Cardiovascular magnetic resonance of pulmonary artery growth and ventricular function after Norwood procedure with Sano modification

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Abstract

For hypoplastic left heart syndrome (HLHS), there have been concerns regarding pulmonary artery growth and ventricular dysfunction after first stage surgery consisting of the Norwood procedure modified with a right ventricle-to-pulmonary artery conduit. We report our experience using cardiovascular magnetic resonance (CMR) to determine and follow pulmonary arterial growth and ventricular function in this cohort.

Following first stage palliation, serial CMR was performed at 1 and 10 weeks post-operatively, followed by cardiac catheterization at 4 – 6 months. Thirty-four of 47 consecutive patients with HLHS (or its variations) underwent first stage palliation. Serial CMR was performed in 20 patients. Between studies, ejection fraction decreased (58 ± 9% vs. 50 ± 5%, p < 0.05). Pulmonary artery growth occurred on the left (6 ± 1 mm vs. 4 ± 1 mm at baseline, p < 0.05) but not significantly in the right. This trend continued to cardiac catheterization 4–6 months post surgery, with the left pulmonary artery of greater size than the right (8.8 ± 2.2 mm vs. 6.7 +/- 1.9 mm, p < 0.05). By CMR, 5 had pulmonary artery stenoses initially, and at 2 months, 9 had stenoses. Three of the 9 underwent percutaneous intervention prior to the second stage procedure.

In this cohort, reasonable growth of pulmonary arteries occurred following first stage palliation with this modification, although that growth was preferential to the left. Serial studies demonstrate worsening of ventricular function for the cohort. CMR was instrumental for detecting pulmonary artery stenosis and right ventricular dysfunction.

Background

Hypoplastic left heart syndrome is a congenital cardiac malformation involving hypoplasia of the ascending aorta, aortic valve atresia or stenosis, a hypoplastic left ventricle, and mitral atresia or hypoplasia[1]. Until the past few years, the standard surgical approach to hypoplastic left heart syndrome has either been a staged surgical palliation, with the first step being the modified...
Norwood procedure[2], or cardiac transplantation[3,4]. The first stage surgical palliation involves aortic arch augmentation, atrial septectomy, and an aorto-pulmonary shunt for pulmonary blood flow. While surgical survival has improved at many institutions, the overall surgical mortality of this first stage of palliation remains significant[5,6]. Recently, a large number of institutions (including the University of Virginia) have switched to the "Sano" modification of the Norwood procedure, with improved short-term results in some, but not all centers[7,8]. This "Sano" modification of the Norwood procedure uses a valveless right ventricle-to-pulmonary artery conduit in place of the aorto-pulmonary shunt for pulmonary blood flow. However, concern remains regarding the growth of the pulmonary arteries and right ventricular function with this surgical modification, which involves a ventriculotomy in the systemic right ventricle[9]. While echocardiography has become the primary imaging modality in pediatric cardiology, it is limited in its ability to image the branch pulmonary arteries after this surgical intervention.

At the University of Virginia, because of these concerns it became our clinical practice to perform a cardiovascular magnetic resonance (CMR) study prior to discharge and at two months of age, followed by cardiac catheterization at 4 – 6 months of age, in children with hypoplastic left heart syndrome. The next stage of surgical palliation was usually performed after 4 – 6 months of age, and involved ligation and division of the right ventricle-to-pulmonary artery conduit, and creation of a superior vena cava-to-pulmonary artery anastomosis. If CMR defined any significant pulmonary artery stenosis or coarctation, earlier transcatheter intervention was undertaken.

The intent of this study was to report on the CMR assessment of growth of the pulmonary arteries and right ventricular function after the Norwood procedure with Sano modification for hypoplastic left heart syndrome.

**Methods**

Approval for the study was obtained from the University of Virginia Institutional Review Board Human Investigations Committee. We retrospectively reviewed the results of all children admitted following birth to the University of Virginia with the diagnosis of hypoplastic left heart syndrome (or its variations) from 2002 to the end of 2006. The time period was chosen because in mid-2002 our institution switched from the "standard" modified Norwood procedure[2,10] to the Sano modification[8,11]. (Figure 1) The procedure was carried out with arterial cannulation via the innominate artery and regional perfusion with minimal use of deep hyperthermic circulatory arrest. The neoaortic arch was constructed utilizing pulmonary homograft. The right ventricular to pulmonary artery con-
duit was constructed using either 5 or 6 mm ringed polytetrafluoroethylene graft, running to the patient's right of the neoaorta, and a chimney patch created and anastomosed to the confluence of pulmonary arteries distally. The chimney patch was constructed using a 0.4 mm thick polytetrafluoroethylene cardiovascular patch and the ringed polytetrafluoroethylene conduit. The polytetrafluoroethylene patch was cut into an elliptical shape, and a 6 mm hole was created in the center of the patch using an aortic punch. The conduit was anastomosed to the opening in the patch using a 6-0 prolene suture, and the chimney patch was then anastomosed to the pulmonary artery confluence. A 4.8 mm aortic punch was used to create a ventriculotomy in the right ventricular outflow tract. This right ventriculotomy is used for the proximal anastomotic site for the right ventricle-to-pulmonary artery conduit. The conduit size was 5 mm in patients < 3.5 kg, and 6 mm in the remainder. The same surgical and cardiology team was involved in all cases.

Following an episode of unrecognized conduit and pulmonary artery stenosis leading to cardiovascular collapse, we began a clinical program of surveillance by CMR for the development of significant pulmonary artery stenosis or coarctation of the aorta. CMR was performed in patients prior to discharge after first stage surgery, and again at 2 months post-operatively. By prospective protocol, CMR was also performed at 1 year of age in patients with persistent late ventricular dysfunction as defined by follow-up echocardiography.

Studies were performed with general anesthesia and endotracheal intubation, which allowed the patients to remain still for the studies. Cardiac CMR was performed on a 1.5 Tesla Sonata scanner (Siemens Medical Solutions, Erlangen, Germany). The patient was placed supine in a two-channel head coil with monitoring of electrocardiogram, blood pressure, and oxygen saturation. Steady state free precession (SSFP) cine imaging was performed with repetition time of 2.7 ms, echo time 1.3 ms, temporal resolution 19 ms, slice thickness 4 mm, flip angle 27°, field of view 200 mm, matrix 76 × 192, and 4–5 signal averages during free breathing. Spatial resolution for SSFP was 2.6 × 1.0 × 4.0 mm. Axial and right ventricular short-axis image stacks were obtained without a gap. In addition, velocity encoded gradient echo cine imaging was obtained perpendicular to the proximal portion of the right ventricle-to-pulmonary artery conduit and in the plane of the proximal branch pulmonary arteries with repetition time of 4 ms, echo time of 3.6 ms, temporal resolution of 29 ms, slice thickness 4 mm, flip angle 30°, field of view 200 mm, matrix 93 × 256, velocity encoded at 300 cm/s, and 3 signal averages during free breathing. Spatial resolution for velocity encoded images was 2.2 × 0.8 × 4.0 mm. Finally, a 3-dimensional contrast-enhanced CMR angiogram was obtained during infusion of 0.2 mM/kg of gadolinium-DTPA. The angiogram was obtained in 1 slab with repetition time of 3.75, echo time 1.4 ms, slice thickness of 0.9 mm, flip angle 30°, field of view 200 mm, matrix 75 × 320, and 6 signal averages. Spatial resolution for CMR angiogram images was 2.7 × 0.6 × 0.9 mm.

Dedicated analysis software (Argus, Siemens Medical Solutions, Malvern, PA) was utilized to calculate end-diastolic ventricular volumes and systolic function from the short axis SSFP cine images. The anterior-posterior diameter of the branch pulmonary arteries was measured from the velocity encoded cine images and confirmed by the CMR angiogram, and the point of measurement was at the hilum. SSFP cine images were not used for this measurement because of off-resonance flow effects that prevented adequate visualization of the branch pulmonary arteries. Significant pulmonary artery stenosis or coarctation were defined by CMR as an abrupt luminal narrowing > 40% [12]. Right ventricle-to-pulmonary artery conduit regurgitation volume and fraction was measured from the velocity encoded imaging obtained perpendicular to the conduit using Argus software. The CMR angiogram was viewed on the Argus 3-dimensional workstation as a multiplanar reformat and maximum intensity projection.

At time of CMR, all patients also had transthoracic echocardiography to compare estimates of ventricular function, and diagnoses of pulmonary artery stenoses and aortic coarctation. (Figure 2) Pulmonary artery stenosis was diagnosed by demonstrating a qualitative luminal narrowing on the color Doppler signal, rather than by Doppler-derived gradients as there were high velocities from the proximal conduit. Two-dimensional imaging by echocardiography was not able to evaluate the branch pulmonary artery anatomy after surgical palliation with the right ventricle-pulmonary artery conduit. Echocardiographic definition of coarctation was a peak instantaneous Doppler-derived gradient in the aorta of > 20 mmHg using both proximal and distal velocities in the complete modified Bernoulli equation [13].

All patients underwent cardiac catheterization prior to the second stage surgery, which was intended at 4–6 months of age. Right ventricular ejection fraction was calculated by calibrated biplane Simpson's rule [14]. Given the difficulty with interpretation of multiple pressure gradients in series, and that a large gradient is normally present across the right ventricle-pulmonary artery conduit, only the presence of a gradient at the site of angiographic luminal narrowing in the branch pulmonary artery was used to define a significant pulmonary artery stenosis. A significant coarctation was defined by catheterization as a gradient of > 20 mmHg in the presence of angiographic
narrowing[15]. Significant coarctations underwent percutaneous balloon angioplasty[16,17], and success was defined as a gradient of < 10 mmHg without significant drop in cardiac output.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Statistical Analysis
Serial measurements for patients were compared using analysis of variance for repeated measures, and comparison between patients was analyzed using unpaired t tests, with statistical significance defined as p < 0.05.

Results
Demographics
From 2002 to 2006, 47 newborns with hypoplastic left heart syndrome (or its variations, see Table 1) were admitted to the University of Virginia. Six patients received palliative care only and expired shortly thereafter. Seven patients with HLHS and high-risk features underwent hybrid palliation, and have been previously reported on by our group[18]. The remaining 34 patients underwent the Norwood procedure with Sano modification at an age of 9 +/- 8 days (range 1 – 47 days), with survival to hospital discharge in 26 of 34. Initially, the first 9 infants underwent surgical intervention, and the 6 survivors were followed without CMR screening. Following these first 9 patients, we then began the CMR screening program for the reasons noted above. For the remainder of the study period 25 infants underwent surgical palliation, of which 5 patients expired prior to hospital discharge, with cardiac CMR being performed in the remaining 20 patients. There were no complications from the anesthesia for the CMR study.

CMR evaluation of the right ventricle
From the initial pre-discharge CMR study to the 2-month study, right ventricular volumes increased (19 ± 6 mL vs. 32 ± 5 mL, p < 0.05) but were not different compared with body growth (102 ± 33 mL/m² vs. 105 ± 33 mL/m², p = NS), and right ventricular ejection fraction decreased (58.0 ± 8.9% vs. 49.9 ± 5.4%, p < 0.05). (Figure 3) The right ventricular ejection fraction as seen on the cardiac catheterization prior to the 2nd stage surgical palliation was 45 ± 9%. A comparison between echocardiographic and CMR estimates of right ventricular function is shown in Figure 4. There is overlap in CMR-determined right ventricular ejection fraction between the different echocardiographic classifications of ventricular function. The CMR-determined right ventricular ejection fraction in the group with "good" systolic function by echocardiography was 53 ± 8%, with 25 ± 11% in the moderate group. The single patient with an echocardiographic estimate of "poor" function had an ejection fraction of 16%.

CMR evaluation of the branch pulmonary arteries
At time of initial CMR, the right and left pulmonary arteries were of similar size (4.6 ± 0.9 mm vs. 4.4 ± 1.0 mm, p = NS). However, pulmonary artery growth occurred mainly in the left pulmonary artery (6.3 ± 1.1 mm vs.4.4 ± 1.0 mm at baseline, p < 0.05), but not significantly in the right (5.2 ± 1.5 mm vs. 4.6 ± 0.9 mm at baseline, p = NS), with the left pulmonary artery larger at time of the 2nd CMR (6.3 ± 1.1 mm vs. 5.2 ± 1.5 mm for the right pulmonary artery, p < 0.05). (Figures 5 &6) This trend appeared to continue to the cardiac catheterization at 4 +/- 1 months post surgery, with the left pulmonary artery of significantly greater size than the right (8.8 ± 2.8 mm vs 6.7 ± 1.9 mm for the right pulmonary artery, p < 0.05).

By CMR, 5 patients had pulmonary artery stenoses defined at the two-week study, and at the two-month study 9/20 had pulmonary artery stenoses. Three of these underwent early percutaneous intervention for severe unilateral stenoses. On all 9 patients with CMR-defined pulmonary artery stenosis, cardiac catheterization confirmed the diagnosis. In those patients without CMR-defined pulmonary artery stenosis, no significant pulmonary artery stenosis was found at time of pre-operative cardiac catheterization.

Table 1: Anatomic diagnoses of the cohort are listed.

<table>
<thead>
<tr>
<th>Anatomic Diagnoses</th>
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<tbody>
<tr>
<td>Hypoplastic left heart syndrome</td>
<td>30</td>
</tr>
<tr>
<td>Heterotaxy/Unbalanced AV canal with left ventricular hypoplasia</td>
<td>3</td>
</tr>
<tr>
<td>Double outlet right ventricle with left ventricular hypoplasia</td>
<td>1</td>
</tr>
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However, the ability of echocardiography to diagnose CMR-diagnosed pulmonary artery stenosis was poor, with only a 6% sensitivity (1 of 18 stenoses were diagnosed by echocardiography). There were no false positive diagnoses of pulmonary artery stenosis by echocardiography.

There was no significant change in conduit regurgitant fraction (15 ± 4% vs. 16 ± 5%) between studies.

**CMR evaluation of the aortic coarctation**

While 9 patients were defined by CMR at the 2-week study as having a coarctation, clinically it was determined that these did not require reintervention at that time. Among these 9 patients, coarctations in 6 persisted or worsened by the 2-month study, and resolved in 3. 2 additional patients developed a significant coarctation that was defined on the 2-month study. Ten of the 26 1st stage survivors underwent percutaneous coarctation intervention, which was judged successful in 7, and one was felt not to have clinical coarctation despite the CMR findings. This was related to an artifact caused by a metal surgical clip. Of the patients not diagnosed by CMR with a coarctation, one was found to have a coarctation at time of the preoperative cardiac catheterization.

Echocardiography agreed with CMR-diagnosed coarctation in 7 of 10 patients who underwent cardiac catheterization. A single patient erroneously diagnosed with a
coarctation by CMR was thought not to have a significant
gradient by Doppler, and two unsedated patients did not
have adequate arch views to determine the presence of
coarctation by echocardiography.

Those patients not having a diagnosis of recurrent coarctation
had a right ventricular ejection fraction by CMR of 48 +/- 8%
as compared to those with recurrent coarctation their
ejection fraction was 41 +/- 12% (p = NS).

**Discussion**
In this cohort of patients, CMR demonstrates an important
role in the detection of surgical issues complicating
the Norwood procedure with Sano modification. It was
able to define pulmonary artery stenosis with 100% sensi-
tivity and specificity, and has already been proven to be instrumental in the evaluation of right ventricular func-
tion and aortic coarctation.

Pulmonary artery growth in this cohort of infants with
hypoplastic left heart syndrome after the Norwood proce-
dure with Sano modification was asymmetric, with greater
growth in the left pulmonary than the right. This asymme-
try of growth may be related to both the direction of the flow
from the right ventricle-to-pulmonary artery conduit,
which is preferential to the left pulmonary artery, and that
the right pulmonary artery must then pass under the
reconstructed aortic arch. This is in contrast to the stand-
ard Norwood palliation, which involves a modified Bla-
lock Taussig shunt, which frequently comes off of the
right-sided innominate artery and inserts onto the right
pulmonary artery. Previous work has shown asymmetric
growth of the pulmonary arteries after the right-sided
modified Blalock Taussig shunt, with the right pulmonary
artery larger than the left [19]. In either type of surgical
shunt, pulmonary artery asymmetry of growth may have
important late implications which have not been yet
defined.

For diagnosing recurrent or persistent coarctation of the
aorta, the CMR has been described as highly sensitive and
specific [12,20]. However, in 1 patient, the CMR incor-
rectly gave a suspicion of a coarctation, and in that patient
the clinical diagnosis was confounded by femoral arterial
occlusion. The patient had been referred for early cardiac
catheterization, which determined no gradient across the
aortic arch which was widely patent on angiography. Ret-
rospective review found a surgical clip casting an artifact
obscuring the aortic isthmus. It is possible that the use of
a phase contrast velocity encoding sequence through the
area of concern for coarctation may be useful in clarifying
this. Therefore, we believe that in the absence of such
imaging artifacts, CMR has an excellent ability to define
the pulmonary artery and aortic anatomy after the Nor-
wood procedure with Sano modification. However, in our
patient series, there was one patient incorrectly diagnosed
with coarctation by CMR. In that patient, an aortic luminal
narrowing was seen on CMR. Since cuff blood pressures and
Doppler echocardiography demonstrated no gradient across
the coarctation site, this was felt to be hemodynamically insignificant. This is likely related to the observation
that not all anatomic narrowings will produce significant hemodynamic obstructions, which may be ameliorated by vessel wall compliance and presence of collateral vessels.

In this cohort of patients, in which the single ventricle is
of right ventricular morphology and in which a ventricu-
lotomy was performed, there was a significant depression of systolic function, as measured by serial
study. In addition, out of 26 initial hospital survivors, 2
subsequently underwent cardiac transplantation with
another currently being listed. The indication in all 3 such
patients was symptomatic heart failure. It is possible that
the ventriculotomy plays a role in the development of late
ventricular dysfunction, as has been noted in other centers
[21]. It is also possible that recurrence of coarctation, with
its attendant increased afterload on the right ventricle,
may contribute to ventricular dysfunction. In our cohort
of patients, we found a non-significant trend of increased
ventricular dysfunction in the group with recurrent coarc-
tation. Importantly, we took an approach of early percuta-
neous intervention to any new diagnosis of recurrent
coarctation, on the assumption that the afterload reduc-
tion was important in these patients' management.

Both the survival to discharge and the interstage mortality
in this cohort of patients following the Norwood proce-
dure with Sano modification were similar to other reports
in the current era[5,8,10,22,23], and has been associated
with improved peri-operative hemodynamic stability[9].
However, it may be that this is a trade-off for later ven-
tricular dysfunction.

Limitations of the present study include the different
imaging modalities to evaluate right ventricular, pulmo-
nary artery, and aortic anatomy and function. However,
previous work has demonstrated excellent correlation
between CMR and cardiac catheterization for right ven-
tricular volumes and function[24,25], for pulmonary
artery anatomy[26], and for coarctation evaluation[27].

**Conclusion**
Development of significant pulmonary artery stenosis,
coarctation, and right ventricular dysfunction occurs in a
portion of patients undergoing the Norwood palliation
with Sano modification for hypoplastic left heart syn-
drome. Cardiovascular magnetic resonance is instrument-
ental in surveillance for such complications.
Abbreviations
HLHS: Hypoplastic left heart syndrome; CMR: Cardiovascular magnetic resonance imaging.

Competing interests
DLS, BBP, and GPM have no conflicts of interest to disclose. CMK has research equipment support from Siemens Medical.

Authors' contributions
DLS designed the study, collected data, and drafted the manuscript. BBP performed the surgeries and drafted a portion of the manuscript. GPM participated in study design and data collection. CMK participated in study design and data collection, and drafted a portion of the manuscript. All authors read and approved the final manuscript.

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