Maladaptive Aortic Properties in Children After Palliation of Hypoplastic Left Heart Syndrome Assessed by Cardiovascular Magnetic Resonance Imaging

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Background—The status of the reconstructed aorta in hypoplastic left heart syndrome is considered an important determinant of long-term prognosis. Therefore, we assessed the anatomy, elastic properties, and viability of the aorta and right ventricular function in patients with hypoplastic left heart syndrome by cardiovascular magnetic resonance imaging.

Methods and Results—Cardiovascular magnetic resonance imaging was performed in 40 patients with hypoplastic left heart syndrome (age, 6.0±2.2 years) and 13 control subjects (age, 6.6±2.2 years). Aortic dimensions and distensibility were calculated at different locations of the aorta using gradient-echo cine imaging at 3.0 T. Additionally, pulse-wave velocity, right ventricular ejection fraction, and aortic late gadolinium enhancement for viability assessment were measured. Compared with control subjects, patients with hypoplastic left heart syndrome had increased axial diameters of the aortic root (36.0±5.5 versus 24.1±2.7 mm/m²; P<0.01), ascending aorta (32.0±5.0 versus 21.3±1.5 mm/m²; P<0.01), and transverse aortic arch (22.7±5.2 versus 18.7±2.5 mm/m²; P<0.01). Wall distensibility was reduced in the ascending aorta (4.1±2.4 versus 13.5±7.2 10⁻⁶ mm Hg⁻¹; P<0.01) and transverse aortic arch (5.4±3.6 versus 10.3±3.5 10⁻³ mm Hg⁻¹; P<0.01). Pulse-wave velocity trended higher in patients (P=0.06). Reduced distensibility in the ascending aorta correlated with the amount of late gadolinium enhancement in a volume that included the aortic root and the ascending aorta (r=−0.72, P<0.01), and both parameters correlated with decreased right ventricular ejection fraction.

Conclusions—Adverse aortic properties post palliation of hypoplastic left heart syndrome manifest themselves by aortic dilatation, decreased distensibility, and increased volume of nonviable aortic wall tissue. The negative association between aortic late gadolinium enhancement and right ventricular ejection fraction suggests unfavorable aortic-ventricular coupling. The potential impact of these findings on long-term right ventricular function should be evaluated in future studies.  

Key Words: aorta, heart defects, congenital, hypoplastic left heart syndrome, imaging, magnetic resonance imaging

Hypoplastic left heart syndrome (HLHS), a fatal disease of the newborn if left untreated, comprises a spectrum of complex cardiac anomalies characterized by marked hypoplasia of left ventricular structures and the ascending aorta. Palliative reconstructive surgery has become the preferred treatment option and is accomplished in 3 stages. The first stage, the Norwood operation, involves formation of a neo-aorta using graft material. Stage 2 aims to create a bidirectional cavopulmonary connection at stage 3. The aortic reconstruction as part of the Norwood operation is an important determinant of morbidity. Previous reports indicate that this so-called neoaorta tends to dilate throughout childhood compared with normal aortic dimensions. In addition, impaired aortic distensibility in the reconstructed transverse arch measured with echocardiography has been reported.

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Normally, the thoracic aorta acts as a compliant tube that buffers pulsatile output from the heart. Aortic distensibility and pulse-wave velocity (PWV) are 2 parameters that are closely tied to the elastic buffering function of the aorta. In
patients with HLHS after the Norwood operation, the bioelastic properties of the reconstructed aorta are of particular concern because the right ventricle (RV) is more sensitive to increased afterload than the left ventricle. However, comprehensive data on the anatomic and functional status of the reconstructed aorta in HLHS are still lacking.

Cardiovascular magnetic resonance (CMR) imaging is increasingly used to evaluate the cardiovascular system in congenital heart disease and has recently been established as a noninvasive tool for the assessment of aortic distensibility and PWV, as not being constrained by limited windows, and as being useful for assessing regional elastic properties of the aorta at multiple locations. CMR can also be used to detect fibrotic tissue by late gadolinium enhancement (LGE) imaging. We used 3.0-T CMR to evaluate aortic distensibility, aortic PWV, and LGE of the aortic root and ascending aorta, as well as their impact on RV function in children with HLHS after 3-stage palliation.

Methods

Patients

The study population consisted of 40 patients with HLHS and 13 control subjects without any cardiovascular disease. All patients with HLHS had undergone 3-stage surgical palliation with reconstruction of the complete aortic arch during the Norwood operation and creation of a fenestrated intraaortal lateral tunnel at the third stage. Spontaneous closure occurred in 3 patients, and 16 patients underwent percutaneous closure of the fenestration. The characteristics of the study population, aortic arch reconstruction technique, and medication use in patients with HLHS are listed in Table 1.

For the CMR study, sedation with propofol and midazolam was used in all patients. Heart rate, respiratory motion, oxygen saturation, and noninvasive blood pressure were monitored during examination.

Findings were compared with those of the control children referred for diagnostic magnetic resonance imaging (MRI) of the central nervous system by the Department of Pediatric Neurology in whom cardiac pathology had been excluded. Immediately after central nervous system MRI, all control subjects underwent noncontrast-enhanced CMR imaging. In 3 control subjects, CMR was performed without any sedation.

The investigation protocol was approved by the local research ethics committee. Informed consent was obtained from all people who had the care and custody of the child.

CMR Data Acquisition

CMR studies were performed with a 3.0-T CMR scanner (Achieva 3.0T X series, Philips Medical Systems, Best, the Netherlands) using a phased-array coil for cardiac imaging, or in the smallest children, a coil for extremities (SENSE Cardiac coil, SENSE Flex-L coil, Philips Medical Systems).

Aortic dimensions and the aortic lumen area (for assessment of aortic distensibility) were measured by gradient-echo cine imaging with retrospective ECG gating using a stack of parallel, contiguous, 5-mm-thick, sagittally angulated views of the aortic arch. On these images, we identified the maximal diameters for each of 5 selected measuring points (Figure 1) by picking for each measurement location the slice with maximum aortic diameter. Additionally, views perpendicular to the aortic axis were acquired at each measurement point to determine the maximum axial aortic diameter.

The cine sequence parameters were as follows: field of view, 280×224 mm; voxel size, 1.88×1.94×6 mm; repetition time/echo time, 4.4/2.5 milliseconds; 25 cardiac phases; non–breath-hold; number of repetitions, 2; and scan duration, 3 to 6 minutes. For assessment of RV ejection fraction (RVEF), a stack of short-axis slices was acquired with the same non–breath-hold gradient-echo cine protocol.

LGE images were acquired in patients with HLHS 10 to 15 minutes after contrast injection with an inversion-recovery 3-dimensional turbo-field echo sequence (field of view, 300×178×80 mm; voxel size, 1.17×1.27×10 mm; repetition time/echo time, 3.7/1.83 milliseconds; flip angle, 15°). The time after inversion was adjusted to null the signal in the aortic wall. Healthy control subjects did not receive any gadolinium contrast because of a veto by the local research ethics committee.

Phase-contrast cine imaging was applied to assess aortic PWV between the ascending aorta at the level of the sinotubular junction and the proximal descending aorta, with a slice plane intersecting the aorta at both locations at an approximately right angle (parameters: field of view, 270×270 mm; voxel size, 1.64×1.4×7 mm; repetition time/echo time, 4.4/2.7 ms; velocity encoding, 200 cm/s).

Additionally, high-resolution gadolinium-enhanced magnetic resonance (MR) angiography was performed in patients with HLHS for comprehensive 3-dimensional visualization of the aorta (Figure 2) using a keyhole technique (field of view, 380×380 mm; 70 slices; keyhole percentage, 20%; 20 dynamics; repetition time/echo time, 2.4/0.93 milliseconds; scan duration, 0:40 minutes). Gadolinium (Magnevist, Bayer Schering Pharma AG, Berlin, Germany) at a dose of 0.1 mmol/kg was injected intravenously at a rate of 2 mL/s, followed by a normal saline flush at the same rate.

Overall image quality was considered good or excellent in all patients, except in regions in close proximity to metallic implants. LGE imaging was completed and of diagnostic quality in 28 patients with HLHS, and phase-contrast cine imaging was applied in 17.

Table 1. Characteristics of HLHS Patients and Healthy Control Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients</th>
<th>Healthy Children</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>40</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Male/female, n</td>
<td>27/13</td>
<td>6/7</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>6.0±2.2</td>
<td>6.6±2.2</td>
<td>0.17</td>
</tr>
<tr>
<td>Age at TCPC, y</td>
<td>2.5±0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>20.4±7.1</td>
<td>21.9±5.4</td>
<td>0.13</td>
</tr>
<tr>
<td>Body height, cm</td>
<td>112.7±13.7</td>
<td>117.8±15.3</td>
<td>0.19</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>0.8±0.2</td>
<td>0.8±0.2</td>
<td>0.14</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>77.5±15.7</td>
<td>92.9±16.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>86.6±17.7</td>
<td>97.1±10.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>46.5±8.7</td>
<td>58.1±13.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>40.1±9.6</td>
<td>38.3±8.3</td>
<td>0.85</td>
</tr>
<tr>
<td>Oxygen saturation, %</td>
<td>90.0±4.1</td>
<td>96.4±2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVEF, %</td>
<td>50.5±11.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of aortic arch reconstruction, n (%)</td>
<td></td>
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<tr>
<td>Use of a bovine pericardial patch</td>
<td>33 (83)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of pulmonary homograft material</td>
<td>7 (18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>3 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>15 (38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>3 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>32 (80)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenprocoumon</td>
<td>3 (8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TCPC indicates total cavopulmonary connection. Values are mean±SD when appropriate. P values are from the Mann–Whitney U test.
Dilatation of the ascending aorta and proximal aortic arch, as well as at 2 levels in the descending aorta: level 1, at the isthmus of the aorta; and level 2, above the diaphragm. Distensibility was calculated as follows:

$$\text{Distensibility} (10^{-3} \text{ mm Hg}^{-1}) = \frac{(A_{\text{max}} - A_{\text{min}}) \times (P_{\text{max}} - P_{\text{min}})}{A_{\text{min}}}$$

where $A_{\text{max}}$ and $A_{\text{min}}$ represent the maximal and minimal cross-sectional lumen area of the aorta on cine MRI images, and $P_{\text{max}}$ and $P_{\text{min}}$ are the systolic and diastolic blood pressures (in millimeters of mercury), respectively. Blood pressure was obtained noninvasively with a MR-compatible vital signs monitor with sphygmomanometer (In Vivo Precess 3160, In Vivo, Orlando, Fla). The sphygmomanometer cuff was placed around the right arm.

PWV in patients and heart-healthy control subjects was determined from aortic flow-versus-time curves using phase-contrast cine acquisitions in a segment between the ascending aorta and proximal descending aorta. PWV was calculated as the ratio of the aortic segment length ($\Delta x$ [meters]; Figure 3A) and the time delay of the distal flow curve relative to the proximal flow curve ($\Delta t$ [seconds]; Figure 3B): $\text{PWV} = \frac{\Delta x}{\Delta t}$. The technique of PWV quantification is relatively immune to angle offsets. It will not cause a shift of the curve or of the foot of the systolic upslope on the velocity-versus-time curves.

LGE was scored in a volume that included the aortic root and the ascending aorta on axial images (Figure 4A and 4B). LGE was considered present within the aortic wall if a bright signal exceeded a threshold of 3 SD above the mean signal intensity in a region of nonenhancing aortic wall. The relative amount of LGE (percent) was determined by calculating the total volume with hyperenhancement and dividing by the total aortic wall volume. LGE volumes were evaluated for all slices covered by the 3-dimensional LGE acquisition, which extended 4 cm from the aortic root along the ascending aorta.

RV volumes at end diastole and end systole and volumetric RVEF were quantified by manual planimetry of cine images. Forward stroke volume was calculated as the RV volume at end diastole minus the RV volume at end systole. Volumetric RVEF was calculated by dividing the stroke volume by the end-diastolic volume.

**CMR Data Analysis**

All images were analyzed with dedicated CMR software (ViewForum release 6.3, Philips Medical Systems). Aortic diameters were measured in all patients with HLHS and all control children during systole on axial and sagittal gradient-echo cine images in 5 selected segments: aortic root, ascending aorta, transverse aortic arch, aortic isthmus, and descending aorta (Figure 1). The ascending aorta and the transverse aortic arch are those parts of the aorta that include graft material from surgical reconstruction. The aortic root contains the former pulmonary root, and the descending aorta consists of native wall tissue. Aortic diameters were measured twice independently; the average value was used for further analysis.

Aortic distensibility was measured in patients and healthy control subjects from 2-dimensional cine images in the ascending aorta and transverse aortic arch, as well as at 2 levels in the descending aorta: level 1, at the isthmus of the aorta; and level 2, above the diaphragm. Distensibility was calculated as follows:

$$\text{Distensibility} (10^{-3} \text{ mm Hg}^{-1}) = \frac{(A_{\text{max}} - A_{\text{min}}) \times (P_{\text{max}} - P_{\text{min}})}{A_{\text{min}}}$$

where $A_{\text{max}}$ and $A_{\text{min}}$ represent the maximal and minimal cross-sectional lumen area of the aorta on cine MRI images, and $P_{\text{max}}$ and $P_{\text{min}}$ are the systolic and diastolic blood pressures (in millimeters of mercury), respectively. Blood pressure was obtained noninvasively with an MR-compatible vital signs monitor with sphygmomanometer (In Vivo Precess 3160, In Vivo, Orlando, Fla). The sphygmomanometer cuff was placed around the right arm.

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**Statistical Analysis**

Statistical analysis was performed with SPSS (version 15, SPSS Inc, Chicago, Ill) and the R program, especially the “irr” package for reliability analysis. For all aortic diameters, interrater agreement was measured by intraclass correlation coefficients. The means from the 2 measurements were used for further computations.

All continuous variables were described by mean ± SD. The sample size in control subjects was small, and we found different high variances of CMR variables. The Mann–Whitney $U$ test for independent samples was used to compare patients and control subjects. Because multiple tests were performed for the same outcome variables at several aortic locations, $P$ values of distensi-
bility and aortic diameters were adjusted by the Bonferroni-Holm procedure. In addition, t tests were performed to check for the consistency of significant differences. The statistical power for comparisons of measurements with nonsignificant differences between patients and volunteers was estimated for effect sizes corresponding to aging-related differences of aortic diameters, distensibility, and PWV observed in younger (20 to 29 years of age) and older (50 to 59 years) healthy volunteers. Correlations were described by scatterplots, including a locally weighted polynomial regression fit (locally weighted scatterplot smoothing method).

Figure 3. A and B, Analysis of PWV. A, Sagittal image of the thoracic aorta shows the sites where phase-contrast cine images were acquired. The distance (Δx) between the ascending and proximal descending aortas was measured first. B, The transit time of the systolic pulse wave across the aortic arch (Δt) was determined from the midpoints of the systolic upslope (ta) on the flow-vs-time curves. The difference in ta for ascending and descending aorta locations defined Δt, and pulse wave was estimated as Δx/Δt.

Strength of association was measured by Spearman correlation coefficients. All tests were 2 tailed, and values of \( P < 0.05 \) were considered to indicate statistical significance.

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

Results

Patients with HLHS and the control children were comparable in age, weight, body height, body surface area, and pulse

Figure 4. A, Axial LGE image of the ascending aorta of a 5-year-old boy with HLHS after 3-stage surgical palliation showing distinct high signal intensity of the aortic wall. B, Analysis of the extent of LGE of the axial stack.
pressure. Oxygen saturation was lower in patients with HLHS than in the control group (P<0.01; Table 1). All patient characteristics in Table 1 were not significantly different between the subgroups with and without phase-contrast and LGE measurements.

Aortic Dimensions
Aortic dimensions, normalized by body surface area, are shown in Table 2. Patients with HLHS showed significantly increased axial and sagittal (normalized by body surface area) diameters of the aortic root (P<0.01), ascending aorta (P<0.01), and transverse aortic arch (axial, P<0.01; sagittal, P<0.01) compared with the heart-healthy children. Diameters of the aortic isthmus and the descending aorta were not significantly different. Measurements of aortic diameters proved to be substantially reproducible.

Distensibility, PWV, and RV Function
Aortic distensibility at the level of the ascending aorta and the transverse aortic arch was clearly decreased in patients with HLHS compared with control subjects (P<0.01; Table 3). Aortic distensibility at levels 1 and 2 of the descending aorta was not significantly different between the patient group and the control group. The distensibility of the ascending aorta correlated modestly with reduced volumetric RVEF (Spearman rank correlation, r=0.53; P<0.01) and with the extent of LGE (r=−0.72, P<0.01; Table 4 and Figure 5A and 5B) in patients with HLHS. PWV in the transverse aortic arch trended higher in patients with HLHS (P=0.06; Table 3).

The diameters of the native ascending aorta at birth, measured by echocardiography in the intensive care unit, averaged 17.7±7.8 mm/m² (range, 7.8 to 35.4 mm/m²). There was no correlation between the diameter of the ascending aorta at birth and RVEF (r=−0.17, P=0.33). The statistical power was >85% for all cases with nonsignificant differences in Tables 2 and 3 (aortic diameters and aortic distensibility in descending aorta and PWV) using effect size estimates, representative of the age-related progression of subclinical disease.21

Late Gadolinium Enhancement
LGE was quantified in a volume covering the aortic root and the native ascending aorta, as well as the patch, including the ascending neoaorta. The extent of LGE ranged from 18% to 73% of wall volume. There was a moderate negative correlation (r=−0.5, P<0.01) between the amount of aortic LGE and volumetric RVEF (Table 4 and Figure 6). No correlation was found between aortic LGE and the diameter of the ascending aorta at birth (r=0.05, P=0.8).

Reproducibility of Aortic Measurements
Measurements of aortic diameters proved to be substantially reproducible. The intraclass correlation coefficient ranged from 0.63 to 0.89.

Discussion
In this study, the aortic root, ascending aorta, and transverse aortic arch of patients with HLHS after the Norwood opera-
tion were characterized by increased size, reduced vascular distensibility, and the presence of aortic LGE. Reduced distensibility and the extent of LGE correlated with decreased RV function.

Aortic Dimensions
In patients with HLHS, we found significant dilatation of the aortic root, which is the former pulmonary root, as well as of the ascending aorta and the transverse aortic arch, which includes graft material. A previous echocardiographic study by Mahle et al. showed significantly enlarged diameters of the transverse aortic arch in HLHS using long-axis suprasternal views. We additionally examined sagittal and axial dimensions of the aortic root, ascending aorta, and descending aorta by MRI (Figure 2).

Reasons for dilatation of the neoaorta in patients with HLHS after surgery can be attributed to the following constraints. First, the diameter of the pulmonary root, which is used to create the neoaortic root, is larger than the aortic root of healthy subjects and determines the size of the neoaortic root. Second, the increased diameters of the ascending aorta and transverse aortic arch are a consequence of surgical implantation of the aortic patch to compensate for underdevelopment of these vascular structures.

Our patients with HLHS showed normal diameters of the aortic isthmus (see Table 2) but an oversized aortic root and significant dilation of the reconstructed part of the aorta. The combination of these features leads to disharmonious and incongruous contours and shapes of the neoaorta (see Figure 2). The abnormal aortic shape, in combination with altered elastic properties, may influence the aortic blood flow and the elastic buffering capacity of the ascending aorta. Normal flow characteristics include a right-handed helix in the upper aortic arch during systole, a retrograde end-systolic flow down the inside curvature of the ascending aortic arch, and flow vortexes in the coronary sinuses. In patients with ascending aortic aneurysms, anomalous flow patterns have been demonstrated, and in patients with bicuspid aortic valves, such abnormal flow profiles lead to increasing ascending aortic dilatation. However, the effects of the disharmonious aortic arch on aortic flow patterns in HLHS remain unclear and require further investigation.

Distensibility, PWV, and RV Function
The distensibility of the ascending aorta and transverse aortic arch was markedly decreased in our patients with HLHS compared with healthy control subjects. A previous ultra-
sound study by Cardis et al\textsuperscript{4} reported a reduced distensibility of the transverse aortic arch in HLHS. We expanded on this study by also measuring the distensibility of the ascending and descending aortas. Reduced distensibility of the ascending aorta correlated significantly with reduced RVEF.

The decreased distensibility of the ascending aorta and transverse aortic arch in patients with HLHS may be due primarily to the use of noncompliant patch material in the ascending aorta and the transverse aortic arch. Second, the aorta is completely surrounded by fibrous tissue after reconstruction. Third, considering that HLHS is characterized by aortic arch hypoplasia, intrinsic aortic wall abnormalities similar to those found in patients with coarctation may contribute to decreased distensibility. In patients with coarctation, histological examination of aortic tissue showed increased collagen content and decreased smooth muscle cell density in the precoarctation aortic wall.\textsuperscript{28} As a consequence, clinical studies recently found increased aortic stiffness after coarctation repair.\textsuperscript{29,30} It also has been reported that damage of the vasa vasorum results in a decrease in ascending aortic distensibility.\textsuperscript{31,32}

Because aortic buffering is an important determinant of cardiac output,\textsuperscript{33} the increased aortic stiffness in patients with HLHS may have an adverse effect on aortic-ventricular coupling by causing afterload elevation. If severe and left untreated, it may eventually result in consecutive ventricular hypertrophy and failure.\textsuperscript{34} Similar adverse effects of surgical aortic repair and its detrimental effect on ventricular function were described previously for patients after the Ross procedure.\textsuperscript{10} In patients with HLHS after the Norwood operation, the bioelastic properties of the reconstructed aorta are of particular concern because the RV is maladapted to function as a systemic pressure pump\textsuperscript{7} and therefore is more sensitive to increased afterload than the left ventricle. Accordingly, chronically impaired aortic elasticity may represent an important risk factor for single-ventricle patients and a potential burden across the complete lifespan. Furthermore, one can speculate that with advancing age, alterations of the elastic properties of the native aortic wall in patients with HLHS after the Norwood operation may result in a higher susceptibility for early atherosclerotic lesions and hypertension. At this point, our patient population did not show arterial hypertension; an increased stiffness of the proximal aorta did not appear to lead to systemic arterial hypertension in our patients with HLHS with a mean age of 6 years.

Although aortic distensibility and PWV provide similar information about aortic bioelastic function,\textsuperscript{11} we found a significantly decreased distensibility of the ascending aorta and transverse aortic arch compared with healthy control subjects, whereas PWV trended higher only in patients with HLHS. These differences may be due to the low number of PWV measurements in patients with HLHS (n=17) as a result of a technical problem mentioned in Methods. Furthermore, aortic distensibility and aortic PWV are not interchangeable parameters of vascular elasticity. Distensibility represents a localized measurement of elasticity,\textsuperscript{5} whereas PWV provides information about the vascular elasticity measured along the ascending aorta, transverse arch, and proximal descending aorta (Figure 3A). One can speculate that the normally structured wall of the descending aorta partly compensates for the low elasticity of the ascending aorta and transverse arch because only the latter sections contain graft material.

Late Gadolinium Enhancement

LGE of the aorta occurred in all patients with HLHS at sites with graft material such as the ascending aorta, but LGE was also detected in areas with native wall tissue like the aortic root. The extent of LGE correlated with decreased distensibility of the ascending aorta, and both parameters also correlated with reduced RVEF.

LGE is widely accepted as a histologically validated marker of fibrosis and scarred tissue in various organs and was validated in histological studies.\textsuperscript{14,15,35,36} Aortic wall LGE was previously observed in Takayasu disease, a result of inflammation of the arterial wall.\textsuperscript{37} Harris et al\textsuperscript{38} observed LGE of the ascending aorta after congenital heart surgery. The mechanisms of arterial wall LGE in patients with HLHS are not completely understood, although the LGE undoubtedly reflects an increase of the contrast distribution volume. In addition, our findings might be explained by the following facts: Ascending aortic LGE in our patients with HLHS in particular is related to the incorporation of patch material. However, the increased LGE found in the aortic root and native part of the ascending aorta indicates intrinsic aortic wall abnormalities. Structural changes of the ascending aorta in various forms of congenital heart disease have been described by Niwa et al.\textsuperscript{39} They observed abnormalities of smooth muscle, elastic fibers, collagen, and ground substance of the medial layer. Schoof et al\textsuperscript{40} found in an animal study increased collagen deposition in the extracellular matrix of pulmonary autografts implanted in the aortic position. Therefore, the LGE of the aortic root (the former pulmonary root) may be due not only to intrinsic abnormalities but also to the exposure to systemic blood pressure.

To the best of our knowledge, the implications of aortic wall LGE for aortic function and aortic-ventricular coupling in patients with HLHS have not previously been studied. We surmise from our results that patients with a greater extent of LGE may be at higher risk for later RV failure.

Methodical Aspects

Our study has shown that CMR is a unique imaging tool to delineate aortic anatomy in HLHS after palliation in a single, comprehensive, \textasciitilde 40-minute long examination. A distinguishing feature of our study was the use of a 3.0-Tesla scanner to compensate for the inherent loss of signal-to-noise ratio when small fields of view are used in children.

Limitations

No long-term follow-up data were available. Therefore, the prognostic value of our findings is unknown. Future studies are required to investigate the long-term effects of reduced aortic elasticity on systemic RV function. However, our present findings may serve as baseline data.

In addition, the blood pressure measurements between patients with HLHS and the control group were significantly different, which is probably explained by higher blood pressures.
in 3 control subjects who underwent CMR without sedation. Pulse pressures, which are used to estimate the vascular distensibility, were not different between the 2 groups.

The MR protocol could not be fully completed in some patients for the following reasons. First, some patients awoke early from sedation. Second, some images could not be used for further analysis because of image artifacts caused by metallic implants. In particular, these artifacts affected phase-contrast measurements for PWV analysis. We cannot exclude the possibility that the lack of phase-contrast data in a subgroup of patients biased the difference of the PWV measurements between patients and healthy volunteers because RVEF was lower in the patients without phase-contrast measurements (48.0±11.4% versus 58.9±6.8% in patients with phase-contrast measurements; P=0.023). Another limitation is the small number of control subjects.

Conclusions
Dilatation and reduced distensibility of the aortic root, ascending aorta, and transverse aortic arch in children with HLHS after 3-stage palliation are common. A markedly decreased distensibility in the ascending aorta correlated with reduced systolic RV function. Impaired ascending aortic elasticity is associated with aortic LGE, suggestive of fibrosis and scar tissue. Our results help improve our understanding of aortic biophysical properties after extensive surgical reconstruction and emphasize the need for follow-ups with MRI.

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Disclosures
None.

References
CLINICAL PERSPECTIVE

In children with hypoplastic left heart syndrome, the status of the reconstructed aorta after the Norwood operation is of potential prognostic importance. Dilatation and an impaired distensibility of the neoaorta have already been reported in previous echocardiographic and angiocardioGraphic studies. However, comprehensive data on the anatomic and functional properties of the reconstructed aorta and their potential influence on right ventricular function in hypoplastic left heart syndrome are still lacking. The present study used cardiovascular magnetic resonance imaging to evaluate the anatomy, bioelastic properties, viability of the aorta and right ventricular ejection fraction in 40 patients with hypoplastic left heart syndrome. Compared with control subjects, patients with hypoplastic left heart syndrome had an increased aortic size and reduced aortic bioelasticity (distensibility and pulse-wave velocity). Fibrosis was detected with cardiovascular magnetic resonance imaging in the proximal aorta using the well-proven late gadolinium enhancement technique. Aortic late gadolinium enhancement correlated inversely with reduced right ventricular ejection fraction and distensibility in the ascending aorta. These findings suggest unfavorable aortic-ventricular coupling, which may contribute to a higher risk for later right ventricular failure. This study may help improve our understanding of aortic biophysical properties after extensive surgical reconstruction of the aorta. The results may serve as baseline data for further longitudinal studies in children with hypoplastic left heart syndrome to establish the prognostic value of anatomic and bioelastic aortic properties measured by cardiovascular magnetic resonance imaging.
Maladaptive Aortic Properties in Children After Palliation of Hypoplastic Left Heart Syndrome Assessed by Cardiovascular Magnetic Resonance Imaging

Inga Voges, Michael Jerosch-Herold, Jürgen Hedderich, Charlotte Westphal, Christopher Hart, Michael Helle, Jens Scheewe, Eileen Pardun, Hans-Heiner Kramer and Carsten Rickers

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