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Increased myocardial contractility in short-term Type 1 diabetic patients: an echocardiographic study

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Summary. Cardiac function was investigated by echocardiography in 24 short-term Type 1 diabetic patients with a mean diabetes duration of 7 years (range 4–14 years) during conditions of ordinary metabolic control. Compared to 24 age and sex matched normal control subjects, measurements of myocardial contractility as left ventricular fractional shortening and mean circumferential shortening velocity were increased by 12% and 20% respectively. Another 8 Type 1 diabetic patients were examined during conditions of poor (hyperglycaemia and ketosis) and good metabolic control. Following improved glycaemic control, left ventricular fractional shortening and mean circumferential shortening velocity decreased by 16% and 24% respectively. Our findings show that short-term Type 1 diabetes is associated with increased myocardial contractility. Furthermore, this condition is related to the state of metabolic control.

Key words: Echocardiography, left ventricular function, Type 1 diabetes, metabolic control, diabetic cardiopathy.

From studies of blood flow to different organs in short-term diabetic patients, evidence has accumulated indicating a state of hyperperfusion, at least during conditions of poor metabolic control. Thus an increase in renal plasma flow in diabetic patients with a duration of disease of less than 10 years has been reported by several authors [1–5]. Also in the retina [6], the cerebrum [7], and in the subcutaneous tissue [8], increased blood flow has been observed.

Presently information on cardiac function in short-term Type 1 diabetes and its possible relation to the state of metabolic control is very scarce.

Therefore we performed echocardiography in 24 short-term Type 1 diabetic patients on standard insulin therapy, and in 8 short-term Type 1 diabetic patients before and after proper metabolic control had been achieved.

Subjects and methods

Subjects

Twenty-four Type 1 diabetic patients on ordinary subcutaneous insulin therapy (12 females and 12 males), and 24 age and sex matched normal control subjects, were investigated. Individual clinical data are given in Table 1. Mean age of diabetic patients was 29 years, with mean duration of disease 8 years. Mean blood glucose profile (measured every second hour for a 24-h period during in-patient conditions 3–4 days before the echocardiographic examination) was 12.9 mmol/l, mean fasting blood glucose at the day of examination was 10.3 mmol/l and mean haemoglobin Alc (HbAlc) was 7.2% (normal range 4.3–5.5%). None of the patients had albuminuria or proliferative retinopathy (4 patients had microaneurysms), or other disease than diabetes. Normal control subjects and the diabetic patients were investigated during outpatient conditions.

Further, we examined 8 Type 1 diabetic patients (1 woman and 7 men), mean age 31 years. Six of these diabetic patients had newly diagnosed insulin-dependent diabetes mellitus, while the remaining two patients, who had had diabetes for 7 and 12 years, were examined during admission because of malregulation. The patients were examined during the state of poor metabolic control and after 4 to 14 days of improved metabolic control. Individual clinical data are given in Table 2. At the first examination, mean blood glucose was 17.1 mmol/l and ketone bodies were present in the urine, but none were acidotic. Three patients had begun insulin therapy at the examination. At the second examination, mean blood glucose was 7.6 mmol/l, and there was no ketonuria. Both examinations were performed during admission from 09.00 to 12.00 hours.

All patients gave informed consent to the investigation, which was in accordance with the declaration of Helsinki.

Echocardiography

After 10 min of rest in a supine position, blood pressure was measured using a sphygomanometer with Korotkoff's phase 1 and 5 sounds indicating systolic and diastolic blood pressure respectively. Two-dimensional echocardiography and M-mode echocardiography were performed with a simultanous electrocardiogram. The echocardiographic equipment used were: an ATL 315A video display, an ATL 850A

Table 1. Clinical data in 24 short-term Type 1 diabetic patients

Patient/sex	Age (years)	Body mass index (kg/m^2)	Duration of disease (years)	Blood glucose profile (mmol/l)	Fasting blood glucose (mmol/l)	HbAlc (%)	Retinopathy
1 M	29	24.8	2	13.2	15.3	6.4	-
2 M	37	21.7	3	17.4	10.8	8.8	-
3 F	33	21.2	7	16.2	8.1	7.5	-
4 F	26	20.8	15	10.6	19.5	6.7	+
5 F	36	21.7	7	14.0	7.2	6.9	-
6 F	22	21.2	7	8.3	5.3	7.0	-
7 M	34	26.0	12	8.3	9.3	7.1	+
8 M	38	22.6	4	8.9	11.1	6.4	-
9 F	24	27.5	8	10.9	7.5	9.2	-
10 F	22	24.7	11	14.9	12.2	7.3	-
11 M	22	23.5	8	16.2	6.7	9.0	+
12 M	30	24.0	12	15.0	5.2	5.5	-
13 F	29	18.5	7	12.8	19.0	7.7	-
14 F	23	26.6	13	8.6	15.1	5.7	+
15 M	34	22.4	5	15.6	6.7	6.9	-
16 M	26	20.8	14	11.0	8.6	7.0	-
17 M	33	23.6	7	11.8	4.2	7.0	-
18 M	23	21.1	10	15.0	10.3	9.7	-
19 M	38	23.5	12	13.6	12.5	7.3	-
20 M	25	24.5	1	16.1	16.1	7.6	-
21 F	24	21.6	5	14.1	13.3	7.1	-
22 F	27	21.0	7	8.8	4.9	5.8	-
23 F	21	21.5	5	17.2	8.8	8.0	-
24 F	44	20.0	10	9.9	9.5	5.9	-
Mean	29.2	22.7	8	12.9	10.3	7.2	
1 SD	6.4	2.2	3.8	3.0	4.3	1.1	

(F) and (M) signify female and male. Body mass index: (weight in kg)/(height in meters)^2. Blood glucose profile: mean of 12 determinations during 24 h. (+/-) signify presence or absence of retinal microaneurysms

Table 2. Clinical data in 8 Type 1 diabetic patients during poor metabolic control (PMC) and following improved metabolic control (IMC)

Patient	Sex (female/male)	Age (years)	Duration of disease (years)	Body mass index (kg/m^2)	Mean blood glucose		24-h urinary ketone bodies	
					PMS (mmol/l)	IMC (mmol/l)	PMC (+/-)	IMC (+/-)
I	male	34	7	23.3	15.7	4.2	+	-
II	male	22	0	17.2	18.9	8.4	+	-
III	male	30	0	21.3	14.7	6.3	+++	-
IV	female	20	0	24.0	18.3	6.3	+	-
V	male	27	0	21.3	20.2	8.0	+++	-
VI	male	40	0	22.1	12.0	6.9	+	-
VII	male	36	0	21.9	20.4	12.5	+++	-
VIII	male	38	12	23.6	16.5	8.2	+	-
Mean		30.9		21.8	17.1	7.6		
1 SD		7.4		2.1	2.9	2.4		

Body mass index: (weight in kg)/(height in meters)^2. Mean blood glucose: mean of 6 measurements

real time scan controller, an ATL pulsed echo 600B (Advanced Technology Laboratories Inc., USA), and a Honeywell 1856 visiocorder (Honeywell, USA). The two-dimensional echo was used to ensure absence of wall asynergy and localization of optimal M-mode measurements of the internal end-systolic diameter (LVIDs) and the internal end-diastolic diameter (LVIDd) of the left ventricle just below the mitral valve. Left ventricular ejection time (LVET) was measured from the opening to the closure of the aortic valve [9]. Mean of 5 expiratory cardiac cycles was used. Paperspeed was 50 mm/sec.

Definitions

End-systolic volume (SV) and end-diastolic volume (DV) of the left ventricle were calculated as described by Teichholtz [10]: ventricular volume: $\frac{7}{2.4+D} \times D^3$, where D is the left ventricular internal short diameter; cardiac output: (DV-SV) × heart rate; fractional shortening (FS%): $\frac{LVIDd-LVIDs}{LVIDd}$%; mean velocity of circumferential shortening (Vcf): FS%/LVET. To eliminate confounding differences in height and weight of the diabetic patients and the control subjects, parameters, including ventricular volumes and diameters, were corrected for body surface area using the formula of Du Bois.

Table 3. Haemodynamic and echocardiographic parameters in 24 short-term Type 1 diabetic patients

Patient	Mean arterial blood pressure mmHg	Heart rate (beats/min)	Diastolic diameter (mm/m^2)	Systolic diameter (mm/m^2)	Ejection time (ms)	Mean circumferential shortening velocity (circumf./s)
1	97	56	28	13	300	1.76
2	85	81	28	17	286	1.34
3	83	74	26	17	263	1.27
4	78	75	30	18	269	1.47
5	83	88	25	16	269	1.27
6	76	68	30	17	295	1.49
7	90	76	23	14	288	1.31
8	70	89	26	19	252	1.09
9	83	85	27	18	288	1.18
10	90	86	25	17	250	1.22
11	80	67	29	18	288	1.25
12	80	62	28	17	327	1.19
13	97	98	27	15	220	1.95
14	87	59	24	12	400	1.28
15	88	72	24	14	275	1.52
16	90	91	23	12	-	-
17	83	66	27	19	269	1.12
18	80	82	31	19	287	1.37
19	97	68	27	17	294	1.19
20	90	60	28	19	308	1.05
21	90	72	31	18	317	1.32
22	93	68	31	21	311	1.03
23	93	48	27	17	317	1.12
24	80	83	29	17	250	1.70
Mean	86	74	27.3	16.7	288	1.32
1 SD	7.1	12.4	2.4	2.3	35	0.23
Normal control subjects (n = 24)						
Mean	88	66	27.9	18.5	311	1.10
1 SD	9.8	11.8	2.8	2.9	26	0.20
	(NS)	($p<0.025$)	(NS)	($p<0.05$)	($p<0.02$)	($p<0.005$)

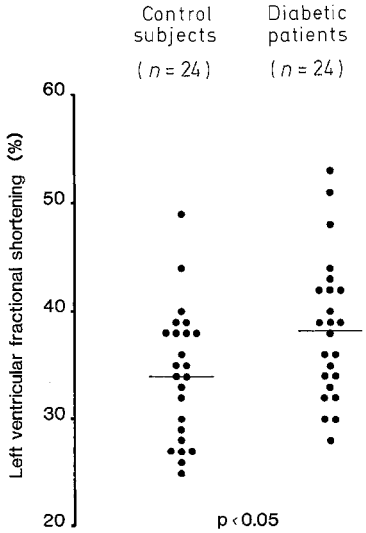

Fig. 1. Left ventricular fractional shortening (%) in 24 short-term Type 1 diabetic patients and in 24 age and sex-matched normal control subjects

Calculations and statistics

The echocardiographic recordings were described without knowledge of the status of the subject examined. The recordings in the group of diabetic patients investigated before and during improved metabolic control were described in pairs to ensure identical levels in measuring the diameter of the left ventricle.

Statistical evaluation was performed using the two-tailed paired and non-paired Student's t-test. Data are given as mean and range, or as mean ± 1 SD, with a level of significance $p<0.05$.

Results

Results from the echocardiographic examination in 24 short-term diabetic patients and 24 normal control subjects are shown in Table 3. Mean arterial blood pressure was not significantly different in the two groups, while heart rate was 12% ($p<0.025$) higher in the diabetic patient group. End diastolic diameter did not show differences between the groups but end systolic diameter was significantly lower in the diabetic patient group ($p<0.05$). FS% was 12% ($p<0.01$) higher in the diabetic patient group ($38\pm7\%$) than in the group of normal control subjects ($34\pm6\%$) (Fig. 1). Also Vcf was significantly increased among the diabetic patients (23%) ($p<0.005$). Calculation of ventricular volumes showed an insignificant increase in stroke volume in the diabetic patient group. Because of higher heart rate in the diabetic patient group, cardiac output (cardiac index) was found significantly higher ($p<0.01$) in this group (3.2 ± 0.7 l/min $\times$ m^2) as compared to the group of nor-

Table 4. Haemodynamic and echocardiographic parameters in 8 Type 1 diabetic patients during poor metabolic control (PMC) and following improved metabolic control (IMC)

Patient	Mean arterial blood pressure (mm Hg)		Heart rate (beats/min)		Diastolic diameter (mm/m^2)		Systolic diameter (mm/m^2)		Ejection time (ms)		Mean circumferential shortening velocity (circumf./s)	
	PMC	IMC	PMC	IMC	PMC	IMC	PMC	IMC	PMC	IMC	PMC	IMC
I	80	77	74	66	26	27	16	19	269	269	1.39	1.02
II	92	75	72	67	30	30	18	20	240	259	1.42	1.23
III	93	83	84	62	27	27	18	18	245	308	1.45	1.07
IV	87	87	53	47	28	28	17	19	359	490	1.08	0.64
V	103	87	75	56	31	30	18	19	350	341	1.20	1.05
VI	97	83	87	60	30	30	19	20	286	390	1.30	0.94
VII	115	92	69	63	30	30	18	22	286	290	1.40	0.84
VIII	97	97	71	68	27	27	17	17	298	295	1.28	1.19
Mean	96	85	73	61	28.6	28.6	17.6	19.3	292	330	1.32	1.00
1 SD	11	7	10	7	1.8	1.5	0.9	1.4	44	77	0.13	0.19
	($p<0.02$)		($p<0.05$)		(NS)		($p<0.02$)		(NS)		($p<0.001$)	

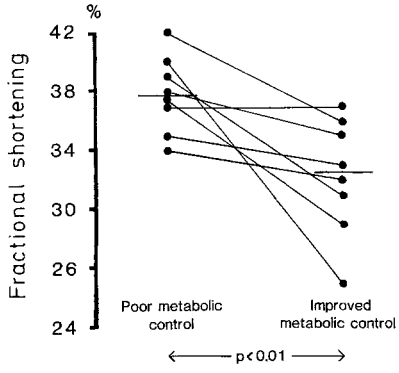

Fig. 2. Left ventricular fractional shortening (%) in 8 Type 1 diabetic patients during poor and following improved metabolic control

mal control subjects (2.6 ± 0.5 l/min $\times$ m^2). No significant correlation was found between either FS%, Vcf or cardiac output and HbAlc and blood glucose.

Results from the paired observations in the 8 Type 1 diabetic patients during poor and following improved metabolic control are shown in Table 4. Both heart rate and mean arterial blood pressure decreased significantly following improved metabolic control. End diastolic diameter was unchanged, while end systolic diameter increased significantly ($p<0.02$) following improved control. The parameters of contractility decreased significantly following improved glycaemic control (FS% from $38 \pm 3\%$ to $32 \pm 4\%$ ($p<0.01$) (Fig. 2) and Vcf by 24% ($p<0.001$) (Table 4). Calculation of ventricular volumes showed unchanged diastolic volume, but significantly increased systolic volume and significantly decreased stroke volume, together with decreased heart rate resulting in significantly ($p<0.01$) reduced cardiac output (index) following improved metabolic control (from 3.5 ± 0.7 l/min $\times$ m^2 to 2.7 ± 0.5 l/min $\times$ m^2).

Day to day variation was assessed in 8 normal control subjects. The percent mean variation was: FS% $8.2 \pm 5.9\%$, Vcf $10.0 \pm 8.1\%$ and cardiac index $9.6 \pm 5.5\%$.

Discussion

The present study demonstrates clearly that short-term (less than 15 years duration) uncomplicated Type 1 diabetes is associated with increased fractional shortening and increased mean circumferential shortening velocity of the left ventricle, and that this enhanced myocardial contractility is related to metabolic control.

Necropsy studies have suggested a specific diabetic cardiopathy [11], and evaluation of cardiac function by non-invasive techniques such as systolic time intervals and echocardiography have provided evidence of subclinical cardiomyopathy in diabetic patients [12–15]. In studies where potentially important factors such as age of the patient, duration of diabetes and presence of clinical microvascular complications have been considered, the prevalent finding have been signs of impaired left ventricular function in patients with long duration of disease and presence of severe microvascular complications [12, 14]. Impaired cardiac function has been suggested on the basis of an increased pre-ejection period - left ventricular ejection time - ratio [12], disturbed relation between mitral valve movement and left ventricular wall movement [14] and by decreased fractional shortening [16]. On the other hand, pre-ejection period - left ventricular ejection time - ratio has been found within normal limits in short-term uncomplicated diabetes [12].

The present finding of increased myocardial contractility is not inconsistent with the above mentioned reports, since we have been dealing exclusingly with rather short-term patients without signs of microvascular disease except for a few cases showing a light degree of background retinopathy. Thus a longitudinal prospective study would be needed in order to further elucidate the relationship between diabetes duration, clini-

cal microvascular complications and cardiac function in Type 1 diabetes.

The pathogenesis of increased myocardial contractility cannot be deduced from the present study. Myocardial contractility may be enhanced due to elevated sympathetic activity [17], altered myocardial metabolism, or be secondary to increased peripheral circulatory demands. Further studies will be required in order to identify the factors and mechanisms behind the increased contractility.

While FS% and Vcf are reliable parameters of myocardial contractility [9], there are considerable problems in determining left ventricular volumes and cardiac output from measurement of the short diameter of the left ventricle [18] as described by Teichholz [10]. However, we think our observation of increased heart rate, increased contractility and identical left ventricular internal diastolic diameter in the diabetic patient group compared to the normal control subjects is highly suggestive of increased cardiac output in short-term uncomplicated diabetes. In this context it is of particular interest that our preliminary report, which suggests significant alterations in cardiac output secondary to changes in metabolic control in Type 1 diabetic patients [19], has recently been confirmed by a Xenon-wash out technique [20]. Our suggestion of cardiac output in short-term Type 1 diabetic patients would be completely compatible with our knowledge of increased blood flow to the kidneys [2-4], the retina [6, 21] and the peripheral tissues [8, 22] of these patients. Until now there are no other reports comparing indices of cardiac output in Type 1 diabetic patients with normal subjects, and the present suggestion based on indirect meassurements awaits confirmation.

From our finding of normalization of myocardial contractility following improved glycaemic control it can be concluded, however, that the degree of metabolic control is an important factor in this condition. Further, this finding might be of clinical relevance since haemodynamic changes such as localized hyperperfusion has been suggested as an important component in the development of diabetic microvascular disease [23].

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