Original Article

Evaluation of left ventricular function in diabetics with ischemic heart disease

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Summary:

Background: Diabetes mellitus is a major risk factor for coronary artery disease, with a higher incidence of myocardial infarction and sudden death. Left ventricular dysfunction is difficult to diagnose and to differentiate into diastolic and systolic dysfunction on the basis of medical history, physical examination, electrocardiography (ECC) and chest radiography. Two-dimensional, M-mode, and Doppler echocardiography are excellent for diagnosing left ventricular dysfunction. M-mode echocardiography was used for diagnosing left ventricular systolic dysfunction, while Doppler echocardiography has become well accepted as a reliable, reproducible and practical noninvasive method for the diagnosis of left ventricular diastolic dysfunction.

Subjects and methods: eighty four (84) males, type 2 diabetic patients with ischemic heart disease, their mean age was 60 ± 7 years, in addition to fourty six (46) non diabetics again with ischemic heart disease matched for sex and age served as control were involved in this study. Each patient was subjected to medical history, clinical examination, blood pressure measurement, physical measurement, lipid profile estimation, ECG, chest x-ray, M-mode and Doppler echocardiography to assess their left ventricular function, whether they suffer left ventricular diastolic dysfunction or systolic dysfunction and or combined systolic and diastolic dysfunction.

Results: The result of this study demonstrated that diabetic subjects were more prone to develop ST elevation myocardial infarction and isolated diastolic dysfunction of impaired relaxation type (74%). However, echocardiography clarify that small percentage of those patient suffer an isolated systolic dysfunction (26%).

Conclusion: Higher percent of diabetic subjects suffer ST elevation myocardial infarction and they were found to develop diastolic dysfunction.

Key words: left ventricular function, diabetes mellitus, ischemic heart disease.

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Introduction:

Diabetes Mellitus (DM) is a major risk factor for coronary artery disease with a higher incidence of myocardial infarction (Ml) and sudden death. Re-infarction rate are even higher following MI in diabetics in comparison with non-diabetic subjects (1). It increases the cardiovascular death rate twofold in men and fourfold in women. Thus, individuals with DM have an increased incidence of ischemic heart disease. The etiology of this liability is probably multifactorial and includes factors such as accelerated atherosclerosis and myocardial cell dysfunction secondary to chronic hyperglycemia (2). Other risk factors for macrovascular diseases in diabetic individuals include dyslipidemia, hypertension, obesity, reduced physical activity, and cigarette smoking. Determinants of microvascular dysfunction in DM, such as hyperglycemia and insulin resistance, and other factors including sympathetic overdrive, endothelial dysfunction, and left ventricular hypertrophy of concentric remodeling contribute to the development of diastolic dysfunction. Systolic failure may be a further consequence because of impairment of both diastolic properties and coronary microcirculation (3). At the bedside diastolic dysfunction is difficult to diagnose and to differentiate from systolic dysfunction on the basis of medical history, physical examination, electrocardiography (ECG) and chest radiography. Two-dimensional and m-mode echocardiography are excellent for diagnosing systolic dysfunction, and Doppler echocardiography has became well accepted as a reliable, reproducible and practical noninvasive method for diagnosis and longitudinal follow-up of patients with diastolic dysfunction (4). This study was aimed to evaluate and assess the left ventricular diastolic and systolic function of diabetic patients with acute coronary syndrome (ST elevation myocardial infarction, non STEMI, angina, and unstable angina).

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Patients and Methods:

One hundred and thirty (130) males were involved in this study. They were classified as eighty four (84) subjects (patients group) with type 2 Diabetes Mellitus of more than 15 years duration proved to have ischemic heart disease with a mean age of 60 ± 7 years and fourty six (46) non diabetics again with ischernic heart disease matched for age (mean age 58 ± 8 years) served as control (control group). Each

subject was submitted for medical history, clinical examination, physical measurements (height, weight, and body mass index), blood pressure measurement, M-mode and Doppler echocardiography (Philips EnVisor 2005 2B with a transducer operating at 2.5-3.5 MHz), in addition to an ECG and chest X- ray. 5 ml of blood was withdrawn and send to the lab. of Baghdad-Medical City Teaching Hospital for lipid profile estimation. This study was conducted in the echocardiographic unit of Baghdad-Medical City Teaching Hospital and Iraqi center for heart disease, during the period between June 2007 and July 2008. Left ventricular internal dimensions at diastole (LVIDd) and systole (LVIDs), interventricular septum thickness, posterior wall thickness, ejection fraction (EF %) and fractional shortening (FS%) were measured, using M-mode echocardiography to assess left ventricular systolic function. While, the left ventricular diabolic function was determined by pulsed Doppler echocardiography that involved recordings of transmitral inflow velocities from a 2x2mm sample volume positioned at mitral valve leaflet tips traced along the black-white interface, to measure peak E and A wave velocities and their ratio (E/A ratio), E-wave deceleration time (DT) and isovolumic relaxation time (IVRT).

Statistical analysis: All calculations and analyses were performed using Statistical Package for the Social Sciences (SPSS version 11.5 for windows). Echocardiographic data was presented as mean ± Standard deviation (SD) for continuous variables. The student t-test was used to compare variables of patients with that of control. The level of statistical significance was defined as $P < 0.05$, which was obtained by comparing the calculated t-value to the tabulated t-value 95% confidence interval.

Results:

Anthropometric data and demographic characteristics of 130 subjects involved in this study are shown in table (1). It is clear from this table that there were no significant differences in age, height, weight, body mass index and blood pressure levels between the patients group and control. However, all subjects were non smokers, non obese, not hypertensive. Regarding the type of ischemia, the results of this study revealed that ST elevation myocardial infarction (STEMI) was present in 53% of diabetics (45 out of 84) when compared with 20% of diabetics who suffer non ST elevation myocardial infarction (non STEMI), 17% with chronic stable angina, and 10% with unstable angina.

Table 1: Anthropometric data and demographic characteristics of subjects involved in this study.

Parameter	Diabetics	Control	P value
Number (males)	N = 84	N = 46	……
Age (years)	60 ± 7	58 ± 5	0.134
Height (cm)	166.2 ± 8.1	165.9 ± 7.4	0.172
Weight (kg)	75.6 ± 5.4	74.7 ± 6.8	0.791
BMI (kg/m^2)	28.1 ± 1.4	27.8 ± 1.5	0.368
SBP(mmHg)	131 ± 6	129 ± 5	0.060
DBP (mmHg)	82 ± 3	81 ± 6	0.321

Values were expressed as mean ± SD.
P-values more than 0.05 were considered to be statistically not significant.
BMI = body mass index. SBP = systolic blood pressure. DBP = diastolic blood pressure.

Table 2 clarifies the comparison between diabetic patients and control with respect to lipid profile levels. Apart from the significant difference in HDL (P = 0.001), small differences in Triglycerides, Cholesterol, LDL, and VLDL values of diabetics when compared with that of non diabetic control subjects were noticed. However, these differences were not statistically significant ($P > 0.05$), which reflect matched lipid profile values.

Table 2: Comparison of the Lipid profile values between diabetics and control.

Lipid profile	Diabetics (n=84)	Control (n=46)	P value
Triglycerides (mg/dl)	188 ± 53	187±22	0.511
Cholesterol (mg/dl)	199 ±29	198 ±15	0.293
LDL (mg/dl)	121 ±13	119 ± 16	0.365
VLDL (mg/dl)	37 ±10	36 ± 4	0.486
HDL (mg/dl)	39 ± 2	42 ± 3	0.001*

Values were expressed as mean ± SD.
*** P-values less than 0.05 were considered to be statistically significant.**

The data obtained from table 3 illustrated several mitral inflow parameters that evaluate left ventricular diastolic function (diastolic filling and pressure); E wave represents early mitral inflow velocity, A wave represents mitral inflow velocity during atrial contraction, their ratio (E/A ratio), IVRT and DT. What was noticed from this table that there was a significant decrease in peak E velocity and E/A ratio ($P< 0.05$). While, there were a significant increase in peak A velocity, DT of E wave and in IVRT ($P < 0.05$). In addition to an increase in the PWT and IVST, these parameters might reflect the presence of left ventricular hypertrophy. Accordingly, diastolic dysfunction of impaired relaxation pattern involved an E/A ratio < 1 or DT > 24o msec. in patient less than 55 years old and an E/A ratio < 0.8 and DT > 24o

msec. in patient more than 55 years old, or an IVRT > 100 msec. (1, 12). Thus, those patients with such Doppler transmitral inflow and M-mode echo parameters suffer diastolic dysfunction. Consequently, in this study, 62 out of 84 (74%) diabetic patients with these findings were classified to have an isolated diastolic dysfunction. When the Echocardiographic parameters values of the remained twenty two (26%) diabetic patients and that of control were compared, table 4 demonstrated that there were a statistically significant increase in LVIDd and LVIDs ($P < 0.05$). In addition, there were a statistically significant decrease in EF% and FS% ($P < 0.05$), with a non significant decrease in IVST and PWT ($P > 0.05$). However, systolic dysfunction was defined by EF% <50% and FS% < 25% (5). This means that those patients developed an isolated systolic dysfunction since they have these M-mode echo values in addition to the normal Doppler transmitral inflow parameters (peak E velocity and E/A ratio, DT of E wave and IVRT).

Table 3: The comparison of echocardiographic parameters between diabetic patients with diastolic dysfunction and control subjects.

Echocardiographic Parameters	Diabetics With DD (n=62) Mean ± SD	Control (n=46) Mean ± SD	P value
LVIDd (cm)	4.80 ± 0.32	4.77 ± 0.35	0.230
LVIDs (cm)	2.82 ± 0.36	2.79 ± 0.34	0.200
IVST (cm)	1.18 ± 0.61	0.89 ± 0.13	0.0001*
PWT (cm)	1.14 ± 0.87	0.88 ± 0.11	0.0001*
Fractional shortening (FS %)	39.87 ± 4.42	39.47± 5.33	0.637
Ejection Fraction (EF %)	68.43 ± 6.77	69.41± 6.08	0.160
Peak E velocity (cm/s)	72.12 ±16.60	79.38 ± 4.53	0.002*
Peak A velocity (cm/s)	102.04 ±14.6	64.54 ± 6.29	0.0001*
E/A ratio	0.70 ± 0.13	1.23 ± 0.13	0.0001*
D time of E wave (msec.)	244.60 ± 28.2	180.13 ± 11.7	0.0001*
IVRT (msec.)	146.37 ± 16.3	100.84 ± 6.87	0.0001*

Values were expressed as mean ± SD.
*** P-values less than 0.05 were considered to be statistically significant.**
DD = diastolic dysfunction

Table 4: Comparison of echocardiographic parameters between diabetic patients with systolic dysfunction (sd) and control subjects.

Echocardiographic Parameters	Diabetics with sd (n=22)	Control (n=46) Mean ± SD	P value
LVIDd (cm)	5.93± 0.42	4.77 ± 0.35	0.0001*
LVIDs (cm)	4.56 ± 0.75	2.79 ± 0.34	0.0001*
IVST (cm)	0.84 ± 0.13	0.89 ± 0.13	0.133
PWT (cm)	0.85 ± 0.14	0.88 ± 0.11	0.309
Fractional shortening (FS %)	22.84± 4.76	39.47± 5.33	0.0001*
Ejection Fraction (EF %)	34.28± 4.38	69.41± 6.08	0.0001*
Peak E velocity (cm/s)	81.16 ± 4.71	79.38 ± 4.53	0.206
Peak A velocity (cm/s)	62.85 ± 5.79	64.54 ± 6.29	0.373
E / A ratio	1.28 ± 0.12	1.23 ± 0.13	0.148
D time of E wave (msec.)	178.57±7.49	180.13± 1.77	0.444
IVRT (msec.)	102.46±7.04	100.84 6.87	0.581

Values were expressed as mean ± SD.
***P-values less than 0.05 were considered statistically significant. sd= systolic dysfunction.**

Discussion:

Diabetes mellitus influences the myocardium mainly through macro- and microangiopatlny. Metabolic disturbances cardiac autonomic neuropathy and frequently coexisting hypertension. These complications can seldom be found in an isolated form in individual patient, often overlapping and potentiating each other (6). Hence, the importance of assessment of left ventricular functions of diabetic patients with coronary artery disease in order to reduce the effect of diabetes on cardiac function, M-mode and Doppler echocardiography are known to be very important for providing evidence about systolic and diastolic performance of ischemic heart in diabetics. In order to exclude the possibility that differences in the results between patients and control groups were caused solely by differences in age, BMl, blood pressure level, and lipid profile values, comparison was made between both groups involved in this study matched for age, BMI, and lipid profile, however they were nonsmokers (Table 1, 2). Thus it is possible to exclude the possible effect of these factors on the result. Specifically, the BMI was less than 28.1 kg/ m^2, where BMl of 30 kg/m^2 is used as a cutoff for obesity with its risk for the development of complication of ischemic heart including left ventricular diastolic dysfunction (7). Moreover, the guideline of seventh report of the joint National Committee in 2003 (JNC/7. 2003), provide a new category of Bp levels, as normal, prehypertension, and hypertension (stage 1 and stage II). Consequently, all subjects involved in this study were considered as prehypertensives (8), since that their BP level fluctuate between 120-140 mmHg systolic and less

than 90 mmHg diastolic. While, blood pressure levels of both groups were matched, the additional pathological effect of blood pressure level on left ventricular functions was excluded too. The same thing applied regarding lipid profile levels, where the result of this study revealed matched lipid profile levels of both group (table 2). From the results of the present study, high percentage of diabetic patients (74%) who developed diastolic dysfunction are those with myocardial infarction with respect to smaller percentage (26%) of those who found to have systolic dysfunction (9, 10). Left ventricular diastolic dysfunction is more common following Ml in diabetic patients. Meanwhile, acute myocardial infarction is characterized by regional myocardial damage that may lead to systolic and/or diastolic dysfunction. In addition, myocardial ischemia, cell necrosis. Microvascular dysfunction and regional wall motion abnormalities will influence the rate of active relaxation of the ventricles, Moreover, interstitial edema, fibrocellular infiltration, and scar formation will directly affect LV chamber stiffness. These issues proved to be significant factors in the development of abnormal left ventricular filling and hence left ventricular diastolic dysfunction (11). From the results of the present study (table 3), the significant statistical decreases in peak E velocity, E/A ratio and the significant increases in peak A velocity, DT of E wave and in IVRT, reflect that these pateints had mild diastolic dysfunction of the left ventricle which represents the earliest stage of diastolic dysfunction that involved impaired LV relaxation with initially normal LV filling pressures. Consequently, this impaired relaxation might lead to decreased early filling (E wave) and increased filling with atrial contraction (A wave) in which that the mitral inflow patterns show an E/A less than I, the IVRT is prolonged (>100 msec.), with prolongation of DT > 200 msec, (12). Furthermore, the compensatory hyperdynamic response of the remaining non-ischemic myocardium has, however, has been shown to be impaired, this might be a reflection of the diabetic systolic and diastolic myopathy (diabetic cardiomyopathy) induced by altered cellular calcium balance and exacerbated by accelerated ventricular hypertrophy (13). Moreover, as it was noticed from table 2, in diabetic patients, the significant higher values of left ventricular posterior wall thickness and interventricular septal wall thickness reflect the development of left ventricular hypertrophy (LVH). The development of LVH within the diabetics is due to the sequence of biologic events that lead to the increment in the LV mass due to increased stress that lead to deformation and alterations matrix metalloproteases enzyme expression and activation (14). Determinants of microvascular dysfunction in DM such as hyperglycemia and insulin resistance, and factors including sympathetic overdrive, endothelial dysfunction and left ventricular concentric remodeling, also contribute to the development of diastolic dysfunction. Likewise, Diastolic dysfunction has been recognized during the early as well during the post-MI phase with or without left ventricular systolic dysfunction. In the acute phase of Ml both an abnormal relaxation pattern and restrictive left ventricular filling pattern are present. Abnormal relaxation filling, is the most pronounced filling pattern after one year post MI which might be related to the remodeling process including compensatory hypertrophy, scarring of the infarct zone leading to a non-uniform relaxation of the left ventricle. Left ventricular remodeling process following the very early phase post Ml includes the scarring process with collagen deposition in the infracted and non-infracted myocardium (15, 16). The association of DM with Ml in the development of diastolic dysfunction and or systolic dysfunction suggest the following mechanisms for diastolic dysfunction in patients with diabetes; excessive myocardial fibrosis, interstitial accumulation of glycoproteins, slow sarcoplasmic reticulum calcium reuptake, or altered release from a dysfunctional coronary endothelium of mediators such as nitric oxide and endothelin. Furthermore, diabolic dysfunction is likely the result of both accumulation of collagen and myocyte injury in the heart. This may explain the greater prevalence of diastolic dysfunction in type 11 diabetes, because aging-related increments in cardiac collagen are likely additive, although less satisfactory glycemic control may be an important factor as well (15, 17) . On the other hand. As it was mentioned earlier, the Doppler transmitral flow parameters reflect the diastolic dysfunction, since that the remained 26% of diabetic patients (table 4) discovered to have only systolic dysfunction using M-mode echo parameters, therefore there were no significant statistical differences of Doppler transmitral flow parameters when compared with those of control group. These results reflect the effect of ischemia on the development of diabolic dysfunction, which may coexists in patients with systolic dysfunction (18). Because systole and diastole are closely coupled in the cardiac cycle, it is possible that functional abnormalities of intracellular calcium handling and the interaction of rnyofilament resulting in diastolic abnormalities also affect systolic function (19). Because the severity of systolic and diastolic dysfunctions occurs in a continuous spectrum, some patient may have more dominant features of diastolic dysfunction or diastolic heart failure, whereas the others have combined systolic and diastolic dysfunction. In addition, left ventricular systolic dysfunction is a common and more frequently observed in diabetic men than in women. The majority of patients with left ventricular systolic dysfunction shows none of the cardinal symptoms or signs of heart failure and can be regarded as having asymptomatic left ventricular systolic dysfunction (20).

Conclusion:

This study conclude that higher percent of diabetic patients with coronary artery disease developed an isolated left ventricular diastolic dysfunction as compared to those diabetics who were found to have an isolated left ventricular systolic dysfunction. In addition, most diabetics herein suffer ST elevation myocardial infarction with respect to other type of acute coronary syndrome (non STEMI, unstable angina, stable angina).

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