Real-Time Magnetic Resonance Assessment of Septal Curvature Accurately Tracks Acute Hemodynamic Changes in Pediatric Pulmonary Hypertension

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Background—This study assesses the relationship between septal curvature and mean pulmonary artery pressure and indexed pulmonary vascular resistance in children with pulmonary hypertension. We hypothesized that septal curvature could be used to estimate right ventricular afterload and track acute changes in pulmonary hemodynamics.

Methods and Results—Fifty patients with a median age of 6.7 years (range, 0.45–16.5 years) underwent combined cardiac catheterization and cardiovascular magnetic resonance. The majority had idiopathic pulmonary arterial hypertension (n=30); the remaining patients had pulmonary hypertension associated with repaired congenital heart disease (n=17) or lung disease (n=3). Mean pulmonary artery pressure and pulmonary vascular resistance were acquired at baseline and during vasodilatation. Septal curvature was measured using real-time cardiovascular magnetic resonance. There was a strong correlation between mean pulmonary artery pressure and $SC_{\text{min}}$ at baseline and during vasodilator testing ($r=−0.81$ and $−0.85$, respectively; $P<0.01$). A strong linear relationship also existed between pulmonary vascular resistance and minimum septal curvature indexed to cardiac output both at baseline and during vasodilator testing ($r=−0.88$ and $−0.87$, respectively; $P<0.01$). Change in septal curvature metrics moderately correlated with absolute change in mean pulmonary artery pressure and pulmonary vascular resistance, respectively ($r=0.58$ and $−0.74$; $P<0.01$). Septal curvature metrics were able to identify vasoresponders with a sensitivity of 83% (95% confidence interval, 0.36–0.99) and a specificity of 91% (95% confidence interval, 0.77–0.97), using the Sitbon criteria. Idiopathic pulmonary arterial hypertension subgroup analysis revealed 3 responders with $\Delta SC_{\text{min}}$ values of 0.523, 0.551, and 0.568. If the middle value of 0.551 is taken as a cutoff, the approximate sensitivity would be 67% and the specificity would be 93%.

Conclusions—Septal curvature metrics are able to estimate right ventricular afterload and track acute changes in pulmonary hemodynamics during vasodilator testing. This suggests that septal curvature could be used for continuing assessment of load in pulmonary hypertension. (Circ Cardiovasc Imaging. 2014;7:706-713.)

Key Words: hypertension, pulmonary ■ pediatrics ■ vasodilator agents

Cardiovascular magnetic resonance (CMR) is increasingly used in pulmonary hypertension (PH) because of its ability to accurately measure right ventricular (RV) volumes and function. In adults, conventional breath-held, cardiac-gated CMR is easy to use and has proven prognostic utility. However, conventional CMR is problematic in pediatric PH because many of these children find breath-holding difficult. Thus, real-time CMR is a more attractive option, and this technique has recently been used to successfully assess the RV in children with PH.

Optimal management of PH also benefits from assessment of either mean pulmonary artery pressure (mPAP) or indexed pulmonary vascular resistance (PVRi). Although the reference standard method of measuring mPAP and PVRi is cardiac catheterization, noninvasive methods are used during routine follow-up. For instance, mPAP and PVRi can be noninvasively estimated using CMR by measuring interventricular septal curvature. In adults, septal curvature measured using conventional CMR strongly correlates with mPAP and PVRi. However, the use of septal curvature has not been validated in children, particularly those imaged with real-time CMR. Furthermore, the ability of septal curvature to track changes in mPAP or PVRi has not been definitively proven, which is vital if septal curvature is to be used to assess response to therapy or disease progression.

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The main aims of this study were (1) to demonstrate that real-time CMR-derived septal curvature is abnormal in pediatric PH; (2) to assess the relationship between septal curvature and both mPAP and PVRi in pediatric PH; and (3) to evaluate the ability of septal curvature to track acute changes in mPAP and PVRi.

This study was performed in large cohort of pediatric patients with PH who were undergoing CMR-augmented cardiac catheterization with vasodilator testing as part of their clinical care. In this technique, real-time CMR is performed with invasive catheters in situ, allowing simultaneous assessment of mPAP, PVRi, and septal curvature.1011 Thus, it represents the optimal setting for investigating the relationship between these metrics.

**Methods**

**Study Population**

Consecutive children with a history of PH (defined as a previous invasively measured mPAP ≥25 mm Hg or an estimated systolic pulmonary artery pressure >50 mm Hg measured from tricuspid regurgitant jet on echocardiography) referred for clinical CMR-augmented cardiac catheterization between December 2009 and August 2013 were considered for inclusion into this study. Referral criteria were as follows: (1) mPAP and PVRi assessment after initial diagnosis of PH; (2) clinical worsening; and (3) assessment on PH-specific therapy. The inclusion criterion was mPAP ≥25 mm Hg. Exclusion criteria were (1) complex congenital lesions or univentricular circulations and (2) large cardiac shunt (Qp:Qs>1.2:1 or <0.8:1). All patients were in sinus rhythm at the time of cardiac catheterization. A control population of 15 healthy pediatric volunteers also underwent CMR and assessment of septal curvature without concomitant cardiac catheterization or general anesthetic. Ethics approval was obtained from the National Ethics Committee, and all parents/legal guardians gave consent.

**CMR-Augmented Cardiac Catheterization**

All examinations were performed in an interventional magnetic resonance (MR) suite that consisted of a 1.5T CMR scanner (Avanto; Siemens Medical Solutions, Erlangen, Germany) and a biplane angiography system (Axiom Artis; Siemens Medical Solutions, Erlangen, Germany) separated by a radio frequency–shielded door.11 A 12-element phased array coil was used for signal reception, and a vectorcardiogram system was used for cardiac gating. Inhaled sevoflurane was used for maintenance of general anesthesia during the whole procedure. After routine invasive measurement of RV and right atrial pressure, a 5F to 6F balloon tipped wedge monitoring catheter was fluoroscopically guided into either the left or right pulmonary artery. The catheter was positioned so that balloon tip inflation allowed measurement of pulmonary capillary wedge pressure. Once a stable position was achieved, the patient was transferred to the adjoining CMR scanner on a moveable table.13 Baseline measurements were acquired in the CMR scanner as described in the next section. Vasodilator testing was performed using 100% of oxygen (O2) and 20 ppm of nitric oxide (NO) in all cases. Vasodilator gases were administered to the patients while they were in the CMR scanner by introducing them into the inlet anesthetic tubing. A commercial delivery system (INOvent Datex-Ohmeda, Madison, WI) that was calibrated before each study was used to dispense NO. Repeat hemodynamic measurements were only made after 10 minutes of vasodilator exposure to ensure a steady state had been reached. Vasodilators were administered until all repeat measurements had been made. Invasive femoral artery pressure, heart rate, and pulse oximetry were measured throughout the study.

**CMR Protocol**

The following CMR protocol was performed at baseline (21% FiO2) and during an acute vasodilator phase (20 ppm NO and 100% FiO2). All image processing was performed using in-house plug-ins for the open-source OsiriX digital imaging and communications in medicine software.14 Flow imaging was performed using a velocity-encoded phase-contrast MR sequence during free breathing (acquisition time, 1–3 minutes). To overcome problems associated with flow errors in the dilated main pulmonary artery, pulmonary blood flow (Qp) was measured by summing the flow in the branch pulmonary arteries.4 In addition, phase-contrast MR data were segmented using a semiautomatic vessel edge detection algorithm with operator correction and Qp was calculated as previously described.3 mPAP was recorded during flow imaging, and pulmonary capillary wedge pressure was evaluated at the end of flow imaging (required wedge catheter balloon inflation). PVRi was calculated by dividing the transpulmonary gradient (mPAP–pulmonary capillary wedge) by the body surface indexed total pulmonary blood flow (Wood units/m2 [WUm2]).

Biventricular volumetric and functional assessment was performed using real-time radial k-t sensitivity encoding sequence. This sequence has been previously described and validated in children with congenital heart disease.10 It provides high spatiotemporal resolution real-time imaging and permits data acquisition during normal ventilation. This is vital when performing CMR-augmented catheterization because apneic scans may increase mPAP and PVRi. Although this was a real-time sequence, it was possible to R-wave trigger the start of acquisition for each slice. This allowed timing synchronization between septal curvature and both the R-wave and the ECG-gated flow data. The scans were planned in the ventricular short axis with 7 to 13 contiguous slices required to cover both the ventricles. The biventricular end-diastolic volume and end-systolic volume were measured by manual segmentation of the endocardial borders excluding trabeculations. Segmentation of the epicardial border of the RV at end-systole allowed calculation of RV free-wall mass. Ventricular stroke volume, ejection fraction, and tricuspid regurgitation fraction (TRF) were calculated as previously described.4

In the control population, biventricular volumetric assessment was performed using the same real-time radial k-t SENSE sequence. These scans were performed in unsedated children during free breathing and processed in the same way as the patient population.

**Septal Curvature Calculations**

Septal curvature was measured in the short-axis plane at the level of the left ventricular (LV) papillary muscles in patients and healthy children. This ensured that neither the outflow tracts nor valve tissue was in the images. The septum and lateral wall were segmented using a previously described registration-based algorithm built into the OsiriX software.17 Segmentation was initialized by drawing 3-point arcs on the endocardial surface of RV septal wall and the epicardial surface of the LV free wall in a single frame (Figure 1). These regions of interest were then propagated through time and manually corrected if necessary. The curvature of the septal and lateral walls was interpolated at the aortic ejection fraction (Figure 1). The aortic ejection fraction was from 0 to 321 ms.

![Figure 1](http://circimaging.ahajournals.org/)

**Figure 1.** A, Regions of interest applied to lateral free wall and septum during left ventricular bowing. B, Curvature across 1 cardiac cycle in the septum (red line), lateral wall (green line), and curvature ratio (blue line). Aortic ejection was from 0 to 321 ms.
lateral walls in each frame was then calculated as the inverse of the circle circumscribed by the 3 points in the regions of interest. The final septal curvature was calculated as the ratio of the septal and lateral wall curvatures. Negative septal curvature denoted a leftward convexity of the septum (septum bowing into the left ventricle). Minimum septal curvature ($SC_{min}$) was taken as the lowest or most negative value of the septal curvature time curve. Minimum septal curvature indexed to Qp ($SC_{min}/Qp$) was used a surrogate for PVRi.

### Statistical Analysis

All statistical analyses were performed using SPSS v21 and Prism 5F (GraphPad). Data are presented as median (interquartile range, IQR) unless it was more appropriate to describe the range, in which case this is explicitly stated. Mann–Whitney test was used to assess the difference between the populations, and Wilcoxon signed-rank test was used to assess the difference between hemodynamic parameters at baseline and during vasodilation. The relationship between the septal curvature and the invasive hemodynamic data was explored using Pearson correlation. ANCOVA was used to assess the difference between regression lines at baseline and during vasodilator testing. A $P$ value of <0.05 was considered statistically significant.

Two investigators analyzed the septal curvature in a randomized group of 20 studies including both controls and patients with PH. Intraobserver variability was performed on a similar randomized group. Both interobserver and intraobserver variability were explored using the intraclass correlation coefficient. Receiver–operating characteristic curve analysis was performed to evaluate the diagnostic accuracy of septal curvature metrics in identifying patients with vasoresponder status using the Sitbon criterion defined as a decrease in mPAP of ≥10 mm Hg reaching a mPAP value of ≤50 mm Hg and an increased or unchanged cardiac output. The optimum cutoff value was chosen to maximize the Youden index (sensitivity + specificity –1).

### Results

#### Study Population

During the study period, 118 patients underwent CMR-augmented cardiac catheterization, of which 114 fulfilled the inclusion criteria (mPAP≥25 mm Hg). Sixty-four patients were excluded because of either large cardiac shunts (with Qp:Qs>1.2:1 or <0.8:1) or univentricular hearts/complex congenital heart disease. Thus, the study population consisted of 50 patients, with a median age of 6.7 years (range, 0.45–16.5 years) and a female preponderance (n=35, 70%). In the study population, 30 of 50 had idiopathic pulmonary arterial hypertension (IPAH), 17 of 50 had pulmonary arterial hypertension associated with congenital heart disease, and 3 of 50 had PH associated with lung disease. In the pulmonary arterial hypertension associated with congenital heart disease group (Table 1), all patients were post repair of their primary lesion. The median age at surgery was 0.07 years (range, 0.01–3.47 years), with all but 1 patient undergoing repair within the first year of life. Four patients had small residual defects with no discernable shunt (1 atrial septal defect, 1 patent foramen ovale, and 2 tiny apical ventricular septal defects).

The median baseline mPAP was 47.0 mm Hg (36.0–62.3 mm Hg), PVRi was 11.8 WU/min (7.8–17.8 WU/min), and Qp was 3.2 L/min/m² (2.3–3.9 L/min/m²). Patient clinical data and CMR-derived LV and RV volumetric data are detailed in Tables 2 and 3, respectively. Median TRF was 10.3 ms (5.5–16.5 years) and the median RR interval to the end of aortic ejection (as measured using phase contrast MR) was 321 ms (164–425 ms) and the median RR interval was 770 ms (611–926 ms).

### Table 1. Primary Congenital Heart Defects in 17 Patients

<table>
<thead>
<tr>
<th>Type of Defect</th>
<th>Status</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDA*</td>
<td>Postligation</td>
<td>5</td>
</tr>
<tr>
<td>Transposition of the arteries†</td>
<td>Post ASO</td>
<td>5</td>
</tr>
<tr>
<td>AVSD</td>
<td>Post fully operative repair</td>
<td>2</td>
</tr>
<tr>
<td>Coarctation of the aorta‡</td>
<td>Post fully operative repair</td>
<td>2</td>
</tr>
<tr>
<td>Perimembranous VSD</td>
<td>Post fully operative repair</td>
<td>2</td>
</tr>
<tr>
<td>Aortopulmonary window</td>
<td>Post fully operative repair</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>17</td>
</tr>
</tbody>
</table>

*PDA, patent ductus arteriosus; AVSD, atrioventricular septal defect; ASO indicates arterial switch operation; PDA, patent ductus arteriosus; and VSD, ventricular septal defect.

††One patient in this group had a patent foramen ovale.

‡‡Two patients in this group had small residual apical VSDs with a Qp:Qs ratio of 1.1:1.

One patient in this group had a small atrial septal defect.

#### Feasibility and Variability

Septal curvature analysis was feasible in all subjects (patients and controls). The automated segmentation took ≈1 minute and manual correction took another 2 to 3 minutes. The interobserver intraclass correlation coefficient for assessment of $SC_{min}$ was 0.977 (95% confidence interval [CI], 0.944–0.99) and the intraobserver intraclass correlation coefficient was 0.966 (95% CI, 0.955–0.966). A representative septal curvature curve for the whole cardiac cycle is shown in Figure 1. The median time from the R-wave to $SC_{min}$ was 440 ms (360–480 ms). For comparison, the median time from the R-wave to the end of aortic ejection (as measured using phase contrast MR) was 321 ms (164–425 ms) and the median RR interval was 770 ms (611–926 ms).

### Table 2. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)</th>
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</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>6.7 (4.5–11.2)</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>79.5 (64.5–98.5)</td>
</tr>
<tr>
<td>$O_2$ saturations (%)</td>
<td>95.0 (92.0–97.0)</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>0.85 (0.67–1.16)</td>
</tr>
<tr>
<td>RV mass (g)</td>
<td>47.9 (35.9–65.6)</td>
</tr>
<tr>
<td>RVESVi (ml/m²)</td>
<td>73.0 (60.8–86.5)</td>
</tr>
<tr>
<td>LVEDVi (ml/m²)</td>
<td>28.5 (24.0–41.3)</td>
</tr>
<tr>
<td>L VESVi (ml/m²)</td>
<td>59.5 (49.3–67.3)</td>
</tr>
<tr>
<td>RVO (L/min/m²)</td>
<td>21.0 (16.8–25.0)</td>
</tr>
<tr>
<td>LVCI (L/min/m²)</td>
<td>3.2 (2.4–3.9)</td>
</tr>
</tbody>
</table>

Values are represented as median (interquartile range). BSA indicates body surface area; IQR, interquartile range; LVCI, left ventricular cardiac index calculated using volumetric data; LVEDVi, indexed left ventricular end-diastolic volume; L VESVi, indexed left ventricular end-systolic volume; and RVESVi, indexed right ventricular end-diastolic volume; and RVO, indexed right ventricular end-systolic volume.
Septal Curvature in PH Patients and Normal Controls

There was a significant difference ($P<0.001$) between median $SC_{\min}$ in the patient group ($-0.23$; IQR, $-0.36$ to $0.07$) compared with the control group ($1.06$; IQR, $0.98$–$1.12$). In addition, there was no overlap between $SC_{\min}$ (range, $0.902$–$1.175$) in normal controls and $SC_{\min}$ in patients (range, $0.556$–$0.796$) as shown in Figure 2. Median age of the control population was $11.8$ years (IQR, $10.3$–$13.4$ years), which was significantly older than the patient population ($P=0.002$). However, there was no correlation between $SC_{\min}$ and age in either the controls ($r=0.29$; $P=0.29$) or patients ($r=-0.063$; $P=0.66$). In addition, in an age-matched sample of the patient population, ($n=15$; median age, $11.8$ years), there was still a significant difference in $SC_{\min}$ (patient=$-0.18$; IQR, $-0.48$ to $0.21$ versus control=$1.06$; IQR, $0.98$–$1.1$; $P<0.0001$).

Septal Curvature Correlations With Hemodynamics

There was a good correlation between mPAP and $SC_{\min}$ at baseline and during vasodilator testing ($r=-0.81$ and $-0.85$, respectively; $P<0.001$). The relationship between mPAP and $SC_{\min}$ was similar in both conditions (mPAP=$-43.2\times SC_{\min}+42.3$ at baseline and mPAP=$-40.1\times SC_{\min}+41.5$ during vasodilation), and on ANCOVA, there was no difference ($P=0.50$) between the regression lines (Figure 3).

There was a curvilinear relationship between PVRi and $SC_{\min}$ (Figure 4A). However, there was a strong linear relationship between PVRi and $SC_{\min}/Qp$ (Figure 4B) both at baseline and during vasodilator testing ($r=-0.88$ and $-0.87$, respectively). In addition, there was no significant difference in the regression equations in the 2 conditions ($PVRi=-55.1\times SC_{\min}/Qp+4.4$ at baseline and $PVRi=-50.0\times SC_{\min}/Qp+10.7$ during vasodilation, $P=0.66$).

In this small patient group, no correlation between $SC_{\min}$ and TRF or QRS duration could be demonstrated ($P=0.60$ and $0.90$, respectively).

Septal Curvature and Acute Changes in Hemodynamics

During vasodilator testing, mPAP fell to median of $38$ ($27$–$56$ mm Hg) and median PVRi fell to $8.5$ ($5.2$–$17$ WUm$^2$). Septal curvature was successfully assessed in all patients in both conditions. Change in $SC_{\min}$ and $SC_{\min}/Qp$ moderately correlated with absolute change in mPAP and PVRi, respectively ($r=0.58$ and $-0.74$, $P<0.01$), as seen in Figure 5A and 5B.

Septal Curvature and Vasoresponder Status

Six patients (12%) fulfilled the Sitbon criteria for vasoresponsivity (fall in mPAP of $\geq 10$ mm Hg to a mPAP of $\leq 40$ mm Hg, with an increase or no change in Qp). On receiver-operating characteristic curve analysis (Figure 6), the optimal cutoff value of $\Delta SC_{\min}$ for identification of vasoresponders (defined by the Sitbon criteria) was $0.466$ (area under the curve, $0.90$; $P=0.001$).

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**Table 3. Hemodynamic Data Pre- and Postvasodilation**

<table>
<thead>
<tr>
<th>Hemodynamic Parameter</th>
<th>Prevasodilation</th>
<th>Postvasodilation</th>
<th>Wilcoxon Signed-Rank Test Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial systolic (mm Hg)</td>
<td>82.0 (76.0–89.0)</td>
<td>83.0 (76.0–89.5)</td>
<td>0.86</td>
</tr>
<tr>
<td>Arterial diastolic (mm Hg)</td>
<td>48.0 (41.5–51.0)</td>
<td>48.0 (45.0–52.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>Arterial mean (mm Hg)</td>
<td>61.0 (55.5–67.0)</td>
<td>62.0 (57.0–67.5)</td>
<td>0.57</td>
</tr>
<tr>
<td>PAP systolic (mm Hg)</td>
<td>65.0 (53.0–85.5)</td>
<td>54.0 (41.5–78.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PAP diastolic (mm Hg)</td>
<td>30.0 (19.5–41.5)</td>
<td>24.0 (15.5–34.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PAP mean (mm Hg)</td>
<td>47.0 (36.0–62.3)</td>
<td>37.5 (27.0–56.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>10.0 (8.0–11.0)</td>
<td>10.0 (8.0–11.0)</td>
<td>0.99</td>
</tr>
<tr>
<td>TPG (mm Hg)</td>
<td>37.5 (28.0–54.0)</td>
<td>28.0 (20.5–43.5)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Qp (L/min)</td>
<td>3.2 (2.3–3.9)</td>
<td>2.9 (2.2–4.1)</td>
<td>0.19</td>
</tr>
<tr>
<td>PVRi (WUm$^2$)</td>
<td>11.8 (7.8–17.8)</td>
<td>8.3 (5.2–16.6)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Values are represented as median (interquartile range). PAP indicates pulmonary artery pressure; PCWP, mean pulmonary capillary wedge pressure; PVRi, indexed pulmonary vascular resistance; Qp, pulmonary flow; and TPG, transpulmonary gradient. *Significant changes.

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**Figure 2.** Minimum septal curvature ($SC_{\min}$) in controls and patients with a mean pulmonary artery pressure $\geq 25$ mm Hg. Solid lines indicate mean and 95% confidence intervals; dashed lines indicate lower limit of normal population and upper limit of patient group. PH indicates pulmonary hypertension.

**Figure 3.** Relationship between minimum septal curvature ($SC_{\min}$) and mean pulmonary artery pressure (mPAP). Red circles are at baseline; blue triangles are during vasodilator testing.
Discussion
Assessment of pulmonary hemodynamics is vital in the management of pediatric PH. The most commonly used noninvasive method is measurement of tricuspid regurgitation velocity using Doppler echocardiography. Unfortunately, tricuspid regurgitation is absent in ≈9% of children with PH, and there are concerns about its reliability. Thus, an alternative approach is desirable, and several adult CMR studies have shown that septal curvature correlates well with pulmonary artery pressure. However, this is the first pediatric CMR study to investigate the relationship between septal curvature and pulmonary hemodynamics. Furthermore, it is the first study to compare septal curvature with simultaneously acquired pulmonary hemodynamic data. This was possible because of the use of MR-augmented cardiac catheterization, which allows CMR to be performed with pressure catheters in situ. The main findings were as follows: (1) there was a significant difference in septal curvature parameters between normal controls and children with PH; (2) septal curvature-derived metrics correlated with mPAP and PVRi in patients; and (3) septal curvature-derived metrics were able to track acute changes in pulmonary hemodynamics during vasodilator testing. We think that these results show that septal curvature metrics \((SC_{\text{min}})\) could be used as a noninvasive adjunct to catheter assessment in pediatric PH.

In healthy children, LV pressure exceeds RV pressure throughout the cardiac cycle. This gives the LV a circular shape in the short axis, and in this study, all healthy children had a \(SC_{\text{min}} \approx 1\). However, in PH, the LV–RV pressure gradient is reduced or even reversed, causing the septum to become either flattened or bow into the LV. Thus, \(SC_{\text{min}}\) was <1 in all our patients, and there was no overlap with the healthy population. This raises the possibility that \(SC_{\text{min}}\) could be used as a screening tool for PH in children. Unfortunately, the current study was not designed to test this capability, and therefore, no strong conclusions can be made without further work.

In the patient population, we have shown that \(SC_{\text{min}}\) significantly correlates with mPAP and that it occurs ≈100 ms after aortic valve closure. This leads to an overlap between late RV systole and early LV diastole, and during this period, the trans-septal pressure gradient is at its highest. Thus, the septum is mechanically deformed most at this point in the cardiac cycle. Other factors, such as tricuspid regurgitation and prolonged QRS duration/right bundle branch block, also theoretically affect septal curvature, although in our study no correlations were demonstrated.

The correlations found in this study were not sufficient for septal curvature to be used as a replacement for catheterization or as an accurate method of estimating mPAP. Nevertheless, CMR assessment of septal curvature could still have an important role to play in patient management, particularly during follow-up. Currently, CMR is mainly used to evaluate ventricular volumes and function in PH. However, RV failure only represents part of the pathophysiology of the disease, the other part being increased ventricular afterload. We have shown that septal curvature metrics can provide an approximation of RV afterload, and if combined with CMR, volumetry may provide a more comprehensive assessment of PH.

We also demonstrated that changes in \(SC_{\text{min}}\) and \(SC_{\text{min}}/Qp\) correlated reasonably well with changes in mPAP and PVRi during vasodilator testing. Hemodynamic response to vasodilators provides information about prognosis and operability.

![Figure 4](http://circimaging.ahajournals.org/)

Figure 4. A, Relationship between minimum septal curvature \((SC_{\text{min}})\) and indexed pulmonary vascular resistance \((PVRi)\). B, Relationship between minimum septal curvature/indexed cardiac output \((SC_{\text{min}}/Qpi)\) and PVRi. Red circles are at baseline; blue triangles are during vasodilator testing.

![Figure 5](http://circimaging.ahajournals.org/)

Figure 5. A, Relationship between change in mean pulmonary artery pressure \((mPAP)\) and change in minimum septal curvature \((SC_{\text{min}})\). B, Relationship between change in indexed pulmonary vascular resistance \((PVRi)\) and minimum septal curvature/indexed cardiac output \((SC_{\text{min}}/Qpi)\).
Chronic changes in afterload. Clearly, acute vasodilator testing opens up the possibility of using septal curvature to monitor hemodynamic changes. The ability to track acute hemodynamic changes without invasive monitoring is essential. Irrespective of the vasodilator used, continuous monitoring of heart rate, cuff blood pressure, and saturations would be a prerequisite of noninvasive testing. The drawback of using NO to an awake patient via a facemask is that it often causes dyspnea and may not be the safest option when performing vasodilator testing. Unfortunately, it is associated with greater systemic effects and may not be the safest option when performing vasodilator testing without invasive monitoring. In conclusion, we have shown that septal curvature–derived metrics correlate with pulmonary hemodynamics in pediatric PH. In addition, we have shown that septal curvature metrics can track change in hemodynamics during acute vasodilator testing. We think that these findings demonstrate that septal curvature assessed using real-time CMR is a practical and accurate method of assessing SC in children with PH.

Limitations
The main limitation of this study was that all patients were under general anesthesia. This was necessary because the study was performed during MR-augmented catheterization, which in our institution is always done under general anesthesia. Thus, we are unable to definitely say that the relationships seen in this study reflect the situation in awake children. Nevertheless, even though pulmonary artery pressure may be different, there is no reason to think that the mechanical underpinning of the relationship will change. A further related issue is that real-time imaging may not perform as well in awake children with irregular breathing patterns. Ventricular volumes assessed using the same real-time imaging in awake children do compare well with the reference standard breath-hold techniques. Consequently, we think that the real-time imaging would be sufficient even in this group of pediatric patients, although formal testing is required. It would also be important to confirm prognostic ability of septal curvature metrics measured with routine CMR.

Conclusion
In conclusion, we have shown that septal curvature–derived metrics correlate with pulmonary hemodynamics in pediatric PH. We think that these findings demonstrate that septal curvature assessed using real-time CMR may have an important role in estimating afterload during routine follow-up of children with PH.

Sources of Funding
We acknowledge the support received from the British Heart Foundation and UK National Institute of Health Research (NIHR). This report is independent research by the National Institute for Health Research Biomedical Research Centre Funding Scheme. The views expressed in this publication are those of the authors and not

Figure 6. Receiver-operating characteristic curve of the performance of change in minimum septal curvature ($\Delta SC_{\text{min}}$) for identification of patients who are classified as vasoresponders by the Sitbon criteria. $\Delta SC_{\text{min}}$ cutoff value of 0.466 (area under the curve, 0.90; 95% confidence interval, 0.80–0.99) provided the greatest diagnostic accuracy (sensitivity=83%, specificity=91%).

(pulmonary arterial hypertension associated with congenital heart disease),32 and most importantly optimum treatment strategies (IPAH).30,33,34 Specifically, in IPAH, calcium channel blockers are only recommended in patients classified as vasoresponders (using specific criteria). Thus in IPAH, vasoresponsivity is invasively assessed at diagnosis and repeatedly reassessed in vasoresponders to ensure a continued response. Unfortunately, catheterization in the pediatric population often require general anesthesia, which carries a risk in children with PH. Consequently, it would be useful if invasive assessment were only performed in children in whom vaso-reactivity was uncertain. We have shown that septal curvature change can predict vasoresponder status (as defined by the Sitbon criteria) with high specificity and moderate sensitivity in both the IPAH subgroup and the total study population. This means that any patient who has a positive septal curvature response is almost certain to be a true vasoresponder and does not necessarily need catheterization. However, patients who have minimal or absent septal curvature response should be catheterized, as they will be a mixture of true and false negatives. If CMR were to be used in this manner, one issue that needs resolving is how to safely administer NO to an awake child in a CMR scanner. Previous studies have shown that it is possible to administer NO to an awake patient via a mask or nasal cannula.35–38 However, it would be vital to demonstrate that the delivered dose and any nitrogen dioxide build up could be accurately monitored. An alternative approach is a noninhalational vasodilator (ie, prostacyclin), which should induce changes in septal curvature, as deformation is primarily a mechanical process. The main benefit of using prostacyclin is that it is easier to administer in the CMR scanner. Unfortunately, it is associated with greater systemic effects and may not be the safest option when performing vasodilator testing without invasive monitoring. Irrespective of the vasodilator used, continuous monitoring of heart rate, cuff blood pressure, and saturations would be a prerequisite of noninvasive testing. The ability to track acute hemodynamic changes opens up the possibility of using septal curvature to monitor chronic changes in afterload. Clearly, acute vasodilator testing is not an adequate model of response to therapy or disease progression. Nevertheless, animal studies have used MR to track chronic changes in RV afterload,39 and it would be useful to confirm this in pediatric patients.

One major difference between our study and previous adult studies was the use of real-time CMR. Children with PH are often dyspneic and find conventional breath-hold CMR difficult to perform.4 The benefit of real-time CMR is that it can be performed during free breathing, making it feasible in pediatric PH.4 The drawback of real-time CMR is that it is usually acquired at low temporal and spatial resolution, which can affect accuracy.16 Recently, novel high-resolution real-time sequences have been developed and validated in the pediatric population. In this study, we used one such technique (radial k-t SENSE) that has a similar spatial and temporal resolution to conventional breath-hold cine imaging.16 This is vital because the septum often displays a flicking motion that is difficult to appreciate at low temporal resolution. Because the correlation between $SC_{\text{min}}$ and mPAP was similar to previously reported results, we think that the temporal resolution of this sequence is sufficient to accurately assess $SC_{\text{min}}$. Therefore, we think that real-time CMR is a practical and accurate method of assessing SC in children with PH.
necessarily those of the National Health Service, the NIHR, or the Department of Health.

Disclosures

None.

References


In this study, 50 children (median age, 6.7 years) with pulmonary hypertension underwent a combined cardiovascular magnetic resonance catheter study, which allowed simultaneous assessment of pulmonary artery pressure and septal curvature. Significant correlations were demonstrated between mean pulmonary artery pressure and septal curvature at baseline and during vasodilator testing ($r=-0.81$ and $r=-0.85$, respectively). A strong linear relationship also existed between pulmonary vascular resistance and minimum septal curvature indexed to cardiac output both at baseline and during vasodilator testing ($r=-0.88$ and $r=-0.87$, respectively; $P<0.001$). This suggests that septal curvature may be of use in making an estimate of right ventricular load during follow-up. This is particularly true because change in septal curvature also correlated with change in hemodynamics during vasodilator testing. In addition, these metrics could be used to identify vasoressponders with a high specificity in all patients in the study population and in the idiopathic pulmonary arterial hypertension subgroup (n=30). This may allow better identification of patients who need formal invasive testing of vasoresponsiveness, reducing the total number of catheterizations these children must undergo.
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_Circ Cardiovasc Imaging_. 2014;7:706-713; originally published online April 25, 2014; doi: 10.1161/CIRCIMAGING.113.001156

_Circulation: Cardiovascular Imaging_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 1941-9651. Online ISSN: 1942-0080

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