Assessment of Left Ventricular Dyssynchrony in Patients With Conduction Delay and Idiopathic Dilated Cardiomyopathy

Head-to-Head Comparison Between Tissue Doppler Imaging and Velocity-Encoded Magnetic Resonance Imaging

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OBJECTIVES This study sought to compare tissue Doppler imaging (TDI) with velocity-encoded (VE) magnetic resonance imaging (MRI) for left ventricular (LV) dyssynchrony assessment.

BACKGROUND Cardiac resynchronization therapy (CRT) is proposed for patients with heart failure, depressed LV function, and a wide QRS complex. Selection is based mainly on electrocardiogram criteria, but recent data suggest that intraventricular dyssynchrony may be preferred for selection. An LV dyssynchrony can adequately be assessed with TDI, but this has not been compared directly with other imaging modalities. A VE MRI potentially allows direct myocardial wall motion measurements similar to TDI.

METHODS Twenty patients with heart failure, systolic LV dysfunction, and a wide QRS complex were included, as well as 10 normal individuals with normal QRS duration and LV function. The TDI and VE MRI data were acquired to study intraventricular dyssynchrony.

RESULTS Left ventricular dyssynchrony was not observed in normal individuals (mean dyssynchrony 2 ± 15 ms on TDI; mean -5 ± 17 ms on MRI, p = NS). In patients, mean LV dyssynchrony was 55 ± 37 ms on TDI; 49 ± 38 ms on MRI (p = NS). Good correlation between both modalities was observed (linear regression TDI = 0.99 × MRI − 5, n = 30, r = 0.98, p < 0.01). The MRI showed a small, nonsignificant underestimation of 5 ± 8 ms compared with TDI. Agreement between MRI and TDI for classification according to severity of LV dyssynchrony (minimal, intermediate, and extensive) was excellent (κ ± SE = 0.96 ± 0.07, p < 0.01) with 95% of patients classified identical.

CONCLUSIONS Both MRI and TDI yield comparable information on LV dyssynchrony; MRI is useful in the selection of patients for CRT.

Cardiac resynchronization therapy (CRT) has been proposed for treatment in patients with severe heart failure symptoms, depressed left ventricular (LV) function, and left bundle branch block morphology on the electrocardiogram (1). Improvement in symptoms and LV function has been shown in 70% to 80% of the patients after CRT (2–4). Candidates who may benefit from CRT are mainly selected by electrocardiogram criteria. Current inclusion criteria are a wide QRS complex (>120 ms), New York Heart Association (NYHA) functional class III or IV, and depressed LV ejection fraction <35%. However, 20% to 30% of the patients do not have a response to CRT, emphasizing the need for additional selection criteria. Several studies have shown that the main predictor of response to CRT may be the presence of intra-LV dyssynchrony (5–7). It was subsequently pointed out that electrical dyssynchrony (wide QRS complex) does not accurately reflect intra-LV dyssynchrony, but rather corresponds to interventricular (LV vs. right ventricle) dyssynchrony, suggesting that the surface electrocardiogram may not be optimal for patient selection (8,9). The LV dyssynchrony (i.e., the mechanical delay between septum and lateral wall contraction) can be adequately assessed by echocardiography using tissue Doppler imaging (TDI) (5–7,10,11).

The LV dyssynchrony assessment on TDI has not been compared directly with other imaging modalities. Recent studies have suggested magnetic resonance imaging (MRI) for assessing LV dyssynchrony. In particular, magnetic resonance tagging with strain analysis of the LV myocardium was applied to derive LV dyssynchrony, comparing the results with TDI (12). Velocity-encoded (VE) MRI, when applied for myocardial wall motion measurement (13,14), potentially allows direct myocardial wall motion measurement similar to TDI (i.e., comparing velocity graphs obtained in different parts of the myocardial wall during systole). Paelinck et al. (15) compared TDI with VE MRI when studying diastolic function in patients with...
hypertensive heart disease but normal or slightly reduced systolic function. Good agreement was found between MRI and TDI, but LV dyssynchrony was not evaluated. This issue was explored in the current study. Accordingly, 20 consecutive patients with heart failure (NYHA functional class III or IV), systolic LV dysfunction, and wide QRS complex underwent TDI and VE MRI. The LV dyssynchrony was assessed by comparison of peak systolic velocities of the basal septum and lateral wall. In addition, 10 normal individuals with normal LV function and a narrow QRS complex were studied.

**MATERIALS AND METHODS**

**Patients and study protocol.** The study population consisted of 20 consecutive patients (15 men, 5 women, mean age 57 ± 15 years) with heart failure (NYHA functional class III or IV), systolic LV dysfunction, and wide QRS complex underwent TDI and VE MRI. The LV dyssynchrony was assessed by comparison of peak systolic velocities of the basal septum and lateral wall. In addition, 10 normal individuals with normal LV function and a narrow QRS complex were studied.

Ten normal individuals (8 men, 2 women, mean age 57 ± 9 years) with normal QRS duration < 85 ms (mean ± SD, 81 ± 2 ms on electrocardiogram) and normal LV function were evaluated for comparison. Within 1 week (mean ± SD, 6 ± 4 days), patients and normal individuals underwent TDI and VE MRI, and LV dyssynchrony was evaluated. The study protocol was approved by the local medical ethics committee, and informed consent was obtained in all individuals before participation in the study.

**Tissue Doppler imaging with echocardiography.** Patients and normal individuals were imaged in the left lateral decubitus position using a commercially available system (Vingmed Vivid Seven, General Electric-Vingmed, Milwaukee, Wisconsin). Images were obtained using a 3.5-MHz transducer at a depth of 16 cm in the parasternal and apical views (standard long-axis and two- and four-chamber images). Standard two-dimensional and color Doppler data, triggered to the QRS complex, were saved in cine loop format. For TDI, color Doppler frame rates varied between 80 and 115 frames/s depending on the sector width of the range of interest; pulse repetition frequencies were between 500 Hz and 1 kHz, resulting in aliasing velocities between 16 and 32 cm/s. Intraventricular LV dyssynchrony was studied from the color Doppler images by off-line analysis using commercial software (Echopac 6.1, General Electric-Vingmed). The TDI data were analyzed by an experienced observer blinded to the clinical and MRI data. Sample volumes were placed at the basal level in the septum and lateral wall (using the four-chamber images) to derive velocity graphs. From these data, the time from the beginning of the QRS complex (on electrocardiogram) to peak systolic velocities in the septum and lateral wall were assessed, and the difference between these two peak systolic velocities was calculated as a measure of intraventricular dyssynchrony (referred to as the septal-to-lateral delay) (5–11). Interobserver and intraobserver agreement for assessment of the septal-to-lateral delay were 90% and 96%, respectively (16).

**Velocity-encoded MRI.** Within 1 week of the echocardiographic examination, MRI was performed using a 1.5-T MRI scanner (ACS-NT15 Gyroscan with the Powertrack 6000 gradient system; Philips Medical Systems, Best, the Netherlands). The body coil was used for transmission, and a five-element phased-array synergy cardiac coil was placed on the chest for signal reception. After scout images, standard two-chamber and four-chamber long-axis series for planning purposes [conform standard cardiac MR protocols (17), using balanced fast-field echo (18)], and an LV short-axis series for LV function analysis (19,20) were acquired, a three-directional VE MRI (21) was performed in the four-chamber orientation. Imaging parameters were as follows: echo time/repetition time, 5.0/6.9; flip angle, 50°; field-of-view, 370 mm; scan matrix, 128 × 76; slice thickness, 8 mm; four signal averages, gated cardiac triggering with retrospective reconstruction of 30 phases. Velocity was encoded in all three directions with a velocity sensitivity of 20 cm/s. The flow velocity was acquired in the ascending aorta using VE MRI with a velocity sensitivity of 150 cm/s (22).

The MRI data were analyzed by an experienced observer blinded to the clinical and echocardiographic data. Sample volumes were placed at the basal level of the septum and lateral wall in the 30 phase images of the MRI with the velocity encoded in the direction of the long axis of the LV. The mean velocity over the sample volume was measured, resulting in the myocardial wall velocity over one average cycle. During contraction and relaxation, the basal level moves, requiring manual correction for the placement of the sample volumes in each of the 30 phases. Intraobserver and interobserver variations of the image analysis were determined by repeated analysis by one observer (blinded to the first analysis with an interval >1 month) and additional image analysis of a second observer (blinded to the results from the first observer).

**Assessment of LV function and LV volumes with cine MRI.** The LV function analysis (19,20) is performed on the short-axis series using MASS analytical software (Medis, Leiden, the Netherlands), yielding end-systolic and end-diastolic LV volumes, and the ejection fraction was...
derived. In the presence of significant mitral regurgitation, the aortic volume flow was determined using Flow software (Medis), and the LV ejection fraction was obtained from the true systolic stroke volume, determined from the volume flow in the ascending aorta and the LV end-diastolic volume (23).

**Statistical analysis.** Continuous data were expressed as mean ± SD. Paired data were compared using the Student \( t \) test. A \( p \) value < 0.05 was considered significant. Agreement for dysynchrony classification with TDI and MRI, respectively, was assessed from a 3 \( \times \) 3 table using weighted \( \kappa \) statistics (Fleiss-Cohen weighting). Correlation between the dysynchrony measurements from TDI and MRI was examined using a Pearson correlation coefficient. Relations were determined by linear regression analysis. Bland-Altman analysis (24) was performed to study the differences in dysynchrony assessed with MRI and TDI, respectively. Intraobserver and interobserver variation for LV dysynchrony assessment with MRI was studied by calculating the coefficient of variation (defined as the standard deviation of the differences between the two series of measurements divided by the mean of both measurements) with confidence interval. For statistical analysis, SPSS for Windows version 11.0.1 (SPSS Inc., Chicago, Illinois) was used.

**RESULTS**

The study population consisted of 20 consecutive patients (15 men, mean age 57 ± 15 years) with heart failure (mean NYHA functional class 3.2 ± 0.4), systolic LV dysfunction (mean LV ejection fraction 40 ± 11\%), wide QRS complex (mean QRS duration 133 ± 19 ms), with LBBB or interventricular conduction delay. The baseline characteristics of the patients are summarized in Table 1.

Ten normal individuals (8 men, mean age 57 ± 9 years) with a normal QRS duration (mean 81 ± 2 ms), normal LV function (mean LV ejection fraction 65 ± 14\%) and normal LV volumes (mean LV end-systolic volume 58 ± 36 ml, mean LV end-diastolic volume 157 ± 55 ml) were evaluated for comparison.

**Table 1.** Baseline Characteristics of Patients

| Age (yrs) | 57 ± 15 |
| Gender (male/female) | 15/5 |
| Mean NYHA functional class | 3.2 ± 0.4 |
| NYHA functional class III | 16 |
| NYHA functional class IV | 4 |
| Mean QRS duration (ms) | 133 ± 19 |
| Mean LV ejection fraction (%) | 40 ± 11 |
| Mean LV end-diastolic volume (ml) | 215 ± 55 |
| Mean LV end-systolic volume (ml) | 93 ± 44 |
| Medication |  |  |  |
| Diuretics | 18 (90\%) |
| ACE inhibitors | 19 (95\%) |
| Beta-blockers | 15 (75\%) |
| Anticoagulants/aspirin | 20 (100\%) |

ACE = angiotensin-converting enzyme; LV = left ventricular; NYHA = New York Heart Association.

In Figure 1, an example of the assessment of LV dysynchrony in a normal individual is shown. Sample volumes are placed in the basal part of the septum and lateral wall. Velocities measured in these sample volumes are presented in velocity graphs. Sample volumes are also placed at the basal level of the septum and lateral wall, similarly to TDI (Fig. 1B). In this normal individual, no LV dyssynchrony was found (septal-to-lateral delay 0 ms). In Figure 2, an example of the LV dyssynchrony assessment in a patient is presented. A septal-to-lateral delay in peak systolic velocity of 115 ms was found with TDI and of 116 ms was found with MRI.

Intraobserver and interobserver variations of LV dysynchrony assessment with MRI were determined by repeated analysis by the same observer and one additional observer. The coefficient of variation (defined as the standard deviation of the differences between the two series of measurements divided by the mean of both measurements) was 10\% for both the intraobserver as well as the interobserver variation, with a confidence interval for both ranging from −11 ms to 8 ms. Differences in results for LV dyssynchrony measurement for the repeated analysis were statistically nonsignificant.

None of the normal individuals showed LV dyssynchrony, and the mean mechanical septal-to-lateral delay was −2 ± 15 ms on TDI as compared with −5 ± 17 ms on MRI (\( p = \) NS). In patients, the mean septal-to-lateral delay was 55 ± 37 ms on TDI, as compared with 49 ± 38 ms on MRI (\( p = \) NS).

In Figure 3, the correlation between LV dyssynchrony measured with TDI and MRI is presented. The differences between the results from both modalities are examined conformed to statistics described Bland and Altman (24). In Figure 3A, the extent of LV dyssynchrony measured by MRI is plotted versus the extent of LV dyssynchrony measured by TDI. A good correlation between the two techniques was observed (linear regression \( Y = aX + b \), with a \( (\pm SE) = 0.99 \pm 0.04 \) and b \( \pm SE = -5 \pm 2, n = 30, r = 0.98, p < 0.01 \)).

When the comparison was limited to the patients only, the correlation between TDI and MRI was also very good \( (Y = aX + b \text{ with } \pm SE = 1.0 \pm 0.1 \text{ and } b \pm SE = -6 \pm 4, n = 20, r = 0.97, p < 0.01) \).

The differences between MRI and TDI (Bland-Altman analysis) are presented in Figure 3B. The MRI showed a small nonsignificant underestimation of 5 ± 8 ms for LV dyssynchrony as compared with TDI. The confidence intervals ranged from −22 ms to 11 ms. For patients only, the underestimation of MRI versus TDI was 6 ± 9 ms (\( p = \) NS). The confidence intervals ranged from −24 ms to +13 ms.

The patients were categorized into three groups according to the extent of LV dyssynchrony on TDI: minimal LV dyssynchrony (<50 ms), intermediate LV dyssynchrony (50 to 80 ms), and extensive LV dyssynchrony (>80 ms). The results are presented in a 3 \( \times \) 3 table (Table 2). An excellent
agreement between MRI and TDI classification was found ($\kappa \pm SE = 0.96 \pm 0.07$, $p < 0.01$), 95% of the patients were classified as identical. On TDI, eight patients (40%) had minimal or no LV dyssynchrony (septal-to-lateral delay <50 ms), with a mean septal-to-lateral delay of 19 ± 18 ms; on MRI, nine patients (45%) were classified with minimal or no LV dyssynchrony on MRI, with a mean delay of 14 ± 17 ms ($p = NS$ vs. TDI). Intermediate LV dyssynchrony (septal-to-lateral delay between 50 ms and 80 ms) was observed in six patients (30%) on TDI, and in five patients

![Figure 1. Example of the assessment of left ventricular (LV) dyssynchrony in a normal individual. In the color-coded tissue Doppler images (TDI) (A, four-chamber view), sample volumes are placed in the basal part of the septum and lateral wall. Velocity graphs derived from the velocities measured in these sample volumes are presented in the right panel of A. In this normal individual, LV dyssynchrony is not present, as indicated by a septal-to-lateral delay in peak systolic velocity (arrow) of 0 ms. (B) The accompanying velocity encoded magnetic resonance imaging is presented. Similar to TDI, sample volumes are placed at the basal level of the septum and lateral wall. The velocity graphs are presented in panel C, confirming the absence of LV dyssynchrony (septal-to-lateral delay 0 ms).](image-url)
The mean septal-to-lateral delay was 59 ± 12 ms on TDI as compared with 57 ± 9 ms on MRI (p = NS). Extensive LV dyssynchrony (septal-to-lateral delay >80 ms) was noted in six patients (30%) both on TDI and MRI, respectively; the mean septal-to-lateral delay was 99 ± 15 ms on TDI as compared with 96 ± 10 ms on MRI (p = NS).

**DISCUSSION**

Cardiac resynchronization therapy is the proposed treatment in patients with LBBB or interventricular conduction delay and idiopathic dilated cardiomyopathy (1). Current selection criteria for CRT are a wide QRS complex (>120 ms) on electrocardiogram, systolic LV dysfunction with

*Figure 2.* Example of left ventricular (LV) dyssynchrony assessment in a patient. (A) The color-coded tissue Doppler images four-chamber view. The velocity graphs are presented in the right panel of A. There is extensive LV dyssynchrony with a septal-to-lateral delay in peak systolic velocities of 115 ms (arrows). The accompanying velocity encoded magnetic resonance imaging and velocity graphs are presented in panels B and C, respectively, confirming extensive LV dyssynchrony with a septal-to-lateral delay of 116 ms.
NYHA functional class III or IV, and a depressed LV ejection fraction. The relatively high percentage of non-responders to CRT (varying from 20% to 30%), however, indicates that additional criteria are needed (2–4). The presence of LV dyssynchrony has been proposed as an alternative criterion (5–7). Leclercq et al. (8) and Kass (9) showed that mechanical dyssynchrony in LV contraction determined from the septal-to-lateral delay in myocardial wall contraction is not reflected by electrical dyssynchrony (wide QRS complex) on electrocardiogram.

The method of choice for assessment of LV dyssynchrony is echocardiography using TDI (5–7,10,11). To our knowledge, this technique has not yet been validated against any other technique that can assess LV dyssynchrony. In the current study, velocity-encoded MRI was compared with TDI in a group of 20 patients with LBBB or interventricular conduction delay and idiopathic dilated cardiomyopathy. Also, 10 normal individuals with a normal QRS duration (<85 ms) and normal LV function and volumes were included for comparison. None of the normal individuals showed LV dyssynchrony on either TDI or MRI. For the patients, a strong correlation between TDI and MRI for assessment of LV dyssynchrony was obtained. Linear regression for all data resulted in a strong linear relation between MRI and TDI (Y = 0.99X − 4.9, n = 30, r = 0.98, p < 0.01). The differences between MRI and TDI (Bland–Altman analysis) are presented in (B). The MRI showed a small nonsignificant underestimation of 5 ± 8 ms for LV dyssynchrony as compared with TDI (dashed lines). The confidence intervals ranged from −22 ms to 11 ms (dotted lines).

The results of the current head-to-head comparison between TDI and MRI indicate that both modalities can be used interchangeably for LV dyssynchrony assessment. Cardiac MRI is of potential interest for evaluation of potential candidates for CRT because not only is LV dyssynchrony relevant for optimal prediction of response to CRT but also other factors are important in the patient selection for CRT. These factors include the size and shape of the LV (LV volumes and ejection fraction) and the presence and transmurality of scar tissue in the location where the LV lead should be positioned (25–27). An MRI can potentially provide all of this information with high accuracy because of the high spatial and temporal resolution of the technique.

Study limitations. In the current study, only patients with nonischemic cardiomyopathy were included; additional studies in patients with ischemic cardiomyopathy are needed. The temporal resolution achieved with MRI is three- to four-fold lower than the temporal resolution achieved with TDI. With MRI, the velocity was encoded not only in the direction of the long axis, but in all three directions. Only the velocity encoded in the direction of the long axis was used for analysis. Three-directional encoding results in a lower temporal resolution than one-directional encoding. The temporal resolution was still sufficient to accurately determine the LV dyssynchrony from the septal-

Table 2. Agreement Between LV Dyssynchrony Measurements With TDI and MRI

<table>
<thead>
<tr>
<th>MRI</th>
<th>&lt;50 ms</th>
<th>50–80 ms</th>
<th>&gt;80 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>T Minimal dyssynchrony (&lt;50 ms)</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D Intermediate dyssynchrony (50–80 ms)</td>
<td>1</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>I Extensive dyssynchrony (&gt;80 ms)</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
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κ ± SE = −0.96 ± 0.07, p < 0.01.

LV = left ventricular; MRI = magnetic resonance imaging; TDI = tissue Doppler imaging.
REFERENCES