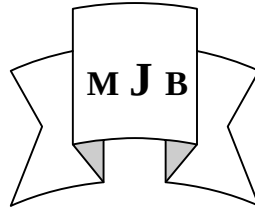


## Left Ventricular Dysfunction in Diabetes Mellitus Echocardiographic Study

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### **Abstract**

Diabetes mellitus induces a pattern of myocardial pathology known as a specific diabetic cardiomyopathy and to evaluate the presence of this phenomenon we measured various parameters of left ventricular function by echocardiography as it is available in merjan teaching hospital , and these parameters including :

1. Ejection fraction
2. Fractional shortening
3. Inter-ventricular septal thickness
4. Posterior left ventricular wall thickness

The results of our study show that diabetic patients have left ventricular dysfunction as compared with control group by a reduction in EF and FS and increase in the thickness of (IVS) and (pw) of the left ventricle.(The results are statistically significant,  $P < 0.005$ ).

Although patients with non-insulin dependent diabetes developed left ventricular dysfunction more than patients with insulin dependent diabetes and female patients are more affected than male patients especially in NIDDM ( the difference is statistically not significant,  $P > 0.1$ ).

LVD occurs more frequently with prolonged duration of the disease in both types of diabetes (the difference is statistically not significant,  $P > 0.1$ ).

### **Abbreviations**

|       |                                         |
|-------|-----------------------------------------|
| LVD   | left ventricular dysfunction            |
| DM    | Diabetes Mellitus                       |
| IDDM  | Insulin dependent diabetes mellitus     |
| NIDDM | Non-insulin dependent diabetes mellitus |
| EF    | Ejection fraction                       |
| FS    | Fractional shortening                   |

|       |                                                     |
|-------|-----------------------------------------------------|
| IVS   | Inter-ventricular septum                            |
| PW    | Posterior wall of left ventricle                    |
| ESV   | End systolic volume                                 |
| EDV   | End diastolic volume                                |
| LVIDS | Left ventricular internal dimension at end systole  |
| LVIDD | Left ventricular internal dimension at end diastole |

### الخلاصة

داء السكري يسبب نوع من امراض القلب يعرف بصورة خاصة بالاعتلال السكري للعضلة القلبية ولتقييم حدوث هذه الظاهرة قمنا بعمل قياسات متعددة لوظيفة البطين الايسر باستخدام جهاز الايكو الموجود في مستشفى مرجان التعليمي وهذه القياسات تتضمن .:

- 1- معامل الدفع في القلب .
- 2- معامل التقصر في القلب.
- 3- سمك الجدار الحاجز بين البطينين.
- 4- سمك الجدار الخلفي للبطين الايسر .

نتائج البحث تظهر ان مرضى السكري لديهم اختلال في وظيفة البطين الايسر مقارنة بالناس الطبيعيين ( المفحوصين في مجموعة المقارنة ) بوجود نقص في :

- 1- معامل الدفع في القلب .
- 2- معامل التقصر في القلب.

مع زيادة في :

- 1- سمك الجدار الحاجز بين البطينين.

- 2- سمك الجدار الخلفي للبطين الايسر

النتائج احصائيا مهمة (  $P < 0.005$  )

كذلك مرضى السكري الغير معتمد على الانسولين يصابون باختلال وظيفة البطين الايسر اكثر من مرضى السكري المعتمد على الانسولين والمرضى الاناث يصابون اكثر من الذكور وخصوصا في السكري الغير معتمد على الانسولين

( الاختلاف غير مهم احصائيا ) ( $P > 0.1$ ) اختلال وظيفة البطين الايسر تحدث بصورة اكثر مع ازدياد فترة الإصابة للسكري بنوعيه :

( الاختلاف غير مهم احصائيا ) ( $P > 0.1$ ).

### Introduction

Cardiovascular disease is the most common cause of death in patient with diabetes mellitus[1].

Variable evidence has implied the existence of a specific cardiac disease of diabetes termed variously as Diabetic Cardiopathy or Diabetic Cardiomyopathy, which might

contribute to increase mortality of diabetes. This evidence has accumulated from non-invasive cardiac testing and has incorporated pathological abnormalities mainly from post-mortem material . [2, 3]

Specific diabetic cardiopathy has been suggested to be partly involved in the development of cardiac failure in diabetic patients. [4, 5]

Congestive heart failure occurs more frequently in diabetic than non-diabetic patients despite a similar extent of coronary artery disease as noted in several studies. [6, 7]

Both types of diabetes are associated with increased cardiovascular complications, the most common of which are ischemic cardiomyopathy and left ventricular dysfunction. The extent of an independent disease, diabetic cardiomyopathy, was suggested by initial anatomic studies, experimental models, and more recently, by epidemiological studies. The exact cause of this ventricular dysfunction is not known, several mechanism have

been proposed, such as metabolic abnormalities of glucose transport, cellular overload in fatty acid metabolites, alteration in calcium uptake by the sarcoplasmic reticulum leading to cellular calcium overload, coronary microangiopathy, structural collagen abnormalities, interstitial and perivascular fibrosis or the presence of autonomic neuropathy. The condition is characterized by abnormal left ventricular filling suggesting poor compliance or prolongation of left ventricular relaxation.[8,9,10]

So the aim of our study is to evaluate the presence of pre- clinical

myocardial damage in insulin and non-insulin dependent diabetic patients

by assessment with echocardiography and the results compared

with that of control subjects.

The echocardiographic assessment of left ventricular function in

this study was done by measuring:

EDV - ESV

$$1. EF \text{ which is equal to } \frac{\text{EDV} - \text{ESV}}{\text{EDV}} \times 100$$

LVIDD - LVIDS

$$2. FS \text{ which is equal to } \frac{\text{LVIDD} - \text{LVIDS}}{\text{LVIDD}} \times 100$$

3. Inter ventricular septal thickness.

4. Posterior left ventricular wall thickness.

Adult normal values: [11,12]

|     |              |
|-----|--------------|
| EF  | $67\% \pm 8$ |
| FS  | $31\% \pm 2$ |
| IVS | $9 \pm 3$ mm |
| PW  | $9 \pm 3$ mm |

### **Patients and Methods**

At merjan teaching hospital we studied 50 diabetic patients who attended babel centre for diabetes. 25 patients (50%) 12 male and 13 females on insulin therapy, aged 16-38 years (mean age 32.4 years) and 25 patients (50%) 10 male and 15 female on oral hypoglycemic agents aged 45-68 years (mean age 52.3 years).

The duration of the disease was 5 years and more (5-22 years) were only included in the study.

Forty non-diabetic control subjects were randomly selected from the population divided into two groups: 20 subjects in the first group (C1) comprised age and sex matched for insulin dependent diabetic patients and 20 subjects in the second group (C2) comprised age and sex matched for non-insulin dependent diabetic patients as shown in table (1).

Group C1 aged 15-38 years, (mean age 35.8 years) and group C2 aged 43-67 years, (mean age 50.6 years).

Diabetic patients and non-diabetic control subjects were identified from the initial study population by the following exclusion criteria:

1. History of myocardial infarction, angina pectoris, valvular heart disease and any other cardiac disease.
2. History of cerebro-vascular accident [C.V.A] or other arterial diseases.
3. History of any disease known to affect cardiac function such as thyroid diseases.
4. History of hypertension.
5. Drug therapy other than insulin or oral hypoglycemic agents.

On examination of both diabetic patients and control subjects the

heart rate range from 70-90 beats/min (because the heart rate outside 60-100 beats/min limits the alteration in the diastolic in flow), [11,13] also all were normotensive (blood pressure  $\leq 130/80$ ) and all had normal resting ECG at the time of the study .

The diabetic patients and control subjects were asked to attend the

echocardiographic department and examined by (Philips Envisor, version B.O.2) and recording :-

Ejection fraction , fractional shortening and thickness of inter-ventricular septum and posterior wall of the left ventricle at end-diastole . [11,14]

**Table 1** Clinical characteristic of the study groups

|                                | Male with<br>IDDM  | Female<br>with<br>IDDM | Control<br>group C1 | Male with<br>NIDDM | Female<br>with<br>NIDDM | Control<br>group C2 |
|--------------------------------|--------------------|------------------------|---------------------|--------------------|-------------------------|---------------------|
| Age                            | 18-35<br>years     | 16-38<br>years         | 15-38<br>years      | 45-64<br>years     | 50-68<br>years          | 43-65<br>years      |
| Duration<br>Of<br>diabetes     | 6-18<br>years      | 7-22<br>years          |                     | 6-15<br>years      | 5-18<br>years           |                     |
| Heart rate                     | 70-90<br>beat/min. | 70-90<br>beat/min.     | 80-90<br>beat/min.  | 75-90<br>beat/min. | 80-90<br>beat/min.      | 80-90<br>beat/min.  |
| Systolic<br>blood<br>pressure  | 110-130<br>mm Hg   | 125-130<br>mm Hg       | 120-130<br>mm Hg    | 120-130<br>mm Hg   | 120-130<br>mm Hg        | 120-130<br>mm Hg    |
| Diastolic<br>blood<br>pressure | 70-80<br>mm Hg     | 75-80 mm<br>Hg         | 75-80 mm<br>Hg      | 75-80 mm<br>Hg     | 70-80 mm<br>Hg          | 70-80 mm<br>Hg      |

**Results**

In our study, 50 diabetic patients and 40 control subjects matched

for age and sex, all with normal heart rate, blood pressure and resting

ECG were evaluated by echocardiography for the presence of left ventricular dysfunction.

Table (2): Shows the results of echocardiographic study of insulin dependent, non-insulin dependent and control groups (C1 and C2) these results are shown in:

Figure (1): Shows a reduction in EF in insulin dependent group compared with C1 control group and in non-insulin dependent group

compared with C2 control group. (The results are statistically significant,

$P < 0.005$ ).

Figure (2): Shows a reduction in FS in insulin dependent group compared with C1 control group and in non-insulin dependent group compared with C2 control group. (The results are statistically significant,

$P < 0.005$ ).

Figure (3): Shows an increase in the thickness of inter-ventricular septum between insulin dependent group compared with C1 control group

and in non-insulin dependent group compared with C2 control group.

(The results are statistically significant,  $P < 0.005$ ).

Figure (4): Shows an increase in the thickness of posterior left ventricular wall compared with C1 control group and in non-insulin dependent group compared with C2 control group. (The results are statistically significant,  $P < 0.005$ ).

Table (3): Shows that (44%) of non-insulin dependent diabetic patients developed LVD while only (28%) of insulin dependent diabetic patients developed LVD. (the results are statistically not significant,  $p > 0.1$ ).

Also shows that 18 patients (36%) were found to have left ventricular dysfunction.

Table (4): Shows that (43%) of diabetic female developed LVD while

only (27%) of male developed LVD. (The results are statistically not significant,  $p > 0.1$ ).

Table (5): Shows the incidence of left ventricular dysfunction in female according to the type of diabetes. (The results are statistically not significant,  $p > 0.1$ )

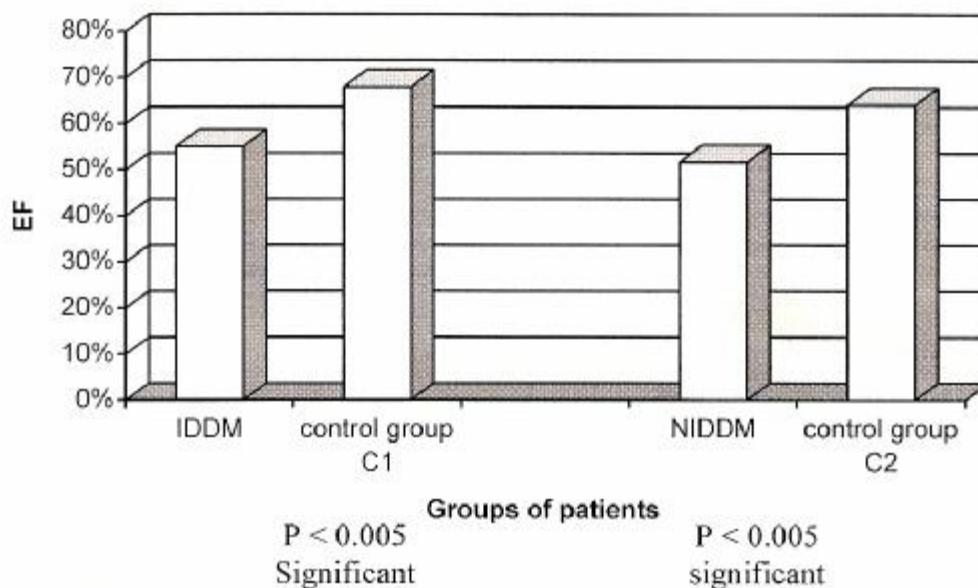
Table (6): Shows the incidence of left ventricular dysfunction in male according to the type of diabetes. (The results are statically not significant,  $P > 0.1$ ).

Table (7): Shows that LVD occurs more frequently with prolonged duration of the disease in both IDDM and NIDDM. (The results are statistically not significant,  $P > 0.1$ ).

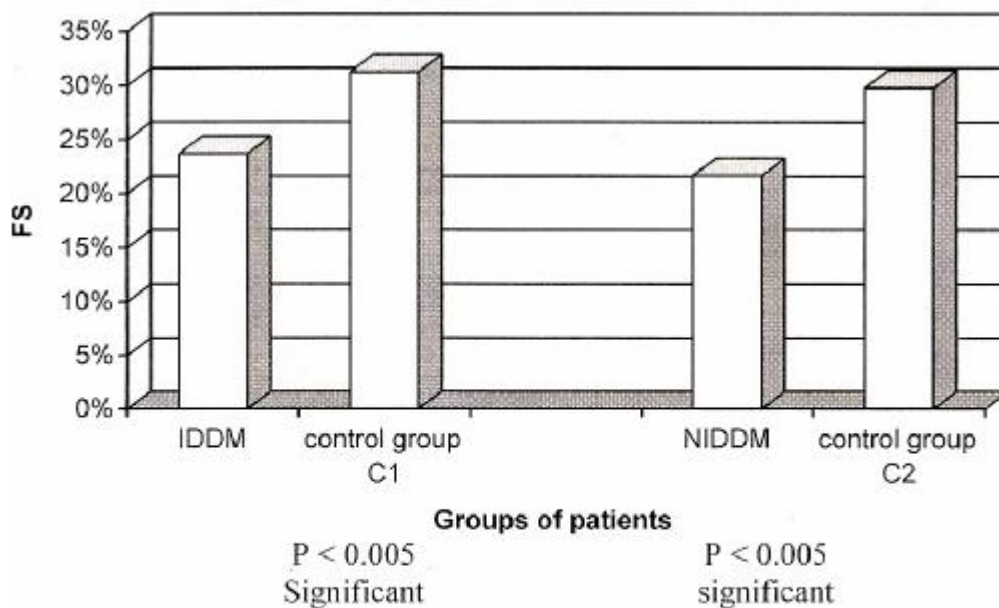
**Table 2** Results of echocardiography study

|     | IDDM 25 patients  | Control group C1 20 patients | NIDDM 25 patients | Control group C2 patients 20 |
|-----|-------------------|------------------------------|-------------------|------------------------------|
| EF  | 55.1% $\pm$ 7.6   | 67.9% $\pm$ 3.4              | 51.8% $\pm$ 6.8   | 64.2% $\pm$ 2.8              |
| FS  | 23.7% $\pm$ 4.2   | 31.2% $\pm$ 0.9              | 21.7% $\pm$ 3.9   | 29.8% $\pm$ 0.7              |
| IVS | 10.8 mm $\pm$ 1.6 | 9.6 mm $\pm$ 0.8             | 11.9 mm $\pm$ 1.1 | 9.8 mm $\pm$ 0.7             |
| PW  | 11.0 mm $\pm$ 1.4 | 9.7 mm $\pm$ 1.3             | 12.3 mm $\pm$ 1.3 | 10.2 mm $\pm$ 0.9            |

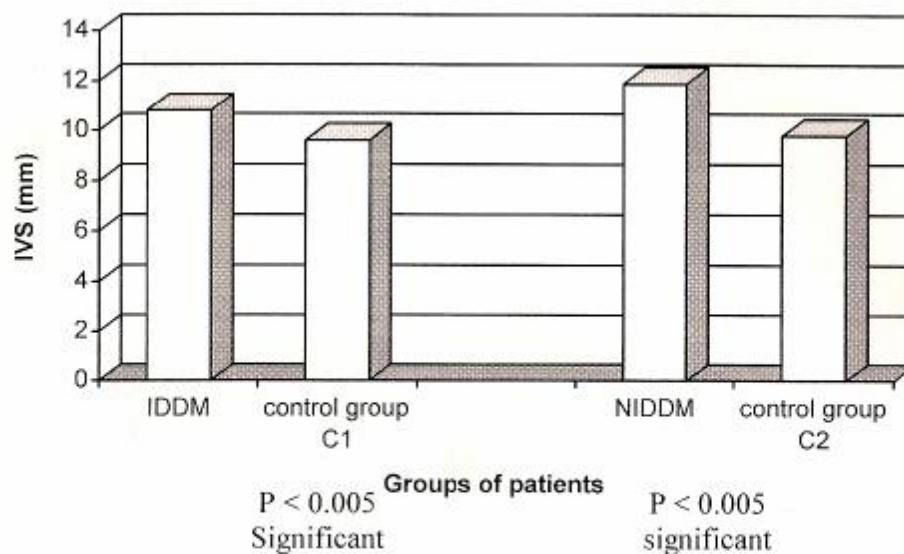
Mean  $\pm$  SD



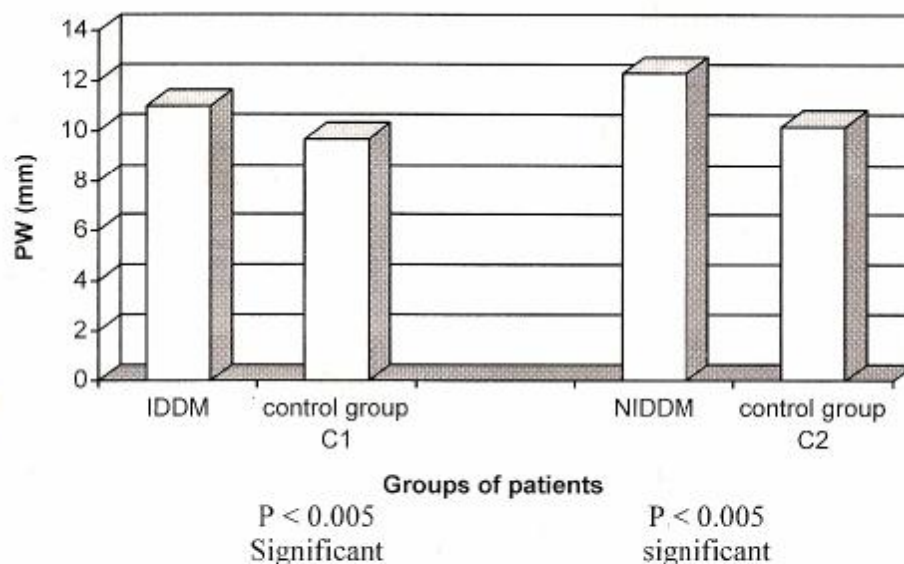
**Figure 1** The results of (EF) from echocardiographic study



**Figure 2** The results of (FS) from echocardiographic study



**Figure 3** The results of inter ventricular septal thickness from echocardiographic study



**Figure 4** The results of posterior left ventricular wall thickness from echocardiographic study

**Table 3** Left ventricular dysfunction in diabetic patients (according to the type of diabetes)

|       | Positive |    | Negative |    | Total |
|-------|----------|----|----------|----|-------|
|       | No.      | %  | No.      | %  |       |
| IDDM  | 7        | 28 | 18       | 72 | 25    |
| NIDDM | 11       | 44 | 14       | 56 | 25    |
| Total | 18       | 36 | 32       | 64 | 50    |

P > 0.1 not significant

**Table 4** Left ventricular dysfunction according to the sex of diabetic patients

|        | Positive |    | Negative |    | Total |
|--------|----------|----|----------|----|-------|
|        | No.      | %  | No.      | %  |       |
| Female | 12       | 43 | 16       | 57 | 28    |
| Male   | 6        | 27 | 16       | 73 | 22    |
| Total  | 18       | 36 | 32       | 64 | 50    |

P > 0.1 not significant

**Table 5** Left ventricular dysfunction among female patients

|       | Positive |    | Negative |    | Total |
|-------|----------|----|----------|----|-------|
|       | No.      | %  | No.      | %  |       |
| IDDM  | 4        | 30 | 9        | 70 | 13    |
| NIDDM | 8        | 53 | 7        | 47 | 15    |
| Total | 12       | 43 | 16       | 57 | 28    |

P > 0.1 not significant

**Table 6** Left ventricular dysfunction among male patients

|       | Positive |    | Negative |    | Total |
|-------|----------|----|----------|----|-------|
|       | No.      | %  | No.      | %  |       |
| IDDM  | 3        | 25 | 9        | 75 | 12    |
| NIDDM | 3        | 30 | 7        | 70 | 10    |
| Total | 6        | 27 | 16       | 73 | 22    |

P > 0.1 not significant

**Table 7** Left ventricular dysfunction according to the duration of IDDM and NIDDM

|       | LVD in diabetes < 10 years |    | LVD in diabetes ≥ 10 years |    | Total |
|-------|----------------------------|----|----------------------------|----|-------|
|       | No.                        | %  | No.                        | %  |       |
| IDDM  | 2                          | 29 | 5                          | 71 | 7     |
| NIDDM | 3                          | 27 | 8                          | 73 | 11    |
| Total | 5                          | 28 | 13                         | 72 | 18    |

P > 0.1 not significant

### **Discussion**

The existence of diabetic cardiomyopathy has been proposed because evidence has accumulated for the presence of myocardial dysfunction in diabetic patient in the absence of ischemic , valvular or hypertensive heart disease . [15, 16]

From our study we found that EF and FS are decreased in diabetic patients than in control subjects ( these results are statistically significant ,  $p < 0.005$  ) , also we found that inter-ventricular septum and posterior left ventricular wall are thicker in diabetic patients than in control subjects ( these

results are statistically significant ,  $p < 0.005$  ) , so 18 patients developed LVD among 50 diabetic patients included in this study . Also we found that left ventricular dysfunction occurs more frequently in non-insulin dependent diabetic patients than in insulin dependent diabetic patients , ( but the results are statistically not significant  $p < 0.1$  ) and this may be due to a low number of patients [17] , and these results may be related to that insulin dependent diabetic patients are quite well identified from the disease onset and clinical features appeared as soon Langerhan's Islets are damage by viral or auto immune events while in

NIDDM an overt clinical feature appeared slowly , in which vascular and myocardial damage started before the dysmetabolic events become clear , while hyperinsulinaemia , microalbuminuria , advanced glycated end products and lipid abnormalities could lead to reduction in ventricular compliance which if long standing , may enhance left ventricular mass [18] . The development of left ventricular muscle stiffness due to elevated tissue calcium levels , associated with defective sarcoplasmic reticular calcium- ATPase and a redistribution of myosin isoenzymes from the most active V1 from to the least active V3 from was experimentally demonstrated in NIDDM , so vascular wall changes and increase left ventricular mass typically associated with generalized cardiovascular metabolic disease might be the primary consequence of NIDDM , also aging process may play a role in NIDDM , which is principally a disease of middle age , and elderly while IDDM is principally a disease of young . [19,20]

Also we found that female patients are more affected than male patients especially in NIDDM , we found also that left ventricular dysfunction occurs more frequently with prolonged duration of the disease , ( the results are statistically not significant ,  $p < 0.1$  ) , and these results may be due to close relationship between the duration of diabetes and the presence of microangiopathic complications , which has been reported by some authors as diabetic myocardiopathy which is a disease showing intramural microvascular endothelial proliferation , swelling as well as sub-endothelial accumulation of acid glycogen deposition cells and increase amount of collagen , glycoproteins , triglycerides in the myocardium . [21,22]

According to this study and others done before using different methods we found that Myocardial involvement in D.M. is functionally important and increases with prolongation of the duration of the disease initially impairing early diastolic relaxation and when more extensive , probably in combination with hypertrophy and reduced myocardial perfusion further impairing relaxation and contraction such abnormality have been called a diabetic cardiomyopathy . [23,24]

### **Conclusions and Recommendations**

1. Ejection fraction and fractional shortening are decreased in diabetic patients than in control subjects .
2. Inter-ventricular septum and posterior left ventricular wall are thicker in both insulin dependent diabetic patients and non-insulin dependent diabetic patients than in control subjects .
3. The incidence of LVD is numerically more in non-insulin dependent diabetic patients than in insulin dependent diabetic patients and in female patients more than in male patients and it is related to the duration of diabetes , but these results are statistically not significant and this may be due to a low number of patients included in this study .
4. Our study supports previous findings that LVD occurs in diabetic patients without overt evidence of heart disease .
5. Every patient with D.M. should be examined by echocardiography especially in non-Insulin dependent diabetic patients to detect early cardiac changes.
6. We have to start treatment for any diabetic patient with LVD, as soon as possible, to improve the prognosis .

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