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SUBCLINICAL DIABETIC CARDIOMYOPATHY—ASSESSMENT BY SYSTOLIC TIME INTERVALS

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SUMMARY

Left ventricular performance in diabetics without hypertension, ischemic heart disease, or clinical evidence of other heart diseases was assessed by systolic time intervals and echo-cardiography. The PEP/LVET ratio was 3.48% higher in diabetics than in controls. There was good correlation of abnormality of PEP/LVET ratio with duration of diabetes. There was no correlation with age of patient or severity of diabetes. There was good correlation between abnormal PEP/LVET and incidence of retinopathy and nephropathy. This suggests the possibility of the presence of subclinical diabetic cardiomyopathy in these individuals.

INTRODUCTION

Accelerated coronary artery disease and hypertension are well-known features of Diabetes mellitus and account for much of the morbidity and mortality of this condition. It has been noted however that congestive heart failure and cardiomegaly occur in diabetics independent of these two conditions.[1] Histopathological reports[2-4] and studies of left ventricular functions in diabetics by non-invasive methods[5-7] have led to the concept of a separate entity of heart disease in diabetics called Diabetic Cardiomyopathy.[8]

If Diabetic Cardiomyopathy is a distinct condition, it may pass through a subclinical phase when left ventricular function is impaired and this phase could be detected by using sensitive and accurate non-invasive methods of evaluating left ventricular function.[6] Systolic time interval estimation and echo-cardiography are now accepted as sensitive and accurate non-invasive methods of evaluating left ventricular function.[9-11]

This paper presents a study of left ventricular function in diabetics without clinical heart disease by systolic time intervals.

MATERIAL AND METHODS

CASE MATERIAL AND CRITERIA FOR SELECTION: The clinical material consisted of diabetics admitted as inpatients at the Diabetes Research Centre, Madras. Patients were subjected to an initial thorough clinical examination. Blood pressure recordings were done on 3 consecutive days. A complete hemogram, X-ray chest and 12 lead ECG were done. After these initial tests, patients were screened and those with anemia, hypertension, evidence of ischemic or other heart diseases, respiratory or other systolic diseases, or obvious

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infections were excluded. Patients with body weight exceeding 15% of the ideal body weight were also excluded. Only patients who were in sinus rhythm, free from signs or symptoms of congestive cardiac failure, and normal C-T ratio on chest PA view, were considered for the study. Chronic smokers and alcoholics were also excluded.

After this rigorous exclusion list, 50 diabetic patients were taken up for the study. The clinical data of these patients is presented in Table 1.

TABLE 1.—*Clinical Data of 50 Diabetics*

Age	Sex	Duration of Diabetes	No.	Treatment	No.
20-65	Males (36)	10 years	38	Insulin	7
	Females (14)	10-15 years	3	Insulin + oral drugs	17
		15 years	9	Oral drugs	12
				Irregular treatment	14

Biochemical profiles of the patients included an oral G.T.T., lipid analysis and lipoprotein patterns, serum total proteins, electrophoresis and uric acid. At the time of the study all patients were in an uncontrolled diabetic state.

There were 6 patients with mild diabetes, 16 patients with moderate diabetes and 28 patients with severe diabetes. The criteria for severity of diabetes was as follows:

Severity of diabetes	Fasting Blood Sugar	Post prandial Blood sugar
Mild	<120	<200
Moderate	120-180	200-300
Severe	>180	>300

Kidney function tests including urea, creatinine, creatinine clearance, and 24 hour proteinuria were done in all cases and the presence of nephropathy was noted. Fundus examination was done in all cases by direct ophthalmoscopy after full mydriasis and the presence of retinopathy was noted.

Control group:

One hundred and thirty four age matched healthy non-diabetics none of whom had any history of diabetes in the family, formed the control group. There were 111 males and 23 females.

Systolic time intervals: (S.T.I.)

The test was done in the post-absorptive state, the patients having missed their morning dose of drugs. The S.T.I. were estimated at an identical time of the day (between 10 A.M. and 11 A.M.) in the diabetics and controls. During held expiration a 10 second recording was made of simultaneous carotid pulse tracing, phonocardiogram, and Lead 2 electrocardiogram at a paper speed of 100 mm/second using a Gallileo 3 channel recorder. The lead in which the onset of depolarisation was well defined was used. This was usually L II. In a few cases, other limb leads were used. The QS_2, LVET and PEP were measured.

The PEP/LVET ratio was calculated in each case. To correct for the heart rate, the S.T.I. indices namely QS_2I, LVETI and

PEPI were calculated using the regression equation formulae of Weissler.[10]

RESULTS

The systolic time intervals in 50 diabetic patients and 134 controls expressed as LVETI, PEPI and PEP/LVET are shown in Table 2.

TABLE 2.—*Systolic Time Intervals in Diabetics and Controls*

	LVETI	PEPI	PEP/LVET
Diabetics (n = 50)	404 ± 8	153 ± 13	0.461 ± 0.034
Controls (n = 134)	418 ± 10	127 ± 15	0.342 ± 0.053
P. Value	<0.05	<0.01	<0.001

The mean PEP/LVET ratio was higher in diabetics than controls and the difference was highly significant statistically ($P < 0.001$). The mean PEP/LVET ratio was 34.8% higher in the diabetics. Thirty-nine out of 50 diabetics (78%) exhibited an abnormal PEP/LVET ratio, taking 0.407 as upper limit of normal (mean value of the controls + 1 S.D.). Taking 2 S.D. for calculation, 22 out of 50 diabetics (44%) showed abnormal PEP/LVET ratios.

The PEPI was significantly prolonged in diabetics ($P < 0.01$). There was also a significant shortening of the LVETI in diabetics ($P < 0.05$). The abnormality in PEP/LVET was more in males than in females. There was no correlation of the abnormality of PEP/LVET with age and even patients below 30 years of age had significant increase of the PEP/LVET ratio.

The patients were then studied with regard to duration of diabetes (i.e., from the day the disease was detected). There was good correlation between abnormal PEP/LVET ratio and duration of diabetes (Table 3).

There was no direct correlation between the severity of diabetes and abnormal PEP/LVET ratio (Table 4).

Patients were subdivided according to the mode of therapy, and the PEP/LVET ratios were compared (Table 5).

TABLE 3.—*Correlation Between Duration of Diabetes and Abnormal PEP/LVET RATIO*

Duration	No. of patients	No. with abnormal PEP/LVET	%age abnormality
10	38	28	73.6
10-15	9	8	88.8
15	6	3	100.0

TABLE 4.—*Severity of Diabetes and Abnormal PEP/LVET RATIO*

Severity	No. of patients	No. with abnormal PEP/LVET	% age abnormality
Mild	6	4	66.6
Moderate	16	14	87.5
Severe	28	21	78.5

There was no significant difference in PEP/LVET ratio in patients on different

TABLE 5.—*PEP/LVET in Diabetics Subdivided According to Therapy*

Mode of therapy	No. of patients	PEP/LVET	Significance (P value)
Insulin	7	0.477 ± 0.101	
Oral drugs	12	0.450 ± 0.125	N.S. (P >0.50)
Insulin + Oral drugs	17	0.416 ± 0.208	N.S. (P >0.50)
Irregular treatment	14	0.540 ± 0.090	N.S. (P >0.50)

therapies. The mean PEP/LVET was higher in diabetics with uncontrolled diabetes which was however not significant statistically.

The 39 patients with abnormal PEP/LVET ratios were then analysed to note the incidence of associated microangiopathic complications Table 6 shows the results.

TABLE 6.—*Associated Complications in Patients with Abnormal PEP/LVET Ratio*
Total 39 cases

Complication	No.	% age
Retinopathy alone	9	23.7
Nephropathy alone	6	15.3
Retinopathy + Nephropathy	10	25.6
Total No. with complications	25	64.1
Without complications	14	35.9

64.1% of patients with abnormal PEP/LVET values had associated microangiopathic complications.

DISCUSSION

Assessment of L.V. function by non-invasive methods such as systolic time intervals and echo-cardiography are now established procedures. In diabetic patients without ischemic heart disease, left ventricular dysfunction has been noted by both these methods. PEP/LVET ratio is an excellent index of L.V. function. The mean ratio was 34.8% higher in diabetics compared to controls. There were significant changes in diabetics compared to controls. There were significant changes in diabetics in the other systolic time intervals as well. LVETI is shorter and PEPI is longer in diabetics compared to controls.

Analysis of patients with abnormal PEP/LVET ratio showed that 64.1% had other evidences of microangiopathy such as retinopathy or nephropathy. It must be stressed that if finer techniques such as fluorescein angiography had been applied, more cases of retinopathy would probably have been detected and thus the correlation could have been still better.

The strict selection of patients free from angina and previous myocardial infarction and with normal ECG's and chest radiographs would exclude coronary artery disease as a cause of the L.V. dysfunction noted in diabetics in this study. In this context, it is interesting to note that even in patients with chronic coronary artery disease without myocardial infarction, the systolic time intervals are normal at rest,[12, 13] or even in the presence of angina.

The presence of L.V. dysfunction in the absence of clinical evidence of heart disease points to the possible existence of subclinical Diabetic Cardiomyopathy in

these patients. The exact nature of the L.V. dysfunction remains uncertain because both systolic time intervals and echocardiography are purely non-invasive. The answer to the problem could possibly come from invasive studies such as endomyocardial biopsy. However, since all patients were asymptomatic this procedure has not been attempted in this study.

Histopathological studies[8] and endomyocardial biopsies[2] in diabetics have shown presence of microangiopathic changes in the heart. The small vessel involvement consisted of endothelial proliferation, subendothelial fibrosis and exudative deposits of hyaline. These have been suggested to be the cause of Diabetic Cardiomyopathy, and working hypothesis for its pathogenesis has been put forward by Zoneraich[8] (Fig. 1).

PATHOGENESIS OF CARDIOMYOPATHY IN DIABETES MELLITUS

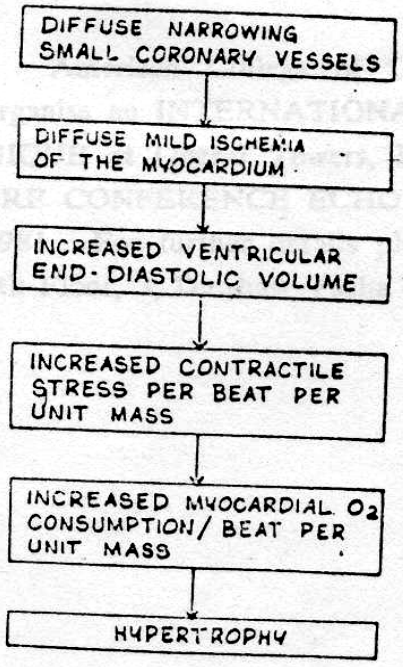

Fig. 1.

Sykes *et al*[14] have shown that the abnormal systolic time intervals in diabetics could be brought back to normal after metabolic control of diabetes. This raises the possibility whether the L.V. dysfunction observed could be due to a purely metabolic derangement. Alternatively, a metabolic derangement leading to reversible changes in the small blood vessels is also possible..

Serial follow-up studies and invasive techniques such as endomyocardial biopsy might throw more light on the nature of left ventricular dysfunction in diabetic patients.

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NEWS

American College of Chest Physicians (Western Indian Chapter) will organise an INTERNATIONAL CONFERENCE ON NON-INVASIVE TECHNIQUE at Oberoi Towers, Bombay, on 6,, 7 and 8th December, 1981. A PRE CONFERENCE ECHO CARDIOLOGY will be held on 5th December, 1981. For further details please contact Dr. Ashok Tulpule, Apeejay House, 7th Floor, 3, Dinshaw Vacha Road, Bombay 400 020.