Ventricular kinetic energy may provide a novel noninvasive way to assess ventricular performance in patients with repaired tetralogy of Fallot

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ABSTRACT

Objective: Ventricular kinetic energy measurements may provide a novel imaging biomarker of declining ventricular efficiency in patients with repaired tetralogy of Fallot. Our purpose was to assess differences in ventricular kinetic energy with 4-dimensional flow magnetic resonance imaging between patients with repaired tetralogy of Fallot and healthy volunteers.

Methods: Cardiac magnetic resonance, including 4-dimensional flow magnetic resonance imaging, was performed at rest in 10 subjects with repaired tetralogy of Fallot and 9 healthy volunteers using clinical 1.5T and 3T magnetic resonance imaging scanners. Right and left ventricular kinetic energy (KERV and KE LV), main pulmonary artery flow (Q MPA), and aortic flow (Q AO) were quantified using 4-dimensional flow magnetic resonance imaging data. Right and left ventricular size and function were measured using standard cardiac magnetic resonance techniques. Differences in peak systolic KERV and KE LV in addition to the Q MPA/KERV and Q AO/KE LV ratios between groups were assessed. Kinetic energy indices were compared with conventional cardiac magnetic resonance parameters.

Results: Peak systolic KE RV and KE LV were higher in patients with repaired tetralogy of Fallot (6.06 ± 2.27 mJ and 3.55 ± 2.12 mJ, respectively) than in healthy volunteers (5.47 ± 2.52 mJ and 2.48 ± 0.75 mJ, respectively), but were not statistically significant (P = .65 and P = .47, respectively). The Q MPA/KERV and Q AO/KE LV ratios were lower in patients with repaired tetralogy of Fallot (7.53 ± 5.37 mL/[cycle mJ] and 9.65 ± 6.61 mL/[cycle mJ], respectively) than in healthy volunteers (19.33 ± 18.52 mL/[cycle mJ] and 35.98 ± 7.66 mL/[cycle mJ], respectively; P < .05). Q MPA/KERV and Q AO/KE LV were weakly correlated to ventricular size and function.

Conclusions: Greater ventricular kinetic energy is necessary to generate flow in the pulmonary and aortic circulations in repaired tetralogy of Fallot. Quantification of ventricular kinetic energy in patients with repaired tetralogy of Fallot is a new observation. Future studies are needed to determine whether changes in ventricular kinetic energy can provide earlier evidence of ventricular dysfunction and guide future medical and surgical interventions. (J Thorac Cardiovasc Surg 2015;149:1339-47)
With advancements in technology and surgical technique, most patients now undergo corrective surgical repair early in life and live into adulthood. Surgical correction of TOF typically involves ventricular septal defect closure, placement of an outflow patch. Expected disruption of the pulmonary valve that results in pulmonary regurgitation has been associated with progressive RV dilatation and ventricular dysfunction. Alterations in hemodynamics that frequently occur after repair ultimately contribute to poor long-term outcomes, including progressive exercise intolerance, ventricular arrhythmia, and sudden cardiac death.

Cardiac magnetic resonance (CMR) has become the gold standard to monitor patients with repaired TOF (rTOF). Volumetric and functional CMR parameters are used to guide the decision of when to perform pulmonary valve replacement to protect from the long-term sequelae of chronic pulmonary insufficiency. Monitoring with conventional CMR relies on detecting underlying morphologic changes, such as RV dilatation, to signify dysfunction. The newer 4-dimensional (4D) flow magnetic resonance imaging (MRI) technique can detect abnormal RV diastolic flow patterns in rTOF even when RV volumes or function is not substantially abnormal. Although pulmonary valve replacement results in reversal of RV dilation, the risk of cardiac death and arrhythmias may not be averted. More sensitive markers of RV dysfunction could help guide therapy and timing of pulmonary valve insertion.

Ventricular kinetic energy (KE) measurements provide a novel method of monitoring cardiac function and may provide an earlier imaging biomarker of declining ventricular efficiency in patients with rTOF compared with conventional measurements of ventricular size and function, which are based on morphologic changes. Previous studies have demonstrated the feasibility of calculating KE noninvasively with 4D flow MRI. In addition, 4D flow MRI provides aortic and main pulmonary artery (PA) flow data allowing the relationship of KE and the generated ventricular outflow to be evaluated. Traditionally, the ventricular–vascular relationship or coupling is described by elastance of each component, derived from pressure-volume loops. With the availability of 4D flow MRI, an analogous ventricular KE and vascular outflow relationship can be studied. To our knowledge, there have been no previous studies that have examined ventricular KE measurements in patients with rTOF. The purpose of this study was to assess differences in ventricular KE between rTOF and healthy volunteers using 4D flow MRI.

MATERIALS AND METHODS

Subjects

This single-center prospective cohort study was approved by the university Institutional Review Board. Data were acquired in compliance with all applicable Health Insurance Portability and Accountability Act regulations. Written informed consent was obtained from all subjects. For subjects aged 18 years or less, written informed consent was obtained from parents or legal guardians and assent obtained from subjects aged 6 years or more. Ten patients with rTOF (age 20.6 ± 12.2 years) and 9 healthy volunteers (age 38.9 ± 15.1 years) were included in this study. Healthy volunteers responded to public recruitment advertisements and were selected to participate after passing a health screening for cardiovascular disease. All subjects underwent CMR examinations after obtaining appropriate consent/assent.

Cardiac Magnetic Resonance

In subjects with rTOF, the clinically indicated CMR performed to measure ventricular size and function was followed by an investigational 4D flow MRI acquisition. Subjects with rTOF were scanned at 1.5T (HDx, GE Healthcare, Waukesha, Wis) or 3.0T (MR750, GE Healthcare), depending on the clinical availability of the scanners at the time of the examination and need for sedation. In healthy volunteers, 4D flow MRI and 2-dimensional cine balanced steady-state free precession were performed on 3.0T scanners (MR750, GE Healthcare).

Details of the 4D flow MRI sequence, phase contrast with vastly undersampled isotropic projection reconstruction (PC VIPR), have been reported. Briefly, 4D flow MRI parameters were as follows: field of view = 250 to 320 mm, spatial resolution = 1.3 mm isotropic, repetition time = 8.8 to 10.9 ms (1.5T) and 6.2 to 3.7 ms (3.0T), echocardiography time = 2.8 to 3.7 ms (1.5T) and 2.0 to 2.2 ms (3.0T), velocity

Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>BSA</td>
<td>body surface area</td>
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<tr>
<td>CMR</td>
<td>cardiac magnetic resonance</td>
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<tr>
<td>EDVI</td>
<td>end-diastolic volume index</td>
</tr>
<tr>
<td>EF</td>
<td>ejection fraction</td>
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<tr>
<td>ESVI</td>
<td>end-systolic volume index</td>
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<tr>
<td>4D</td>
<td>4-dimensional</td>
</tr>
<tr>
<td>IV</td>
<td>intravenous</td>
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<tr>
<td>KE</td>
<td>kinetic energy</td>
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<tr>
<td>KE&lt;sub&gt;LV&lt;/sub&gt;</td>
<td>left ventricular kinetic energy</td>
</tr>
<tr>
<td>KE&lt;sub&gt;RV&lt;/sub&gt;</td>
<td>right ventricular kinetic energy</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricular</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>PA</td>
<td>pulmonary artery</td>
</tr>
<tr>
<td>PC VIPR</td>
<td>vastly undersampled isotropic projection reconstruction</td>
</tr>
<tr>
<td>Q&lt;sub&gt;AO&lt;/sub&gt;</td>
<td>aortic flow</td>
</tr>
<tr>
<td>Q&lt;sub&gt;MPA&lt;/sub&gt;</td>
<td>main pulmonary artery flow</td>
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<tr>
<td>rTOF</td>
<td>repaired tetralogy of Fallot</td>
</tr>
<tr>
<td>RV</td>
<td>right ventricular</td>
</tr>
<tr>
<td>TOF</td>
<td>tetralogy of Fallot</td>
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Without surgical intervention, the natural history of tetralogy of Fallot (TOF) can lead to mortality rates of 25% in infants with severe obstruction within the first year of life and up to 95% by age 40 years. TOF is the most common cyanotic congenital heart disease accounting for 9% to 14% of all congenital cardiovascular defects. With advancements in technology and surgical technique, most patients now undergo corrective surgical repair early in life and live into adulthood. Surgical correction of TOF typically involves ventricular septal defect closure, placement of an outflow patch. Expected postoperative pulmonary regurgitation has been associated with progressive RV dilatation and ventricular dysfunction. Alterations in hemodynamics that frequently occur after repair ultimately contribute to poor long-term outcomes, including progressive exercise intolerance, ventricular arrhythmia, and sudden cardiac death.

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The KE of a voxel of blood was calculated using the equation \( KE = \frac{1}{2} m v^2 \), where the mass \( m \) represents the voxel volume multiplied by the density of blood \((1.05 \text{ g/mL})\) and the velocity \( v \) of each voxel was determined from 4D flow MRI. \( K_{RV} \) and \( K_{LV} \) were determined from the sum of the KE of the voxels within the segmented RV or LV blood pool, respectively, at each phase of the cardiac cycle. In the KE equation and concurrent with previous studies, the directionality component of velocity is removed because velocity is squared. Therefore, blood flowing in opposite directions within the ventricle would lead to additive KE values. KE values were calculated in millijoules and measured at 20 phases throughout the cardiac cycle.

### Data Analysis
Statistical analyses were conducted using SPSS version 20 (SPSS Inc, Chicago, Ill). Differences in peak systolic \( K_{RV} \) and \( K_{LV} \) in addition to the \( Q_{MPS}/K_{RV} \) peak systolic and \( Q_{MPS}/K_{LV} \) peak systolic ratios between rTOF and healthy volunteer groups were assessed using the Wilcoxon rank-sum test. The \( Q_{MPS}/K_{RV} \) peak systolic and \( Q_{MPS}/K_{LV} \) peak systolic ratios were measured as a marker of ventricular-vascular efficiency or ventricular KE loss. This is a novel ratio that allows quantitative evaluation of the relationship between ventricular outflow and KE. \( K_{RV} \) and \( Q_{MPS}/K_{RV} \) were compared with the RV EF, EDVI, and ESVI using the Pearson correlation coefficient. \( K_{LV} \) and \( Q_{MPS}/K_{LV} \) were also compared with the LVEF, EDVI, and ESVI using the Pearson correlation coefficient.

### RESULTS
Ten patients with rTOF (age 20.6 ± 12.2 years, 5 female) and 9 healthy volunteers (age 38.9 ± 15.1 years, 3 female) were included in this study. Characteristics of the rTOF group are summarized in Table 1. A total of 7 of the 10 patients with rTOF had transannular patch correction. The type of repair in the other 3 patients was not available. All subjects with rTOF underwent surgical correction when they were aged less than 2 years. None of the patients had significant residual ventricular septal defects, and all had some degree of pulmonary insufficiency. Seven subjects with rTOF were symptomatic at the time of CMR, including fatigue, palpitations, dyspnea, or chest discomfort.

Figure 1 shows the distribution of RV KE during systole and early diastole in a healthy volunteer and a subject with rTOF. During systole in healthy volunteers, the focal red signal in Figure 1 shows the highest KE at the RV outflow tract. During diastole, the highest KE was seen along the RV inner curvature, between the tricuspid valve.

### TABLE 1. Characteristics of subjects with repaired tetralogy of Fallot

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age at time of CMR (y)</th>
<th>Gender</th>
<th>BSA (m²)</th>
<th>Type of repair</th>
<th>Prior shunt</th>
<th>Age of last repair</th>
<th>Symptoms at time of CMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>F</td>
<td>0.98</td>
<td>Transannular patch</td>
<td>N/A</td>
<td>2 mo</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>M</td>
<td>0.96</td>
<td>Transannular patch and pulmonary valvectomy</td>
<td>Blalock–Taussig</td>
<td>6 mo</td>
<td>Dyspnea on exertion</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>F</td>
<td>1.17</td>
<td>Transannular patch</td>
<td>Blalock–Taussig ×2</td>
<td>8 mo</td>
<td>Palpitations, chest discomfort</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>F</td>
<td>1.51</td>
<td>Transannular patch</td>
<td>N/A</td>
<td>6 mo</td>
<td>Palpitations</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>F</td>
<td>1.59</td>
<td>Transannular patch</td>
<td>Blalock–Taussig</td>
<td>2 y</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
<td>F</td>
<td>1.62</td>
<td>Transannular patch</td>
<td>N/A</td>
<td>2 y</td>
<td>Fatigue</td>
</tr>
<tr>
<td>7</td>
<td>19</td>
<td>M</td>
<td>1.90</td>
<td>Transannular patch</td>
<td>N/A</td>
<td>10 mo</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>34</td>
<td>M</td>
<td>2.17</td>
<td>N/A</td>
<td>Waterston</td>
<td>16 y</td>
<td>Palpitations</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>M</td>
<td>2.31</td>
<td>N/A</td>
<td>Waterston</td>
<td>N/A</td>
<td>Palpitations</td>
</tr>
<tr>
<td>10</td>
<td>43</td>
<td>M</td>
<td>1.71</td>
<td>N/A</td>
<td>Waterston</td>
<td>N/A</td>
<td>Shortness of breath</td>
</tr>
</tbody>
</table>

CMR, Cardiac magnetic resonance; BSA, body surface area; N/A, not available.

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and the RV outflow tract. This distribution of RV KE was typical for the healthy volunteer group. In those with rTOF, the highest KE was seen along the RV outflow tract in both diastole and systole because of the presence of pulmonic regurgitation. This distribution of RV KE was typical for the rTOF group.

Table 2 summarizes volumetric CMR measurements, ventricular KE calculations, and flow measurements. The mean peak systolic KE<sub>RV</sub> in patients with rTOF, 6.06 ± 2.27 mJ, was higher than in healthy volunteers, 5.47 ± 2.52 mJ, although this difference was not significant (P = .65) (Figure 2, A). The mean peak systolic KE<sub>LV</sub> in patients with rTOF, 3.55 ± 2.12 mJ, was also slightly higher than in healthy volunteers, 2.48 ± 0.75 mJ (P = .47) (Figure 2, A). When corrected for body surface area (BSA), peak systolic KE<sub>RV</sub> and KE<sub>LV</sub> remained higher in those with rTOF (3.89 ± 1.30 mJ/m<sup>2</sup> and 3.55 ± 2.12 mJ/m<sup>2</sup>, respectively) than in healthy volunteers (2.97 ± 1.36 mJ/m<sup>2</sup> and 2.48 ± 0.75 mJ/m<sup>2</sup>, respectively; P = .15 and P = .08, respectively). There was no significant difference between BSA-corrected Q<sub>MPA</sub> (P = .25) and Q<sub>AO</sub> (P = .17) between rTOF and healthy volunteers (Table 2).

The mildly higher Q<sub>MPA</sub> and Q<sub>AO</sub> in healthy volunteers compared with rTOF is attributable to a larger scale increase in flow relative to increase in BSA. The Q<sub>MPA</sub>/KE<sub>RV</sub> and Q<sub>AO</sub>/KE<sub>LV</sub> ratios were lower in subjects with rTOF than in healthy volunteers (P < .05) (Figure 2, B). The differences in BSA-corrected Q<sub>MPA</sub> and Q<sub>AO</sub> (1.3× and 1.3× higher in healthy volunteers, respectively) were less compared with the differences in Q<sub>MPA</sub>/KE<sub>RV</sub> and Q<sub>AO</sub>/KE<sub>LV</sub> (2.02 and 2.76 higher in healthy volunteers, respectively). In subjects with rTOF with pulmonary or aortic insufficiency, the Q<sub>MPA</sub>/KE<sub>RV</sub> and Q<sub>AO</sub>/KE<sub>LV</sub> ratios were adjusted to include all forward flow, rather than net flow. These adjusted ratios remained significantly lower in subjects with rTOF than in healthy volunteers (P < .05).

The relationships between Q<sub>MPA</sub>/KE<sub>RV</sub> and Q<sub>AO</sub>/KE<sub>LV</sub> and standard CMR measurements of EDVI, ESVI, and EF are shown in Table 2. Although there was a moderately positive correlation between ventricular-vascular efficiency and RV EDVI and RV ESVI in subjects with rTOF (r = 0.67, P = .03), the other comparisons did not reach

**FIGURE 1.** A and B, Healthy volunteer RV KE maps in a long-axis orientation. The KE values of each voxel of blood in the segmented plane where the highest KE values are marked in red. Note that highest KE values are seen along the RV outflow tract during systole and along the RV inner curvature during diastole. C and D, rTOF RV KE maps oriented along the RV outflow tract. Note that highest KE values are seen along the RV outflow tract during systole and diastole because of the presence of pulmonic regurgitation in this patient. KE, Kinetic energy.
TABLE 2. Summary of standard volumetric and kinetic energy measurements in healthy volunteers and subjects with repaired tetralogy of Fallot

<table>
<thead>
<tr>
<th></th>
<th>Healthy volunteers</th>
<th>rTOF</th>
<th>P values</th>
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<tbody>
<tr>
<td>RVESVI (mL/m²)</td>
<td>74 ± 18</td>
<td>116 ± 52</td>
<td>.03</td>
</tr>
<tr>
<td>RVEDVI (mL/m²)</td>
<td>31 ± 9</td>
<td>60 ± 27</td>
<td>.007</td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>58 ± 8</td>
<td>48 ± 6</td>
<td>.005</td>
</tr>
<tr>
<td>LVEDVI (mL/m²)</td>
<td>78 ± 17</td>
<td>71 ± 20</td>
<td>.33</td>
</tr>
<tr>
<td>LVESVI (mL/m²)</td>
<td>30 ± 8</td>
<td>31 ± 12</td>
<td>.93</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62 ± 3</td>
<td>56 ± 7</td>
<td>.02</td>
</tr>
<tr>
<td>Mean peak systolic KE&lt;sub&gt;RV&lt;/sub&gt; (mJ)</td>
<td>5.5 ± 2.5</td>
<td>6.1 ± 2.3</td>
<td>.65</td>
</tr>
<tr>
<td>Mean peak systolic KE&lt;sub&gt;RV&lt;/sub&gt;/BSA (mJ/m²)</td>
<td>3.0 ± 1.4</td>
<td>3.9 ± 1.3</td>
<td>.15</td>
</tr>
<tr>
<td>KE&lt;sub&gt;RV&lt;/sub&gt;/BSA (mJ/m²)</td>
<td>2.5 ± 0.8</td>
<td>3.5 ± 2.1</td>
<td>.47</td>
</tr>
<tr>
<td>Mean peak systolic KE&lt;sub&gt;LV&lt;/sub&gt; (mJ)</td>
<td>1.4 ± 0.4</td>
<td>2.2 ± 1.1</td>
<td>.08</td>
</tr>
<tr>
<td>KE&lt;sub&gt;LV&lt;/sub&gt;/BSA (mJ/m²)</td>
<td>42.4 ± 9.8</td>
<td>32.4 ± 26.7</td>
<td>.25 (NS)</td>
</tr>
<tr>
<td>Qmpa/BSA (mL/cycle*m²)</td>
<td>45.8 ± 9.8</td>
<td>34.3 ± 23.6</td>
<td>.17 (NS)</td>
</tr>
<tr>
<td>Qmpa/KE&lt;sub&gt;RV&lt;/sub&gt; peak/BSA</td>
<td>19.3 ± 18.4</td>
<td>7.5 ± 5.4</td>
<td>.015</td>
</tr>
<tr>
<td>Qmpa/KE&lt;sub&gt;LV&lt;/sub&gt; peak/BSA</td>
<td>36.0 ± 7.7</td>
<td>9.7 ± 6.6</td>
<td>.0003</td>
</tr>
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</table>

Pearson correlation

<table>
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<tr>
<th></th>
<th>R</th>
<th>R</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qmpa/KE&lt;sub&gt;RV&lt;/sub&gt; vs RVEF</td>
<td>0.46</td>
<td>0.06</td>
<td>.21 (healthy), .87 (rTOF)</td>
</tr>
<tr>
<td>Qmpa/KE&lt;sub&gt;RV&lt;/sub&gt; vs RVESVI</td>
<td>-0.14</td>
<td>0.68</td>
<td>.72 (healthy), .03 (rTOF)</td>
</tr>
<tr>
<td>Qmpa/KE&lt;sub&gt;LV&lt;/sub&gt; vs LVEF</td>
<td>0.20</td>
<td>0.60</td>
<td>.61 (healthy), .07 (rTOF)</td>
</tr>
<tr>
<td>Qmpa/KE&lt;sub&gt;LV&lt;/sub&gt; vs LVEDVI</td>
<td>0.53</td>
<td>0.09</td>
<td>.14 (healthy), .80 (rTOF)</td>
</tr>
</tbody>
</table>

SD, Standard deviation; rTOF, repaired tetralogy of Fallot; RVESVI, right ventricular end-systolic volume index; RVEF, right ventricular ejection fraction; LVEDVI, left ventricular end-systolic volume index; LVESVI, left ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; KE<sub>RV</sub>, right ventricular kinetic energy; KE<sub>LV</sub>, left ventricular kinetic energy; Qmpa, main pulmonary artery flow; Qao, aortic flow.

statistical significance. In Figure 3, subjects with rTOF were grouped according to normal and abnormal standard RV volumetric measurements and peak KE<sub>RV</sub> was plotted. No significant KE<sub>RV</sub> differences were seen between these subgroups.

DISCUSSION

In this study, time-resolved KE in the RV and LV of healthy volunteers and subjects with rTOF was calculated noninvasively using 4D flow MRI. Although KE<sub>RV</sub> and KE<sub>LV</sub> were higher in subjects with rTOF compared with healthy volunteers, Q<sub>MPA</sub> and Q<sub>AO</sub> were the same between groups. This reflects the decreased ventricular-vascular efficiency in rTOF for both pulmonary and systemic circulations. These observations may indicate that patients with rTOF have greater energy loss in the RV and LV compared with healthy volunteers without a corresponding ability to generate increased pulmonary or systemic flow. This study helps illustrate the complex relationship between KE and flow between the ventricles and vasculature, within the LV and RV, and during systole and diastole in patients with rTOF compared with healthy volunteers.

Previously, accurate measurements of cardiac pressure and energy required invasive methods such as cardiac catheterization, limiting their utility in standard clinical practice. The development of 4D flow MRI has provided a noninvasive method of collecting 4D velocity data needed to determine pressure, flow, and energy measurements throughout the cardiac cycle. Noninvasive measurements of KE in the LV and RV were first described in prior studies using 4D flow acquisitions and were thought to provide a nondirectional measure of the amount of work invested in overcoming the inertia of intracardiac blood during the cardiac cycle. Although KE comprises only approximately 1% of the total LV work and 6% of total RV work at rest, it plays a larger role in the myocardial work under exercise conditions than at rest. Furthermore, over longer time spans any inefficiencies will contribute to excess work and presumably earlier failure.

To our knowledge, this study was the first to measure time-resolved KE<sub>RV</sub> and KE<sub>LV</sub> in subjects with rTOF using 4D flow MRI. Initial studies using MRI to calculate KE during early diastole using a single slice estimated total KE<sub>LV</sub> to be 4 to 5 times higher than the values measured in that single slice. However, these studies considered only the rotating vortex-like portion of flow without the straight streams of blood flow. Diastolic KE was later quantified in the RV by Fredricksson and colleagues with 4D flow MRI using calculated pathlines forward and backward in time from the isovolumetric contraction. Subsequently, Carlsson and colleagues calculated KE<sub>RV</sub> and KE<sub>LV</sub> throughout the cardiac cycle using a method similar to that used in our study. The peak systolic KE values calculated in our healthy volunteers were 2.48 ± 0.75 mJ in the LV and 5.47 ± 2.52 mJ in the RV, whereas Carlsson and colleagues obtained values of 4.9 ± 0.4 mJ in the LV and 7.5 ± 0.8 mJ in the RV. The lower KE values calculated using our 4D flow MRI technique are probably related to the fact that the peak velocities measured using PC VIPR were lower than those measured using Cartesian-based 4D flow MRI methods used by Carlsson and colleagues because of temporal blurring and averaging of velocities over the length of the scan. Because KE is proportional to the velocity squared, small differences in velocity are magnified when calculating KE values. Future studies using both approaches for 4D flow MRI will be necessary to confirm this. A benefit of using PC VIPR for 4D flow MRI is that it provides a larger field of view and higher spatial resolution than Cartesian approaches in the same scan acquisition time.

Previous research has shown the mortality rate in rTOF increases from 0.27% per year to 0.94% per year in the third decade of life, with sudden cardiac death as the major
cause of death.\textsuperscript{25} It often may be too late to intervene by the

time conventional measures such as LVEF have declined,
because the patient’s risk of sudden cardiac death has

already increased.\textsuperscript{26} Even after repair of TOF, research
comparing patients with rTOF with healthy subjects found

an increased number of vortical flow patterns in the RV,
illustrating altered intracardiac flow patterns.\textsuperscript{7} RV-PA

coupling has been shown to be impaired in patients with

rTOF and proposed as a maladaptive response of the
pulmonary arterial system to chronic RV hemodynamic

derangements.\textsuperscript{27} Disorganized flows within the ventricle

may contribute to KE but not necessarily to ventricular

outflow, representing ventricular-vascular inefficiency.
Ericksson and colleagues\textsuperscript{28} reported higher KE\textsubscript{LV} in

patients with dilated cardiomyopathy than in healthy

volunteers despite similar stroke volumes in both groups.
Although the ventricular-vascular relationship has been

expressed as the ratio between arterial elastance and

end-systolic elastance,\textsuperscript{14} we used the relationship between

peak systolic KE and ventricular outflow to serve as an

indirect measure of ventricular-vascular inefficiency with

respect to the blood pool. The range of Q\textsubscript{MPA}/KE\textsubscript{RV} and

Q\textsubscript{AO}/KE\textsubscript{LV} efficiency ratios was relatively large in our

healthy volunteers, and this could be explained by the small

peak systolic KE denominator component of 1.83 to 3.80

mJ in the LV and 1.03 to 9.18 mJ in the RV. Although the

KE values and flows were similar throughout healthy

volunteers, a wider range of normal values would be

expected when the ratio is taken. The rTOF ventricular

efficiency ratios had a narrower range due to the higher

peak systolic KE values.

Overall, there were no strong correlations between

(A) KE\textsubscript{RV}, KE\textsubscript{LV}, Q\textsubscript{MPA}/KE\textsubscript{RV}, and Q\textsubscript{AO}/KE\textsubscript{LV} and

(B) conventional measurements of ventricular size or

function. These results indicate that ventricular KE and

the flow/KE ratios are an earlier indicator of abnormal

cardiac function than EDVI, ESVI, and EF. We hypothesize

that these altered hemodynamics precede the gross

morphologic changes of the myocardium that are quantified

with these standard cardiac measurements. Consequently,
KE as a reflection of disordered flow and ventricular

inefficiency may provide an earlier indicator of ventricular
dysfunction.

Although altered hemodynamics may precede gross

morphologic changes in the myocardium, the relationship
among KE, hemodynamic derangements, and microscopic

myocardial changes warrants further study. Moderate RV

or LV systolic dysfunction has been associated with poor

clinical status of long-term survivors with rTOF, and

reduced LVEF in patients with rTOF has been shown to

be one of the strongest predictors of mortality.\textsuperscript{5,27} Further

studies have shown correlation between RV and LV

systolic dysfunction, suggesting unfavorable ventriculo-

ventricular interactions.\textsuperscript{27,29} Our results demonstrate

increased KE and decreased efficiency in both the RV and

LV of patients with rTOF. We found higher KE in the LV

compared with the RV, which is compatible with previous

findings.\textsuperscript{10,13} Of note, Carlsson and colleagues\textsuperscript{12} reported

higher peak systolic KE in the RV than the LV. However,

the exact mechanisms of how altered hemodynamics and

energy might contribute to ventricular dysfunction are

unclear. LV contraction contributes to RV pressure
development, and RV loading affects LV function, but

additional factors such as shared myocardial fibers and

septal deviation have been implicated in producing

unfavorable interventricular interactions that contribute to

ventricular dysfunction in rTOF.\textsuperscript{5,30} This ventricular
dyssynchrony reduces net cardiac output and reduces

FIGURE 2. A, Peak systolic KE\textsubscript{RV} and KE\textsubscript{LV} comparison between subjects with rTOF and healthy volunteers. Differences in KE\textsubscript{RV} (P = .65) and KE\textsubscript{LV} (P = .47) are not statistically significant. B, Ratios of outflow to peak systolic ventricular KE as markers for ventricular-vascular efficiency. Q\textsubscript{MPA}/KE\textsubscript{RV} was significantly lower in rTOF than in healthy volunteers (P = .015). Q\textsubscript{AO}/KE\textsubscript{LV} was also significantly lower in rTOF than in healthy volunteers (P = .0003). KE, Kinetic energy; rTOF, repaired tetralogy of Fallot; LV, left ventricular; RV, right ventricular; Q\textsubscript{mpa}, main pulmonary artery flow; KE\textsubscript{RV}, right ventricular kinetic energy; Q\textsubscript{ao}, aortic flow; KE\textsubscript{LV}, left ventricular kinetic energy.
myocardial efficiency. Ventricular strain, or local myocardial deformation, evaluated by CMR and echocardiography speckle-tracking may be an earlier predictor of regional ventricular dysfunction compared with EF in patients with rTOF. Whether microscopic myocardial changes or changes in KE and altered hemodynamics...
provide better indicators for declining ventricular function warrant further investigation.

In addition to examining biventricular KE, we also explored the time-resolved KE changes throughout the cardiac cycle. As in previous studies, we observed 1 systolic and 2 diastolic KE peaks. Carlson and colleagues showed that the KE was highest along the RV outflow tract during systole and that the KE was highest from the tip of the tricuspid valve to the center of the ventricle during diastole. Our findings showed a similar distribution of KE in healthy volunteers throughout the cardiac cycle. In subjects with rTOF, higher diastolic KE was seen along the RV outflow tract because of the presence of locally increased retrograde flow from pulmonic regurgitation.

Study Limitations

Although the magnitude images from 4D flow MRI have lower contrast between blood-pool and myocardium than steady-state free precession images, Roldan-Alzate and colleagues reported that ventricular volumes measured using this method are accurate. Using a time average of the magnitude images allowed for a single ventricular segmentation to be performed on images intrinsic to the 4D flow MRI data. An alternative would have been to segment the ventricles on all phases using time-resolved magnitude images. However, this method would be more time-consuming. Using time averaged images in the segmentation would be more limited in the setting of hyperdynamic ventricular motion but would be less limited in the setting of decreased ventricular wall motion.

Some of the subjects with rTOF were scanned at 1.5T and others at 3T, whereas all healthy volunteers were scanned at 3T with minor differences in parameters between 1.5 and 3T. This introduces a possible source of variability in the data. In addition, 3 subjects with rTOF did not receive IV contrast because of IV access difficulty and poor renal function. Although previous studies have shown that phase-contrast imaging after IV contrast administration improves signal to noise, adequate phase-contrast imaging was obtainable both before and after contrast.

Other limitations of this study include the small size of the 2 cohorts and heterogeneity of the subjects with rTOF. The study could have been strengthened with age and BSA-matched healthy volunteers, which may have reduced differences in flow data. Further studies in subjects with rTOF with similar repairs and with imaging performed earlier after repair will be necessary to determine the longitudinal significance of quantifying these hemodynamic abnormalities on long-term outcomes. Although we calculated the intraventricular KE, we did not account for the earliest stages of generating ventricular energy at the myocardial level, which other studies have evaluated. Also, the ventricular efficiency ratio proposed in this study used the peak systolic ventricular KE and aortic or main PA outflow. This was introduced as one marker for ventricular efficiency with respect to KE of the ventricular blood pool. An alternative consideration of ventricular efficiency could include the myocardial work that relates to generating ventricular outflow, which was not directly evaluated in this study. Correlation with pressure-volume loops available through catheterization would offer further insight into the degree of myocardial work that is transferred into KE. Finally, these metrics were all obtained at rest in the supine position. Patients with rTOF often have decreased exercise tolerance, which may be a reflection of inefficient ventricular contractions. During exercise, the flow rates and flow patterns that were observed in this study would likely change with KE playing a larger role.

CONCLUSIONS

Quantification of increased ventricular KE in patients with rTOF is a new observation. Our study illustrates the complex relationship between ventricular KE and flow through the great vessels. KE and KE were higher and QMPA/KE and QMPA/KE ratios were lower in patients with rTOF than in healthy volunteers. This is indicative of significantly greater energy losses in the RV and LV in patients with rTOF without a corresponding ability to generate increased pulmonary or systemic flow. Also, KE constitutes a greater portion of the total work in the right side of the heart than in the left side of the heart at baseline and during activity. Future studies may determine a closer relationship of KE and KE with exercise performance and capacity than standard CMR measurements. Although KE measurements derived from 4D flow MRI provide a novel noninvasive method of monitoring cardiac function, future investigations will be needed to determine whether changes in ventricular KE can provide earlier evidence of ventricular dysfunction and guide future medical and surgical interventions.

Conflict of Interest Statement

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References


