Cardiac Magnetic Resonance Imaging After Stage I Norwood Operation for Hypoplastic Left Heart Syndrome

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Background—After the Norwood operation, a patient’s suitability for proceeding to a bidirectional cavopulmonary connection (BCPC) is assessed by a combination of echocardiography and diagnostic cardiac catheterization. In this study, we describe the results of 37 patients who underwent cardiovascular magnetic resonance (MR) assessment before BCPC.

Methods and Results—Cardiovascular MR and echocardiography were performed in 37 infants with hypoplastic left heart syndrome before BCPC, and the findings were compared with surgical findings. MR assessment of ventricular function and valvar regurgitation were compared with echocardiography. MR exhibited high sensitivity and specificity for identification of neoaortic (sensitivity 86%, specificity 97%) and left pulmonary artery (sensitivity 100%, specificity 94%) obstruction. Echocardiography exhibited poor sensitivity for identification of vascular stenosis. The mean right ventricular ejection fraction calculated from the MR data was $50 \pm 10\%$. There was general agreement between MR and echocardiographic measures of ventricular function, although patients with good function on echocardiography demonstrated a wide range of ejection fractions. There was good agreement between MR and echocardiography for identification of valvar regurgitation.

Conclusions—Cardiovascular MR can be used to define ventricular and valvar function and vascular anatomy in infants with hypoplastic left heart syndrome after the Norwood operation. We have shown how this information can be used to plan the BCPC and identify any revisions or additional valvar surgery. (Circulation. 2005;112:3256-3263.)

Key Words: heart defects, congenital ■ magnetic resonance imaging ■ pediatrics ■ surgery

Hypoplastic left heart syndrome (HLHS) has an incidence of approximately 1 in 5000 births.1-2 Palliative reconstructive surgery has become the preferred treatment option, although cardiac transplantation may offer better long-term survival.3 Palliative reconstructive surgery is performed over 3 stages. The Norwood procedure, performed in the first week of life, involves anastomosis of the main pulmonary artery to the hypoplastic aorta. A 3.5-mm modified Blalock-Taussig shunt (MBTS) maintains pulmonary blood flow, and the atrial septum is excised, which enables unrestricted pulmonary venous return.4

At 3 to 9 months, a bidirectional cavopulmonary connection (BCPC) is created with anastomosis of the superior vena cava to the right pulmonary artery, insertion of a patch dividing the superior vena cava from the right atrium, and removal of the MBTS shunt. The final stage is the creation of a total cavopulmonary connection, usually performed at 2 to 4 years of age.5 Success of the BCPC is dependent on preoperative anatomic and functional assessment.6-7 Cardiac catheterization is used to delineate anatomy and to measure the pulmonary vascular resistance (PVR).6,7 Echocardiography is used to assess valvar and right ventricular function. Cardiac catheterization is associated with morbidity and occasional mortality in this group of patients8 and leads to significant exposure to medical radiation.9 Echocardiography can be used to risk-stratify patients before BCPC.6,7 However, because of the limited sensitivity of echocardiography in detecting great vessel stenosis, it cannot be used as a noninvasive alternative to cardiac catheterization.10 Furthermore, echocardiography only provides a semiquantitative assessment of ventricular and valvar function.

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Cardiovascular magnetic resonance (MR) imaging is increasingly used to assess congenital heart disease. Gadolinium-enhanced MR angiography is an accurate alternative to diagnostic angiography in the infant population, being successfully used to diagnose pulmonary and aortic obstruction. The use of MR in anatomic delineation after the Norwood procedure has been described in case reports but not in a large patient group. Velocity-encoded phase-contrast MR and MR volumetry are accurate methods of measuring flow and right ventricular function in children. PVR cannot be measured with cardiovascular MR. However, there is evidence to suggest that raised PVR is not commonly present in patients with HLHS before BCPC, with one study demonstrating a mean PVR of 1.9±0.8 Wood units. In addition, PVR has not been shown to be a significant predictor of mortality after BCPC.

In 2001, cardiovascular MR was introduced as an alternative to catheterization in some patients for pre-BCPC assessment in our unit. The rationale was that cardiovascular MR is a proven technique for assessing cardiac anatomy and function and that measurement of PVR is not vital for preoperative assessment. In the group assessed by MR, there was agreement with surgical findings and a similar postoperative course as for patients who had cardiac catheterization. In view of the significant risks attached to cardiac catheterization and the satisfactory information derived from MR, in 2002, it was decided that all patients would undergo MR rather than catheter assessment before BCPC. In these patients, a standardized MR protocol was used, and information about echocardiographic findings, surgical findings, and outcome was collated. The purpose of the present study is to demonstrate that MR provides comprehensive preoperative assessment and can thus replace catheterization without any adverse effects on outcome.

Methods

Study Population

Thirty-seven consecutive infants with HLHS after Norwood operation underwent MR between 2002 and 2004. All patients with HLHS undergoing BCPC were included. All parents/guardians gave informed consent. General anesthesia was used in all patients, which allowed better control of cardiopulmonary function and easier respiratory suspension, thus improving image quality and shortening study time. Respiratory motion was suspended during “apneic” scans through withdrawal of ventilatory support. End-tidal carbon dioxide, oxygen saturations, and noninvasive blood pressure were monitored to assess cardiorespiratory stability. General anesthesia was induced and maintained with sevoflurane, and paralysis was obtained with atracurium.

Cardiac MR Imaging Protocol

All images were obtained with a 1.5-T MR scanner with a 2-element phased-array coil for signal reception and the body coil for signal transmission (Philips Medical Systems). A vector ECG system was used for cardiac synchronization. The MR scan time was between 45 and 60 minutes. All subsequent scan parameters are described in Table 1.

MR Anatomic Imaging

3D Bright-Blood MRI

The 3D bright-blood imaging was performed with a multislab, multiphase 3D steady state free precession (SSFP) sequence that covered the heart in axial sections. To cover the whole volume of the thorax, 8 to 12 3D slabs were acquired. Each slab was acquired in one 10- to 15-second apnea. As previously described, misalignment of slabs acquired in different apneas is not a significant problem in patients undergoing BCPC. In one 10- to 15-second apnea. As previously described, misalignment of slabs acquired in different apneas is not a significant problem in patients undergoing BCPC. In one 10- to 15-second period of apnea.

Single-Slice 2D MR Cine Imaging

Interactive real-time SSFP was used to plan and save the geometries of subsequent cine imaging planes during free breathing. Two-dimensional cine imaging was performed with an SSFP sequence. Cine images were acquired in the vertical and horizontal long axis and the right ventricular outflow tract (Figure 1). Each cine image was acquired in a single 10- to 15-second period of apnea.

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<tr>
<th>TABLE 1. Sequence Parameters</th>
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<td>3D SSFP</td>
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<tr>
<td>FOV, mm</td>
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<tr>
<td>TR, echo time</td>
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<td>TR, repetition time</td>
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<tr>
<td>NSA, number of signal averages</td>
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<td>SENSE, sensitivity encoding</td>
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Gd MRA indicates gadolinium-enhanced MR angiography; FOV, field of view; RFOV, rectangular field of view; TR, repetition time; NSA, number of signal averages; and SENSE, sensitivity encoding.
Black-Blood MR Imaging
Black-blood images were acquired with a 2D turbo spin-echo sequence triggered at end diastole. Images of the Blalock-Taussig shunt, the branch pulmonary arteries, and aortic arch were acquired at end diastole in 2 perpendicular longitudinal planes. Each image was acquired in a single 10- to 15-second period of apnea.

MR Functional Imaging

MR Flow Quantification
Neoaorta flow data were acquired with a velocity-encoded fast-field-echo sequence. A dedicated nonlinear phase correction filter, based on Chebichev polynomials (Philips Medical Systems), was used to correct for phase errors introduced by eddy currents and Maxwell terms.

MR Volumetry
MR volumetry was with a short-axis multislice SSFP technique. To cover the ventricular volume, 7 to 10 slices were acquired in multiple 10- to 15-second periods of apnea (2 slices per apnea).

MR Data Analysis

Anatomic Analysis
Volume rendering of the blood pool (with both 3D SSFP and MR angiograms) was performed with an automated segmentation technique (Viewforum 4.1, Philips Medical Systems). Anatomy was assessed with a combination of the sequences described. The diameter of any stenotic vessels and the diameter of the vessel distal to the obstruction were measured from black-blood and angiographic images. Obstruction was categorized as severe (obstruction ≥40% of the diameter of normal distal vessel), mild/moderate (obstruction 10% to 39%), and none/trivial (obstruction <10%).

Ventricular Volume Measurements
Right ventricular end-diastolic volume (RVEDV) and end-systolic volume (RVESV), indexed to body weight, were measured from the short axis SSFP data with a semiautomatic edge-detection algorithm with operator correction (EasyVision 9, Philips Medical Systems). Body weight rather than body surface area was used for indexing because it is not dependent on complex equations that may not be valid in this patient group.

Right ventricular stroke volume (RVSV)=RVEDV−RVESV

Quantification of Neoaortic Valve and AV Valve Incompetence
Neoaortic blood flow was calculated with phase-contrast MR data with a semiautomatic vessel edge-detection algorithm (Flow, Medis) with operator correction. Neoaortic forward volume (FV) and neoaortic regurgitant volume (RV) were measured.

Neoaortic regurgitation fraction=$\frac{\text{Neoaortic RV}}{\text{Neoaortic FV}} \times 100$

Calculation of tricuspid valve regurgitation fraction (RF) combines data from a breath hold and free-breathing scan; previous work has shown that it is a valid method for calculating regurgitation fraction. An RF of >10% was taken as demonstrating valvar regurgitation.

Tricuspid RF=$\frac{\text{RVSV−Neoaortic FV}}{\text{RVSV}} \times 100$

Echocardiographic Assessment
Transsthoracic echocardiography was performed before cardiac MR (Sonos 5500, Philips Medical Systems). Intracardiac and vascular anatomy was assessed with 2D echocardiography. Color and continuous-wave Doppler were used to assess the functional significance of any stenoses. Ventricular function was assessed semiquantitatively and categorized as good, moderate, or poor. If valvar regurgitation was seen on color Doppler, this was categorized as mild, moderate, or severe. The MR operators (V.M., A.M.T., and R.R.) were not blinded to the echocardiographic data.

Surgical Assessment
The surgeons were aware of the echocardiographic and MR findings before surgery. In all patients, pulmonary arteries were dissected as part of the BCPC and directly visualized by the surgeon. The surgeon’s criterion for significant obstruction in the pulmonary arteries was visualized stenosis of approximately >40%. The pressure gradient between the neoascending aorta and femoral artery was measured in all patients at the time of surgery. The neoaorta was dissected and visualized in all patients with a pressure gradient >10 mm Hg, or MR or echocardiographic evidence of narrowing.

Right ventricle ejection fraction (RVEF)=$\frac{\text{RVSV}}{\text{RVEDV}} \times 100$
Directly visualized neoaortic obstruction >40% was deemed significant. All significant vascular obstructions were repaired.

**Statistical Analysis**

Data are expressed as mean±SD. The paired Student’s t test was used to compare the oxygen saturation data before and after BCPC operation. Sensitivity, specificity, positive predictive value, and negative predictive value were used to compare MR and echocardiography with the surgical findings. Correlation coefficients and Bland-Altman analysis were used to compare right ventricular stroke volume (RVSV) to neoaortic FV. Bias was the mean of the difference between the 2 methods, and agreement was the mean±2 SDs. A probability value of <0.05 was taken as statistically significant. Statistical analysis was performed with Matlab (Mathworks, USA).

**Results**

**Study Population**

The mean age at Norwood operation was 4.2±3.6 days. The mean age of patients at cardiovascular MR was 181±61 days, with a mean weight at the time of MR imaging of 6.3±1.0 kg.

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<th>Severe</th>
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<th>None</th>
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<td>Neoaorta</td>
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<td>RPA</td>
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<td>LPA</td>
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RPA indicates right pulmonary artery.

Values shown are number of patients with vascular obstruction of the neoaorta, RPA, or LPA identified with MR. Obstruction was categorized as severe (≥40%), mild/moderate (10% to 39%), and none/trivial (<10%).

**Vascular Anatomy**

**Aortic and Upper-Body Vessel Assessment**

The MRI protocol (as outlined in the Methods) was completed in all patients. Thirty-six patients were successfully extubated after general anesthetic. One patient with severe tricuspid regurgitation (TR) who was clinically unstable before cardiovascular MRI had a failed extubation after the procedure and required ventilation until the BCPC was performed. The mean time between MR and BCPC surgery was 45±4.9 days, and the mean age at BCPC was 224±72 days.

All patients successfully underwent BCPC, with good postoperative outcome. There has been no short-term mortality or requirement for reintervention in the patients in this study (2-month follow-up period). There was a significant improvement in the peripheral oxygen saturation in air from 74±6% to 81±5% (P<0.001) after the BCPC operation.

**Table 2. MR Identification of Vascular Stenosis**

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Figure 2. Volume-rendered gadolinium-enhanced MR angiograms of patients with HLHS. a, Patient with severe neoaortic narrowing (note the complex 3D structure) and tenting of the right pulmonary artery. b, Right pulmonary artery stenosis just distal to the insertion of the MBTS. c, Bilateral superior vena cava. d, Proximal LPA stenosis.
the balloon dilation were unsatisfactory. Comparison of echocardiographic and surgical identification of neoaortic obstruction ≥40% is shown in Table 3. The sensitivity of echocardiographic assessment of the neoaorta was 42%, the specificity was 97%, the positive predictive value was 0.75, and the negative predictive value was 0.88. There was complete agreement between the MR and surgical delineation of head and neck vessel anatomy and obstructions. There were no abnormal venous collaterals identified on MR or echocardiography or at surgery. The MBTS and the native aorta to neoaortic connection were patent in all patients.

**Pulmonary Vasculature**

Pulmonary artery stenoses identified on MR are shown in Table 2, and examples are shown in Figures 2 and 3. In all cases, right pulmonary artery reconstruction was performed as part of the BCPC. Comparison of MR and surgical identification of severe left pulmonary artery (LPA) stenosis is shown in Table 4. The sensitivity of MR assessment of the LPA was 100%, the specificity was 94%, the positive predictive value was 0.71, and the negative predictive value was 1.0. Comparison of echocardiographic and surgical identification of significant LPA stenosis is shown in Table 4.

The sensitivity of echocardiographic assessment of the LPA was 20%, the specificity was 100%, the positive predictive value was 1.0, and the negative predictive value was 0.89. No obstruction to the pulmonary venous system was noted on MR or echocardiography.

**Cardiac Function**

From MR volumetric analysis, mean right ventricular end-diastolic volume indexed to weight was $4.8 \pm 1.7$ mL/kg, mean RVSV indexed to weight was $2.6 \pm 1.3$ mL/kg, and mean right ventricular ejection fraction was 50% (range 25% to 79%). From echocardiographic assessment, 27 patients were categorized as having good ventricular function, 8 patients moderate function, and 2 patients poor function. A plot of right ventricular ejection fraction against echocardiographic groups is shown in Figure 4. Progression to BCPC was delayed in the 2 patients who had poor ventricular function on MR and echocardiography; however, both responded to maximal medical therapy with improvement in ventricular function and successful completion of the BCPC. The correlation coefficient between RVSV and neoaortic stroke volume in patients with no or trivial valvar regurgitation was

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<th>TABLE 3. Comparison of Identification of Significant Neoaortic Obstruction</th>
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Echo indicates echocardiographic.

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<th>TABLE 4. Comparison of Identification of Significant LPA Obstruction</th>
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<td>5</td>
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<td>MR negative</td>
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Echo indicates echocardiographic.
Figure 4. Scatterplot of right ventricular ejection fraction (RVEF) against echocardiographic classification of right ventricular (RV) function.

0.95 (P<0.05), the bias was −0.01 mL/kg, the upper limit of agreement was 0.32 mL/kg, and the lower limit of agreement was −0.34 mL/kg.

**Valvar Regurgitation**

Cardiovascular MR identified 13 patients with TR (RF >10%) and 24 patients with no or trivial TR (RF <10%). In patients with TR identified with MR, the mean RF was 18±12%. Echocardiography identified 2 patients with severe TR, 12 patients with mild/moderate TR, and 23 patients with trivial/no TR. A plot of RF against echocardiographic groups is seen in Figure 5. One patient with echocardiographic evidence of mild/moderate TR had no evidence of TR on MR. Tricuspid valve annuloplasty (at the time of BCPC) was performed on the patient with an RF of 56%. The patient with an RF of 28% had a severe aortic arch narrowing, repair of which (at the time of BCPC) significantly reduced the degree of TR, as assessed by perioperative echocardiography.

Cardiovascular MR identified 1 patient with neoaortic regurgitation (RF=14%) and 36 patients with no or trivial neoaortic regurgitation (RF <10%). Echocardiography identified 2 patients with mild/moderate neoaortic regurgitation and 35 patients with trivial/no neoaortic regurgitation.

**Discussion**

Assessment before BCPC in patients with HLHS is achieved with a combination of cardiac catheterization and echocardiography.6,7 There are risks attached to invasive catheterization,24 particularly in patients with HLHS who are at risk of MBTS occlusion.6 Furthermore, there are increasing concerns about the long-term effects of exposure to medical radiation.9 In addition, echocardiography is user-dependent and only provides semiquantitative information.

In the present study, we have demonstrated that cardiovascular MR provides comprehensive anatomic and functional assessment and can thus replace catheterization without any adverse affects on outcome. In addition, we have demonstrated that echocardiography is not a suitable replacement to cardiac catheterization.

**Vascular Anatomy**

Neoaortic coarctation and branch pulmonary artery stenosis are causes of BCPC failure.25 Significant vascular obstructions must be relieved before or at the time of BCPC. Right pulmonary artery reconstruction is necessary as part of the BCPC, and thus, definition of proximal right pulmonary artery anatomy is not crucial. Identification of neoaortic and LPA stenosis, however, is vital. Although echocardiography can identify candidates for low-risk BCPC,6,7 identification of neoaortic coarctation and pulmonary artery stenosis is difficult.6,10 Cardiovascular MR can accurately define aortic and pulmonary artery anatomy in the infant population.12-13 It has been used in small groups of patients with HLHS to delineate vascular anatomy after the Norwood procedure.14-16 In the present study, MR angiography was used to obtain 3D images of the vasculature, and “black blood” was used to accurately measure vascular dimensions. MR had a very high sensitivity and specificity for identification of neoaortic and LPA obstructions that required surgical repair. In the 1 false-negative result, MR did identify a degree of neoaortic narrowing (33%). In the 3 cases of false-positive MR results (1 neoaorta, 2 LPA), the surgeon confirmed a degree of vascular narrowing but not severe enough to require repair. It is the policy of our unit to surgically assess vessels with preoperative evidence of obstruction; however, visual inspection increases the invasiveness of the BCPC operation. Our results suggests that in patients with no MR, evidence of vascular obstruction visual inspection is not required, because in this group, no vascular obstructions were identified at surgery. However, patients with any narrowing on MR should undergo vascular inspection. In keeping with previous studies,5,10 echocardiography had a low sensitivity for identification of neoaortic or LPA obstruction that required surgical repair, which suggests that it is an unsuitable replacement for x-ray angiography.

One benefit of cardiac catheterization is the possibility of balloon angioplasty of any vascular narrowing (particularly neoaortic coarctation) before BCPC.25 However, there is evidence that re-coarctation is more common in patients who undergo angioplasty rather than surgical repair.26 For this reason, the preferred option in our center is to perform surgical repair of coarctation at the time of the BCPC. Two patients with significant coarctation identified on MR underwent balloon angioplasty to relieve the aortic obstruction. In
both cases, angioplasty was unsuccessful, and aortic repair was required at the time of BCPC.

**Ventricular Function**

There is no “gold standard” method of measuring ventricular volumes. One method of validation is to compare MR volumetry with phase-contrast flow, because RVSV should equal neoaoortic stroke volume in patients with no regurgitation or trivial valvar regurgitation. We have demonstrated good correlation, minimal bias, and narrow limits of agreement between RVSV and neoaoortic stroke volume. This suggests that MR is an accurate method of measuring right ventricular volumes and function in this group of patients. Accurate quantification of ventricular function is important for risk stratification and timing of BCPC. Comparison with semiquantitative echocardiographic assessment showed general agreement between the 2 modalities; however, in those patients classified as having good function echocardiographically, right ventricular ejection fraction ranged from 38% to 79%, overlapping with those patients classified as having moderate function (36% to 47%). Because we have demonstrated the accuracy of MR volumetry, these results suggest that echocardiography overestimates ventricular function in some patients. The right ventricle in the present group of patients was dilated compared with normal subjects. The mean right ventricular end-diastolic volume measured 4.8 mL/kg compared with the combined normal right and left ventricular volumes (an appropriate comparison because the single ventricle is dealing with the entire cardiac output) of 4.2 mL/kg. The results of the present study suggest that the “usual” right ventricular ejection fraction after the Norwood procedure is ≈50%.

**Valvar Regurgitation**

A combination of phase-contrast MR and MR volumetry is used to quantify valvar regurgitation. Phase-contrast MR has been validated in small-diameter vessels and children. We have demonstrated close agreement between RVSV and neoaoortic FV in patients without valvar regurgitation. There was good agreement between the MR regurgitation fraction and the echocardiographic groupings. However, in the present study, 1 case of TR and 1 case of neoaoortic regurgitation were not identified by MR. In both cases, valvar regurgitation was mild on echocardiography, and identification did not change patient management. Another method of assessing valvar regurgitation is to directly image the valve with phase-contrast MR. This method may have greater sensitivity for identification of valvar regurgitation. It was not used in the present study because there are some concerns about the accuracy of through-plane flow measurement of regurgitant jets. A combination of direct valve phase-contrast MR and the method used in the present study may have greater sensitivity and accuracy.

**Optimized Protocol**

We found that the 3D SSFP sequence was redundant in anatomic delineation. Therefore, we suggest that MR angiography, black-blood imaging, and 2D cine imaging are the only sequences required for anatomic delineation. We also suggest direct phase-contrast imaging of the tricuspid valve in addition to MR volumetry. This should improve the sensitivity of MR for identification of tricuspid valve regurgitation.

**Study Limitations**

The main limitation of the present study was that the surgeon was not blinded to the MR findings and the MR operators were not blinded to the echocardiographic findings. Preoperative assessment is an important part of surgical planning, and therefore, it was not possible to blind the surgeon. Echocardiography is performed routinely before MR under general anesthetic, and findings were known to the MR operator to aid the MR examination and to not place the patient at a disadvantage. However, this may have resulted in a higher sensitivity and specificity of MR than in a blinded study. In the present study, PVR was not measured. Raised PVR is unusual in this group of patients owing to the restrictive nature of the MBTS, and when present, it is not a significant predictor of mortality after BCPC. Therefore, we believe that measurement of PVR is not mandatory before BCPC. The Sano modification to the Norwood procedure, which utilizes a right ventricular to pulmonary artery conduit rather than an MBTS, is being performed with increasing frequency. The present study does not address the anatomic accuracy or the possible anesthetic complications in this group. However, because the assessment does not involve specific characteristics of the systemic-pulmonary connection, we believe that MR assessment would be suitable for patients who have undergone the Sano procedure. We did not compare x-ray angiography and cardiovascular MR in the present study because the risk of performing 2 general anesthetics was not justifiable in infants with HLHS.

**Conclusions**

We have shown that cardiovascular MR can be used to define ventricular and valvar function and vascular anatomy in a group of infants with HLHS after the Norwood operation. We have shown how this information can be used to plan the BCPC and identify any revisions or additional valvar surgery. All patients in the present study had a good postoperative outcome, which suggests that MR can be used to replace cardiac catheterization in this patient group.

**Acknowledgments**

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