Echocardiographic evaluation of fibrous replacement in the myocardium of patients with Duchenne muscular dystrophy

Kazuo Miyoshi

Abstract

Objectives—To study myocardial echo amplitude in Duchenne muscular dystrophy and to examine the implications of increased echo amplitude.

Design—Regional echo amplitude, wall motion, and uptake of thallium-201 were examined in the left ventricular wall and the relation between these variables was investigated.

Setting—Hara National Sanatorium, Japan.

Patients—Seven healthy controls aged 10–28 years and 14 patients with Duchenne muscular dystrophy aged 12 to 30 years.

Interventions—Echocardiography with a sector scanner (Hitachi EUB-150, Japan) and a 3.5 MHz transducer (Hitachi EUP-S21, Japan); thallium-201 myocardial single photon emission computed tomography at rest with a rotating gamma camera system (Hitachi RC-135DT, Japan).

Main outcome measures—Echo amplitude of the myocardium, thickness and wall motion of the posterior wall and ventricular septum, and myocardial uptake of thallium-201.

Results—Areas of increased echo amplitude were detected along the outer half of or throughout the posterior wall of left ventricle in nine of the 14 patients. Their posterior walls showed significantly decreased maximal systolic and diastolic endocardial velocities (mean (SE) 31.4 (16.0) and 55.6 (53.5) mm/s) compared with normal subjects (57.7 (19.4) and 113.0 (27.5) mm/s), and decreased uptake of thallium-201. Their ventricular septa, however, showed normal echo amplitude and wall motion and normal uptake of thallium-201.

Conclusion—Areas of increased echo amplitude were detected in the posterior walls of left ventricles of patients with Duchenne muscular dystrophy. These areas were suspected to be the sites of myocardial fibrosis.

Duchenne muscular dystrophy is known to affect the heart. Typically, extensive replacement of myocardial fibres with connective tissue is found at necropsy. The posterobasal and lateral walls of left ventricle are the sites of the most extensive myocardial fibrosis. Electrocardiography, vectorcardiography, echocardiography, and radionuclide imaging are used to detect cardiac involvement in patients. The most commonly recognised electrocardiographic features are tall R waves in right precordial lead and deep Q waves in the limb leads and lateral precordial leads. Radionuclide imaging showed areas of hypoperfusion in the wall of the left ventricle and echocardiography showed a reduced maximal diastolic endocardial velocity and ejection fraction.

I know of no attempts to assess the extent of fibrous replacement in myocardium by echocardiography and to relate it to wall motion in Duchenne muscular dystrophy. Though myocardial fibrosis was assessed by echocardiography in myocardial infarction and cardiomyopathy, and an attempt was made to relate regional echo amplitude to left ventricular function in left ventricular hypertrophy. The posterior wall, which is the area of the left ventricle most extensively affected in Duchenne muscular dystrophy, is easily accessible by cross sectional and M mode echocardiography. When I examined by

Figure 1 Cross sectional and M mode echocardiograms from a 12 year old control. On the cross sectional echocardiogram epicardium and pericardium produced the strongest echo and myocardium weak homogenous speckle echoes. On the M mode echocardiogram myocardium produced a weak homogenous echo between the endocardium and the epicardium and pericardium with no reduction in wall motion. IVS, interventricular septum; LV, left ventricle; LA, left atrium; AML, anterior mitral leaflet; ENDO, endocardium; RV, right ventricle; MYO, myocardium; EPI, epicardium; PERI, pericardium.
Echocardiographic evaluation of fibrous replacement in the myocardium of patients with Duchenne muscular dystrophy

Figure 2 Cross sectional and M mode echocardiograms from a 30 year old patient with Duchenne muscular dystrophy showing a strong echo band in the outer half of myocardium in the long axis view of the cross sectional echocardiogram (arrows). A simultaneous M mode echocardiogram showed this echo band as thick band near the epicardium and pericardium (arrows). Wall motion is not impaired in this patient. See legend to figure 1 for abbreviations.

Figure 3 Cross sectional and M mode echocardiogram of a 24 year old patient with Duchenne muscular dystrophy. An abnormally strong echo band was detected in the outer half of myocardium of the posterior wall of left ventricle in the long axis view of the cross sectional echocardiogram (arrows). This echo band was detected as a thick band in the myocardium near the epicardium on M mode echocardiogram (arrows). Posterior wall motion was considerably reduced. See legend to figure 1 for abbreviations.

echocardiography the myocardium of the posterior wall of left ventricle in patients with Duchenne muscular dystrophy. I detected abnormally strong echoes in the myocardium. I have compared these abnormal echoes with the results of thallium-201 single photon emission computed tomography and with wall motion on the M mode echocardiogram.

Patients and methods

PATIENTS

I examined 14 patients with Duchenne muscular dystrophy aged 12 to 30 years and seven healthy controls aged 10-28. In all cases, the diagnosis was established on the basis of family history, high concentrations of serum creatine kinase, and other clinical investigation.

ECHOCARDIOGRAPHIC TECHNIQUE

Echocardiography was performed with a sector scanner (Hitachi EUB-150, Japan) and a 3-5 MHz transducer (Hitachi EUP-S21, Japan) and recorded on Polaroid films. The cross sectional echocardiograms were obtained by a sector scan along the long and short axis of left ventricle at the left fourth or fifth intercostal space and an M mode scan was performed simultaneously at the level of the chordae tendineae. To evaluate the echo pattern of the left ventricular wall the total gain setting and the depth gain setting were adjusted to an optimum level by hand so that there were no noise echoes in the left ventricular area. I measured the left ventricular systolic and diastolic dimensions (LVDs and LVDd), the systolic and diastolic posterior wall thickness of left ventricle (WTs and WTd), and the systolic and diastolic ventricular septal thickness (IVSTs and IVSTd). The ejection fraction (EF) was calculated according to the method described by Pombo et al. The maximal systolic endocardial velocity (SEVM) and the maximal diastolic endocardial velocity (DEVM) were measured by drawing a tangent to the steepest portion of the systolic and diastolic endocardial excursions and the slopes in mm/s measured according to the method described by Ishikawa et al. The same method was used to calculate the maximal systolic and diastolic endocardial velocities of ventricular septum (IVSVs and IVSvd).

THALLIUM-201 MYOCARDIAL SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

Thallium-201 myocardial single photon emission computed tomography was performed with the subject at rest. After injection of thallium-201, data on single photon emission computed tomography were collected by a rotating gamma camera system (Hitachi RC-135DT, Japan).

Results

On the cross sectional echocardiograms from the controls the strongest echoes came from the epicardium and pericardium. The myocardium produced homogeneous weak speckle echoes. On M mode echocardiograms from the controls the myocardium appeared as a weak homogeneous echo between the endocardium and the epicardium and pericardium (fig 1).

Five of fourteen patients with Duchenne muscular dystrophy had normal echoes and normal wall motion. The remaining nine patients had abnormally strong echoes on cross sectional and M mode echocardiograms. These echoes were of two types. One was an abnormally strong echo band in the outer half of the myocardium adjacent to the epicardium of the posterior wall of left ventricle on the cross sectional echocardiogram. In the simultaneous M mode echocardiogram there was a
Duchenne muscular dystrophy

Myocardial single photon emission computed tomography

Relation between echo patterns in posterior wall and left ventricular dimensions and wall motion (mean & SE)

<table>
<thead>
<tr>
<th>Controls</th>
<th>Duchenne muscular dystrophy</th>
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<tbody>
<tr>
<td>Normal</td>
<td>Abnormally strong echoes</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>(n = 5)</td>
</tr>
<tr>
<td>LVDs (mm)</td>
<td>30.1 (6.8)</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>45.4 (8.2)</td>
</tr>
<tr>
<td>EF (%)</td>
<td>65.8 (7.7)</td>
</tr>
<tr>
<td>LVEDd (mm)</td>
<td>47.0 (7.2)</td>
</tr>
<tr>
<td>IVSTd (mm)</td>
<td>11.7 (0.7)</td>
</tr>
<tr>
<td>SEVM (mm/s)</td>
<td>31.4 (10.4)</td>
</tr>
<tr>
<td>DEVM (mm/s)</td>
<td>113.0 (27.5)</td>
</tr>
<tr>
<td>Ventricular septum:</td>
<td></td>
</tr>
<tr>
<td>IVSTs (mm)</td>
<td>3.9 (1.7)</td>
</tr>
<tr>
<td>IVSTD (mm)</td>
<td>6.9 (1.7)</td>
</tr>
<tr>
<td>IVSS (mm/s)</td>
<td>39.9 (10.2)</td>
</tr>
<tr>
<td>IVSVD (mm/s)</td>
<td>35.9 (10.0)</td>
</tr>
</tbody>
</table>

LVDs and LVDD, left ventricular systolic and diastolic dimensions; EF, ejection fraction; WTd, and WTs, systolic and diastolic left ventricular posterior wall thickness; SEVM and DEVM, systolic and diastolic endocardial velocity; IVSTs and IVSTD, systolic and diastolic ventricular septal thickness; IVSS and IVSVD, maximal systolic and diastolic endocardial velocity of ventricular septum. *p < 0.05 compared with controls.

Discussion

The abnormally strong echo bands and speckle echoes that I detected in the myocardium of the posterior wall of patients with Duchenne muscular dystrophy coincided with one of the sites in the left ventricle most severely affected by fibrous replacement in Duchenne muscular dystrophy. 1, 2 In the present patients I have no direct evidence that these abnormal echoes indicate the site of fibrous replacement. None the less, the fact that the walls with abnormal echoes showed considerably reduced uptake of thallium-201 supports the hypothesis that there were areas of fibrosis. This evidence accords with reports that abnormally strong echoes were seen in the areas of myocardial scar tissue of myocardial infarction 3 and the areas of connective tissue or myocardial degeneration in cardiomyopathy. 4

The presence of collagen in tissue considerably increases ultrasonic attenuation, absorption, and velocity in tissue. Also collagen in its native state is more dense (1.16–1.33 g/cm³) than soft tissue, which has a density near to that of water. 4 These facts indicate that the acoustic impedance of connective tissue is different from that of myocardial tissue. When fibrous replacement advances and the connective tissue grows large enough in relation to the wave-

Figure 4 Thallium-201 myocardial single photon emission computed tomography in the same patient as shown in figure 3. Uptake of thallium-201 was reduced in the posterobasal (arrows) and apical walls of the left ventricle.

Figure 5 Cross sectional and M mode echocardiograms from a 24 year old patient with Duchenne muscular dystrophy. Abnormally strong specular echoes were detected throughout myocardium of the posterior wall of left ventricle (arrows). These abnormal echoes appeared as multiple lines on the M mode echocardiogram (arrows). Posterior wall motion was much reduced, whereas the septal wall showed normal echoes and normal wall motion. See legend to figure 1 for abbreviations.

the myocardium and considerably reduced posterior wall motion (fig 5). Myocardial single photon emission computed tomography at rest showed reduced uptake of thallium-201 in the posterior wall in the area that showed the abnormally strong speckle echoes (fig 6). The table shows that wall motion was reduced in the posterior walls showing abnormal echoes. In most of the patients who showed abnormally strong echoes in their posterior walls the ventricular septum did not show abnormally strong echoes or decreased uptake of thallium-201 (fig 6).

thick band near the echo of the epicardium and pericardium. Five patients showed these abnormally strong echo bands. In two wall motion was normal (fig 2) and in three it was decreased (fig 3). Single photon emission computed tomography showed that the uptake of thallium-201 was reduced in the area of the posterior wall that showed the abnormally strong echo band (fig 4). Abnormally strong specular echoes were seen throughout the myocardium of posterior wall of left ventricle in other patients with Duchenne muscular dystrophy. A simultaneous M mode echocardiogram showed multiple lines throughout
length of ultrasound, the ultrasound will be strongly reflected at the interface of myocardial tissue and connective tissue. Such specular interfaces are detectable when they are perpendicular to the ultrasound beam. This means that fibrous replacement of posterior wall is clearly detectable in the long axis view. I believe that the abnormally strong echo band and speckle echoes are made up of these reflected ultrasound beams. The fact that none of the nine patients with posterior wall abnormalities had similar abnormalities in their septal walls supports my hypothesis.

However, there are practical limitations in the detection of fibrous replacement by echocardiography if the area of connective tissue is smaller than the wavelength of the ultrasound. Then two different and adjacent points of fibrosis in the myocardium will become one point on the echocardiogram and small areas of connective tissue throughout the myocardium will be difficult to detect. Despite this limitation it is important to examine not only cardiac function but also fibrous replacement when echocardiography is performed in patients with Duchenne muscular dystrophy.

2 Frankel KA, Rossor RI. The pathology of the heart on progressive muscular dystrophy: epimyocardial fibrosis. *Hum Pathol* 1976;7:375-85.
8 Shapiro LM, Moore RB, Logan-Sinclair RB, Gibson DG. Relation of regional echo amplitude to left ventricular function and the echocardiogram in left ventricular hypertrophy. *Br Heart J* 1984;52:99-105.