Assessment of Pulmonary Arterial Pressure by Velocity-Encoded Cine Magnetic Resonance Imaging in Children With Congenital Heart Disease

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Background: Velocity-encoded cine magnetic resonance imaging (VEC-MRI) has recently been reported as effective for assessing not only pulmonary blood flow (Qp) but also pulmonary arterial pressure (PAP) in adults. However, there have been few reports on the usefulness of VEC-MRI for assessing PAP in children with congenital heart disease (CHD).

Methods and Results: We evaluated 34 children with CHD. Qp and systemic blood flows (Qs) were determined by cardiac catheterization and VEC-MRI. The right-to-left Qp ratio (R/L) was measured by pulmonary perfusion scintigraphy and VEC-MRI. The pulmonary-to-systemic blood pressure ratio (Pp/Ps) was determined by cardiac catheterization. The acceleration time (AcT), ejection time (ET), peak velocity (PV), acceleration volume (AcV), and maximal change in flow rate during ejection (MCFR) in the pulmonary arteries, which were standardized by body surface area, were determined by VEC-MRI. The children were divided into 2 groups according to Pp/Ps. The Qs, R/L ratio and Qp/Qs obtained by VEC-MRI strongly correlated with those obtained by catheterization and scintigraphy. No significant differences in AcT, ET, AcT/ET, PV, or AcV were observed between the 2 groups. However, a significant difference was observed in MCFR. Furthermore, a significant correlation was observed between the MCFR and Pp/Ps.

Conclusions: This study clearly demonstrated that VEC-MRI is useful for assessing not only blood flow, but also PAP, by referring to MCFR in children. (Circ J 2013; 77: 3015–3022)

Key Words: Congenital heart disease; Pulmonary arterial hypertension; Pulmonary arterial pressure; Velocity-encoded cine magnetic resonance imaging (VEC-MRI)
adults. However, there have been few reports on the usefulness of VEC-MRI for assessing PAP in children.

The present study tested the following hypotheses: measurements of Qp and systemic blood flow (Qs) obtained using VEC-MRI are valid in children without shunt lesions (Part 1); the ratio of pulmonary-to-systemic blood flow (Qp/Qs) obtained by VEC-MRI correlates with that obtained by cardiac catheterization in children with shunt lesions (Part 2); and the VEC-MRI method is useful for assessing PAP in children with CHD (Part 3).

Methods

Subjects

From June 2006 to November 2008, we prospectively enrolled 34 clinically stable children with CHD who ranged in age from 4 months to 16 years (Table 1). All children were admitted to the Department of Pediatrics of Asahikawa Medical University Hospital. A total of 15 children without shunt lesions were enrolled in Part 1 of the study; of these, 10 had undergone intracardiac surgical repair for coarctation of the aorta (n=4), tetralogy of Fallot (n=3), transposition of the great arteries (n=2), or atrioventricular septal defect (AVSD; n=1). The remaining 5 children had aortic stenosis. Of the 19 children with shunt lesions who were enrolled in Part 2 of the study, 5 had a ventricular septal defect (VSD), 5 had an atrial septal defect (ASD), 4 had a patent ductus arteriosus, 3 had a single ventricle, 1 had double outlet right ventricle, and 1 had AVSD. Patients who underwent Blalock-Taussig shunting were excluded from this study. For Part 3 of the study, the subjects were divided into 2 groups according to the ratio of pulmonary pressure (Pp) to systemic pressure (Ps), as measured by cardiac catheterization, to give a low PAP group (Pp/Ps <0.25, n=17) and a high PAP group (Pp/Ps ≥0.25, n=17). All the children and their parents were fully informed about the procedures, risks, and benefits of the study, and written informed consent was given before the study.

Cardiac Catheterization

Cardiac catheterization was performed under the same anesthesia protocol for all patients, which included the intravenous infusion of pentobarbital or midazolam, blood sampling for measurement of oxygen content, and measurement of both pulmonary and systemic arterial pressures. Qp/Qs was derived from oximetric measurements using the Fick method. Qs was obtained by the thermodilution method (Cardio Master RMC-3100; Nihon Koden, Tokyo, Japan).

Pulmonary Perfusion Scintigraphy

Pulmonary perfusion scintigraphy was performed using a gamma camera (GCA-9300A/DI; Toshiba Medical, Tokyo, Japan) following the administration of 46–185 MBq of 99mTc-MAA, depending on the patient’s age. We collected dynamic SPECT data for 5 min (30 rounds), beginning immediately after infusion of the isotope. After the construction of lung images, we selected regions of interest (ROI) in the right and left lungs from the available image and then evaluated the right-to-left Qp (R/L) ratio.

VEC-MRI

A Magnetom Symphony Sonata gradient system (Siemens, Munich, Germany; 1.5 T) was used to perform VEC-MRI. Images were captured every 28 ms with body and spine array coils using the phase-contrast method; the optimal time to echo was set at 3.2 ms, and the flip angle was set at 30°. The slice thickness ranged from 3 to 5 mm, the field of view ranged from 128 to 320 mm, and the optimal flow rate sensitivity was set at 300 cm/s. The cross-sections used included those of the ascending aorta, the main pulmonary artery, and the right and left pulmonary arteries, which were perpendicular to the direction of blood flow. We used cine-MRI to image these cross-sections using the phase-contrast method. Both magnitude and phase-contrast images were obtained. The ROI was established using the corresponding blood vessel and then the flow rate was calculated using the Argus analysis software (Siemens Medical Solutions, Munich, Germany) included with the Magnetom Vision console (Siemens). The time-velocity and time-flow curves in the ROI during 1 cardiac cycle were automatically reconstructed. Using the time-velocity curve, we calculated the acceleration time (AcT), defined as the time from the onset of flow to the peak velocity (PV) in the main pulmonary artery, and the ejection time (ET) (Figure 1). Acceleration volume (AcV), defined as the volume ejected during the AcT, and the MCFR, defined as the maximal value of the ascending slope of the flow rate, were measured using the time-flow curve.

Standardization Methods

We considered it necessary to standardize the VEC-MRI param-

### Table 1. Demographic and Hemodynamic Data

<table>
<thead>
<tr>
<th></th>
<th>Part 1 Without shunt (n=15)</th>
<th>Part 2 With shunt (n=19)</th>
<th>Part 3 Low PAP (n=17)</th>
<th>Part 3 High PAP (n=17)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6.4±5.0</td>
<td>3.2±3.2</td>
<td>6.5±4.1</td>
<td>2.7±3.8</td>
<td>NS</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>0.7±0.3</td>
<td>0.6±0.3</td>
<td>0.9±0.4</td>
<td>0.5±0.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>sPAP (mmHg)</td>
<td>32±12</td>
<td>30±15</td>
<td>21±3</td>
<td>39±14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>18±6</td>
<td>19±12</td>
<td>13±3</td>
<td>25±9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>dPAP (mmHg)</td>
<td>9±5</td>
<td>14±8</td>
<td>10±4</td>
<td>20±17</td>
<td>0.04</td>
</tr>
<tr>
<td>ABP (mmHg)</td>
<td>97±16</td>
<td>100±12</td>
<td>106±13</td>
<td>88±12</td>
<td>NS</td>
</tr>
<tr>
<td>Qp/Qs</td>
<td>1.00</td>
<td>1.79±0.98</td>
<td>1.35±0.54</td>
<td>1.58±1.05</td>
<td>0.03</td>
</tr>
<tr>
<td>Pp/Ps</td>
<td>0.33±0.14</td>
<td>0.30±0.18</td>
<td>0.20±0.04</td>
<td>0.47±0.02</td>
<td>&lt;0.01</td>
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<tr>
<td>Rp (Um²)</td>
<td>1.5±1.2</td>
<td>1.7±1.2</td>
<td>1.0±0.5</td>
<td>2.5±1.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cardiac index (L·min⁻¹·m⁻²)</td>
<td>4.9±1.0</td>
<td>4.7±1.2</td>
<td>5.2±1.1</td>
<td>4.9±1.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

ABP, arterial blood pressure; BSA, body surface area; dPAP, diastolic PAP; mPAP, mean PAP; NS, not significant; PAP, pulmonary arterial pressure; Pp/Ps, ratio of pulmonary-to-systemic blood pressure; Qp/Qs, ratio of pulmonary-to-systemic blood flow; Rp, pulmonary arterial vascular resistance; sPAP, systolic PAP.
Assessment of PAP by VEC-MRI

Statistical Analysis

All data are expressed as mean±SD. To assess the correlations among the data obtained, we used Spearman’s rank correlation test. Multiple linear regression analysis was conducted using induced variables for PAP, as measured during cardiac catheterization, and independent variables for the 6 parameters were obtained by VEC-MRI. We used the Statistical Package for the Social Sciences version 19 (SPSS Inc, Chicago, IL, USA). P<0.05 was considered statistically significant.

Table 2. AUCs of 3 Different Standardization Methods Using ROC Curve Analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No revision</th>
<th>BSA revision</th>
<th>Cardiac cycle revision</th>
<th>Square root of cardiac cycle revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>AcT</td>
<td>0.464</td>
<td>0.875</td>
<td>0.600</td>
<td>0.531</td>
</tr>
<tr>
<td>ET</td>
<td>0.289</td>
<td>0.806</td>
<td>0.540</td>
<td>0.405</td>
</tr>
<tr>
<td>AcT/ET</td>
<td>0.554</td>
<td>0.886</td>
<td>0.664</td>
<td>0.599</td>
</tr>
<tr>
<td>PV</td>
<td>0.578</td>
<td>0.862</td>
<td>0.671</td>
<td>0.644</td>
</tr>
<tr>
<td>AcV</td>
<td>0.651</td>
<td>0.931</td>
<td>0.730</td>
<td>0.696</td>
</tr>
<tr>
<td>MCFR</td>
<td>0.848</td>
<td>0.900</td>
<td>0.858</td>
<td>0.862</td>
</tr>
</tbody>
</table>

AcT, acceleration time; AcV, acceleration volume; AUC, area under the ROC curve; ET, ejection time; MCFR, maximal change in flow rate during ejection; PV, peak velocity; ROC, receiver-operating characteristic.
obtained by these 2 methods were strongly correlated ($r=0.832$, $P<0.005$, $n=11$). Finally, a comparison of the ratio of right-to-left Qp measured using VEC-MRI (MRI-R/L) to the same ratio measured using pulmonary perfusion scintigraphy (Scinti-R/L) revealed a significant correlation between the results obtained by these methods ($r=0.705$, $P<0.005$, $n=13$; Figure 2D).

**Results**

**Part 1 Study: Children Without Shunt Lesions**

The demographic and hemodynamic data of the children in this study group are shown in Table 1 and the comparison of the blood flow volume of the main pulmonary artery (MRI-Qp) with that of the ascending aorta (MRI-Qs) measured using VEC-MRI is shown in Figure 2A. This comparison revealed a significant correlation between these parameters ($r=0.932$, $P<0.001$, $n=15$). Next, a comparison of the blood flow volume of the main pulmonary artery (MRI-Qp) with the sum of the blood flow volumes of the right and left pulmonary arteries (MRI-Qp [Rt + Lt]) measured using VEC-MRI revealed a significant correlation between these parameters ($r=0.927$, $P<0.001$, $n=15$; Figure 2B). Further, a comparison of the Qs measured using VEC-MRI (MRI-Qs) and that measured using cardiac catheterization with thermodilution (Thermo-Qs) is shown in Figure 2C. The results obtained by these 2 methods were strongly correlated ($r=0.832$, $P<0.005$, $n=11$). Finally, a comparison of the ratio of right-to-left Qp measured using VEC-MRI (MRI-R/L) to the same ratio measured using pulmonary perfusion scintigraphy (Scinti-R/L) revealed a significant correlation between the results obtained by these methods ($r=0.705$, $P<0.005$, $n=13$; Figure 2D).

**Part 2 Study: Children With Shunt Lesions**

The demographic and hemodynamic data of the children in the study group are shown in Table 1. A comparison of the Qp/Qs measured using VEC-MRI (MRI-Qp/Qs) with the same parameter measured using the Fick method (Fick-Qp/Qs), which is based on oximetry of blood samples taken during cardiac catheterization, is shown in Figure 3. This comparison revealed a significant correlation between the 2 methods ($r=0.897$, $P<0.001$, $n=19$).
Part 3 Study: Assessment of PAP Using VEC-MRI

The demographic and hemodynamic data of the children in the study group are shown in Table 1. The mean age of the children was 6.5±4.1 years in the low PAP group (Pp/Ps <0.25) and 2.7±3.8 years in the high PAP group (Pp/Ps ≥0.25). Significant differences were found between the low and high PAP groups for several parameters, including BSA, systolic PAP, mean PAP, diastolic PAP, Qp/Qs, Pp/Ps, and the pulmonary arterial vascular resistance. There were no significant differences in arterial blood pressure or cardiac index between the low and high PAP groups. To select a suitable standardization method, we conducted a ROC analysis and calculated the AUC. The results of this analysis are presented in Table 2. Division by the BSA was taken as the most suitable method for standardization of the parameters of AcT, ET, AcT/ET, PV, AcV, and MCFR.

A series of comparisons between the low and high PAP groups in terms of the standardized parameters AcT, ET, AcT/ET, PV, AcV, and MCFR are shown in Figure 4. No significant difference between groups was observed in terms of the AcT, ET, AcT/ET, PV, and AcV parameters; however, a significant difference was observed in the MCFR (P<0.001). Correlations, obtained by univariate and multivariate analyses, between Pp/Ps and the results of the various VEC-MRI measure-
Determined, and the results showed a very good correlation between Qs and Qp measured using VEC-MRI was.

CHD, who have a small physique and a rapid heart rate. MRI, as a noninvasive test, is currently being used for hemodynamic assessment in children with CHD after a Glenn procedure. In contrast, the VEC-MRI method is excellent because it allows for calculation of the blood flow in each of the 3 blood vessels with different flow directions and diameters, together with that of the comparison aimed at determining whether the sum of the blood flow in 2 blood vessels is identical to that found in another blood vessel, showed a very good correlation. These results reflected the accuracy of VEC-MRI measurements.

We also examined the validity of the absolute value of perfusion measured using VEC-MRI. In a study conducted in swine, Kuehne et al attempted to compare the results of cardiac output put measurements obtained using the thermodilution method to those obtained using VEC-MRI. However, to date, there are still few reports on studies of children. In the present study, a comparison of cardiac output (Qs) measured using the thermodilution method with that measured using VEC-MRI showed a good correlation (Figure 2C). We also compared VEC-MRI with pulmonary perfusion scintigraphy. The ratio of perfusion between the right and left pulmonary arteries measured using VEC-MRI showed a good correlation with that obtained using pulmonary perfusion scintigraphy (Figure 2D). Lung perfusion scintigraphy does not allow for an accurate calculation of the ratio of perfusion between the right and left pulmonary arteries in children with CHD after a Glenn procedure. In contrast, the VEC-MRI method is excellent because it allows for calculation of the blood flow volume in the right and left pulmonary arteries regardless of the presence or absence of circulatory shunts.

Next, we conducted a validation study of VEC-MRI in children with shunt lesions. In CHD, Qp/Qs is an important index that already serves as a basis for determining whether surgery is indicated. Beerebaum et al previously reported that VEC-MRI measurements of the Qp/Qs in pediatric patients with ASD or VSD correlated well with those determined using cardiac catheterization. In our study, we extended those observations to CHD children with shunt lesions other than ASD and VSD and found a correlation similar to that noted earlier (Figure 2). This finding suggests that Qp/Qs, which cannot be calculated using Fick’s method in postoperative children because they show a difference in oxygen content between the right and left pulmo-

\[
y = 13.336x - 0.121 \\
R = 0.895, \ n = 34 \ (p<0.001)
\]

![Figure 5](image.png)

Comparison of the standardized maximal change in flow rate during ejection (MCFR) determined by VEC-MRI to Pp/Ps determined by cardiac catheterization. Pp, pulmonary pressure; Ps, systemic pressure; VEC-MRI, velocity-encoded cine magnetic resonance imaging.

MCFR−0.121

Table 3. Results of VEC-MRI Measurements and Univariate and Multivariate Analyses Before and After Standardization Vs. Pp/Ps

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-standardized value</th>
<th>Standardized value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation coefficients</td>
<td>Correlation coefficients</td>
</tr>
<tr>
<td></td>
<td>r</td>
<td>P value</td>
</tr>
<tr>
<td>AcT</td>
<td>−0.236</td>
<td>0.090</td>
</tr>
<tr>
<td>ET</td>
<td>−0.364</td>
<td>0.017</td>
</tr>
<tr>
<td>AcT/ET</td>
<td>−0.080</td>
<td>0.326</td>
</tr>
<tr>
<td>PV</td>
<td>0.165</td>
<td>0.176</td>
</tr>
<tr>
<td>AcV</td>
<td>0.015</td>
<td>0.465</td>
</tr>
<tr>
<td>MCFR</td>
<td>0.615</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

All parameters were standardized using division by the square root of the cardiac cycle length.

VEC-MRI, velocity-encoded cine magnetic resonance imaging. Other abbreviations as in Tables 1, 2.

The results of VEC-MRI measurements and univariate and multivariate analyses before and after standardization are shown in Table 3. Of the individual parameters measured using VEC-MRI, only the standardized MCFR correlated with Pp/Ps in the multivariate analysis. A comparison of the standardized MCFR data and the Pp/Ps ratio determined by cardiac catheterization (Figure 5) revealed an extremely strong correlation between these 2 parameters (r=0.895, P<0.001, n=34) [Pp/Ps=13.336×MCFR−0.121 (r=0.895, n=34, P<0.001)].

**Discussion**

MRI, as a noninvasive test, is currently being used for hemodynamic studies. Therefore, we examined the usefulness of VEC-MRI for hemodynamic assessment in children with CHD, who have a small physique and a rapid heart rate.

To demonstrate that the VEC-MRI technique is accurate in children without a circulatory shunt lesion and who had equivalent Qp and Qs, we conducted a validation study. The equivalence between Qs and Qp measured using VEC-MRI was determined, and the results showed a very good correlation (Figure 2A). In the strict sense, MRI-Qs does not measure systolic coronary blood flow because the flow is measured in the ascending aorta. However, because diastolic coronary blood flow, which accounts for most of the coronary blood flow, is measured by MRI-Qs as a reversed signal and MRI-Qp does not measure the volume of blood returning from the bronchial arteries to the left atrium, it is reasonable to assume that MRI-Qs equals MRI-Qp. Further, the perfusion volume in the right and left pulmonary arteries was calculated separately; the sum was compared with the main pulmonary artery perfusion volume (Figure 2B). The result of the calculation of blood flow in each of the 3 blood vessels with different flow directions and diameters, together with that of the comparison aimed at determining whether the sum of the blood flow in 2 blood vessels is identical to that found in another blood vessel, showed a very good correlation. These results reflected the accuracy of VEC-MRI measurements.
Pulmonary arteries, can be reliably measured using VEC-MRI.

Overall, the evidence presented here confirms that VEC-MRI is useful for hemodynamic assessment in children.

Cardiac catheterization is the gold standard for the measurement of PAP, but because it is an invasive procedure, measurements cannot be performed frequently and evaluation of pulmonary hypertension using cardiac biomarkers is not yet established.17,18 In the echocardiographic examination, pulse Doppler waveforms in the main pulmonary artery are known to have an AcT that correlates with the mean pressure in the pulmonary artery.19 We focused on the shape of the velocity and flow curves obtained using VEC-MRI (Figure 1) and our findings suggested that because children have a rapid heart rate and a small physique, the values might require standardization. Therefore, standardization was performed by focusing on 6 parameters that have been previously reported to correlate with PAP.20–24 By conducting ROC analysis and calculating the AUCs to compare the variability in this standardization, we concluded that using division by the BSA was the most suitable standardization method (Table 2). To the best of our knowledge, no previous studies have corrected the parameters calculated using VEC-MRI for children.

Mousseaux et al previously reported that the AcV obtained using VEC-MRI showed a good correlation with pulmonary vascular resistance.25 They determined the AcV by calculating the cardiac ejection volume, by performing a time integration of the period ranging from the initiation of ejection to the peak in a flow volume curve. Our study showed no significant correlation between the standardized AcV and pulmonary vascular resistance. This may have been because there was no marked difference in pulmonary vascular resistance among the patients in our study. In a previous study of 31 adult patients, Laffon et al showed that PAP could be estimated using VEC-MRI measurement of the PV of the main pulmonary artery;26 however, the calculation method is complicated and no good correlation was found between PV and PAP among the patients in our study. The MCFR, which has been the focus of recent attention, allows for easy calculation of the PAP on the basis of the flow volume curve measured using VEC-MRI; Murayama et al previously reported a correlation between the MCFR and PAP in adults.20,25 In our study, standardized MCFR was the only significant difference observed between the low and high PAP groups (Figure 4). In our study, standardized MCFR was the only significant difference observed between the low and high PAP groups (Figure 4). In our study, standardized MCFR was the only significant difference observed between the low and high PAP groups (Figure 4). In our study, standardized MCFR was the only significant difference observed between the low and high PAP groups (Figure 4).

Study Limitations

This method has a few disadvantages. Although there have been several reported attempts to quantify valvular regurgitation using VEC-MRI, the turbulence creates errors during flow measurement, suggesting that it may be impossible to achieve accurate assessments.26,27 Measurements obtained with VEC-MRI may also be incorrect in the presence of arrhythmia, because such measurements consist of cine-MRI data created by repeatedly superimposing a constant cardiac cycle within a specified time period. Another disadvantage of this technique, which arises because Qp is measured in the proximal side of the pulmonary arteries, is that it does not allow for an accurate evaluation of blood flow in children with systemic-pulmonary collateral circulation flowing into the periphery of these arteries, or in postoperative children who have undergone Blalock-Taussig shunt.

Finally, there are limitations imposed by the use of MRI equipment. Because of the strong magnetic fields involved, VEC-MRI cannot be used in patients wearing metal implants, such as pacemakers and stents. For flow measurements in neonates, the child should weigh approximately 3 kg or more, and the duration of 1 heartbeat should not be less than 600 ms. Sedation is required to protect children against the loud noise emitted by the MRI equipment, but caution in interpreting the resultant data is needed because deep sedation can result in a decrease in the systemic blood pressure or respiratory rate; therefore, the hemodynamics may not necessarily be identical to those of daily life.28

Conclusions

This study clearly demonstrated that VEC-MRI is useful for estimating Qp, Qs, Qp/Qs, and R/L ratio in children with CHD. Moreover, we can diagnose severe pulmonary hypertension using this imaging technique. VEC-MRI is noninvasive and represents a revolutionary diagnostic tool for pediatric cardiology.

Disclosures

Masaya Sugimoto wrote the first draft. We hereby confirm that there are no known conflicts of interest associated with this research and there has been no significant financial support for this work that could have influenced its outcome.

References


