Doppler tissue imaging for assessing left ventricular diastolic dysfunction in heart transplant rejection

S-M Stengel, Y Allemann, M Zimmerli, E Lipp, N Kucher, P Mohacsi, C Seiler

Abstract

Objective—To test the hypothesis that diastolic mitral annular motion velocity, as determined by Doppler tissue imaging and left ventricular diastolic flow propagation velocity, is related to the histological degree of heart transplant rejection according to the International Society of Heart and Lung Transplantation (ISHLT).

Methods—In 41 heart transplant recipients undergoing 151 myocardial biopsies, the following Doppler echocardiographic measurements were performed within one hour of biopsy: transmitral and pulmonary vein flow indices; mitral annular motion velocity indices; left ventricular diastolic flow propagation velocity.

Results—Late diastolic mitral annular motion velocity (A_done) and mitral annular systolic contraction velocity (SC) were higher in patients with ISHLT < IIIA than in those with ISHLT ≥ IIIA (A_done 8.8 cm/s vs 7.7 cm/s (p = 0.03); SC, 19.3 cm/s vs 9.3 cm/s (p < 0.05)). Sensitivity and specificity of A_done < 8.7 cm/s (the best cut off value) in predicting significant heart transplant rejection were 82% and 53%, respectively. Early diastolic mitral annular motion velocity (E done) and flow propagation velocity were not related to the histological degree of heart transplant rejection.

Conclusions—Doppler tissue imaging of the mitral annulus is useful in diagnosing heart transplant rejection because a high late diastolic mitral annular motion velocity can reliably exclude severe rejection. However, a reduced late diastolic mitral annular motion velocity cannot predict severe rejection reliably because it is not specific enough.

(Heart 2001;86:432–437)

Keywords: heart transplant rejection; diastolic function; Doppler tissue imaging; echocardiography

Within the past 20 years, cardiac transplantation has evolved from an experimental surgical procedure to standard care for patients with end stage heart failure. Although there have been significant advances in surgical techniques, in donor and recipient selection criteria, and in the management of transplant patients, allograft rejection remains the primary cause of morbidity in this group of patients.1 As acute rejection is initially asymptomatic, regular rejection surveillance is obligatory. For detecting allograft rejection and monitoring immunosuppressive treatment, clinical and laboratory examinations along with endomyocardial biopsies are conducted following a predetermined time schedule.

Endomyocardial biopsy still represents the gold standard for the detection of acute allograft rejection. Though it has been suggested that various non-invasive methods— including sensitive ECG indices,2 echocardiographic measurements,3,4 phosphorus-31 nuclear magnetic resonance spectroscopy,5 gamma scintigraphy,6 and serological7 and immunological8 tests—could replace endomyocardial biopsy, these techniques have not been proven to be clinically useful.

Doppler tissue imaging and left ventricular diastolic flow propagation velocity measurements are new Doppler techniques for assessing left ventricular diastolic function. Selective measurements of tissue contraction and relaxation velocities at the mitral annulus9 can detect left ventricular dysfunction more accurately than conventional echocardiography.10 11 As left ventricular diastolic dysfunction is an early event during allograft rejection, these techniques may be useful for detecting rejection non-invasively.

Our purpose in this study was to apply these new Doppler techniques to a cardiac transplant population and to assess their reliability in detecting endomyocardial biopsy proven acute allograft rejection.

Methods

STUDY POPULATION

Forty one consecutive adult orthotopic heart transplant recipients (mean (SD) age 53 (13) years; 35 men, six women), referred for routine examination, were included in a prospective study. All the patients were examined for transplant rejection by myocardial biopsy and Doppler echocardiography. The biopsy material was considered adequate in all cases and all the echocardiographic examinations were readable. In all, 151 biopsies and Doppler echocardiographic examinations, including Doppler tissue imaging, were performed. All patients gave their informed consent for their participation in the study, which was approved by the local ethics committee.

ENDOMYOCARDIAL BIOPSY

For monitoring transplant rejection, serial right ventricular endomyocardial biopsies were taken through the right jugular vein. In the first month after transplantation, an endomyocardial biopsy was taken weekly; in the second
month, once every two weeks; from the third to
the sixth month, once every four weeks; and
from the seventh to the 12th month, once every
eight weeks. In the second year, an endomyo-
cardial biopsy was taken once every three
months, and from the third year on, once every
six to 12 months. If required, additional
biopsies were taken.

Cellular rejection was determined using the
International Society of Heart and Lung
Transplantation (ISHLT) criteria\textsuperscript{12}: grade 0 =
no rejection; grade IA = focal (perivascular or
interstitial) infiltrate without myocyte damage;
grade IB = diffuse but sparse infiltrate without
myocyte damage; grade II = one focus only
with aggressive infiltrates and/or myocyte dam-
age; grade IIIA = multifocal aggressive infil-
trates and/or myocyte damage; grade IIIB =
diffuse inflammatory process with myocyte
necrosis; grade IV = diffuse aggressive poly-
ymphophil infiltrate with haemorrhage and
myocyte necrosis. Severe rejection was defined
at ISHLT > IIIA.\textsuperscript{13,14} Histological analyses
were graded by an experienced pathologist
blinded to the Doppler echocardiographic
findings.

The study population was subdivided in two
groups according to the degree of rejection:
ISHLT < IIIA and ISHLT > IIIA. Accord-
ingly, a patient could be in both groups
depending on the degree of rejection at the
time of a particular endomyocardial biopsy.

### Doppler Echocardiography

Doppler echocardiography, including Doppler
tissue imaging, was performed within one hour
of endomyocardial biopsy. Patients underwent
conventional transthoracic M mode cross
sectional echocardiography, as well as Doppler
examination, using an Acuson Sequoia C256
ultrasonography system (Acuson Inc, Moun-
tain View, California, USA). This was
equipped with 2.5–5.0 MHz phased array
cross sectional transducers, second harmonic
imaging, and Doppler tissue imaging software.

All measurements were performed in the
supine left lateral position, according to the
recommendations of the American Society of
Echocardiography.\textsuperscript{15}

Left ventricular M mode measurements
(mm) included septal wall thickness and poste-
rior wall thickness at end diastole, and left ven-
tricular internal diameter at end diastole and
end systole. From the diastolic measurements,
left ventricular mass index (g/m\textsuperscript{2}) was calcu-
lated, using the cube formula.\textsuperscript{16} Apical two and
four chamber views were acquired. Left
ventricular volume measurements for the
calculation of ejection fraction (%) were
performed as recommended by the American
Society of Echocardiography.\textsuperscript{17} The transtho-
racic examination also included spectral pulsed
wave Doppler analysis of transmitral flow
velocity, obtained at the tips of the mitral valve
leaflets. The following transmitral Doppler
variables were obtained: early diastolic flow
velocity (E, cm/s), late diastolic flow velocity
(A, cm/s), E:A ratio, deceleration time of early
transmitral filling (E-dec, ms), isovolumetric
relaxation time (IVRT, ms), and the duration of
late diastolic flow velocity (A-dur, ms).

Examination of the pulmonary veins was
performed using pulsed wave Doppler. The
sample volume was positioned approximately
1 cm within the right upper pulmonary vein.
Measurements in the apical four chamber view
included systolic and diastolic peak flow
velocities (cm/s) and their ratio, flow velocity at
atrial contraction (A wave, cm/s), and A wave
duration (ms).

Doppler tissue imaging is a modification of
the conventional Doppler technology. Using
filtering algorithms, tissue derived slow motion
Doppler signals (\(< 15 \text{ cm/s}\)) can be discrimi-
nated from blood flow velocity signals which
are of much lower intensity in a comparable
velocity range. Tissue derived Doppler signals
can be displayed either as time–velocity trac-
ings or as cross sectional or M mode colour images.18–20

Mitral annular Doppler tissue imaging measurements were performed from the apical four and two chamber views at the lateral, infer-
ior, and anterior site. Because septal wall motion and contraction in transplanted hearts is often paradoxical, delayed, or hypokinetic, we did not consider this site in our analysis.

The Doppler tissue imaging program was set to the pulsed wave Doppler mode. The Nyquist limit was adjusted to a velocity range of −16 to 20 cm/s. Gain was minimised to allow for a clear tissue signal with minimum background noise. Sweep rate was set at 100 mm/s. From the apical four chamber view a 2-mm sample volume was placed at the lateral corner of the mitral annulus. From the apical two chamber view the sample volume was placed at the anterior and inferior corner of the mitral annulus. Mitral annular Doppler tissue imaging measurements (fig 1) were recorded on VHS videotape for off line analysis. These included early (E\text{DTI}, cm/s) and late diastolic mitral annular motion velocity (A\text{DTI}, cm/s), E\text{DTI} : A\text{DTI} ratio, the deceleration time of early diastolic mitral annular motion velocity (E\text{decDTI}, ms), the duration of late diastolic mitral annular isovolumetric relaxation time (IVRT\text{DTI}, ms), mitral annular systolic contraction velocity (SC\text{DTI}, cm/s), and mitral annular systolic con-
traction time (SCT\text{DTI}, ms). All analysed variables were obtained at the lateral, inferior, and anterior site of the mitral annulus and averaged. Each measurement at a given site was performed over three consecutive cardiac cycles and these results were also averaged.

Interobserver variability (between observers x and y) for E\text{DTI} and A\text{DTI} was as follows:

\[
E_{\text{DTI}}: y = 0.048 + 0.809 \times x; r = 0.75, p < 0.0001, n = 138, \text{SEE}_{E\text{DTI}} = 2.0 \text{ cm/s}; \\
A_{\text{DTI}}: y = 0.026 + 0.691 \times x; r = 0.81, p < 0.0001, n = 136, \text{SEE}_{A\text{DTI}} = 1.2 \text{ cm/s}.
\]

Left ventricular diastolic flow propagation velocity was determined using colour Doppler M mode obtained from the apical four chamber view. It was determined as the slope of the first aliasing isovelocity line during early ventricular filling. The slope was assessed 4 cm distal to the mitral valve plane (fig 2).21 All Doppler echocardiographic measurements were performed by two echocardiographers blinded to the histopathological findings.

### Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>ISHLT &lt; IIIA</th>
<th>ISHLT ≥ IIIA</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>25</td>
<td>16</td>
</tr>
<tr>
<td>Number of EMB</td>
<td>128</td>
<td>23</td>
</tr>
<tr>
<td>Number of EMB/patient</td>
<td>5.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>54</td>
<td>50</td>
</tr>
<tr>
<td>Male</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.86 (0.15)</td>
<td>1.77 (0.2)</td>
</tr>
<tr>
<td>Follow up after heart transplant (days)</td>
<td>466 (525)</td>
<td>449 (587)</td>
</tr>
<tr>
<td>Reason for heart transplant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>VHD</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>139 (25)</td>
<td>120 (16)</td>
</tr>
<tr>
<td>LV internal diameter, ES (mm)</td>
<td>29.2 (5.6)</td>
<td>28.5 (6.4)</td>
</tr>
<tr>
<td>LV internal diameter, ED (mm)</td>
<td>42.6 (6.0)</td>
<td>39.9 (6.8)</td>
</tr>
<tr>
<td>Posterior wall thickness, ED (mm)</td>
<td>13.2 (3.3)</td>
<td>13.2 (3.7)</td>
</tr>
<tr>
<td>Septal wall thickness, ED (mm)</td>
<td>13.9 (2.8)</td>
<td>14.8 (3.2)</td>
</tr>
</tbody>
</table>

### Table 2 Doppler echocardiographic indices

<table>
<thead>
<tr>
<th>ISHLT &lt; IIIA</th>
<th>ISHLT ≥ IIIA</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M Mode measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal wall thickness, ED (mm)</td>
<td>13.9 (2.8)</td>
<td>14.8 (3.2)</td>
</tr>
<tr>
<td>Posterior wall thickness, ED (mm)</td>
<td>13.2 (3.3)</td>
<td>13.2 (3.7)</td>
</tr>
<tr>
<td>LV internal diameter, ED (mm)</td>
<td>42.6 (6.0)</td>
<td>39.9 (6.8)</td>
</tr>
<tr>
<td>LV internal diameter, ES (mm)</td>
<td>29.2 (5.6)</td>
<td>28.5 (6.4)</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>11.9 (32)</td>
<td>11.7 (28)</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>58 (14)</td>
<td>55 (13)</td>
</tr>
</tbody>
</table>

| Transmitial Doppler data |
| Early diastolic flow velocity (E) (m/s) | 0.84 (0.23) | 0.82 (0.24) | NS |
| Late diastolic flow velocity (A) (m/s) | 0.44 (0.15) | 0.44 (0.15) | NS |
| E:A ratio | 2.02 (0.68) | 2.05 (0.84) | NS |
| Deceleration time of early transmitial filling (E\text{dec}) (ms) | 134 (39) | 129 (41) | NS |
| Isovolumetric relaxation time (ms) | 90 (25) | 88 (36) | NS |
| Duration of late diastolic flow velocity (A-dur) (ms) | 120 (27) | 126 (37) | NS |

| Pulmonary vein flux indices |
| Systolic peak flow velocity (m/s) | 0.33 (0.11) | 0.32 (0.15) | NS |
| Diastolic peak flow velocity (m/s) | 0.64 (0.18) | 0.63 (0.11) | NS |
| Ratio systolic/diastolic peak flow velocity | 0.54 (0.21) | 0.51 (0.24) | NS |
| Flow velocity of atrial contraction (A, m/s) | 0.23 (0.06) | 0.23 (0.07) | NS |
| Duration of late diastolic flow velocity (A-dur, ms) | 160 (41) | 157 (31) | NS |

Values are n or mean (SD). CAD, coronary artery disease; DCMP, dilated cardiomyopathy; EMB, endomyocardial biopsy; ISHLT, International Society of Heart and Lung Transplantation; VHD, valve heart disease.

**STATISTICAL ANALYSES**

Values are given as mean (SD). Between-group comparisons of continuous demographic, echocardiographic, and Doppler flow velocity data were performed by the unpaired Student t test. Between-group comparisons of categori-
cal data were analysed using a χ² test. Linear regression analysis was applied for analysis of an association between continuous ISHLT values and Doppler echocardiographic indices, and for interobserver variability of Doppler tis-
sue imaging measurements.

For determining the accuracy of Doppler echocardiographic indices in detecting severe rejection, receiver operating characteristic (ROC) analysis was performed at a cut off value of ISHLT < III A or ≥ III A. A probability value of p < 0.05 was considered signifi-
cant.

www.heartjnl.com
Doppler tissue imaging in heart transplant rejection

Table 3 Doppler tissue imaging: mitral annular motion velocity data

<table>
<thead>
<tr>
<th>ISHLT &lt; IIIA</th>
<th>ISHLT ≥ IIIA</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early diastolic mitral annular motion velocity (E&lt;III) (cm/s)</td>
<td>12.7 (3.2)</td>
<td>11.5 (2.5)</td>
</tr>
<tr>
<td>Late diastolic mitral annular motion velocity (∆A&lt;III) (cm/s)</td>
<td>8.8 (2.4)</td>
<td>7.7 (1.8)</td>
</tr>
<tr>
<td>E&lt;III/∆A&lt;III</td>
<td>1.76 (0.48)</td>
<td>1.82 (0.44)</td>
</tr>
<tr>
<td>Duration of late mitral annular motion velocity (∆A&lt;III) (ms)</td>
<td>95 (20)</td>
<td>95 (16)</td>
</tr>
<tr>
<td>Mitral annular isovolumetric relaxation time (IVRT&lt;III) (ms)</td>
<td>116 (27)</td>
<td>110 (35)</td>
</tr>
<tr>
<td>Mitral annular systolic contraction time (∆C&lt;III) (ms)</td>
<td>103 (2.2)</td>
<td>93 (1.7)</td>
</tr>
<tr>
<td>Mitral annular systolic contraction time (∆C&lt;III) (ms)</td>
<td>229 (31)</td>
<td>223 (36)</td>
</tr>
<tr>
<td>LV diastolic flow propagation velocity (slope) (cm/s)</td>
<td>70.5 (33.8)</td>
<td>78.5 (49.7)</td>
</tr>
</tbody>
</table>

Values are mean (SD).

DTI, Doppler tissue imaging; ISHLT, International Society of Heart and Lung Transplantation; LV, left ventricle.

Results

PATIENT CHARACTERISTICS AND CLINICAL DATA

In all, 151 endomyocardial biopsies were obtained, ranging from 1–12 per patient (table 1). In 25 patients (with a total of 128 examinations), ISHLT was < IIIA; in 16 patients (23 examinations), ISHLT was ≥ IIIA.

Endomyocardial histopathology revealed ISHLT rejection grade 0 in 73 samples, grade IA in 30, grade IB in 22, grade II in 3, and grade IIIA in 23. The highest biopsy score obtained during the four month study period was IIIA. The patients’ regular immunosuppression regimen included cyclosporin, azathioprine and prednisone or cyclosporin, and mycophenolate and prednisone. All patients were in New York Heart Association functional class 0 or I.

There was no significant difference between the groups for age, sex, time between heart transplantation and follow up examination, reasons for heart transplantation, blood pressure, or heart rate (table 1). Body surface area was significantly larger in patients without than with severe rejection (ISHLT ≥ IIIA).

DOPPLER ECHOCARDIOGRAPHIC INDICES

M mode measurements, transmitral Doppler flow velocity data, and pulmonary vein flow indices (table 2) showed no significant difference between patients without (ISHLT < IIIA) and with severe transplant rejection (ISHLT ≥ IIIA).

MITRAL ANNULAR MOTION VELOCITY DATA

Both late diastolic mitral annular motion velocity (A<III) and mitral annular systolic contraction velocity (SC<III) were significantly higher in the group without than with severe rejection (table 3). All other mitral annular motion velocity indices, as well as left ventricular diastolic flow propagation velocity, were similar between the study groups (table 3).

Discussion

As heart transplantation is a standard form of care for patients with end stage heart disease, organ rejection is a major clinical problem, and the patient’s immune response has to be suppressed permanently. To optimise medical immunosuppressive treatment, allograft rejection needs to be detected at an early stage. So far, endomyocardial biopsy has been and is the gold standard, though many clinical approaches have been undertaken to find a less invasive method with sufficient accuracy to detect allograft rejection.

Table 4 Doppler tissue imaging: association between mitral annular motion velocity and flow propagation variables versus ISHLT values for assessing heart transplant rejection

<table>
<thead>
<tr>
<th>y Intercept</th>
<th>Slope</th>
<th>r</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early diastolic mitral annular motion velocity (E&lt;III) (cm/s)</td>
<td>14.6</td>
<td>−0.003</td>
<td>−0.095</td>
</tr>
<tr>
<td>Late diastolic mitral annular motion velocity (∆A&lt;III) (cm/s)</td>
<td>9</td>
<td>−0.004</td>
<td>−0.178</td>
</tr>
<tr>
<td>E&lt;III/∆A&lt;III</td>
<td>1.75</td>
<td>0.02</td>
<td>0.045</td>
</tr>
<tr>
<td>Duration of late mitral annular motion velocity (∆A&lt;III) (ms)</td>
<td>78.4</td>
<td>−1.55</td>
<td>−0.095</td>
</tr>
<tr>
<td>Mitral annular isovolumetric relaxation time (IVRT&lt;III) (ms)</td>
<td>96.1</td>
<td>−1.12</td>
<td>−0.063</td>
</tr>
<tr>
<td>Mitral annular systolic contraction time (∆C&lt;III) (ms)</td>
<td>114</td>
<td>0.83</td>
<td>0.031</td>
</tr>
<tr>
<td>Mitral annular systolic contraction time (∆C&lt;III) (ms)</td>
<td>153.5</td>
<td>−2.83</td>
<td>−0.105</td>
</tr>
<tr>
<td>Mitral annular systolic contraction time (∆C&lt;III) (ms)</td>
<td>232.1</td>
<td>−3.98</td>
<td>−0.136</td>
</tr>
<tr>
<td>LV diastolic flow propagation velocity (slope) (cm/s)</td>
<td>69</td>
<td>3.01</td>
<td>0.088</td>
</tr>
</tbody>
</table>

DTI, Doppler tissue imaging; ISHLT, International Society of Heart and Lung Transplantation; LV, left ventricle.
Changes in myocardial structure caused by rejection induced oedema, lymphocyte infiltration, increased mass, and myocardial necrosis have been shown to compromise myocyte function, resulting in increased myocardial stiffness and abnormal relaxation. Doppler tissue imaging, a non-invasive ultrasound procedure, is capable of selectively measuring the low velocity, high amplitude Doppler signals reflected by moving myocardium, while filtering out the high velocity, low amplitude signals emitted by moving blood cells. Doppler tissue imaging is an accurate method of detecting diastolic dysfunction, a condition that is known to be an early manifestation of rejection. However, in the present study—which included more than 150 endomyocardial biopsies among 41 heart transplant recipients—late diastolic mitral annular motion velocity analysis proved to be only moderately reliable in detecting severe allograft rejection. Neither early diastolic mitral annular motion velocity nor flow propagation velocity obtained during early left ventricular filling was associated with the degree of transplant rejection.

**TRADITIONALLY EMPLOYED ECHOCARDIOGRAPHIC METHODS FOR DETECTING HEART TRANSPLANT REJECTION**

There are several reasons why conventionally employed echocardiographic measurement variables have notoriously low sensitivity for detecting acute rejection. Wall thickness and left ventricular mass determinations are rather crude measurements which are influenced by operator dependent errors in performing M mode echocardiography. Pathophysiologically, rejection induced myocardial oedema manifested by an echocardiographically discernible increase in wall thickness is a rather late event. However, enhanced sensitivity of echocardiography for detecting rejection would require the ability to assess early rather than late cardiac alterations. Documenting the latter only enhances the specificity of the method.

In principle, the assessment of left ventricular diastolic function by Doppler echocardiography should allow the sensitive detection of acute rejection, as impaired left ventricular filling caused by myocardial lymphocyte infiltration and oedema occurs much earlier than increased myocardial wall thickness. However, Doppler transmitral and pulmonary venous flow velocity analyses have not upheld their promise in detecting rejection related diastolic dysfunction, for two main reasons. First, transmitral Doppler flow indices are influenced by variables other than ventricular diastolic function, such as age, heart rate, and most importantly ventricular loading conditions; pulmonary venous flow velocity indices are particularly variable, even in individuals without heart disease. Second, denervation of the transplanted heart, with its lack of autonomous regulation and invariable tachycardia, leads to a form of restrictive ventricular filling pattern that amounts to diastolic dysfunction in the absence of acute rejection. The lack of any statistical difference between our two study groups in the traditionally employed Doppler echocardiographic indices is further confirmation of these drawbacks.

**MITRAL ANNULAR MOTION VELOCITY TO DISCERN HEART TRANSPLANT REJECTION**

The main finding of our study—that is, the rather poor specificity of “new” Doppler techniques in detecting severe rejection—is in agreement with other recently published studies that have used a similar study design to ours. For example, Derumeaux and colleagues found values for sensitivity and specificity of 92% using early diastolic mitral annular motion velocity during mild or moderate and severe rejection, in comparison with a healthy group. With increasing rejection grade, early diastolic wall motion velocities decreased significantly (p > 0.001). Puleo and associates tested 121 heart transplant recipients who underwent Doppler tissue imaging at the time of surveillance endomyocardial biopsy. These investigators found a decrease in the peak velocity of E′PV at the inferior wall during moderate allograft rejection (0.14 (0.01) m/s; p < 0.0001) and no change in peak systolic velocity (0.08 (0.02) m/s; NS) in comparison with non-rejecting allograft recipients, with a sensitivity of 76% and a specificity of 88%. In 78 transplant recipients (among whom 75 histological analyses revealed no significant rejection), Mankad and colleagues found a reduction in posterior wall peak systolic and diastolic velocity gradients with rejection (p < 0.05 vs non-rejecting group), as well as a reduction in peak systolic (SCD′TI) and diastolic (EDTI) mitral annular motion velocities (p > 0.001 vs non-rejecting group), with a sensitivity of 93% and a specificity of 71%.

Certain discrepancies between these study findings and ours may have a methodological and technical basis. Pathologically, there was a lack of grade IV rejection and a relatively small number of cases of grade III or more in our study, compared with the studies cited above. This probably impaired the statistical ability to sense a severely blunted mitral annular velocity during diastole. Interobserver variability in off line analysis of Doppler tissue imaging variables was greater in our study than in others, and this may also have hampered the ability of late diastolic annular motion measurements to predict rejection. Both these problems could explain why in our study early diastolic mitral annular motion velocity only showed a trend towards lower values during episodes of rejection, whereas it was significantly lower in the investigations cited above.

The fact that the best threshold of late diastolic mitral annular motion velocity (below 9 cm/s) falsely detected rejection in almost 50% of cases also indicates that the pathophysiological problem of transplant related restriction to left ventricular filling impairs the reliability of any tool assessing diastolic function during the early rejection process.

**CLINICAL IMPLICATIONS AND CONCLUSION**

Diastolic mitral annular motion velocity measurements using Doppler tissue imaging should be employed routinely in the surveillance of
Doppler tissue imaging in heart transplant rejection. However, their value consists in reliably detecting patients not suffering from acute transplant rejection rather than in specifically detecting those with rejection. This is in patients with a late diastolic annular motion velocity above 9 cm/s it may be reasonably safe not to undertake endomyocardial biopsy at any particular point during rejection surveillance.


WEB TOP 10
www.heartjnl.com
These articles scored the most hits on Heart’s web site during July 2001
1 Long term results of mechanical prostheses for treatment of active infective endocarditis JM Guerra, MP Tornos, G Permanyer-Miranda, B Almenr, M Muerta, J Soler-Soler July 2001;86:221–6. (Education in Heart)
4 Matching the right drug to the right patient in essential hypertension MJ Brown July 2001;86:113–20. (Education in Heart)
5 Angiotensin receptor blockers for chronic heart failure and acute myocardial infarction JH McMurtry July 2001;86:97–103. (Education in Heart)
7 Diseases of the thoracic aorta R Erbel August 2001;86:227–34. (Education in Heart)
8 Role of stenting in coronary revascularisation AH Gershick July 2001;86:104–12. (Education in Heart)
9 Guideline for the management of patients with acute coronary syndromes without persistent ECG ST segment elevation February 2001;85:133–42. Visit the Heart website for hyperlinks to these articles, by clicking on “Top 10 papers” www.heartjnl.com
Doppler tissue imaging for assessing left ventricular diastolic dysfunction in heart transplant rejection

S-M Stengel, Y Allemann, M Zimmerli, E Lipp, N Kucher, P Mohacsi and C Seiler

Heart 2001 86: 432-437
doi: 10.1136/heart.86.4.432

Updated information and services can be found at:
http://heart.bmj.com/content/86/4/432

These include:

References
This article cites 30 articles, 4 of which you can access for free at:
http://heart.bmj.com/content/86/4/432#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Hypertension (3006)
Interventional cardiology (2933)
Clinical diagnostic tests (4779)
Echocardiography (2127)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/