Systemic-to-Pulmonary Collateral Flow, as Measured by Cardiac Magnetic Resonance Imaging, Is Associated With Acute Post-Fontan Clinical Outcomes

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Background—Systemic-pulmonary collateral (SPC) flow occurs commonly in single ventricle patients after superior cavo-pulmonary connection, with unclear clinical significance. We sought to evaluate the association between SPC flow and acute post-Fontan clinical outcomes using a novel method of quantifying SPC flow by cardiac magnetic resonance (CMR) imaging.

Methods and Results—All patients who had SPC flow quantified by CMR imaging before Fontan were retrospectively reviewed to assess for acute clinical outcomes after Fontan completion. Forty-four subjects were included who had Fontan completion between May 2008 and September 2010. SPC flow prior to Fontan measured 1.5±0.9 L/min/m², accounting for 31±11% of total aortic flow and 44±15% of total pulmonary venous flow. There was a significant linear association between natural log-transformed duration of hospitalization and SPC flow as a proportion of total aortic (r=0.31, P=0.04) and total pulmonary venous flow (r=0.29, P=0.05). After adjustment for Fontan type and presence of a fenestration, absolute SPC flow was significantly associated with hospital duration ≥7 days (odds ratio [OR]=9.2, P=0.02) and chest tube duration ≥10 days (OR=22.7, P=0.009). Similar associations exist for SPC flow as a percentage of total aortic (OR=1.09, P=0.048 for hospitalization ≥7 days; OR=1.24, P=0.007 for chest tube duration ≥10 days) and total pulmonary venous flow (OR=1.07, P=0.048 for hospitalization ≥7 days; OR=1.18, P=0.006 for chest tube duration ≥10 days).

Conclusions—Increasing SPC flow before Fontan, as measured by CMR imaging, is associated with increased duration of hospitalization and chest tube following Fontan completion. (Circ Cardiovasc Imaging. 2012;5:218-225.)

Key Words: aortopulmonary collaterals ■ cardiac MRI ■ Fontan procedure ■ outcomes ■ single ventricle

In patients with single ventricle physiology, systemic-to-pulmonary arterial collateral vessels (SPCs) long have been observed after superior cavo-pulmonary connection (Stage II). In this group, angiographically visible SPCs have been described in 17% to 85% of patients. In addition to angiographic techniques, attempts to quantify SPC flow have included intraoperative measurements and scintigraphy. Possibly in part because of a lack of a consistent measuring tool, there is disagreement on the clinical impact of and role for targeted therapy of SPCs in Stage II patients.

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We and others recently described and validated a novel method to reliably and objectively quantify SPC flow by cardiac magnetic resonance (CMR) imaging techniques. By this methodology, SPC flow is the average of 2 independent measures: summed pulmonary venous flows minus summed pulmonary arterial flows, and aortic flow minus summed caval flows. It is worth noting that our methodology differs subtly, yet potentially importantly, with that of Grosse-Wortmann et al. We use a direct measurement of inferior vena cava (IVC) flow, while Grosse-Wortmann et al use velocity mapping in the descending aorta as a surrogate measure of IVC flow. This may account for the superior measures of internal consistency (intraclass correlation coefficient of 0.81 versus 0.73, with smaller magnitude of bias by Bland-Altman analysis) that we report. The objective of the current study was to examine the relationship between SPC flow as measured by CMR imaging and acute post-Fontan clinical outcomes. We performed a retrospective cohort study of all patients who had surgical Fontan completion at our...
institution who also had SPC flow quantified by CMR imaging as a Stage II. The primary outcome measures were duration of chest tube and duration of hospitalization. We hypothesized that increasing amounts of SPC flow are associated with increased length of pleural effusion and increased length of hospital stay.

Methods

Subject Ascertainment

The institutional surgical database was queried to find all patients who had surgical Fontan completion between May 1, 2008 and September 30, 2010. This list was cross-referenced against the institutional CMR database to identify all patients who had a CMR study performed prior to Fontan completion. Patients with antegrade pulmonary blood flow were excluded. The CMR reports were reviewed manually to confirm that each subject had SPC flow quantified at the time of CMR imaging as a Stage II prior to Fontan completion. This group constituted our inclusion cohort. At our institution, CMR imaging is performed prior to Fontan completion at the discretion of the patient’s primary cardiologist. The study was approved by the institutional review board, and informed consent was obtained as necessary.

Data Extraction

A detailed retrospective medical record review was performed on all included subjects to extract pertinent demographic, clinical, operative, and outcome variables. These variables were obtained in order to identify factors that may confound or modify the association between measures of SPC flow and clinical outcomes. Demographic factors included age at CMR imaging, gender, age at Stage II, and age at Fontan. Clinical variables included underlying cardiac anatomic diagnosis, staged surgical history, weight at Fontan, duration of effusion and hospitalization after Stage II, and hemoglobin and pulse oximetry at the time of Fontan. The last echocardiogram prior to Fontan was reviewed to grade the degree of ventricular dysfunction and atrio-ventricular (AV) valve regurgitation. If a pre-Fontan cardiac catheterization was performed, hemodynamic measurements were reviewed. Operative variables included cardiopulmonary bypass, aortic cross-clamp, and circulatory arrest times, type of Fontan (extracardiac conduit or intra-atrial lateral tunnel), and the use of a fenestration. Clinical outcome variables included duration of stay in the intensive care unit, duration of total Fontan hospitalization, and duration of chest tube. Duration of chest tube was defined as the total number of days during which a pleural catheter was in place to drain pleural fluid. For example, if a patient had a chest tube in place for 7 days after surgery, then removed for 7 days, and then a pleural catheter was replaced for an additional 7 days, a total of 14 days of chest tube duration would be counted. Duration of mechanical ventilation and duration of inotropic support also were recorded. However, because of very little variance in these outcomes, they were not included in the final analysis.

Statistical Considerations

Demographic, clinical, operative, and outcome variables were summarized using standard descriptive statistics, with normally distributed continuous variables reported as mean ± standard deviation, skewed continuous variables reported as median with range, and categorical variables reported as count with percentage of total. Histograms were generated to display the distribution of clinical outcome variables (duration of chest tube and duration of hospitalization). Because of their skewed distribution with a long right tail, outcome variables were treated as continuous variables after natural log-transformation. Associations between normally distributed continuous predictor and outcome variables were assessed using Pearson correlation testing and linear regression. For ease of clinical applicability, outcome variables were dichotomized based on distributions and preceded from prior publications as follows: chest tube greater than or less than 10 days, hospitalization greater than or less than 7 days, and hospitalization greater than or less than 14 days. These cut points divided subjects into groups that had particularly poor (≥10 days of chest tube drainage or ≥14 days of hospitalization) or particularly good acute clinical outcomes (<7 days of hospitalization). Differences between measures of SPC flow based on these dichotomized outcome variables were tested with Wilcoxon Rank-Sum. Although the primary objective of the study was to examine the association between CMR measures of SPC flow and clinical outcomes, it was necessary to first test for important associations between other covariates and outcomes that might confound the relationship between SPC flow and outcomes. This was accomplished using univariate logistic regression, which identified Fontan type (extracardiac conduit versus intra-atrial lateral tunnel) and use of a fenestration as strong predictors of outcome in our cohort (all patients with intra-atrial lateral tunnels had chest tube duration <10 days, and all unfenestrated patients had hospitalization ≥7 days). Thus, subsequent logistic regression to test the association between measures of SPC flow and outcomes was performed controlling for these 2 important confounders. Statistical significance was established using 2-tailed tests for significance at P<0.05. All statistical analyses were performed using STATA v10.0 (Stata Corp.).

Results

Between May 1, 2008 and September 30, 2010, 162 patients had Fontan completion at our institution and had reached
The majority of subjects were male and the most common anatomic diagnosis was hypoplastic left heart syndrome. By echocardiography prior to Fontan completion, nearly all patients had qualitatively normal ventricular function and no greater than mild AV valve regurgitation. There were no differences in these demographic and clinical variables between the 44 subjects who had CMR imaging performed prior to Fontan and the 118 patients who did not. In addition, there were no sex-based or racial/ethnic-based differences present.

The measures of SPC flow by CMR imaging prior to Fontan are summarized in Table 2. The mean indexed absolute volume of SPC flow was 1.5 L/min/m², which comprised, on average, 31% of the total aortic flow and 44% of the total pulmonary venous flow. There was excellent internal consistency between the 2 independent estimators of SPC flow (rho = 0.81, P < 0.0001; intraclass correlation coefficient = 0.8). With SPC flow included in calculations of total pulmonary blood flow (Qp), Qs was found to be equal to total systemic blood flow (Qsysc + QsVC) at 3.3 L/min/m². Operative and clinical outcome variables are summarized in Table 3. The majority of patients had Fontan completion with an extracardiac conduit, the vast majority of which were fenestrated. The median cardio-pulmonary bypass time was 39 days (range 0 to 458) prior to Fontan completion. The mean indexed absolute volume of SPC flow was 1.5 L/min/m², which comprised, on average, 31% of the total aortic flow and 44% of the total pulmonary venous flow. There was excellent internal consistency between the 2 independent estimators of SPC flow (rho = 0.81, P < 0.0001; intraclass correlation coefficient = 0.8). With SPC flow included in calculations of total pulmonary blood flow (Qp), Qs was found to be equal to total systemic blood flow (Qsysc + QsVC) at 3.3 L/min/m². Operative and clinical outcome variables are summarized in Table 3. The majority of patients had Fontan completion with an extracardiac conduit, the vast majority of which were fenestrated. The median cardio-pulmonary bypass time was 39 days (range 0 to 458) prior to Fontan completion. The mean indexed absolute volume of SPC flow was 1.5 L/min/m², which comprised, on average, 31% of the total aortic flow and 44% of the total pulmonary venous flow. There was excellent internal consistency between the 2 independent estimators of SPC flow (rho = 0.81, P < 0.0001; intraclass correlation coefficient = 0.8). With SPC flow included in calculations of total pulmonary blood flow (Qp), Qs was found to be equal to total systemic blood flow (Qsysc + QsVC) at 3.3 L/min/m². Operative and clinical outcome variables are summarized in Table 3. The majority of patients had Fontan completion with an extracardiac conduit, the vast majority of which were fenestrated. The median cardio-pulmonary bypass time was 39 days (range 0 to 458) prior to Fontan completion. The mean indexed absolute volume of SPC flow was 1.5 L/min/m², which comprised, on average, 31% of the total aortic flow and 44% of the total pulmonary venous flow. There was excellent internal consistency between the 2 independent estimators of SPC flow (rho = 0.81, P < 0.0001; intraclass correlation coefficient = 0.8). With SPC flow included in calculations of total pulmonary blood flow (Qp), Qs was found to be equal to total systemic blood flow (Qsysc + QsVC) at 3.3 L/min/m². Operative and clinical outcome variables are summarized in Table 3. The majority of patients had Fontan completion with an extracardiac conduit, the vast majority of which were fenestrated. The median cardio-pulmonary bypass time was 39 days (range 0 to 458) prior to Fontan completion. The mean indexed absolute volume of SPC flow was 1.5 L/min/m², which comprised, on average, 31% of the total aortic flow and 44% of the total pulmonary venous flow. There was excellent internal consistency between the 2 independent estimators of SPC flow (rho = 0.81, P < 0.0001; intraclass correlation coefficient = 0.8). With SPC flow included in calculations of total pulmonary blood flow (Qp), Qs was found to be equal to total systemic blood flow (Qsysc + QsVC) at 3.3 L/min/m². Operative and clinical outcome variables are summarized in Table 3. The majority of patients had Fontan completion with an extracardiac conduit, the vast majority of which were fenestrated. The median cardio-pulmonary bypass time was 39
minutes. Ten subjects had an additional surgical procedure performed at the time of Fontan completion. There was a wide range of duration of total chest tube time and hospitalization, with a long right tail to the distribution. The median duration of hospitalization was 10 days, with a median chest tube duration of 4.5 days. Dichotomizing chest tube duration at 10 days and hospitalization at 14 days identified the 14 and 14 patients, respectively, who had the worst clinical outcomes. Similarly, dichotomizing hospitalization at 7 days identified the 7 patients who had the best clinical outcome. There were no deaths, cardiac transplantations, or Fontan take-downs in the acute postoperative period for this cohort.

Duration of hospitalization (natural log-transformed values) had a significant linear relationship, with SPC flow expressed either as a percentage of total aortic flow (rho = 0.31, P = 0.04) or total pulmonary venous flow (rho = 0.29, P = 0.05; Figure 2). We were unable to identify a linear relationship between absolute SPC flow and hospital duration, or any measure of SPC flow and duration of chest tube (natural log-transformed values). Subjects with hospital duration less than 7 days (Figure 3) and chest tube duration less than 10 days (Figure 4) had significantly less total SPC flow than subjects who required hospitalization of at least 7 days and chest tube for at least 10 days. When SPC flow is expressed as a proportion of total aortic flow and total pulmonary venous flow, subjects with shorter chest tube requirements had significantly less of a burden from SPC flow than those subjects with longer chest tube needs (Figure 5). There were no significant differences in measures of SPC flow based on hospital length of stay when 14 days was used as a cut point.

The magnitude of the effect size and precision of the estimate were assessed by creating odds ratios (OR) and 95% confidence intervals (CI) using logistic regression. By univariate analysis, there was a significantly increased odds of chest tube duration ≥10 days based on SPC flow as a percentage of both aortic (OR 1.1, 95% CI: 1.02–1.2, P = 0.02) and pulmonary venous flow (OR 1.07, 95% CI: 1.01–1.13, P = 0.02). Similarly, there was an increased odds of hospital duration of at least 7 days based on absolute SPC flow (OR 6.5, 95% CI: 1.1–38, P = 0.04). The direction of the effect for all other measures of SPC flow and clinical outcomes suggested an increased odds of longer chest tube and hospital duration with increasing SPC flow burden; however, the 95% CI included 1, so statistical significance was not achieved for other measures in univariate analyses. For this cohort, however, we first identified the presence of a
measured in absolute terms (L/min/m²) or expressed as a proportion of total aortic or total pulmonary venous flow, those subjects with greater amounts of SPC flow were more likely to require hospitalization of at least 7 days and chest tube duration of at least 10 days. After adjusting for the presence of a fenestration and the Fontan type, the odds of requiring hospitalization of at least 7 days increases by greater than 9-fold for every increase of 1 L/min/m² in total SPC flow. The same increase in SPC flow results in an increased odds of requiring a chest tube for at least 10 days of greater than 22-fold. As an increase in total SPC flow of 1 L/min/m² would represent a fairly large change of slightly greater than 1 standard deviation, it may be more clinically useful to consider the measure of association for an increase in total SPC flow of 0.5 L/min/m². This fairly modest change would result in a 3 times increased odds of prolonged hospitalization and a 4.8 times increased odds of prolonged chest tube duration.

This is the first study to demonstrate a significant association between SPC flow quantified by CMR techniques and post-Fontan clinical outcomes. Prior studies using a variety of other techniques to quantify SPC flow have reported widely inconsistent associations with post-Fontan clinical outcomes. Two groups have attempted to quantify SPC flow intraoperatively at the time of Fontan completion by measuring pulmonary venous return to the heart while on cardio-pulmonary bypass. One group found that more SPC flow predicted higher postoperative systemic venous pressure. In addition, the 4 patients with the most collateral flow all had high Fontan pressures (>17 mm Hg) and subsequent Fontan failure. Conversely, Bradley et al found no association between intraoperative measures of SPC flow and prolonged pleural effusions or hemodynamic parameters like Fontan pressure, common atrial pressure, or transpulmonary gradient after the Fontan procedure. Another approach has been to quantify SPC flow by angiographic techniques. Using a 4-point grading scale, Spicer and colleagues quantified SPC flow at pre-Fontan cardiac catheterization and found increasing severity grades were associated with prolonged drainage of pleural fluid. Using a similar quantification method, McElhinney et al found a seemingly opposite finding, with increasing collateral flow predicting shorter chest tube duration. The direction of this finding has been replicated, but to an extent that did not achieve statistical significance. Finally, SPC flow has been quantified using

Table 4. Measures of Association Between Systemic-Pulmonary Collateral Flow and Clinical Outcomes

<table>
<thead>
<tr>
<th>Measures of SPC Flow</th>
<th>Hospitalization ≥7 d</th>
<th>Hospitalization ≥14 d</th>
<th>Chest Tube ≥10 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)*</td>
<td>P</td>
<td>OR (95% CI)*</td>
</tr>
<tr>
<td>$Q_{col}$ (L/min/m²)$^f$</td>
<td>9.2 (1.4, 61)</td>
<td>0.02</td>
<td>1.46 (0.6, 3.3)</td>
</tr>
<tr>
<td>$Q_{col}/Q_{Ao}$ (%) $^g$</td>
<td>1.09 (1.1, 1.2)</td>
<td>0.048</td>
<td>0.06 (0.99, 1.14)</td>
</tr>
<tr>
<td>$Q_{col}/Q_{PV}$ (%) $^g$</td>
<td>1.07 (1, 1.14)</td>
<td>0.048</td>
<td>0.28 (0.98, 1.09)</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval; OR, odds ratio; $Q_{col}$ systemnic-pulmonary collateral flow; $Q_{Ao}$ aortic flow; $Q_{PV}$ pulmonary venous flow.

Discussion

In this cohort of 44 subjects who had SPC flow quantified by CMR imaging prior to Fontan completion, we have identified significant associations between increasing amounts of SPC flow and worse acute post-Fontan clinical outcomes. Whether fenestration and the Fontan type (extracardiac conduit versus intra-atrial lateral tunnel) as strong independent predictors of outcome. Thus, we also tested for associations between SPC flow and outcomes controlling for these 2 potential strong confounders, and these results are summarized in Table 4. There was a significant increase in the odds of requiring hospitalization of at least 7 days based on absolute SPC flow (OR = 9.2 for every increase of 1 L/min/m², $P = 0.02$), and the proportion of SPC flow expressed as a percentage of total aortic (OR = 1.09 for every 1% increase, $P = 0.048$) and total pulmonary venous flow (OR = 1.07 for every 1% increase, $P = 0.048$). Similarly, there was a significant increase in the odds of requiring a chest tube for at least 10 days based on absolute SPC flow (OR = 22.7 for an increase of 1 L/min/m², $P = 0.009$), and the proportion of SPC flow expressed as a percentage of total aortic (OR = 1.24 for every 1% increase, $P = 0.007$) and total pulmonary venous flow (OR = 1.18 for every 1% increase, $P = 0.006$). We were unable to identify a significant association between any measure of SPC flow and hospital duration dichotomized as <14 days versus ≥14 days.
thermodilution\textsuperscript{16} and whole body scintigraphy\textsuperscript{9} techniques, without demonstrating significant associations with post-Fontan clinical outcomes.

At least in part, the vastly discrepant relationships seen between SPC flow and clinical outcomes likely are due to the lack of a reliable and valid measuring tool. This is where CMR techniques hold tremendous promise. Reported in quick succession by Grosse-Wortman\textsuperscript{10} and our group,\textsuperscript{12} phase-contrast velocity mapping is performed to quantify flow in the following sites: aorta, SVC, IVC, RPA, LPA, RPVs, and LPVs. From these, SPC flow is calculated by 2 independent measures: (1) aortic flow minus summed caval flow, and (2) summed pulmonary venous flow minus summed pulmonary arterial flow. These 2 measures allow performance of an internal check. As we’ve demonstrated, these measurements can be made with a very high degree of reliability.\textsuperscript{12} CMR measures are not limited by the inherent inaccuracies of the Fick principle in estimating flows by oximetry in the cavo-pulmonary circuit, are more quantitative than grading angiography, and are more physiological and less invasive than intraoperative measures of SPC flow.

The 44 subjects comprising this cohort were fairly representative of a typical patient presenting for Fontan completion (Table 1), and were not significantly different than the 118 other patients who had Fontan completion during this time interval but did not have a CMR study performed preoperatively. Instead, these 44 subjects were all referred for pre-Fontan CMR imaging at the discretion of their primary cardiologist, and reflect our institutional trend toward using CMR imaging instead of (or in addition to) cardiac catheterization as part of the pre-Fontan evaluation. No patient in this cohort had embolization of collateral vessels performed prior to the Fontan completion. The measures of SPC flow summarized in Table 2 are consistent with values we have reported previously.\textsuperscript{12} It is worth noting that, with the exception of a single patient, all subjects had measurable SPC flow, with 95\% of subjects having between 0.5 and 2.7 L/min/m\textsuperscript{2} of absolute SPC flow, which contributes 15\% to 49\% of total aortic flow and 22\% to 69\% of total pulmonary venous flow. Our data suggest that virtually all patients with increasing SPC flow associates with poorer outcomes. We had the worst outcome by this measure. In this regard, preoperatively. Instead, these 44 subjects were all referred for pre-Fontan CMR imaging at the discretion of their primary cardiologist, and reflect our institutional trend toward using CMR imaging instead of (or in addition to) cardiac catheterization as part of the pre-Fontan evaluation. No patient in this cohort had embolization of collateral vessels performed prior to the Fontan completion. The measures of SPC flow summarized in Table 2 are consistent with values we have reported previously.\textsuperscript{12} It is worth noting that, with the exception of a single patient, all subjects had measurable SPC flow, with 95\% of subjects having between 0.5 and 2.7 L/min/m\textsuperscript{2} of absolute SPC flow, which contributes 15\% to 49\% of total aortic flow and 22\% to 69\% of total pulmonary venous flow. Our data suggest that virtually all patients with increasing SPC flow associates with poorer outcomes. We had the worst outcome by this measure. In this regard, increasing SPC flow associates with poorer outcomes. We were unable to identify an association between SPC flow and the worst hospitalization times (≥ 14 days).

While we have identified associations between SPC flow and clinical outcomes, this study does not establish a causal relationship. It is tempting to speculate that the additional volume load SPC flow imposes leads to increased ventricular filling pressure and pulmonary arterial pressure. However, this effect has not been consistently demonstrated. Some authors\textsuperscript{8} have reported higher pulmonary arterial pressures with increasing SPC flow, others\textsuperscript{5,17} report lower SVC and ventricular end diastolic pressures, and still others\textsuperscript{10,18} report no association. An alternative hypothesis is that SPC flow is simply a marker of unfavorable underlying anatomy or physiology, which may make a patient a poor Fontan candidate. A number of potential etiologic factors in the development of SPC flow have been suggested, including cyanosis and tissue hypoxia, decreased pulmonary blood flow, and prior mediastinal or pleural inflammation. The development of SPC vessels has been demonstrated experimentally in animal models after unilateral pulmonary arterial ligation,\textsuperscript{18} an effect potentially mediated by vascular endothelium-derived growth factor, a hypoxia-inducible angiogenic factor.\textsuperscript{19} Associations between SPC flow and pulmonary artery size also have been demonstrated clinically in some\textsuperscript{20} but not all\textsuperscript{8} reports. Interestingly, pulmonary artery size measured by CMR imaging has been shown to predict post-Fontan length of stay at our institution in an era before routine quantification of SPC flow.\textsuperscript{21} Vascular endothelium-derived growth factor levels are known to be elevated in patients with cyanotic heart disease,\textsuperscript{22–26} and are higher among single-ventricle patients with angiographically-visible SPC vessels.\textsuperscript{27} Inflammation is also a well-recognized angiogenic stimulus, and SPC flow has been demonstrated to be higher in Stage II patients on the side of the thorax with a prior Blalock-Taussig shunt compared with the contralateral side.\textsuperscript{1,5,16} Finally, SPC flow may be a time-dependent phenomenon among Stage II patients, as a correlation between SPC flow and age has been demonstrated in some but not all\textsuperscript{7,17} studies. It is certainly possible that SPC flow is just a marker of an underlying problem, and it (or more of) these other factors is the actual driver of post-Fontan clinical outcomes.

Perhaps not surprisingly, no consistent benefit to pre-Fontan coil embolization of SPC vessels has been demonstrated. Spicer et al\textsuperscript{6} reported less postoperative chest tube drainage among 11 patients undergoing pre-Fontan coil embolization, a finding that has not been replicated.\textsuperscript{3,5,16,28} Importantly, none of these studies included randomization of patients to a treatment group. In addition, these studies have been limited by the lack of a reliable measure of treatment effect, as they had no method for quantifying collateral flow.

In our cohort, the presence of a fenestration and the type of Fontan (extracardiac conduit versus intra-atrial lateral tunnel) were strong independent predictors of outcome, consistent with prior reports from our institution.\textsuperscript{13,14} Because of this, we controlled for these 2 factors using multivariate logistic regression when determining the strength of the association between measures of SPC flow and acute post-Fontan clinical outcomes (summarized in Table 4). Importantly, significant associations also were identified in univariate analyses, both as a linear relationship between SPC flow (expressed as a proportion of total aortic and total pulmonary venous flow) and natural log-transformed hospital duration (Figure 2), as
well as group differences based on dichotomized clinical outcomes (Figures 3–5).

This study is limited by its retrospective nature. There is also a risk for selection bias, as patients referred for pre-Fontan CMR imaging may have had characteristics that make them systematically more likely to demonstrate an association between SPC flow and clinical outcomes. Although unlikely, we attempted to minimize this possibility by demonstrating similarities between our cohort and the larger Fontan cohort in terms of basic demographic and clinical characteristics. As mentioned, we are unable to prove causation, which can only come from future prospective studies. The strength of the linear association between measures of SPC flow and outcomes was, at best, modest, likely reflecting the fact that SPC flow may be just 1 of many factors that contribute to prolonged length of hospital stay and effusions. However, SPC flow is a potentially modifiable factor, so it may be particularly clinically relevant. In addition, there is a possibility of overfitting the multivariate logistic regression model in attempting to control for 2 confounders in a relatively small sample size. However, significant associations also were found in univariate regression testing, and the direction of the effect sizes did not change after adjustment, suggesting that this was not the case. Finally, the outcome measures were selected because they are easily obtainable and objective. Ultimately, we may be more interested in long-term survival and quality of life, which may or may not be influenced by the same factors that affect short-term chest tube drainage and hospital duration.

**Conclusion**

We have demonstrated for the first time a significant association between CMR measures of SPC flow and acute post-Fontan clinical outcomes. In our cohort, there was a significant linear association between SPC flow expressed as a proportion of total aortic and total pulmonary venous flow and natural-log-transformed hospital duration. After adjusting for the presence of a fenestration and Fontan type, patients with more SPC flow (by any measure) had significantly elevated odds of being hospitalized for at least 7 days and having chest tube duration of at least 10 days. With CMR techniques allowing reliable quantification SPC flow, these data suggest it is now time to: (1) assess how effectively embolization reduces the burden of SPC flow, (2) understand the “natural” history of SPC vessels after Fontan completion, and (3) prospectively evaluate the effect of SPC embolization on clinical outcomes in a randomized, controlled fashion.

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**Disclosures**

None.

**References**


CLINICAL PERSPECTIVE

Systemic-pulmonary collateral (SPC) flow is a well-recognized phenomenon in single ventricle patients after superior cavo-pulmonary connection. The clinical impact of these vessels following Fontan completion is not clear. We have recently described a novel method of quantifying SPC flow by cardiac magnetic resonance (CMR) imaging using phase-contrast velocity mapping techniques. We retrospectively reviewed the acute post-Fontan clinical course of 44 patients who had their burden of SPC flow quantified by CMR imaging prior to Fontan completion. Overall, these patients had a mean SPC flow volume of 1.5 ± 0.9 L/min/m², which comprised 31 ± 11% of total aortic flow and 44 ± 15% of total pulmonary venous flow. We found significant linear associations between increasing amounts of SPC flow and duration of chest tube and hospitalization after Fontan. After adjusting for Fontan type and the presence of a fenestration, there was an increased odds of both prolonged chest tube duration and prolonged hospitalization, based on increasing amounts of all measures of SPC flow. It is unclear from these data whether the presence of SPC flow is the primary driver of a more complicated post-Fontan course, or whether the presence of SPC flow is a marker of underlying unfavorable anatomy or physiology. Future prospective study is needed to better understand the “natural” history of SPC flow in single ventricle patients through the staged surgical pathway, and to examine the efficacy and durability of catheter-based embolization on SPC flow and its effects on longer-term clinical outcomes.
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