Increased Left Ventricular Torsion in Uncomplicated Type 1 Diabetic Patients

The role of coronary microvascular function

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OBJECTIVE — We used speckle tracking echocardiography to study the early changes in left ventricular (LV) torsion in young patients with uncomplicated type 1 diabetes and stress magnetic resonance imaging (MRI) to assess its interrelationships with coronary microangiopathy.

RESEARCH DESIGN AND METHODS — We recruited 33 asymptomatic subjects with type 1 diabetes and 32 age-matched healthy control subjects . All subjects underwent echocardiograms. Stress MRIs were performed in 30 subjects (8 healthy control subjects) to compute myocardial perfusion reserve index (MPRI).

RESULTS — A significant increase in LV torsion (2 ± 0.7 vs. 1.4 ± 0.7°/cm, $P < 0.05$) was identified in longer-term and retinopathy-positive type 1 diabetic subjects (1.9 ± 0.7 vs. 1.4 ± 0.7°/cm, $P < 0.05$) as compared with the healthy control subjects. The MPRI was independently associated with increased LV torsion.

CONCLUSIONS — We demonstrate that LV torsion is increased in young patients with uncomplicated type 1 diabetes and that coronary microvascular disease may play a key pathophysiological role in the development of increased LV torsion.

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There is increasing evidence for the presence of diabetic cardiomyopathy as a separate entity. However, detection of early changes in the myocardium is challenging in patients with diabetes. Speckle tracking echocardiography is a novel method of measuring left ventricular (LV) strain and rotation (1,2). Previous studies with tagged magnetic resonance imaging (MRI) have shown increased torsion in both patients with type 1 and type 2 diabetes (3,4). The main aim of this study was to confirm and extend these findings by exploring the potential pathophysiological mechanisms involved. We utilized speckle tracking to measure LV torsion and stress MRI to compute myocardial perfusion reserve index (MPRI), which is a measure of coronary microvascular function.

RESEARCH DESIGN AND METHODS

— The project was approved by the Multicenter Regional Ethics Committee in Birmingham, U.K. We recruited 65 subjects who provided informed consent: 33 subjects with type 1 diabetes (13 recently diagnosed [diabetes duration <5 years] and 20 with longer-term diabetes [>10 years]) and 32 age- and sex-matched control subjects with no cardiac history or diabetes. All subjects were without evidence of coronary artery disease or heart failure based on history, 12 lead electrocardiograms, a normal ejection fraction on echocardiography, and exercise testing.

Echocardiography was performed with a Vingmed Vivid 7 echocardiographic machine (GE Healthcare, Buckingham, U.K.) using a 2.5-MHz transducer, and standard echocardiographic views were obtained. Cardiac MRI was performed on a 3T Achieva MRI scanner (Philips, Eindhoven, the Netherlands) with a dedicated Sense Cardiac Coil. First-pass images at rest were obtained after Gadolinium contrast injection (0.1 ml/kg body wt, 4 ml/s). For perfusion images, a single-shot turbo field echo Sense pulse sequence was used with three slices per heartbeat. After a gap of 20 min, stress first-pass images were obtained at 3 min of adenosine infusion at a rate of 140 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

Analysis

LV torsion was measured using a speckle tracking system in an EchoPAC workstation (version 4.2.0; GE Healthcare) as previously described (5). Our reproducibility data demonstrated intra-observer and inter-observer variability of 0.24 ± 0.58 (bias ± 1.96 SD) and 0.15 ± 0.69, respectively, which are acceptable. The MPRI was obtained from the ratio of LV relative peak upslope at stress compared with rest as described earlier (6).

Statistics

SPSS (version 15.0; SAS Institute, Cary, NC) was used to perform the statistical operations. Continuous variables are expressed as means ± SD. Comparison between means was performed using ANOVA or χ^2 test. Pearson correlation coefficient (r) was used to describe the relationship between variables. Bland Altman plot was used to assess data reproducibility using MedCalc software (version 9.2.1.0; Mariakerke, Belgium).

RESULTS

— The baseline characteristics are summarized in Table 1. The E/A ratio was the same for those with type 1 diabetes and the healthy control subjects (1.5 ± 0.4 vs. 1.6 ± 0.4, P = NS) and E/E′ was significantly higher in the type 1

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Table 1—*Baseline characteristics and results*

	Newly diagnosed type 1 diabetes	Longer-term type 1 diabetes	Healthy control subjects
n	13	20	32
Sex (% female)	3 (23)	8 (40)	10 (31)
Age (years)	31 ± 10	34 ± 6	30 ± 8
Duration of diabetes (years)	4.8 ± 3	18.4 ± 7	—
A1C (%)	7.4 ± 0.8	8.3 ± 1	—
BMI (kg/m$^{2)}$	23 ± 2	26 ± 3	25 ± 3
Total cholesterol (mmol/l)	4.3 ± 1.2	4.4 ± 0.7	4.9 ± 0.9
HDL cholesterol (mmol/l)	1.5 ± 0.3	1.7 ± 0.5	1.7 ± 0.6
Triglycerides (mmol/l)	1.3 ± 1.2	1.1 ± 0.8	1 ± 0.5
Vo_{2max} (ml · kg^{-1} · min^{-1})	42.6 ± 10.2	35.6 ± 8.4*	44.1 ± 7.2
Retinopathy (%)	5 (38)	12 (60)	—
Peak LV torsion (°/cm)	1.7 ± 0.4	2 ± 0.7*	1.4 ± 0.7
MPRI	2.1 ± 0.2	1.7 ± 0.6*	2.3 ± 0.4

Data are means ± SD. *Significant difference compared with healthy control subjects.

diabetic subjects (7.7 ± 1 vs. 6.4 ± 1, $P <$ 0.001). Overall, the mean MPRI in type 1 diabetic subjects was 1.9 ± 0.5 and significantly lower than in the healthy control subjects (2.3 ± 0.4, $P < 0.05$).

Overall, peak LV torsion was significantly increased in type 1 diabetic subjects compared with healthy control subjects (1.9 ± 0.6 vs. 1.4 ± 0.7°/cm, $P < 0.01$). LV torsion was significantly increased (2 ± 0.7 vs. 1.4 ± 0.7°/cm, $P <$ 0.05) in longer-term type 1 diabetic subjects compared with healthy control subjects and was midway between that of longer-term type 1 diabetic subjects and healthy control subjects in those with recently diagnosed type 1 diabetes (1.7 ± 0.4°/cm). The LV torsion in type 1 diabetic subjects with retinopathy was significantly increased when compared with the healthy control subjects (1.9 ± 0.7 vs. 1.4 ± 0.7°/cm, $P < 0.05$). Type 1 diabetic subjects without retinopathy had nonsignificantly lower LV torsion when compared with subjects with retinopathy (1.7 ± 0.4 vs. 1.9 ± 0.7°/cm, P = NS).

On univariate analysis, LV torsion negatively correlated with MPRI ($r = -0.40$, $P < 0.05$), Vo_{2max} ($r = -0.26$, $P = 0.05$), and anterior-lateral E′/A′ ($r = -0.37$, $P < 0.01$). On multivariate regression analysis, only MPRI ($r = -0.41$, $P < 0.05$) was an independent predictor of LV torsion.

CONCLUSIONS — This study demonstrates for the first time that increased LV torsion complicates longer-term but not recently diagnosed type 1 diabetes. In a previous study of 53 subjects with diabetes without complications, radial contractility was increased and appeared to compensate for reduced longitudinal contractility (7). The longitudinal myocardial fibers are more susceptible to ischemia and fibrosis (8), which may result in a relative increase in short-axis function due to compensatory ventricular remodeling. Tissue doppler analysis in our study showed mild reductions in longitudinal function in type 1 diabetic subjects. Increased torsion may be compensatory for the subclinical reduction in long-axis function. However, the E/A ratio was the same for both groups, suggesting that increased torsion is one of the earliest stages of diabetic cardiomyopathy detected by echocardiography. Indeed, previous studies have shown increased LV torsion in aortic stenosis (9) and hypertrophic cardiomyopathy (10).

This is the first study to demonstrate that MPRI negatively correlates with and is an independent predictor of LV torsion. MPRI has been shown to be a good indicator of coronary microvascular function (11). Our findings imply that myocardial microvascular disease may play a key pathophysiological role in the development of increased torsion in these patients. We found that the longer-term and retinopathy-positive type 1 diabetic subjects exhibited the highest LV torsion with less marked abnormalities than the recently diagnosed and retinopathy-negative diabetic subjects. LV torsion in the healthy control subjects was the lowest of the three subgroups. These data are consistent with those of previous studies in type 1 and type 2 diabetic patients that have suggested a role for myocardial microvascular disease in the development of diabetic cardiomyopathy. Previous studies by our group have demonstrated that in type 1 diabetes, cardiac autonomic neuropathy, which begins at the apex, is associated with impaired myocardial blood flow regulation (12,13). Thus, subclinical dysinnervation of the apex in type 1 diabetic patients may also play a role in increasing apical rotation.

The development of heart failure in diabetic patients is affected by many secondary factors including hypertension, coronary artery disease, renal disease, and dyslipidemia. Our study shows that increased LV torsion may be one of the earliest features of diabetic cardiomyopathy in subjects without these complications. It is tempting to speculate that this may ultimately increase susceptibility to heart failure. If confirmed in large-scale prospective studies, this technique could form the basis of a screening tool for the identification of patients at risk for the development of heart failure resulting in the facilitation of the targeting of preventative approaches.

Limitations of our study are the small sample size and that this was a cross-sectional study and, thus, the natural history of the development and progression of altered torsion is unknown.

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