Acute Effects of Embolizing Systemic-to-Pulmonary Arterial Collaterals on Blood Flow in Patients With Superior Cavopulmonary Connections
A Pilot Study

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Background—The significance and optimal treatment of systemic-to-pulmonary arterial collateral (SPC) vessels in single ventricle patients are poorly understood. The acute efficacy of SPC embolization has not been demonstrated in a quantifiable fashion. We sought to assess the acute efficacy of SPC embolization on blood flow as quantified by phase contrast magnetic resonance imaging and hypothesized that embolization acutely decreases SPC flow and increases systemic blood flow ($Q_s$).

Methods and Results—Six superior cavopulmonary connection patients underwent SPC flow quantification by phase contrast magnetic resonance imaging, including quantification of superior and inferior caval, total pulmonary artery, total pulmonary vein, ascending and descending aortic flows ($Q_{syc}$, $Q_{ivc}$, $Q_{pa}$, $Q_{pv}$, $Q_{ao}$, and $Q_{dao}$, respectively), both immediately before and after cardiac catheterization with coil and particle embolization of angiographically evident SPC vessels. All studies were performed under a single anesthetic. After embolization, we found a significant decrease in SPC flow of 0.9 (range, 0.6–1.3) L/(min·m²) ($P=0.03$); a median reduction of 47% (range, 32–60). There was a significant decrease in the median $Q_s:Q_p$ from 1.3 before to 0.8 after embolization ($P=0.03$), and an increase in $Q_s$ from a median of 3.4 to 4.4 L/(min·m²) ($P<0.05$), and $Q_{syc}$ from a median of 1.7 to 2.3 L/(min·m²) ($P=0.03$).

Conclusions—We report on the acute efficacy of SPC embolization, demonstrating a significant decrease in SPC flow and $Q_s:Q_p$ and increase in $Q_{syc}$ and $Q_s$. Further studies are needed to assess the durability of the procedure and the effect on Fontan and longer-term outcomes. (Circ Cardiovasc Interv. 2013;6:00-00.)

Key Words: aortopulmonary collaterals ■ embolization ■ MRI ■ superior cavopulmonary connection ■ XMR
WHAT IS KNOWN

• The significance and optimal treatment of systemic-to-pulmonary arterial collateral (SPC) vessels in single ventricle patients are poorly understood.
• The acute efficacy of SPC embolization has not been demonstrated in a quantifiable fashion.

WHAT THE STUDY ADDS

• SPC embolization results in a significant acute decrease in SPC flow, pulmonary, and pulmonary-to-systemic flow ratio and increase in superior vena cava flow and systemic flow.
• SPC embolization did not result in an acute change to ventricular loading.
• Using the methodology outlined in this study, we can now determine whether the embolization effects are durable and, even more importantly, whether collateral embolization improves clinical outcomes.

recently demonstrated that higher SPC flow is associated with longer hospital stay and effusion duration after Fontan completion.5

The purpose of this report is to evaluate the efficacy of SPC embolization as determined by immediate pre- and postprocedural SPC flow quantification with MRI. We hypothesized that SPC embolization would result in a significant reduction in SPC flow and increase in systemic blood flow ($Q_s$).

Methods

Data from 6 patients who underwent routine pre-Fontan X-ray magnetic resonance imaging procedures were retrospectively analyzed for this study. X-ray magnetic resonance imaging procedures involved a single anesthetic during which patients underwent diagnostic catheterization and collateral embolization with phase contrast (PC) MRI SPC quantification immediately before and after the embolization procedure.

MRI Studies

MRI scans were performed on a Magnetom Avanto 1.5-T Siemens scanner. All patients underwent immediate precatheterization cardiac MRI consisting of (1) balanced steady-state free precession (bright blood) transverse stack, which extended from the thoracic inlet to the superior portion of the liver, (2) half-Fourier single-shot turbo spin-echo (dark blood) transverse stack spanning the same region, (3) balanced steady-state free precession cine imaging, including a 2-chamber view, 4-chamber view, and short-axis stack for anatomy and to quantify ventricular function, (4) angiography high spatial and temporal resolution magnetic resonance angiography (syngro time-resolved angiography with stochastic trajectories [TWIST]) of the heart and great vessels for anatomy, and (5) through-plane PC-MRI SPC quantification immediately before and after the embolization procedure.

Embolization Procedures

Patients were anesthetized before the MRI studies. All X-ray magnetic resonance imaging cases were performed under one anesthetic and on room air. Monitored physiological variables, such as heart rate, pulse oximetry, noninvasive mean arterial pressure, and end title CO2, were recorded and documented in the anesthesiology record. After completing the MRI, study patients were transferred to the X-ray suite via a Miyabi sliding table (Siemens, Erlangen, Germany) where they underwent routine diagnostic catheterization followed by SPC embolization. Embolization of angiographically evident SPC vessels was performed with a combination of particles (Contour PVA Embolization Particles, Boston Scientific, MA) and MReye coils (Cook Medical Inc, Bloomington, IN). To identify vessels for embolization, digital subtraction angiograms were performed in each subclavian artery as well as intercostal and bronchial arteries. Arterial sources of SPC flow so identified were selectively cannulated with a 4F catheter through which a microcatheter (high flow Renegade, Boston Scientific, Natick, MA) was advanced. Embolization was achieved by infusing particles ranging in size from 500 to 1000μm until distal runoff was obliterated. In larger vessels (proximal diameter > 2 mm), after angiography confirmed cessation of flow, the proximal vessels were occluded with coils. After the embolization procedure, patients were transferred back to the MRI scanner via the Miyabi sliding table for repeat SPC quantification.

Statistical Considerations

Demographic and procedural variables were summarized using standard descriptive statistics and expressed as mean±SD for normally distributed continuous variables, median with range for skewed continuous variables, and count with percentage of total for categorical variables. Pre- versus postembolization SPC estimates were compared for all MRI variables using Wilcoxon paired-signed rank test, and exact probability values were used. The correlation between the number of vessels embolized and the percent reduction in collateral flow was assessed with the Spearman rank-correlation coefficient. All statistical analyses were performed using SPSS v20 (IBM Corporation, Armonk, NY). Statistical significance was established using a 2-tailed probability value of <0.05.

This study was conducted with approval from The Children's Hospital of Philadelphia review board.

Results

Baseline demographic and hemodynamic data are summarized in Table 2 and relevant anatomic and clinical data are summarized in Table 3. There was no statistical difference in heart rate, end-tidal CO2, mean arterial pressure, and pulse oximetry values at MRI before and after the catheterization procedure. Median pulmonary artery pressure and the median

Table 1. Equations Used for Systemic-to-Pulmonary Arterial Collateral Flow Quantification

<table>
<thead>
<tr>
<th>Equation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Q_{coll}$</td>
<td>Collateral flow from estimated systemic flow</td>
</tr>
<tr>
<td>$Q_{syst}$</td>
<td>Systemic flow</td>
</tr>
<tr>
<td>$Q_{pulm}$</td>
<td>Pulmonary flow</td>
</tr>
<tr>
<td>$Q_{coll,pulm}$</td>
<td>Collateral flow from estimated pulmonary flow</td>
</tr>
<tr>
<td>$Q_{coll}$</td>
<td>Average collateral flow</td>
</tr>
</tbody>
</table>

$Q_{coll} = \frac{(Q_{coll,syst} + Q_{coll,pulm})}{2}$

$Q_{syst} = Q_{aortic} - Q_{pulm}$

$Q_{pulm} = Q_{aortic} - Q_{pa}$

Collateral flow and systemic flow ratio and increase in superior vena cava flow.
transpulmonary gradient are shown in Table 2. Table 4 lists the number of vessels embolized, the location of the vessels, and the embolization technique (particle versus coil or a combination of both) used. The PC-MRI derived flows pre- and postembolization procedure are summarized in Table 5 and selected flows are shown in Figure 1.

Change in Collateral Flow

Embolization resulted in a significant decrease in collateral flow \( (Q_{coll}) \) with a median decrease of 0.9 (range, 0.6–1.3) L/(min·m²) \( (P=0.03) \). This equates to a median reduction in collateral flow of 47% (range, 32%–60%) (Figure 1A). When expressed as a percentage of aortic flow or pulmonary venous flow, there was a statistically significant decrease after embolization of 17% (range, 9%–28%) \( (P=0.03) \) and 18% (range, 12%–30%), respectively \( (P=0.03) \). We also found a significant correlation between the number of vessels embolized in a given patient and the percent reduction in collateral flow with more vessels corresponding to higher percent reduction in flow (Spearman correlation = 0.926; \( P<0.01 \)) (Figure 2). Time-resolved contrast injection in the lower extremitry pre- and postprocedure for patient B is shown in Figure 3.

Table 3. Anatomic and Relevant Clinical Data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Anatomy</th>
<th>Additional Surgical History</th>
<th>Previous Embolizations</th>
<th>Other Relevant Clinical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Double outlet right ventricle with mitral atresia</td>
<td>Surgical clipping of RIMA</td>
<td>Stage I complicated by pneumonia and sternal wound infection</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>HLHS</td>
<td>Surgical clipping of RIMA</td>
<td>Laryngomalasias status post trach, multiple episodes of pneumonia, stage I complicated by diaphragm paresis status post plication</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Tricuspid atresia</td>
<td>LPA plasty</td>
<td>LPA stent</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>HLHS</td>
<td>LPA and TV plasty, TV replacement</td>
<td>CoA stent status post stentLPA stentRAD</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Complex heterotaxy with unbalanced CAVC</td>
<td></td>
<td>Severe AVVR, right diaphragm eventration, RAD</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>HLHS</td>
<td></td>
<td>Chylothorax after both operations, right diaphragm paresis status post plication</td>
<td></td>
</tr>
</tbody>
</table>

AVR indicates atriointeravalve regurgitation; CAVC, complete atriointerivalve canal; CoA, coarct; HLHS, hypoplastic left heart syndrome; LPA, left pulmonary artery; RIMA, right internal mammary artery; RAD, reactive airway disease; and TV, tricuspid valve.

Discussion

PC-MRI has been recently shown to be a consistent and precise tool for collateral flow quantification. In this study, we used this method, quantifying collateral flow immediately before and after embolization under the same anesthetic to determine whether and to what degree transcatheter embolization reduces collateral flow in patients with a bidirectional Glenn circulation. In these 6 patients, embolization of SPC vessels resulted in a 47% reduction of collateral flow, which was statistically significant. Along with this reduction in flow, patients had significant increases in systemic as well as superior vena cava flow. In this acute study, we found no change in ventricular loading as determined by the combined systemic and pulmonary venous return. It is noteworthy that despite aggressive embolization, a substantial amount of SPC flow remained after the procedure in our patients. We think these findings are an important step in the effort to clarify the impact of collateral embolization on clinical outcome in single ventricle patients.

The flow changes identified in our study have a number of potential implications. Because systemic output and superior vena caval flow increased, oxygen saturation was maintained despite substantial decreases in pulmonary blood flow. The increase in \( Q_{PV} \) and \( Q_{SV} \) are likely primarily a result of decreased systemic arterial runoff in the setting of unchanged preload making more blood available to supply the systemic circulation.

All patients in our series demonstrated significant reductions in collateral flow. Of note, there was a statistically significant relationship between the degree to which SPC flow decreased and the number of vessels embolized. There is considerable variation among centers in embolization practices. This variation has included not only the decision of which patients should...
undergo embolization, but also which vessels, and by what technique. Coil embolization is a common method used to occlude sources of arterial collateral flow. However, this may not be a particularly effective strategy. Coil embolization for systemic-to-pulmonary collaterals in patients with pulmonary heart disease was originally described primarily for the treatment of major collateral arteries in patients with pulmonary atresia. Subsequently, this same strategy was applied to the current population, although the nature of their collaterals are very different. The vessels, which we occlude with coils, are not the collaterals themselves but rather normal systemic arteries feeding the collaterals. The limitation of this strategy is that the collaterals themselves remain intact. Multiple other systemic arteries have connections allowing them to function as alternative feeders to the same collateral network. An alternative approach is similar to that used for treatment of collateralization in chronic lung diseases where PVA particles are infused through feeder arteries to embolize the smaller caliber arteries closer to the actual collateral connection. We applied this strategy in combination with coil embolization of larger feeder arteries. Although theoretically appealing, as yet there are no data to support the effectiveness of particles versus coil embolization. Further studies will be required to answer such questions.

It is noteworthy that 2 of the 6 patients in this study had surgical clips placed on internal mammary arteries at the time of superior cavopulmonary anastomosis in efforts to decrease collateral flow. Despite this, SPC flow in these patients was high. Given the model for collateral development in this population, it is not surprising that this strategy is not effective. In the study by Bradley et al., SPC flow was higher in patients who had collateral embolization more than 2 months before surgery. These and other observations raise the all-important question: how durable is embolization as a treatment? Further studies will need to be conducted to determine the durability of this procedure as well as the effect on Fontan and longer-term clinical outcomes.

**Limitations**

This study is a retrospective study of 6 patients who underwent SPC quantification by MRI both immediately before and after catheter-based embolization. As such, it is subject to all the limitations and biases inherent in retrospective studies. Furthermore, because we currently tend to perform embolization only on patients with higher than usual collateral burden, the patients reported represent an extreme of the Glenn population in age and collateral burden. This could potentially produce bias in the magnitude of the effect that we have demonstrated in our results. Patients in this series underwent embolization with both particles and coils, which is not the practice at many centers. Thus, our data may not reflect the

**Table 5. Phase Contrast Magnetic Resonance Imaging-Derived Median (Range) Flows, Flow Ratios, Absolute Change, and Percent Change Pre- and Postintervention**

| Phase Contrast Magnetic Resonance Imaging-Derived Median (Range) Flows, Flow Ratios, Absolute Change, and Percent Change Pre- and Postintervention |
|---|---|---|---|---|
| Pre | Post | Absolute Change | Change, % | P |
| $Q_{SVC}$ | 1.7 (0.8 to 2.5) | 2.3 (1 to 2.9) | 0.4 (0.2 to 0.6) | 20 (15 to 25) | 0.03 |
| $Q_{VC}$ | 1.4 (1.2 to 2.7) | 2.2 (1.8 to 3.0) | 0.8 (–0.4 to 1.3) | 66 (–14 to 95) | 0.08 |
| $Q_{Ao}$ | 5.5 (4.5 to 5.8) | 5.7 (4.1 to 6.2) | 0.1 (–1.2 to 0.7) | 2 (–22 to 12) | 0.75 |
| $Q_{SPC}$ | 1.5 (1.0 to 1.9) | 2.1 (1.3 to 2.8) | 0.7 (0 to 1.2) | 53 (5 to 77) | 0.03 |
| $Q_{PA}$ | 1.8 (0.8 to 2.6) | 2.2 (1.0 to 2.9) | 0.3 (–0.1 to 0.7) | 17 (–6 to 47) | 0.08 |
| $Q_{PV}$ | 4.0 (2.6 to 4.4) | 3.3 (1.8 to 4.2) | –0.6 (–1.3 to 0.1) | –15 (–31 to 3) | 0.046 |
| $Q_{VR}$ | 5.5 (4.6 to 5.9) | 5.7 (4.1 to 6.4) | 0 (–1.2 to 1.1) | 0.5 (–23 to 21) | 0.92 |
| $Q_{q}$ | 3.4 (2.4 to 3.9) | 4.4 (3.3 to 5.3) | 1.4 (0.2 to 1.6) | 47 (–6 to 53) | 0.046 |
| $Q_{SPC}$ as % of Ao | 1.25 (0.74 to 1.49) | 0.75 (0.54 to 0.88) | –0.4 (–0.8 to –0.2) | –35 (–54 to –19) | 0.03 |
| $Q_{SPC}$ as % of Ao | 1.9 (1.7 to 2.8) | 1.0 (0.8 to 1.5) | –0.9 (–1.3 to –0.6) | –47 (–61 to –32) | 0.03 |
| $Q_{SPC}$ as % of Ao | 3.62 (29.6 to 48.8) | 20.0 (15.6 to 26.1) | –17 (–28 to –9) | –44 (–62 to –30) | 0.03 |
| $Q_{SPC}$ as % of Ao | 55.2 (42.1 to 67.9) | 32.6 (24.5 to 52.2) | –18 (–32 to –12) | –35 (–52 to –22) | 0.03 |

Flows are in L/(min·m²); $Q_{Ao}$ indicates flow at the aortic valve; $Q_{cp}$ collateral flow; $Q_{SVC}$, inferior vena cava flow; $Q_{PA}$, antegrade pulmonary artery flow; $Q_{PV}$, pulmonary vein flow; $Q_{VR}$, systemic flow; $Q_{SVC}$, superior vena cava flow; and $Q_{VR}$, venous return flow.
results that would be achieved with coil embolization of larger feeding vessels alone. To the extent possible, we attempted to maintain patients in the same physiological state during both MRI procedures and the catheterization with minimal variation in inspired gases or anesthetic. Nonetheless, it is possible that the significant contrast and fluid load given to the patients during the procedure could have introduced a bias into our PC-MRI results.

It is theoretically possible that the embolization coils could affect the flow quantification. However, the platinum coils used have very localized artifacts and are unlikely to significantly affect quantification. Furthermore, there was no difference in the internal consistency of the flow quantification before and after embolization, minimizing this concern.

Lastly, with current technology there is a limit to the spatial resolution of the magnetic resonance angiography.

Figure 1. Plot of phase contrast magnetic resonance imaging-quantified $Q_{\text{coll}}$, $Q_{S}$, $Q_{\text{SVC}}$, and $Q_{PV}$ before and after embolization in patients A–F. The thick black line denotes the difference between the median values before and after the embolization procedure.

Figure 2. Plot of the number of vessels embolized versus the percent reduction in collateral flow.
images, such that small collateral vessels (<1 mm in diameter) cannot be visualized. Consequently, contrast magnetic resonance angiography is currently only useful for seeing the collective effect of collateral flow and for seeing larger collateral vessels. Visualization of smaller vessels requires higher resolution techniques, such as contrast cine X-ray angiograms.

Conclusions

We have demonstrated that SPC embolization results in a significant acute decrease in collateral flow, with a median reduction of 47%. This resulted in significant reduction in total pulmonary blood flow, increase in cavopulmonary blood flow, and increased systemic blood flow, with no decrease in arterial oxygen saturation. The favorable hemodynamic effects of these acute results are encouraging. A larger study with medium and long-term follow-up will be required to determine whether these changes are durable and even more importantly, if collateral embolization improves clinical outcomes.

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Disclosures

None.

References

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