3.2

Direct comparison between tissue Doppler imaging and velocity-encoded magnetic resonance imaging for the assessment of performance and temporal activation of the right ventricle in corrected tetralogy of Fallot patients

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A.E. van der Hulst
A.A.W. Roest
V. Delgado
L.J.M. Kroft
E.R. Holman
N.A. Blom
J.J. Bax
A. de Roos
J.J.M. Westenberg

ABSTRACT

Purpose: To compare velocity-encoded magnetic resonance imaging (VE-MRI) with tissue Doppler imaging (TDI) to assess right ventricular (RV) peak systolic velocities and timings in patients with corrected tetralogy of Fallot (cToF) and healthy subjects.

Materials and Methods: Local institutional review board approval was obtained, and patients or their parents gave informed consent. Thirty-three patients (20 male, 13 female; median age 12 years [11-15] [inter-quartile range]; range 8-18 years) and 19 controls (12 male, 7 female, median age 14 years [12-16], range 8-18 years) underwent VE-MRI and TDI. Peak systolic velocity and time to peak systolic velocity (expressed as percentage of cardiac cycle) were assessed at the RV free wall (RVFW) and RV outflow tract (RVOT). Data were analyzed using linear regression, paired and unpaired tests and Bland-Altman plots.

Results: Good correlation and agreement between the two techniques were observed. Peak systolic velocities: RVFW: r=0.95, mean difference -0.4 cm/s, p<0.01, RVOT: r=0.95, mean difference -0.4 cm/s, p=0.02. Timings: RVFW: r=0.94, mean difference -0.2%, p=0.44, RVOT: r=0.89, mean difference -0.5%, p=0.01. Peak systolic velocities were reduced in cToF patients (RVFW: 8.2 cm/s [6.4-9.7] vs. 12.4 cm/s [10.8-13.8], p<0.01, RVOT: 4.7 cm/s [4.1-7.2] vs. 10.2 cm/s [8.7-11.2], p<0.01). A time delay between the RVFW and RVOT was observed, which was significantly shorter in cToF patients (5.9% [4.9-7.4] vs. 8.4% [6.6-12.4], p<0.01).

Conclusions: VE-MRI and TDI enable assessment of RV systolic performance and timing of velocities at the RVFW and RVOT in cToF patients. Both techniques can be used interchangeably to clinically assess velocities and timings of the RV.
INTRODUCTION

In patients after surgical correction of Tetralogy of Fallot (cToF), right ventricular (RV) dimensions and ejection fraction are important determinants of long-term outcome (1-3). However, these parameters evaluate RV function at a global level. In contrast, assessment of myocardial velocities with echocardiographic tissue Doppler imaging (TDI) permits evaluation of regional RV systolic function and characterization of the RV mechanical activation sequence by timing of peak systolic velocities. Previous studies have shown that assessment of RV myocardial velocities enables reliable quantification of RV performance in various clinical conditions (4-8). In cToF patients, abnormalities in timings of systolic events of the RV free wall (RVFW) and right ventricular outflow tract (RVOT) have been observed, which may contribute to RV failure in cToF patients (9,10). Therefore, comprehensive assessment of velocities and timings of the RVFW and RVOT may provide better understanding of RV failure in cToF patients. Cardiac magnetic resonance imaging (MRI) is the method of reference to assess RV dimensions and function in cToF patients (11). Recently, velocity-encoded MRI (VE-MRI) has been introduced to assess myocardial velocities. In the left ventricle (LV), VE-MRI has been validated against TDI for the assessment of myocardial velocities and timings of peak systolic velocities (12-15). In patients with cToF, the use of VE-MRI to assess myocardial velocities is of interest as it enables comprehensive assessment of RV function in cToF patients during a single integrated MRI examination. Thus far, the application of VE-MRI and TDI to assess RV velocities and timings in different regions of the RV has not been directly compared to our knowledge.

Accordingly, the aim of our study was to compare velocity-encoded magnetic resonance imaging with tissue Doppler imaging to assess peak systolic velocities and timings within the right ventricle in patients with a corrected tetralogy of Fallot and in healthy subjects.

MATERIALS AND METHODS

Study population

All participants or their parents gave written informed consent. Thirty-three patients with corrected tetralogy of Fallot (cToF) [mean age 13 years ± 3 [standard deviation]] were prospectively recruited. In addition, 19 healthy controls with a similar age range were enrolled in the study. All cToF patients and healthy controls underwent transthoracic echocardiography (including TDI and MRI (including VE-MRI)) on the same day. Cardiac MRI was performed to assess peak systolic velocities and timings within the right ventricle in patients with a corrected tetralogy of Fallot and in healthy subjects.

Tissue Doppler imaging

Transcranial echocardiography images were acquired by a single experienced sonographer (8 years experience in echocardiography) using a commercially available system equipped with a 3.5 MHz transducer (Vivid-7,000, GE Vingmed Ultrasound AS, Horten, Norway). Subjects were in the left lateral decubitus position during image acquisition. Acquisition of TDI images was performed with adjusted sector width and angle to align the ultrasound beam with the direction of the myocardial motion. The color frame rate was ≥120 frames/s, yielding a temporal resolution <8.3 ms, and at least three consecutive beats were recorded. Analyses were performed off-line using EchoPac version 108.1.5 (General Electric Medical Systems). Longitudinal myocardial velocity curves were obtained by placing regions of interest (ROI) at the basal RVFW in the 4-chamber view (Figure 1, a and c) and at the lateral RVOT in a dedicated apical RVOT view (Figure 1, b and d), as previously reported (10). Semi-automated tissue tracking was used to maintain the sample area within the ROI throughout the cardiac cycle. Peak systolic velocity was measured at the RVFW (Figure 1c) and at the RVOT (Figure 1d).

In addition, time from R-wave of the ECG to peak systolic velocity was measured at both segments (Figure 1, c and d) and expressed as percentage of the RR interval to ensure accurate comparison of timings between the two techniques. Finally, the time difference between peak systolic velocity at the RVFW and peak systolic velocity at the RVOT was calculated in each cToF patient and control subject.

Magnetic resonance imaging

MRI was performed on a 1.5-Tesla pulsed gradient system (Intera, release 12; Philips Medical Systems, Best, the Netherlands) with 33 mT/m amplitude, 100 mT/m/ms slew rate, and 0.33 ms rise time. A five-element cardiac coil was used for signal reception. Multi-section transverse (16) cine imaging was performed to assess ventricular volumes and ejection fraction. A stack of slices was planned in the transversal plane, covering both ventricles throughout the cardiac cycle. Multi-section cine-images were acquired with a steady-state free precession sequence during breath hold at end-expiration, with scan parameters: repetition time (TR) 3.9ms, echo time (TE) 1.5ms, field of view 350mm; slice thickness 8mm; flip angle 50°; 1.8±2.0×8.0mm acquisition voxel reconstructed into a 1.4×1.4×8.0mm voxel; one signal acquired, 30 phases reconstructed, retrospective gating with 10% acceptance window. VE-MRI was performed in a 4-chamber orientation for the assessment of longitudinal velocity data at the RVFW (Figure 2, a and c), and in a double oblique RVOT view for the assessment of longitudinal velocities at the RVOT (Figure 2, b and d). Imaging parameters for VE-MRI acquisition were: repetition time 5.4ms, echo time 3.4ms, flip angle 10°, slice thickness 8mm, matrix 128×128, field-of-view 370mm actual temporal resolution 10.8ms. Retrospective triggering was used and data acquisition was performed during free breathing. Four signal averages were acquired to increase signal-to-noise ratio. Maximum velocity was set at 20cm/s to assess myocardial velocities. The maximum number of phases was reconstructed, yielding an effective temporal resolution in the velocity graph of approximately 10ms.
Magnetic resonance image analysis

All MRI data were analyzed using the MASS software package (Leiden University, Leiden, The Netherlands). LV and RV end-systolic and end-diastolic volumes were calculated by summation of discs after manual tracing of the endocardial borders at end-systole and end-diastole in all transverse slices. RV and LV ejection fractions were then automatically calculated by the MASS software. For assessment of myocardial velocities, a ROI was placed in the VE-MRI images at the basal RVFW (Figure 2c) and the lateral wall of the RVOT (Figure 2d) in all phases. Manual positioning of the ROI was performed throughout the cardiac cycle to ensure data sampling within the myocardial wall. The average velocity within the ROI was recorded in every cardiac phase. Time-velocity graphs were constructed from the RVFW (Figure 2c) and lateral RVOT segments (Figure 2d). From these graphs, peak systolic velocity and time to peak systolic velocity were derived. Timings are expressed as percentage of the RR interval. In addition, the time difference between peak systolic velocity at the RVFW and peak systolic velocity at the RVOT was calculated in each cToF patient and control subject. Finally, intra-observer and inter-observer agreement for the VE-MRI measurements were assessed in a blinded manner, by re-measuring peak velocities and timings at the RVFW and RVOT in 15 randomly chosen individuals. Intra-observer agreement was evaluated by repeating measurements within one week interval.

Statistical analysis

Continuous variables were tested for normal distribution with the Kolmogorov-Smirnov test. Continuous variables with a normal distribution are expressed as mean ± standard deviation whereas those variables without normal distribution are expressed as median and IQR. Categorical variables are presented as numbers and percentages. Comparisons between cToF patients and controls were analyzed using the Mann-Whitney U-test for continuous data and the Fisher’s exact test for categorical data. Comparisons between TDI and VE-MRI in the full population were analyzed using the paired t-test for normal distributed variables and with the Wilcoxon singed rank test for variables without a normal distribution. Linear regression analysis was used to evaluate the relation between TDI and VE-MRI. Logarithmic transformation was performed before linear regression analysis when variables were not normally distributed. Bland-Altman analysis was performed to assess the agreement between the two techniques. Intra-observer and inter-observer agreement of VE-MRI measurements was assessed using the intra-class correlation coefficient (ICC) for absolute agreement. Data were analyzed using the SPSS 17.0 software (SPSS Inc, Chicago, Illinois). A p-value of <0.05 was considered statistically significant and 95% confidence intervals (CI) were calculated.

RESULTS

Study population

Baseline characteristics of the cToF patients and controls are displayed in Table 1. cToF patients had significantly increased RV end-diastolic and RV end-systolic volumes (Table 1). Furthermore, RV ejection fraction was lower in cToF patients than in controls (median 48%, IQR: 47 to 53% vs. median 53% IQR 50 to 55%, p=0.01). All measurements at the RVFW and RVOT were feasible in each patient and control subject for both imaging techniques.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>cToF patient (n=33)</th>
<th>control (n=19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)*</td>
<td>12 (11-15)</td>
<td>14 (12-16)</td>
<td>0.16</td>
</tr>
<tr>
<td>Gender male/female n (%)</td>
<td>20/13 (60/40)</td>
<td>12/7 (63/37)</td>
<td>0.55</td>
</tr>
<tr>
<td>QRS duration (ms)*</td>
<td>132 (120-150)</td>
<td>96 (90-100)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cardiac cycle (ms)</td>
<td>796 ± 127</td>
<td>846 ± 120</td>
<td>0.16</td>
</tr>
<tr>
<td>BSA (m²)*</td>
<td>1.4 (1.2-1.7)</td>
<td>1.5 (1.4-1.7)</td>
<td>0.09</td>
</tr>
<tr>
<td>Age at corrective surgery (y)*</td>
<td>0.7 (0.5 - 1.1)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Type of corrective surgery n (%)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Infundibulectomy</td>
<td>7 (21)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Transannular patch</td>
<td>20 (61)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>RVOT patch</td>
<td>3 (9)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>PA patch</td>
<td>3 (9)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV-EDV (mL)*</td>
<td>117 (96-150)</td>
<td>141 (126-167)</td>
<td>0.03</td>
</tr>
<tr>
<td>LV-ESV (mL)*</td>
<td>52 (40-69)</td>
<td>62 (54-78)</td>
<td>0.05</td>
</tr>
<tr>
<td>LV-EF (%)</td>
<td>57 (51-60)</td>
<td>55 (53-59)</td>
<td>0.89</td>
</tr>
<tr>
<td>RV-EDV (mL)*</td>
<td>171 (152-205)</td>
<td>149 (128-175)</td>
<td>0.03</td>
</tr>
<tr>
<td>RV-ESV (mL)*</td>
<td>90 (75-106)</td>
<td>72 (59-82)</td>
<td>0.02</td>
</tr>
<tr>
<td>RV-EF (%)</td>
<td>48 (47-53)</td>
<td>53 (50-55)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Abbreviations: BSA: body surface area, EDV: end-diastolic volume, EF: ejection fraction, ESV: end-systolic volume, LV: left ventricle, PA: pulmonary artery, RV right ventricle, RVOT: right ventricular outflow tract. *median and inter-quartile range

TDI versus VE-MRI: peak systolic velocities

Table 2 and Figure 3 summarize the relationship between TDI and VE-MRI to assess peak systolic velocities at the RVFW and RVOT. At the RVFW, a small difference between the techniques was observed (Table 2). An excellent correlation between both techniques was observed in the full population (r=0.95, p<0.01) (Figure 3a). In addition, when the population was divided in cToF patients and controls, excellent correlations were observed between the two techniques (cToF patients r=0.91, p<0.01, controls r=0.90, p<0.01). Bland-Altman analysis showed limits of agreement of -2.3 to 1.5 cm/s (Figure 3b). Finally, intra- and inter-observer agreement of VE-MRI assessment of peak systolic velocities at the RVFW yielded an intra-observer ICC of 0.97 (p<0.01) and an inter-observer ICC of 0.96 (p<0.01). At the RVOT, the assessment of peak systolic velocities yielded a small difference between the two techniques in the full population (Table 2). Furthermore, a strong correlation between TDI and VE-MRI was observed in the full population (r=0.95, p<0.01) (Figure 3c), as well as after dividing...
the population in cToF patients and controls (cToF patients r=0.92, p<0.01, controls r=0.87, p<0.01).

Figure 3d shows the Bland-Altman plots for VE-MRI and TDI agreement. Finally, good intra-observer and inter-observer agreement was noted for the assessment of peak systolic velocities at the RVOT (intra-observer ICC 0.99, p<0.01, inter-observer ICC 0.97, p<0.01).

**TDI versus VE-MRI: timing of peak systolic velocities**

Table 2 and Figure 4 show the relationship between TDI and VE-MRI to measure time to peak systolic velocity corrected by the RR interval. At the RVFW, no significant difference between the techniques was observed (Table 2). In addition, an excellent correlation between TDI and VE-MRI measurements at the RVFW was observed in the full population (r=0.94, p<0.01) (Figure 4a). Furthermore, good correlations between TDI and VE-MRI measurements were noted when the population was divided in cToF patients and controls (cToF patients r=0.86, p<0.01, controls r=0.92, p<0.01). Bland-Altman analysis showed narrow limits of agreement (-3.2 to 2.9%) (Figure 4b). Finally, intra-observer analysis of time to peak systolic velocity at the RVFW yielded an ICC of 0.96 (p<0.01). Assessment of inter-observer agreement of time to peak systolic velocity at the RVFW showed an ICC of 0.92 (p<0.01).

At the RVOT, a small difference between TDI and VE-MRI for time to peak systolic velocity at the RVOT was observed (Table 2). A strong correlation was observed between TDI and VE-MRI (r=0.89, p<0.01) (Figure 4c). After dividing the population in cToF patients and controls, good correlations between TDI and VE-MRI measurements were observed (cToF patients r=0.91, p<0.01, controls r=0.73, p<0.01). Bland-Altman analysis of agreement between VE-MRI and TDI to assess time to peak systolic velocity at the RVOT is displayed in Figure 4d. In addition, intra-observer agreement analysis of time to peak systolic velocity at the RVOT yielded an ICC of 0.89 (p<0.01). Inter-observer agreement of time to peak systolic velocity at the RVOT was 0.84 (p<0.01).

**Table 2. Relationship between TDI and VE-MRI**

<table>
<thead>
<tr>
<th></th>
<th>TDI</th>
<th>VE-MRI</th>
<th>mean-difference</th>
<th>95% CI of difference</th>
<th>p-value paired samples coefficient</th>
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<tbody>
<tr>
<td><strong>Peak systolic velocity</strong></td>
<td></td>
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<tr>
<td>RVFW (cm/s)</td>
<td>91±25</td>
<td>96±20</td>
<td>-0.4±1</td>
<td>-0.7 to 0.2</td>
<td>0.01</td>
</tr>
<tr>
<td>RVOT (cm/s)*</td>
<td>64(46-94)</td>
<td>66(44-99)</td>
<td>-0.4±1</td>
<td>.</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Time to peak systolic velocity</strong></td>
<td></td>
<td></td>
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<tr>
<td>RVFW (%)</td>
<td>145±43</td>
<td>147±44</td>
<td>-2.2±1.6</td>
<td>-6.0 to 3.0</td>
<td>0.24</td>
</tr>
<tr>
<td>RVOT (%)</td>
<td>67±22</td>
<td>72±24</td>
<td>-0.5±1.1</td>
<td>-0.8 to 0.2</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Time difference</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>RVFW-RVOT (%)*</td>
<td>7.2(5.1-10.1)</td>
<td>6.8(5.3-9.2)</td>
<td>-0.4±2</td>
<td>.</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Timings are expressed as percentage of the RR interval. Abbreviations: CI: confidence interval, RVFW: right ventricular free wall, RVOT: right ventricular outflow tract, TDI: tissue Doppler imaging, VE-MRI: velocity encoded magnetic resonance imaging, *median and inter-quartile range

**Figure 1.**

Image analysis of tissue Doppler images. (a): Echocardiographic 4-chamber view of a cToF patient. Red region of interest indicates RVFW myocardial segment where TDI measurements were performed. (b): Echocardiographic apical view of the RVOT of a cToF patient. Red region of interest indicates myocardial RVOT segment where TDI measurements were performed. (c): Example of TDI assessment of peak systolic velocity and time to peak systolic velocity at the RVFW in a cToF patient. Peak systolic velocity can be derived from the time-velocity curve (vertical arrow). Time to peak systolic velocity can be measured by calculating time from R to peak systolic velocity (horizontal arrow). (d): Example of TDI assessment of peak systolic velocity and time to peak systolic velocity at the RVOT in a cToF patient. Peak systolic velocity can be derived from the time-velocity curve (vertical arrow). Time to peak systolic velocity can be measured by calculating time from R to peak systolic velocity (horizontal arrow). Abbreviations: Ao: aorta, LV: left ventricle, RA: right atrium, RV: right ventricle, RVOT: right ventricular outflow tract.
Finally, the time difference between time to peak systolic velocity at the RVFW and at the RVOT was calculated and compared between TDI and VE-MRI. The difference between the two techniques was not statistically significant (Table 2). An excellent correlation was observed between the two techniques for the overall population ($r = 0.79$, $p < 0.01$) and after dividing the population in patients and controls (cToF patient: $r = 0.75$, $p < 0.01$, control $r = 0.76$, $p < 0.01$). Finally, Bland-Altman analysis yielded narrow limits of agreement (-3.6 to 4.4%).

**Patients versus controls: VE-MRI peak systolic velocities and timing of velocities**

The VE-MRI derived peak systolic velocities and time differences between the RVWF and RVOT were compared between cToF patients and controls. The peak systolic velocity at the RVFW was significantly reduced in cToF patients (median: 8.2 cm/s, IQR: 6.4 to 9.7 cm/s vs. median 12.4 cm/s, IQR 10.8 to 13.8 cm/s, $p < 0.01$). Similarly, at the RVOT, the peak systolic velocity was reduced in cToF patients (median 4.7 cm/s, IQR: 4.1 to 7.2, vs. median 10.2 cm/s, IQR: 8.7 to 11.2 cm/s, $p < 0.01$). Finally, the time difference between peak systolic velocity at the RVFW and the RVOT was significantly shorter in cToF patients as compared with controls (median 5.9%, IQR: 4.9 to 7.4%, vs. median 8.4%, IQR: 6.6 to 12.4%, $p < 0.01$).

**DISCUSSION**

Our study provides a direct comparison of tissue Doppler imaging and velocity-encoded magnetic resonance imaging to assess peak systolic velocities and timings of the right ventricular free wall and right ventricular outflow tract in patients with a corrected tetralogy of Fallot and in healthy subjects. The main findings of the present study are: 1) velocity-encoded magnetic resonance imaging and tissue Doppler imaging have a strong correlation and a good agreement for the assessment of peak systolic velocities and timings at the right ventricular free wall and right ventricular outflow tract in patients with corrected tetralogy of Fallot as well as in healthy subjects 2) both velocity-encoded magnetic resonance imaging and tissue Doppler imaging showed reduced peak systolic velocities in patients with corrected tetralogy of Fallot at the right ventricular free wall as well as at the right ventricular outflow tract 3) velocity-encoded magnetic resonance imaging showed that the time difference between peak systolic velocity at the right ventricular free wall and the right ventricular outflow tract was significantly reduced in patients with corrected tetralogy of Fallot.

**VE-MRI: peak systolic velocities**

Evaluation of peak-myocardial systolic velocities enables quantitative assessment of RV performance. Meluzin and co-workers demonstrated a close relationship between peak systolic velocity at the tricuspid valve annulus and RV ejection fraction in healthy subjects as well as in patients with LV failure (7). In addition, in patients with inferior myocardial infarction, Alam et al. demonstrated that measurement of tricuspid valve annular velocities with TDI enabled differentiation between patients...
Figure 3. Correlation and agreement between TDI and VE-MRI for the assessment of peak systolic velocities at the RVFW and RVOT. (a) Correlation between TDI and VE-MRI for the assessment of peak systolic velocity at the RVFW. (b) Agreement between TDI and VE-MRI for the assessment of peak systolic velocity at the RVFW. (c) Correlation between log TDI and log VE-MRI for the assessment of peak systolic velocity at the RV outflow tract. (d) Agreement between TDI and VE-MRI for the assessment of peak systolic velocity at the RV outflow tract. Triangles: cToF patients, squares: controls. Abbreviations: RVFW: right ventricular free wall, RVOT: right ventricular outflow tract, TDI: tissue Doppler imaging, VE-MRI: velocity-encoded magnetic resonance imaging.

Figure 4. Correlation and agreement between TDI and VE-MRI for the assessment of time to peak systolic velocity at the RVFW and RVOT. (a) Correlation between TDI and VE-MRI for the assessment of time to peak systolic velocity at the RVFW. (b) Agreement between TDI and VE-MRI for the assessment of time to peak systolic velocity at the RVFW. (c) Correlation between TDI and VE-MRI for the assessment of time to peak systolic velocity at the RV outflow tract. (d) Agreement between TDI and VE-MRI for the assessment of time to peak systolic velocity at the RV outflow tract. Timings are expressed as percentage of the RR interval. Triangles: cToF patients, squares: controls. Abbreviations: RVFW: right ventricular free wall, RVOT: right ventricular outflow tract.
with and without RV dysfunction (4). In cToF patients, RV dysfunction is commonly observed (1). Cardiac MRI currently is the reference standard to measure volumes and ejection fraction of the RV (11). However, this parameter of RV function may be influenced by pulmonary regurgitation, commonly observed in this group of patients (18). In contrast, assessment of myocardial velocities is much less affected by loading conditions (19) and, therefore, it may provide a more accurate and reliable quantification of RV performance. In addition, myocardial velocities can be assessed at the regional level, providing more detailed information on systolic performance of the different RV components. Recently, VE-MRI was evaluated against TDI to assess LV myocardial velocities (12-15). However, no studies on VE-MRI for the assessment of RV myocardial velocities are available, to our knowledge. Our study provides a comparison of VE-MRI and TDI in healthy subjects and in cToF patients to assess myocardial velocities at the RVFW as well as at the RVOT. Excellent correlations between the two techniques were observed. A small difference between TDI and VE-MRI was observed, with VE-MRI slightly exceeding TDI velocities at both RV regions. The small bias may be explained by acoustic window limitations of TDI, preventing optimal alignment of the ultrasound beam with the myocardial wall in some patients. This may result in an underestimation of peak velocity. Other possible sources of bias may be phase errors or partial volume effects by VE-MRI, or technical differences between TDI (acquiring real-time velocities) and VE-MRI (acquiring a retrospectively-reconstructed time-velocity graph, averaged over 2-3 minutes). However, the observed statistical bias was small (≤0.7 cm/s) and unlikely to be of any clinical relevance.

VE-MRI: timing of peak systolic velocities

In addition to the evaluation of myocardial velocities, VE-MRI has been shown to be a reliable tool for the assessment of timings and dysynchrony of the LV (13,15). The use of VE-MRI to assess RV timings and possible dysynchrony has not been studied, to our knowledge. Our study compared VE-MRI with TDI to assess timings of the RVFW and RVOT in healthy controls as well as in cToF patients. VE-MRI showed close correlation and agreement with TDI at both RV regions. At the RVOT, a small difference between VE-MRI and TDI was observed (0.5%). However, with an average cardiac cycle length of 800 ms in our subjects, this difference equals approximately to 4 ms, which is smaller than the temporal resolution of either technique. Moreover, the assessment of a time difference between the RVFW and the RVOT was highly concordant between TDI and VE-MRI, without a significant difference between the two techniques.

VE-MRI velocities and timings: cToF patients versus controls

In cToF patients, RV dysfunction is commonly observed as a result of volume overload due to pulmonary regurgitation (1,3). Although MRI derived RV end-diastolic volume and ejection fraction are important parameters for clinical decision making in these patients, the exact pathophysiological mechanisms leading to RV failure remain to be elucidated to our knowledge (20). The study of regional peak systolic velocities may contribute to a better understanding of RV failure. A recent study observed reduced velocities at the RVFW in 25 asymptomatic adult cToF patients as compared with 25 healthy controls (5). Our study confirms this finding in young cToF patients. In addition, our study extends these findings by assessing myocardial velocities and timings at the RVOT. In tetralogy of Fallot patients, surgical correction involves relief of the pulmonary stenosis by transannular patching or infundibulectomy. As a result, functional abnormalities of the RVOT are often observed, which have been related to RV performance (10,21). In our study, a reduced peak systolic velocity was observed in cToF patients, providing further evidence of abnormal mechanical performance of the RVOT in these patients.

Finally, time differences between peak systolic velocities at the RVFW and RVOT were evaluated. Investigation of the mechanical activation of the RV may help improve the results of different pacing strategies. The detrimental effects of RV apical pacing have been extensively demonstrated (22-24). In addition, the benefits of cardiac resynchronization therapy (CRT) may be maximized if the mechanical activation sequence of the RV is fully understood. Currently, little is known about the mechanical activation pattern of the different RV regions in either healthy subjects or cToF patients. In our study, a time delay between peak systolic velocity at the RVFW and RVOT was observed both cToF patients and controls. This presence of a time delay within the healthy RV confirms the findings of previous authors (9,10,25). In addition, the time delay within the RV was significantly shortened in cToF patients. These findings may have important clinical implications, as the pathophysiological basis of CRT is restoration of a synchronous contraction pattern and possibly, this concept may not be applied to the RV. In future studies, VE-MRI and TDI should be employed to investigate the RV mechanical activation pattern and its relation with RV performance.

Study limitations

The observed statistical differences in timings of peak systolic velocities at the RVFW and RVOT between VE-MRI and TDI could have resulted from a difference in temporal resolution between the techniques. Nevertheless, the difference in temporal resolution between the techniques was very small (2.5 ms) and therefore unlikely to be relevant in clinical practice.

In conclusion, VE-MRI and TDI can be used interchangeably for the clinical assessment of myocardial velocities and timings of the RV in healthy subjects as well as in cToF patients. Using VE-MRI, significant differences were detected in myocardial velocities as well as timings of the RVFW and RVOT between cToF patients and controls. The assessment of timings of peak velocities at the RVFW and RVOT can aid in future research on the mechanical activation pattern of the RV in healthy subjects and in cToF patients.

In cToF patients, RV dysfunction is commonly observed as a result of volume overload due to pulmonary regurgitation (1,3). Although MRI derived RV end-diastolic volume and ejection fraction are important parameters for clinical decision making in these patients, the exact pathophysiological mechanisms leading to RV failure remain to be elucidated to our knowledge (20). The study of regional peak systolic velocities may contribute to a better understanding of RV failure. A recent study observed reduced velocities at the RVFW in 25 asymptomatic adult cToF patients as compared with 25 healthy controls (5). Our study confirms this finding in young cToF patients. In addition, our study extends these findings by assessing myocardial velocities and timings at the RVOT. In tetralogy of Fallot patients, surgical correction involves relief of the pulmonary stenosis by transannular patching or infundibulectomy. As a result, functional abnormalities of the RVOT are often observed, which have been related to RV performance (10,21). In our study, a reduced peak systolic velocity was observed in cToF patients, providing further evidence of abnormal mechanical performance of the RVOT in these patients.

Finally, time differences between peak systolic velocities at the RVFW and RVOT were evaluated. Investigation of the mechanical activation of the RV may help improve the results of different pacing strategies. The detrimental effects of RV apical pacing have been extensively demonstrated (22-24). In addition, the benefits of cardiac resynchronization therapy (CRT) may be maximized if the mechanical activation sequence of the RV is fully understood. Currently, little is known about the mechanical activation pattern of the different RV regions in either healthy subjects or cToF patients. In our study, a time delay between peak systolic velocity at the RVFW and RVOT was observed both cToF patients and controls. This presence of a time delay within the healthy RV confirms the findings of previous authors (9,10,25). In addition, the time delay within the RV was significantly shortened in cToF patients. These findings may have important clinical implications, as the pathophysiological basis of CRT is restoration of a synchronous contraction pattern and possibly, this concept may not be applied to the RV. In future studies, VE-MRI and TDI should be employed to investigate the RV mechanical activation pattern and its relation with RV performance.

Study limitations

The observed statistical differences in timings of peak systolic velocities at the RVFW and RVOT between VE-MRI and TDI could have resulted from a difference in temporal resolution between the techniques. Nevertheless, the difference in temporal resolution between the techniques was very small (2.5 ms) and therefore unlikely to be relevant in clinical practice.

In conclusion, VE-MRI and TDI can be used interchangeably for the clinical assessment of myocardial velocities and timings of the RV in healthy subjects as well as in cToF patients. Using VE-MRI, significant differences were detected in myocardial velocities as well as timings of the RVFW and RVOT between cToF patients and controls. The assessment of timings of peak velocities at the RVFW and RVOT can aid in future research on the mechanical activation pattern of the RV in healthy subjects and in cToF patients.
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