SCIENTIFIC LETTER

Familial dilated cardiomyopathy: assessment of left ventricular systolic and diastolic function using Doppler tissue imaging in asymptomatic relatives with left ventricular enlargement

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Dilated cardiomyopathy (DCM) has been recognised as a familial condition in a proportion of cases.[1] Left ventricular enlargement (LVE) with normal systolic function is common in asymptomatic relatives of patients with familial DCM; these relatives do not fulfil the diagnostic criteria for DCM. Many such relatives go on to develop overt DCM.[1] Although LV fractional shortening is by definition normal in relatives with LVE, the implication that these relatives have underlying myocardial pathology[2] would suggest that subtle LV systolic and diastolic abnormalities are detectable with appropriate techniques. We hypothesised that Doppler tissue imaging (DTI),[3 4] might reveal subtle abnormalities of systolic and diastolic function that may help to predict asymptomatic relatives with LVE that will go on to develop DCM. The aim of this study was to characterise LV systolic and diastolic function in asymptomatic relatives with LVE, using DTI and conventional echocardiographic techniques.

METHODS

Sixteen asymptomatic relatives with LVE (mean (SD) age 37 (13) years), from 15 families attending a referral centre between 1998 and 1999, underwent echocardiography and were compared with 22 patients with DCM (mean age 43 (9) years) undergoing follow up evaluation during the same time period. The majority of patients with DCM were in New York Health Association (NYHA) class I (9 (41%)) and II (12 (55%)). One patient was in NYHA class III. All of the relatives and patients had the following characteristics: sinus rhythm and a heart rate < 90 beats/min at the time of DTI study; no evidence of moderate to severe mitral regurgitation. Evaluation of asymptomatic relatives was performed following local ethics committee approval. LVE was defined as an LV end diastolic dimension (LVEDD) of greater than 112% of predicted values.[1] Predicted LVEDD was calculated according to the formula of Henry:[5] LVEDD $=$ [45.3 $\times$ body surface area 0.3] $-$ [0.03 $\times$ age] $-$ 7.2. All DCM patients had a predicted LVEDD $>$ 112% and fractional shortening $<$ 25%. Patients with coronary disease, hypertension, or valvar disease were excluded. Forty nine normal volunteers, aged 37 (14) years, without signs or symptoms of heart disease underwent echocardiography. There were no differences in age among relatives with LVE, patients with DCM, and normal controls. Images were taken using an Acuson 128 XP/10 (Mountain View, California) with DTI software. The LV filling signal was traced and the following variables derived: peak velocity of early (E) and late filling (A), deceleration time of E, and isovolumetric relaxation time. Motion of the mitral annulus was obtained with the M mode cursor directed from the apical four chamber view. The amplitude of displacement of the lateral and septal annulus was measured. From the apical four chamber view, a 10 mm sample volume was placed at each annulus. The following measurements of the annular velocities were made from the DTI recordings: systolic velocity, early and late diastolic velocities. All measurements were made in five cardiac cycles and averaged. Data are expressed as mean (SD). Group data were compared using the analysis of variance (ANOVA) with Fisher's PLSD test. A probability value of $p < 0.05$ was considered significant.

RESULTS

Conventional echocardiographic variables, lateral and septal annular excursions, and annular velocities are shown in table 1. LV diastolic dimension was larger in LVE than in controls, but smaller than in DCM. LV fractional shortening was lower in LVE than in controls, but higher than in DCM. Systolic velocities of lateral and septal annulus were lower in LVE than in controls, but higher than in DCM. Early diastolic septal annular velocity was lower in LVE than in controls, whereas early diastolic lateral annular velocity in LVE was not.

DISCUSSION

LV fractional shortening and long axis LV systolic function in LVE are intermediate between those in normal controls and in DCM patients. Longitudinally directed fibres situated in the myocardium of the LV walls play a major role in the maintenance of normal ejection fraction. Mitral annular excursion toward the apex in patients with DCM was reported to be reduced, and to correlate with LV ejection fraction. Systolic velocity of the mitral annulus has also been reported to correlate with LV ejection fraction in patients with DCM.[3] These results suggest that asymptomatic relatives with LVE have impaired LV systolic function compared with normal controls, though LV fractional shortening in LVE is by definition within normal limits.

Diastolic abnormalities are common in DCM. In this study, isovolumic relaxation time was higher in LVE than in normal controls, but was lower than in DCM. Early diastolic septal annular velocity was lower in LVE than in normal controls. These results may suggest minor abnormalities of LV diastolic function in LVE. However, early diastolic lateral annular velocity was not different from that in normal controls. Also, there were few differences in late diastolic velocity between

Abbreviations: DCM, dilated cardiomyopathy; DTI, Doppler tissue imaging; LV, left ventricular; LVEDD, left ventricular end diastolic dimension; LVE, left ventricular enlargement; NYHA, New York Health Association

Table 1 Two dimensional/Doppler echocardiographic findings and annular excursions and velocities

	DCM	LVE	Control
Two dimensional			
LV dimensions			
End diastole (mm)	65 (7)**	56 (4)**‡	46 (4)
End systole (mm)	54 (9)**	39 (4)**‡	27 (4)
Fractional shortening (%)	17 (6)**	31 (3)**‡	41 (5)
Thickness			
IVS (mm)	8 (1)*	8 (1)	9 (1)
Posterior wall (mm)	9 (2)	9 (1)	9 (1)
LA dimension (mm)	39 (6)**	36 (3)*	33 (5)
Doppler			
LV filling flow			
E (cm/s)	61 (19)**	81 (34)‡	77 (14)
A (cm/s)	59 (23)*	45 (13)†	50 (13)
E deceleration time (m/s)	190 (75)**	147 (39)‡	142 (25)
Isovolumic relaxation time (m/s)	100 (17)**	78 (12)*‡	70 (10)
Annular excursion and velocities			
Lateral annulus			
Excursion (mm)	10 (4)**	14 (3)*‡	17 (3)
Systolic velocity (cm/s)	8.4 (3.2)**	12.4 (2.7)*‡	14.0 (2.3)
Early diastolic velocity (cm/s)	11.9 (4.3)**	18.8 (5.0)‡	18.4 (4.2)
Late diastolic velocity (cm/s)	8.7 (2.0)**	10.0 (4.1)*	12.0 (3.2)
Septal annulus			
Excursion (mm)	9 (4)**	13 (3)*‡	15 (2)
Systolic velocity (cm/s)	5.8 (2.4)**	7.9 (1.2)*‡	9.0 (1.3)
Early diastolic velocity (cm/s)	7.8 (2.9)**	10.7 (2.4)*‡	12.2 (2.5)
Late diastolic velocity (cm/s)	8.6 (3.2)	8.4 (2.0)	9.8 (2.2)

DCM, dilated cardiomyopathy; E, early diastolic velocity of LV filling; IVS, interventricular septum; A, late diastolic velocity of LV filling; LA, left atrial; LV, left ventricular; LVE, left ventricular enlargement.
*$p<0.05$, **$p<0.01$ *v* controls.
†$p<0.05$, ‡$p<0.01$ *v* DCM.

lateral and septal annulus. The inconsistent results of assessment of diastolic function contrast with the consistently abnormal indices of LV systolic function in LVE relatives, suggesting that systolic dysfunction precedes diastolic dysfunction.

The majority of relatives with LVE has myocardial disease with inflammatory and/or histopathological abnormalities.[2] These histological changes seem to be associated with impaired LV systolic function in relatives with LVE. Fibrosis in the LV was more commonly found in patients with DCM than those in relatives with LVE, whereas inflammation tended to be more notable among relatives who did not have fibrosis.[2] These results suggest that fibrosis is a later phenomenon in the development of disease. This may partly explain why diastolic dysfunction is less prominent in early disease.

As only a small number of relatives with LVE were studied, our results should be confirmed in a larger study population. Asymptomatic relatives with LVE have impaired LV systolic function compared with normal controls. In contrast, there is little evidence of LV diastolic dysfunction, suggesting that LV systolic dysfunction precedes LV diastolic dysfunction early in the development of DCM. DTI reveals subtle abnormalities of systolic and diastolic function that may help to predict relatives with LVE that will go on to develop DCM.

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REFERENCES

1 **Baig MK**, Goldman JH, Caforio AL, *et al*. Familial dilated cardiomyopathy: cardiac abnormalities are common in asymptomatic relatives and may represent early disease. *J Am Coll Cardiol* 1998;**31**:195–201.
2 **Mahon NG**, Haven AJ, Baig MK, *et al*. Histological and immunohistochemical myocardial abnormalities in early familial dilated cardiomyopathy. *J Am Coll Cardiol* 2000;**35**(suppl A):202A.
3 **Gulati VK**, Katz WE, Follansbee WP, *et al*. Mitral annular descent velocity by tissue Doppler echocardiography as an index of global left ventricular function. *Am J Cardiol* 1996;**77**:979–84.
4 **Nagueh SF**, Middleton KJ, Kopelen HA, *et al*. Doppler tissue imaging: A noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. *J Am Coll Cardiol* 1997;**30**:1527–33.
5 **Henry WL**, Gardin JM, Ware JH. Echocardiographic measurements in normal subjects from infancy to old age. *Circulation* 1980;**62**:1054–61.