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Augmentation of Atrial Contribution to Left Ventricular Filling in IDDM Subjects as Assessed by Doppler Echocardiography

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Left ventricular diastolic function was assessed by pulsed Doppler echocardiography in 21 subjects (mean age 48 yr) with insulin-dependent diabetes mellitus (IDDM) and without evidence of ischemic heart disease and in 21 healthy control subjects of similar age and sex distribution. The peak mitral valve flow velocities during the early rapid filling phase (E) and during late atrial filling (A) were measured, and the ratio of these peak flow velocities (E:A) was calculated. E was similar in both groups, but A was higher ($P < .01$) in the diabetic group. Thus, E:A was lower (1.19 ± 0.24 vs. 1.65 ± 0.67; $P < .01$) in the diabetic subjects than in the control subjects. On subgroup analysis, 6 patients with cardiac autonomic neuropathy had lower E:A than the patients with no such disorder (0.99 ± 0.15 vs. 1.29 ± 0.25; $P < .05$). E:A was not related to the duration of diabetes, presence of retinopathy, HbA_1, or blood glucose levels. In conclusion, the atrial contribution to left ventricular filling seems to be augmented in diabetic subjects. This finding indirectly supports the view that left ventricular compliance is already reduced in asymptomatic diabetic subjects. *Diabetes Care* 12:159–61, 1989

Digitized M-mode echocardiography and radionuclide ventriculography have suggested that abnormal left ventricular diastolic filling is the predominant feature of preclinical diabetic cardiomyopathy (1–4). In this study, we applied pulsed Doppler echocardiography in the assessment of left ventricular diastolic function of asymptomatic diabetic subjects with no clinical heart disease.

MATERIALS AND METHODS

Twenty-one asymptomatic patients with insulin-dependent diabetes mellitus (IDDM) were studied. They had no recent ketoacidosis, hypertension, or other diseases or medication that might affect cardiac function. All patients had a normal 12-lead resting and exercise electrocardiogram and a normal dynamic thallium tomograph. The mean age of the patients (11 women, 10 men) was 47.8 yr (range 37–57 yr), and the duration of diabetes ranged from 6 to 29 yr (mean 15 yr). Seven patients had background retinopathy and two had proliferative retinopathy. Two patients had persistent proteinuria, but none had renal failure as judged by their serum creatinine levels. Nine diabetic subjects were on multiple daily insulin injections, and the remainder of the patients were on a conventional 1–2 injections/day regimen.

The control group consisted of 21 age- and sex-matched volunteers. They were healthy as shown by their medical history, physical examinations, and a 12-lead electrocardiogram. All subjects had a normal exercise electrocardiogram and 2-h oral glucose tolerance test. A Hewlett-Packard 77020A ultrasound color Dop-

pler system was used for M-mode and Doppler echocardiographic studies. Standard recording techniques were used, and analysis of Doppler recordings was made in a method previously described (4,5). The heights of early diastolic flow-velocity peak and late atrial diastolic flow-velocity peak were measured, and the ratio between the heights was calculated. Duration of early flow-velocity peak and its descent slope were also determined (5). The heart-rate variation during deep breathing and the heart rate (30:15) and blood pressure responses to standing up were determined by a standard technique (4).

Blood glucose and HbA_1 concentrations were determined at the time of the study. Data on the patients' HbA_1 measurements during the last 3 yr were gathered, and the mean HbA_1 was calculated from these values (mean = 7 determinations/patient). The differences between the groups were analyzed via Student's *t* test or Mann-Whitney *U* test when appropriate. Standard formulas were used in calculating the linear correlations.

RESULTS

The peak early diastolic flow velocities were similar in the two groups, but the peak atrial flow velocities were higher in the diabetic group ($P < .01$; Table 1). Consequently, the ratio of peak early-to-atrial flow velocity was lower in the diabetic group ($P < .01$). Diabetic subjects had a higher resting heart rate than the healthy subjects ($P < .05$), and in one diabetic subject, analysis of the Doppler study could not be carried out because of tachycardia.

Six diabetic subjects had an abnormal heart rate response to deep breathing (≤10 beats/min) and/or to standing up (≤1.00) as a sign of cardiac autonomic neuropathy. None had postural hypotension (i.e., a fall in systolic blood pressure ≥30 mmHg on standing). The six patients with autonomic neuropathy had a lower ratio of peak early-to-atrial flow velocity than the patients without (0.99 ± 0.15 vs. 1.29 ± 0.25; $P < .05$; Fig. 1).

The peak early-to-atrial flow velocity ratio was not related to the duration of diabetes ($r = -.05$), blood glucose ($r = .03$), HbA_1 ($r = -.20$), mean HbA_1 ($r = -.24$), or heart rate ($r = -.21$), but was inversely related to age ($r = -.44$). The patients with retinopathy did not differ from the remainder of diabetic subjects with respect to this ratio. In the control group, the ratio was inversely related to heart rate ($r = -.55$).

DISCUSSION

The main finding of this study was that peak velocity of the left ventricular filling due to atrial contraction was augmented in diabetic subjects. There was no significant difference among the groups in the peak early filling velocity. Filling abnormalities were most prominent in patients with autonomic neuropathy, which is in accordance with a previous radionuclide study, but were not related to the duration of diabetes or to the degree of metabolic control (3).

Similar patterns of left ventricular filling have been described earlier in hypertrophic cardiomyopathy, hypertension, and coronary artery disease and are thought to reflect decreased left ventricular compliance (5–7).

TABLE 1
Clinical and laboratory data on diabetic and control subjects

	Subjects		
	Control	Diabetic	*P*
Heart rate (beats/min)	63 ± 9	69 ± 9	<.05
Systolic blood pressure (mmHg)	124 ± 9	130 ± 17	NS
Diastolic blood pressure (mmHg)	81 ± 9	80 ± 9	NS
Blood glucose (mM)	5.1 ± 0.4	12.3 ± 5.0	<.001
HbA_1 (%)	6.5 ± 0.7	12.0 ± 2.6	<.001
Heart rate response to deep breathing (beats/min)	19 ± 6	17 ± 10	NS
Heart rate response to standing up (30:15)	1.23 ± 0.18	1.16 ± 0.15	NS
Left ventricular end-diastolic diameter (mm/m^2)	28 ± 2	27 ± 2	NS
Shortening fraction (%)	34 ± 4	35 ± 7	NS
Left ventricular posterior wall thickness (mm)	10 ± 1	10 ± 1	NS
Septal thickness (mm)	10 ± 2	11 ± 2	NS
Peak early flow velocity (cm/s)	70 ± 11	70 ± 17	NS
Peak atrial flow velocity (cm/s)	47 ± 14	60 ± 14	<.01
Peak early-to-atrial flow velocity ratio	1.65 ± 0.67	1.19 ± 0.24	<.01
Duration of early diastolic flow (s)	0.22 ± 0.02	0.23 ± 0.03	NS
Descent slope of early flow-velocity peak (m/s^2)	5.0 ± 1.5	4.3 ± 1.4	NS

Values are means ± SD. $n = 21$/group. NS, not significant.

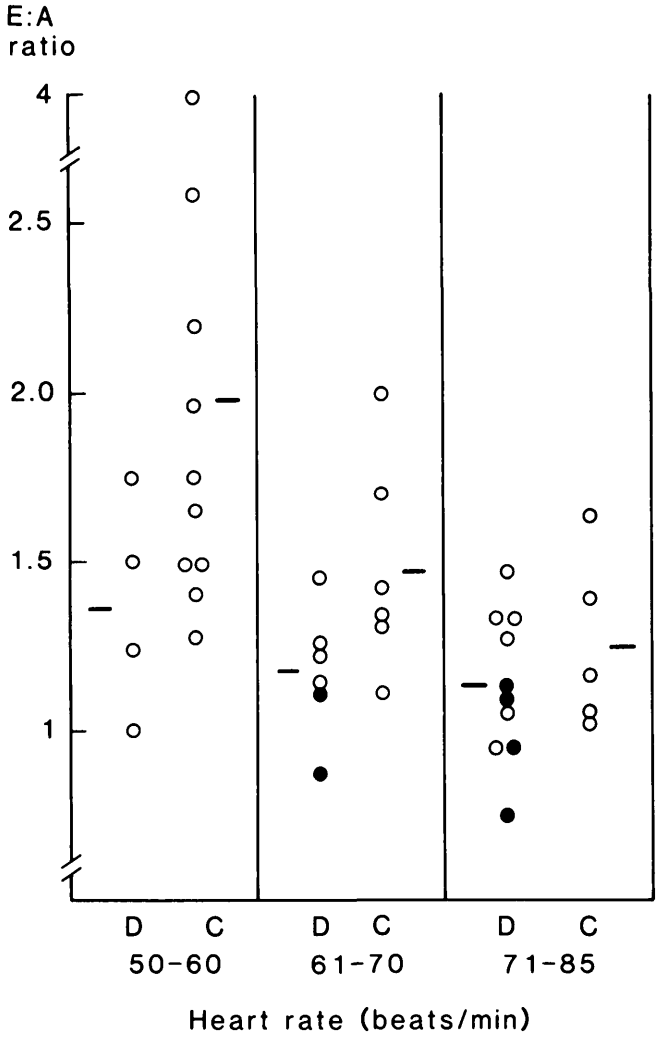

FIG. 1. Ratio of peak early-to-atrial flow velocity (E:A) in diabetic (D) and control subjects (C) divided into 3 groups according to simultaneous heart rate. ●, Diabetic subjects with cardiac autonomic neuropathy.

The diabetic group did not, however, differ from the control group in respect to ventricular wall thicknesses, and none had systemic hypertension. In view of the normal exercise electrocardiography and thallium scintigraphy of the diabetic subjects, it is also unlikely that asymptomatic coronary artery disease has any major impact on the abnormalities. However, it must be emphasized that left ventricular diastolic function is a complex phenomenon modified not only by muscle and chamber stiffness, but also by other factors such as heart rate and loading conditions of the ventricle. In accordance with earlier studies, the diabetic subjects with relatively long-standing disease had a slightly higher heart rate than the control group. Preliminary findings have shown that an acute increase in heart rate decreases the ratio of peak early-to-atrial flow velocity (8). Thus, the slightly higher heart rate of diabetic subjects is likely to exaggerate the difference in this ratio among the groups (Fig. 1). In conclusion, this study shows that the contribution of atrial contraction to left ventricular filling is augmented in patients with IDDM, particularly in those with cardiac autonomic neuropathy. These findings support the view that diabetes may modify myocardial properties and left ventricular compliance. Tachycardia, often associated with long-term disease, interferes with the interpretation of Doppler findings.

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