males and 33 females).

Group IV: included 35 normal individuals with no hypertension and DM as control group (30 males and 25 females). All patients underwent the following:

Clinical examination

Detailed history and through clinical examination were performed. Hypertension was defined and graded according to ESC and ESH guidelines [13]. DM was defined according to European society of cardiology and European Association for the study of Diabetes [14].

Transthoracic 2DE examination

2DE was performed to all subjects with a commercially available ultrasound system (Philips Sonos 5500 with 3.5 MHz probe, Best, The Netherlands). Examination was performed by echo-technician while the patient in the left lateral decubitus position using both apical and parasternal views. The following M-mode parameters were measured: 1) LV systolic (LVSD) and diastolic (LVDD) internal dimensions, 2) Thickness of interventricular septum (IVS) and LV posterior wall (PW) at diastole, 3) LV fractional shortening (FS) by the standard equation: (LVDD – LVSD)/ LVDD, 3) LV mass using the corrected formula [15]:

***Corresponding author:** Dr. Ashraf Mohammed Anwar, MD Cardiology Department, King Fahd Armed Forces Hospital, P.O. Box: 9862, Jeddah 21159, Kingdom of Saudi Arabia, Fax: +966-2-6651868; E-mail: ashrafanwar2000@hotmail.com

Received September 14, 2010; **Accepted** October 20, 2010; **Published** October 22, 2010

Citation: Anwar AM, Mostafa MM, Nosir YFM (2010) Left Ventricular Remodeling in Diabetic Patients with and without Hypertension. J Diabetes Metab 1:108. doi:10.4172/2155-6156.1000108

LV mass (g) = 0.8 {1.04 x (LVDD + IVS + PW)^3 - (LVDD)^3} + 0.6, 4) LV mass index calculated by: LV mass/ body surface area and 5) left atrial (LA) dimension. The interpretation and analysis of echo studies were performed blindly with the study hypothesis and the type of patient group.

Statistical analysis

All data were presented as mean ± SD. Independent sample t-test was used for comparison between the three patients groups and normal group. Comparison between the groups was performed by analysis of variance (ANOVA) test. Frequencies are expressed by percentage with 95% confidence intervals. A single and multiple linear regression analysis with stepwise elimination were performed. LV mass was considered as the dependent variable and the independent variables included in the model were gender, age and the presence or absence of hypertension and DM. The level of significance was set to P <0.05.

Results

Baseline criteria

There were no significant differences between all groups regarding age, sex distribution and body surface area. Comparison between males and females showed no significant difference in LVDD, LVSD, LV wall thickness, LV mass and mass index except for age as the females were older than males. (Table 1) Changes in LV dimensions, wall thickness and mass (Table 2, Table 3).

Effect of DM in normotensive patients

Compared to normal's, Group I patients showed significant increase of LVDD and LVSD (5.7 ± 0.7cm, 4.2 ± 1.0 cm vs 4.7 ± 0.4cm, 3.0 ± 0.5cm respectively; p<0.0001). Values of LV wall thickness (IVS and PW) and mass were significantly higher in Group I than Group IV (all p<0.0001). The prevalence of increased LV wall thickness and mass was 45%.

Variable	Males (n= 139)	Females (n= 61)	P value
	Mean ± SD	Mean ± SD	
Age (yrs)	53.0 ± 11.6	64.6 ± 10.5	0.7
LA (cm)	4.3 ± 0.5	4.3 ± 0.5	0.9
LVDD (cm)	5.8 ± 0.6	5.6 ± 0.7	0.4
LVSD (cm)	4.2 ± 0.8	4.1 ± 0.9	0.8
FS (%)	28.5 ± 7.3	27.8 ± 8.1	0.6
IVS (cm)	1.4 ± 0.2	1.4 ± 0.2	0.6
PW (cm)	1.2 ± 0.1	1.2 ± 0.2	0.5
LV mass (gm)	439.9 ± 100.9	422.2 ± 102.0	0.8
LV mass index (gm/m^2)	306.9 ± 77.4	295.8 ± 79.5	0.9

Table 1: Comparison between males and females.

Variable	**G I** (n= 55)	**G II** (n= 55)	**G III** (n= 55)	**G IV** (n= 35)	P value
Gender Male **Female**	25 (46.5%) 30 (54.5%)	35 (63.6%) 20 (36.4%)	22 (40%) 33 (60%)	30 (54.5%) 25 (46.5%)	0.009
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age (yrs)	55.8 ± 12.8	59.6 ± 9.8	54.2 ± 14.0	55.5 ± 10.2	0.06
LA (cm)	4.3 ± 0.4	4.3 ± 0.5	4.2 ± 0.7	3.6 ± 0.4	0.000
LVDD (cm)	5.7 ± 0.7	5.7 ± 0.5	5.8 ± 0.7	4.7 ± 0.4	0.000
LVSD (cm)	4.2 ± 1.0	4.0 ± 0.6	4.2 ± 0.8	3.0 ± 0.5	0.000
FS (%)	27.0 ± 9.1	29.0 ± 5.7	28.2 ± 6.2	35.7 ± 7.1	0.000
EF (%)	49.5 ± 17.4	53.4 ± 11.1	49.9 ± 11.3	64.3 ± 12.8	0.000
IVS (cm)	1.3 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	1.0 ± 0.1	0.000
PW (cm)	1.2 ± 0.1	1.3 ± 0.2	1.2 ± 0.1	0.9 ± 0.1	0.000
LV mass (gm)	402.6 ± 96.5	462.1 ± 80.8	437.7 ± 116.2	211.9 ± 52.7	0.000
LV mass index (gm/m^2)	280.3 ± 71.5	325.2 ± 71.9	304.4 ± 84.3	149.1 ± 39.8	0.000

Table 2: Comparison between all patient groups.

Group		LA		LVDD		LVSD		FS (%)		LV mass	
		Mean diff	**P value**	**Mean diff**	**P value**	**Mean diff**	**P value**	**Mean diff**	**P value**	**Mean diff**	**P value**
I	**II**	-0.15	1.0	0.55	1.0	2.03	1.0	-2.18	0.8	-59.40*	0.006
	III	1.23	1.0	-0.38	1.0	0.17	1.0	-0.22	1.0	-35.09	0.3
	IV	7.06*	0.000	10.58*	0.000	12.01*	0.000	-8.21*	0.000	190.72*	0.000
II	**I**	0.15	1.0	-0.55	1.0	-2.03	1.0	2.18	0.8	59.43*	0.006
	III	1.38	1.0	-0.93	1.0	-1.85	1.0	1.96	1.0	24.34	1.0
	IV	7.22*	0.000	10.03*	0.000	9.98*	0.000	-6.03*	0.000	250.16*	0.000
III	**I**	-1.23	1.0	0.38	1.0	-0.17	1.0	0.22	1.0	35.09	0.3
	II	-1.38	1.0	0.93	1.0	1.85	1.0	-1.96	1.0	-24.34	1.0
	IV	5.84*	0.000	10.96*	0.000	11.83*	0.000	-7.99*	0.000	225.81*	0.000
IV	**I**	-7.06*	0.000	-10.58*	0.000	-12.01*	0.000	8.21*	0.000	-190.72*	0.000
	II	-7.22*	0.000	-10.03*	0.000	-9.98*	0.000	6.03*	0.001	-250.16*	0.000
	III	-5.84*	0.000	-10.96*	0.000	-11.83*	0.000	7.99*	0.000	-225.81*	0.000

*Significant mean difference

Table 3: Comparison between all groups using Post Hoc Tests.

Predictors	Unstandardized Coefficient		Standardized Coefficient	P value
	Beta	Std. Error	Beta	
Constant	751.94	87.14		0.000
Age	-1.52	0.75	-0.188	0.044
Gender	-18.31	17.48	-0.084	0.29
Hypertension	32.51	17.39	0.151	0.063
DM	-49.68	18.09	-0.233	0.007

Table 4A: Multivariate linear regression analysis.

Predictors	Unstandardized Coefficient		Standardized Coefficient	R	R^2	Adjusted R^2	P value
	Beta	Std. Error	Beta				
Hypertension	123.119	15.966	0.482	0.482	0.233	0.229	0.000
DM	55.721	17.74	0.219	0.219	0.48	0.43	0.002

Table 4B: Single linear regression analysis.

DM versus hypertension

In patients with hypertension only (Group II), thickness of IVS and PW were significantly higher than in patients with DM only (Group I) (1.5 ± 0.2 cm and 1.3 ± 0.2 cm vs.1.3 ± 0.2cm and 1.2 ± 0.1cm; $p<0.001$ respectively). LV mass and mass index were significantly higher also in Group II than in Group I (462.1 ± 80.8 g vs.402.6 ± 96.5 g; $p= 0.001$ and 325.2 ± 71.9 g/m^2 vs. 280.3 ± 71.5 g/m^2; $p=0.002$ respectively). LVDD and LVSD showed no significant difference between both patient groups. The prevalence of increased LV wall thickness and mass was 55%.

Effect of DM in hypertensive patients

Compared to normal's, Values of LVDD, LVSD, wall thickness (IVS and PW) and mass were significantly higher in Group III than Group IV (all $p<0.0001$).Comparison between Group I and Group III showed no significant difference in all values except for IVS thickness which was significantly higher in Group III than Group I (1.3 ± 0.2cm vs 1.4 ± 0.2cm; $p<0.006$). The prevalence of increased LV wall thickness and mass was significantly higher in Group III than both Group I and Group II (75% vs. 45% and 55%).

Regression analysis: (Table 4 (A and B) Multiple linear regression analysis was performed through including age, gender, presence or absence of hypertension and DM and considering LV mass as a dependent variable. As shown in (Table 4-A), age, hypertension and DM were independently associated with an increased LV mass (P: 0.04, 0.06 and 0.007 respectively). (Table 4-B) showed that when single regression analysis was performed including only hypertension and DM, both were significant statistically association with higher LV mass (P: 0.002 and 0.0001 respectively).

LV function and LA dimension

Compared to normals, all patients in Group I, II and III showed significant reduction in LVFS (28.6 ± 7.0 vs 35.7 ± 7.1; $p<0.0001$). LA was significantly larger in all patient groups than in normal's (4.2 ± 0.5 cm vs 3.6 ± 0.4 cm; $p<0.0001$). Comparison between the three patient groups (I, II and III) showed no significant differences in LVFS and LA dimension.

Discussion

It is widely acknowledged that increased LV mass is thought to increase cardiovascular risk through a series of unfavorable metabolic, functional and structural cardiac changes [16]. This explained the facts that an increased LV mass is a premier risk factor for cardiac events e.g. myocardial infarction and heart failure [1,2,17]. Accumulating data from experimental, pathological, epidemiological and clinical studies have shown that DM affects the cardiac function (systolic and diastolic) and structure independent of hypertension, coronary artery disease or any other known risk factors [18-21].

The current study aimed to evaluate the effect of DM on LV internal dimensions, systolic function and LV mass using conventional echocardiography. The study included 3 equal patients groups (DM without hypertension, Hypertension without diabetes and DM with hypertension) and described the changes in echo parameters in each group in comparison with the other groups and with normal individuals.

Struthers and Morris reported that LV hypertrophy was present in 30% of patients with type 2 DM independent of blood pressure or use of antihypertensive medication [22]. The prevalence of LVH increases with the severity of hypertension ranging from 38% to 72% [11]. Our results showed that the prevalence of increased LV wall thickness and mass in patients with DM (Group I) was comparable to those with hypertension (Group II) (45% and 55% respectively). In patients with both hypertension and DM (Group III), the prevalence became significantly higher (75%). Compared to normal individuals, LV mass was significantly higher in all 3 patient groups. When the 3 patient groups were compared with each other, no significant differences in LV wall thickness, systolic function and LV mass were detected.

Chinali [23] demonstrated the high prevalence of other cardiac abnormalities included LA dilatation, reduced midwall shortening and diastolic dysfunction in patients with metabolic syndromes. The prevalence was independent on demographics and individual components of metabolic syndrome [23].

De Simone [24] evaluated 12-year incident heart failure in 2740 participants without prevalent cardiovascular or severe kidney disease, at the time of the first exam of the Strong Heart Study cohort. They concluded that type 2 DM is a potent, independent risk factor for heart failure. Risk of heart failure in diabetic patients cannot be fully explained by incident MI and coexisting cardiovascular risk factors [24]. In the current study, DM was associated with lower LV-FS values than in normals regardless of associated hypertension or not. This finding is not restricted to specific age or sex groups. The current study showed an increased LA size in both diabetic patient groups (normotensive and hypertensive). It was explained as secondary effect to impaired LV systolic and diastolic dysfunction or as an impact of increased LV mass [25]. The cardiac abnormities are probably attributed to direct effect of DM on myocytes including replacement fibrosis caused by focal myocyte necrosis and increased interstitial fibrosis [18]. Many studies described the utility of tissue

Doppler imaging and speckle tracking for early detection of LV systolic and diastolic functions pre-clinically and even before the alteration of conventional 2D echocardiography [26-28].

Many studies [7, 19] described that the association between DM and cardiac abnormalities is more evident in women than men while other studies [6] excluded it. Our results showed that this association is equal in both women and men. This may be attributed to the small percentage of females included in the study.

Our findings may have clinical impact in treating and following up of patients with DM. It will be of great value for the treating physician to assess the parameters of LV hypertrophy and systolic function with the start of treatment and during follow up of diabetic patients with or without associated hypertension.

Study limitation

The study had many limitations including:

1) The number of patients with DM included is small that made the analysis of subgroups is not obtainable. For example differences between type 1 and 2 DM and differences between controlled and uncontrolled DM.

2) The study used the m-mode formula for calculation of LV mass while its calculation by 3-dimensional echocardiography was not performed. The 3D calculation is feasible and accurate; however both techniques (2D and 3D) measurements were moderately correlated [29].

3) The study used FS and EF as indicators of LV systolic function, while the tissue Doppler indices (tissue velocity, strain and strain rate) and speckle tracking were not included.

4) The study described the cardiac abnormalities with the first visit and no follow up data are available. However, to assess the progression or regression of these cardiac abnormalities in response to treatment, a large follow up study is recommended.

Conclusion

The prevalence and severity of increased LV wall thickness and mass in diabetic patients is independent of hypertension. Impaired LV systolic function was associated with DM which explains the increased risk for heart failure.

References

1. Valkili BA, Okin PM, Devereux RB (2001) Prognostic implications of left ventricular hypertrophy. Am Heart J 141: 334-341.
2. Brown DW, Giles WH, Croft JB (2000) Left ventricular hypertrophy as a predictor of coronary heart disease mortality and the effect of hypertension. Am Heart J 140: 848-856.
3. Sundstrom J, Lind L, Ärnlöv J, Zethelius B, Andrén B, et al. (2001) Echocardiographic and electrocardiographic diagnoses of left ventricular hypertrophy predict mortality independently of each other in a population of elderly men. Circulation 103: 2346-2351.
4. Majahalme S, Turjanmaa V, weder A, Lu H, Tuomisto M, et al. (1996) Blood pressure and variability, smoking and left ventricular structure in normotension and in borderline and mild hypertension. Am J Hypertens 9: 1110-1118.
5. Woodiwiss AJ, Libhaber CD, Majane OH, Libhaber E, Maseko M, et al. (2008) Obesity promotes left ventricular concentric rather than eccentric geometric remodeling and hypertrophy independent of blood pressure. Am J Hypertens 21: 1144-1151.
6. Devereux RB, Roman MJ, Paranicas M, O'Grady MJ, Lee ET, et al. (2000) Impact of Diabetes on Cardiac Structure and Function: The Strong Heart Study. Circulation 101: 2271-2276.
7. Ilercil A, Devereux RB, Roman MJ, Paranicas M, O'grady MJ, et al. (2001) Relationship of impaired glucose tolerance to left ventricular structure and function: The Strong Heart Study. Am Heart J 141: 992-998.
8. Verdecchia P, Reboldi G, Schillaci G, Borgioni C, Ciucci A, et al. (1999) Circulating Insulin and Insulin Growth Factor-1 Are Independent Determinants of Left Ventricular Mass and Geometry in Essential Hypertension. Circulation 100: 1802-1807.
9. Galvan AQ, Galetta F, Natali A, Muscelli E, Sironi AM, et al. (2000) Insulin Resistance and Hyperinsulinemia: No Independent Relation to Left Ventricular Mass in Humans. Circulation 102: 2233-2238.
10. Sundstrom J, Lind L, Nyström N, Zethelius B, Andrén B, et al. (2000) Left ventricular concentric remodeling rather than left ventricular hypertrophy is related to the insulin resistance syndrome in elderly men. Circulation 101: 2595-2600.
11. Palmieri V, Bella JN, Arnett DK, Liu JE, Oberman A, et al. (2001) Effect of type 2 Diabetes mellitus on left ventricular geometry and systolic function in hypertensive subjects: Hypertension genetic epidemiology network (HyperGEN) study. Circulation 103: 102-107.
12. Foppa M, Duncan BD, Rohde LE (2005) Echocardiography-based left ventricular mass estimation. How should we define hypertrophy? Cardiovas Ultrasound 3: 17.
13. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, et al. (2007) Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 28: 1462-1536.
14. Rydén L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, et al. (2007) Guidelines on diabetes, pre-diabetes and cardiovascular diseases: executive summary: The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur Heart J 28: 88-136.
15. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, et al. (1986) Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. Am J Cardiol 57: 450- 458.
16. Lorell BH, Carabello BA (2000) Left ventricular hypertrophy: pathogenesis, detection and prognosis. Circulation 102: 470-479.
17. Ghali JK, Liao Y, Simmons B, Castaner A, Cao G, et al. (1992) The prognostic role of left ventricular hypertrophy in patients with or without coronary artery disease. Ann Intern Med. 117: 831-836.
18. Fang ZY, Prins JB, Marwick TH (2004) Diabetic Cardiomyopathy: Evidence, Mechanisms and Therapeutic Implications. Endocr Rev 25: 543-567.
19. Rutter MK, Parise H, Benjamin EJ, Levy D, Larson MG, et al. (2003) Impact of Glucose Intolerance and Insulin Resistance on Cardiac Structure and Function: Sex-Related Differences in the Framingham Heart Study. Circulation 107: 448-454.
20. Mbanya JC, Sobngwi E, Mbanya DS, Ngu KB (2001) Left ventricular mass and systolic function in African diabetic patients: association with microalbuminuria. Diabetes Metab 27: 378-382.
21. Scognamiglio R, Casara D, Avogaro A (2000) Myocardial dysfunction and adrenergic innervation in patients with Type 1 diabetes mellitus. Diabetes Nutr Metab 13: 346-349.
22. Struthers AD, Morris AD (2002) Screening for and treating left ventricular abnormalities in diabetes mellitus: a new way of reducing cardiac deaths. Lancet 359: 1430-1432.
23. Chinali M, de Simone G, Roman MJ, Best LG, Lee ET, et al. (2008) Cardiac markers of pre-clinical disease in adolescents with the metabolic syndrome: the strong heart study. J Am Coll Cardiol. 52: 932-938.
24. de Simone G, Devereux RB, Chinali M, Lee ET, Galloway JM, et al. (2010) Diabetes and incident heart failure in hypertensive and normotensive participants of the Strong Heart Study. J Hypertens 28: 353-360.
25. Gerdts E, Wachtell K, Omvik P, Otterstad JE, Oikarinen L, et al. (2007) Left atrial size and risk of major cardiovascular events during antihypertensive treatment: Losartan Intervention for Endpoint Reduction in Hypertension Trial. Hypertension 49: 311-316.
26. Mogelvang R, Sogaard P, Pedersen SA, Olsen NT, Schnohr P, et al. (2009) Tissue Doppler echocardiography in persons with hypertension, diabetes, or

ischaemic heart disease: the Copenhagen City Heart Study. Eur Heart J 30: 731-739.

27. Gul K, Celebi AS, Kacmaz F, Ozcan OC, Ustun I, et al. (2009) Tissue Doppler imaging must be performed to detect early left ventricular dysfunction in patients with type 1 diabetes mellitus. Eur J Echocardiogr 10: 841-846.

28. Ballo P, Cameli M, Mondillo S, Giacomin E, Lisi M, et al. (2010) Impact of diabetes and hypertension on left ventricular longitudinal systolic function. Diabetes Res Clin Pract 90: 209-215.

29. Takeuchi M, Nishikage T, Mor-Avi V, Sugeng L, Weinert L, et al.(2008) Measurement of left ventricular mass by real-time three-dimensional echocardiography: validation against magnetic resonance and comparison with two-dimensional and m-mode measurements. J Am Soc Echocardiogr 21:1001-1005.