Tissue Doppler time intervals and derived indices in hypoplastic left heart syndrome

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Aims

To describe tissue Doppler time intervals and derived indices in hypoplastic left heart syndrome (HLHS) across surgical stages, taking account of age-related changes in the heart rate. Correlation of the myocardial performance index (MPI) and the systolic to diastolic (S:D) time ratio with other echocardiographic and magnetic resonance imaging (MRI) measures of cardiac performance.

Methods and results

Fifty-seven patients at different stages of HLHS palliation were studied prospectively using tissue Doppler imaging of the right ventricular free wall, with simultaneous cardiac MRI in the majority. Both isovolumic contraction time and isovolumic relaxation time were prolonged compared with the normal left and right ventricle: median (range) \( z \)-scores for the tricuspid annulus 1.9 (–1.2 to 9.3) and 1.3 (–2.0 to 5.5), respectively. When adjusted for heart rate, the ejection, systolic, and diastolic times in HLHS were not significantly different from published normal data. The MPI was increased at all surgical stages in HLHS. Neither MPI nor heart rate-specific S:D time ratio \( z \)-score correlated with MRI ejection fraction or indexed cardiac output when the confounding effect of significant tricuspid regurgitation was taken into consideration.

Conclusion

The prolongation in isovolumic relaxation and contraction times may be due to adaptation or reduced myocardial performance. Differences in the S:D time ratio between surgical stages can be accounted for by the heart rate alone. Neither MPI \( z \)-score nor S:D \( z \)-score correlated with MRI ejection fraction or indexed cardiac output when the confounding effect of significant tricuspid regurgitation was taken into consideration.

Keywords

Congenital heart disease • Tissue Doppler • Hypoplastic left heart • Tei index • Myocardial performance index

Introduction

Hypoplastic left heart syndrome (HLHS) is characterized by severe stenosis or atresia of the aortic and mitral valves, which renders the left heart incapable of supporting the systemic arterial circulation. Affected patients undergo staged surgical palliation over the first years of life resulting in a total cavopulmonary connection (TCPC) with a systemic right ventricle (RV).\textsuperscript{1} The loading conditions of the heart change following each stage of surgery. Initial Norwood surgery\textsuperscript{2} results in a volume-loaded RV due to the inclusion of a systemic to pulmonary artery shunt. Volume loading is eliminated following removal of the systemic to pulmonary artery shunt at the time of the Glenn or hemi-Fontan operation performed during infancy. The completion of the TCPC directs virtually all systemic venous return to the pulmonary arteries.\textsuperscript{3}

Assessment of right ventricular function in this context is known to be difficult, due to a combination of the complex geometry of the RV and abnormal loading conditions.\textsuperscript{4} RV function is known to be of prognostic significance for patients with HLHS,\textsuperscript{5,6} but subjective assessment is prone to error.\textsuperscript{7} Accurate objective assessment of RV function is clinically important, as deterioration may warrant consideration of other treatment options including transplantation.\textsuperscript{8} A variety of techniques may be used including magnetic resonance imaging (MRI), three-dimensional echocardiography, and speckle tracking and Doppler echocardiography.\textsuperscript{4,9,10} MRI requires sedation or general anaesthesia in the paediatric age

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range and many of the echocardiographic techniques require significant post-processing, which limits widespread adoption in routine clinical practice.

Measurement of systolic and diastolic time intervals, by either pulsed Doppler or tissue Doppler imaging (TDI), has been undertaken in HLHS. Derived indices, such as the myocardial performance index (MPI) and systolic to diastolic (S:D) time ratios, have been proposed as useful measures of RV function in HLHS\textsuperscript{11–15} and for the RV in adults.\textsuperscript{16} The S:D ratio was increased in children with idiopathic dilated cardiomyopathy compared with controls.\textsuperscript{17} With respect to the RV, TDI has an advantage over pulsed blood pool Doppler techniques for the calculation of such indices because all of the components can be measured on a single trace and reference data from the paediatric population are available.\textsuperscript{18,19} TDI has the potential to identify pre-symptomatic changes in cardiac function.\textsuperscript{20,21} Due to the fibre orientation in the RV, the ability of TDI to assess longitudinal function makes it particularly suited to the RV.\textsuperscript{10}

There are limitations to the data currently available with respect to TDI in HLHS. Firstly, many reports pre-date the publication of normal TDI time interval data in the paediatric age range, which demonstrated the major impact of heart rate.\textsuperscript{18} This has the potential to confound comparisons between children of different ages and stages of surgical palliation. Secondly, echocardiographic indices, such as MPI or S:D ratio, have been compared with subjective measures such as qualitative assessment of RV function or measures from a single echocardiographic plane,\textsuperscript{12,22} which may themselves be inaccurate. MRI is currently regarded as the most accurate and reproducible technique for measuring ventricular volumes and blood flow. This technique is used for pre-operative assessment of HLHS at our institution.\textsuperscript{23,24}

The aims of this paper are two-fold. The first is to present prospectively acquired TDI data from a cohort of patients with HLHS at different stages of surgical palliation using heart rate-specific z-scores calculated from published reference ranges. This is to allow comparison of patients across operative stages and avoids the confounding effect of the heart rate. Secondly, the absolute values and z-scores of TDI-derived indices were correlated with objective measures of cardiac performance including MRI-derived RV ejection fraction, indexed ventricular volumes, and aortic flow. Where possible, TDI indices were also correlated with other measures of RV systolic and diastolic function such as flow acceleration of the tricuspid regurgitant jet and invasive pressure measurements.

Methods

Study population

This was a prospective cross-sectional study. Patients with HLHS were studied between July 2007 and December 2010. Ethical and institutional approval was obtained (application reference 07/Q0704/3). HLHS was defined as aortic atresia and/or mitral atresia with concordant atrio-ventricular and ventriculo-arterial connections. Patients with critical aortic stenosis with severe hypoplasia of left heart structures palliated towards a single ventricle circulation were included. Patients with abnormal cardiac connections such as those with unbalanced atioventricular septal defects were excluded. Patients were subdivided according to the timing of their study in relation to the operative stage.

Norwood Stage 1 procedure was defined as the modified Norwood operation with systemic to pulmonary artery shunt, followed by the hemi-Fontan operation (superior cavopulmonary connection) and then completion of the cavopulmonary connections (TCPC, fenestrated lateral tunnel technique). To facilitate correlation with other imaging techniques, where possible patients were studied immediately following cardiac MRI. The echocardiographic study was performed under the same general anaesthetic as the MRI scan so that both were performed under equivalent conditions.

Echocardiography

Comprehensive echocardiographic studies were performed using the Philips IE 33 ultrasound system (Philips Inc., Andover, MA, USA). Pulsed-wave tissue Doppler was performed using age appropriate probes (S5-1, SB-3, S12-4). All scans were analysed off-line on an Excelera workstation (Philips Inc., Andover, MA, USA) using a single measurement.

Pulsed tissue doppler

From an apical four-chamber view, the sample volume was placed at the level of the tricuspid annulus on the RV free wall.\textsuperscript{25} The Doppler sweep speed was set to ‘high’, maximizing the frame rate to optimize measurement of time intervals. If the patient was under general anaesthetic for MRI scanning or ventilated on the intensive care unit, a temporary cessation of ventilation avoided respiratory impact on the trace. Patients breathing spontaneously had measurements made in expiration. Measured time intervals included R-R interval, isovolumic contraction time (IVCT), ejection time (ET), and isovolumic relaxation time (IVRT). MPI was calculated as described previously\textsuperscript{26} as well as the systolic time (ST), diastolic time (DT), filling time (FT), and S:D time ratio. A typical tissue Doppler recording with the measured variables and derived indices is shown in Figure 1.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{example figure}
\caption{Pulsed tissue Doppler trace at the tricuspid annulus on the right ventricular free wall. RR interval was measured between two consecutive R waves. (i) Isovolumic contraction time (IVCT); From the end of the a’ wave to the beginning of the s’ wave (ii) Ejection time (ET); From the beginning of the s’ wave to the end of the s’ wave (iii) Isovolumic relaxation time (IVRT); From the end of the s’ wave to the beginning of the e’ wave (iv) Filling duration (FT) was calculated from the RR interval minus (IVCT + ET + IVRT). Myocardial performance index (MPI) was calculated as previously described\textsuperscript{26} (IVCT + IVRT)/ET; Systolic time (ST) = IVCT + ET; Diastolic time (DT) = IVRT + FT; systolic to diastolic (S:D) time ratio = ST/DT.}
\end{figure}
Other echocardiographic parameters: systolic function

In patients with measurable tricuspid regurgitation, the change of velocity over time of the regurgitant jet (\(dV/dT\)) was measured as previously described.\(^{27,28}\) The slope of the tricuspid regurgitant jet was measured between 1 and 3 m/s on a continuous wave Doppler trace. The peak \(s'\) wave velocity was also recorded from the pulsed tissue Doppler trace acquired as described above. Peak \(s'\) wave velocities were converted to \(z\)-scores using published paediatric data.\(^{19}\)

Table 1  Patient demographics

<table>
<thead>
<tr>
<th></th>
<th>Pre-Norwood stage 1 (n = 10)</th>
<th>Pre-hemi-Fontan (n = 28)</th>
<th>Post-hemi-Fontan (n = 21)</th>
<th>Post-TCPC (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at echo, years</td>
<td>2.7 days (2.1)</td>
<td>0.33 (0.13)</td>
<td>2.3 (0.8)</td>
<td>9.8 (2.1)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>3.1 (0.3)</td>
<td>5.2 (1.1)</td>
<td>11.7 (2.4)</td>
<td>31.8 (11.8)</td>
</tr>
</tbody>
</table>

TCPC, Total cavopulmonary connection. All values are mean (SD).

Table 2  Pulsed tissue Doppler parameters

<table>
<thead>
<tr>
<th></th>
<th>Pre-Norwood stage 1 (n = 9)</th>
<th>Pre-hemi-Fontan (n = 28)</th>
<th>Post-hemi-Fontan (n = 21)</th>
<th>Post-TCPC (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frame rate, Hz</td>
<td>169.7 (64.1)</td>
<td>173.4 (65.2)</td>
<td>184.4 (67.5)</td>
<td>189.2 (69.9)</td>
</tr>
<tr>
<td>RR interval, ms</td>
<td>400 (52)</td>
<td>517.1 (87.3)</td>
<td>652.4 (121.7)</td>
<td>778.8 (128.1)</td>
</tr>
<tr>
<td>IVCT, ms</td>
<td>44.0 (15.0)</td>
<td>56.4 (21.5)</td>
<td>81.0 (25.7)</td>
<td>78.2 (38.9)</td>
</tr>
<tr>
<td>ET, ms</td>
<td>192 (46.4)</td>
<td>240 (36.2)</td>
<td>256.2 (47.1)</td>
<td>248.8 (40.3)</td>
</tr>
<tr>
<td>ST, ms</td>
<td>233.3 (43.6)</td>
<td>296.4 (45.0)</td>
<td>337.1 (55.4)</td>
<td>327.1 (57.6)</td>
</tr>
<tr>
<td>IVRT, ms</td>
<td>43 (19.5)</td>
<td>56.4 (21.1)</td>
<td>71.4 (23.1)</td>
<td>68.8 (30.1)</td>
</tr>
<tr>
<td>Filling, ms</td>
<td>124 (36.8)</td>
<td>146.3 (56.9)</td>
<td>243.8 (79.0)</td>
<td>282.9 (153.1)</td>
</tr>
<tr>
<td>DT, ms</td>
<td>166.7 (33.5)</td>
<td>220.7 (64.4)</td>
<td>315.2 (82.6)</td>
<td>451.8 (137.0)</td>
</tr>
<tr>
<td>MPI</td>
<td>0.51 (0.28)</td>
<td>0.48 (0.18)</td>
<td>0.62 (0.22)</td>
<td>0.63 (0.28)</td>
</tr>
<tr>
<td>S.D ratio</td>
<td>1.46 (0.49)</td>
<td>1.46 (0.49)</td>
<td>1.13 (0.31)</td>
<td>0.79 (0.27)</td>
</tr>
<tr>
<td>dV/dT</td>
<td>—</td>
<td>8340 (4572), n = 8</td>
<td>4479 (1707), n = 8</td>
<td>5876 (1545), n = 7</td>
</tr>
<tr>
<td>E/e’</td>
<td>—</td>
<td>11.1 (2.9), n = 9</td>
<td>10.6 (4.5), n = 15</td>
<td>8.7 (3.5), n = 13</td>
</tr>
<tr>
<td>Peak s’</td>
<td>6.6 (1.2)</td>
<td>5.7 (1.3)</td>
<td>6.1 (1.7)</td>
<td>6.5 (2.1)</td>
</tr>
<tr>
<td>Peak s’ z-score</td>
<td>−0.6 (0.2), n = 10</td>
<td>−0.8 (0.2), n = 28</td>
<td>−3.2 (1.1), n = 20</td>
<td>−3.2 (1.0), n = 16</td>
</tr>
</tbody>
</table>

All values are presented in the format of previously published data.\(^{18}\): mean (SD).

Isovolumic contraction time (IVCT), ejection time (ET), isovolumic relaxation time (IVRT), systolic time (ST), diastolic time (DT), myocardial performance index (MPI), systolic to diastolic time ratio (S:D), change in velocity/change in time (dV/dT), E to e’ ratio (E/e’).

Table 3  MRI data

<table>
<thead>
<tr>
<th></th>
<th>Pre-Norwood stage 1 (n = 0)</th>
<th>Pre-hemi-Fontan (n = 19)</th>
<th>Post-hemi-Fontan (n = 13)</th>
<th>Post TCPC (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>iEDV, mL/m²</td>
<td>—</td>
<td>85.2 (14.3)</td>
<td>79.1 (12.5)</td>
<td>73.8 (12.7)</td>
</tr>
<tr>
<td>iESV, mL/m²</td>
<td>—</td>
<td>39.9 (11.3)</td>
<td>30.2 (9.7)</td>
<td>32.7 (7.4)</td>
</tr>
<tr>
<td>iSV, mL/m²</td>
<td>—</td>
<td>45.3 (8.7)</td>
<td>48.7 (5.9)</td>
<td>41.1 (10.2)</td>
</tr>
<tr>
<td>iCO, L/min/m²</td>
<td>—</td>
<td>4.7 (0.9)</td>
<td>4.1 (0.5)</td>
<td>2.8 (0.6)</td>
</tr>
<tr>
<td>iAo, mL/m²</td>
<td>—</td>
<td>44.6 (7.8)</td>
<td>45.2 (7.8)</td>
<td>38.8 (7.4)</td>
</tr>
<tr>
<td>TR %</td>
<td>—</td>
<td>2.4 (3.7)</td>
<td>6.8 (9.4)</td>
<td>3.7 (5.3)</td>
</tr>
<tr>
<td>MRI EF, %</td>
<td>—</td>
<td>54.0 (9.0)</td>
<td>62.6 (8.1)</td>
<td>55.3 (8.1)</td>
</tr>
<tr>
<td>CVP, mmHg</td>
<td>—</td>
<td>10.9 (2.3)</td>
<td>11.3 (2.9)</td>
<td></td>
</tr>
</tbody>
</table>

All values are mean (SD), indexed end-diastolic volume (iEDV), indexed end-systolic volume (iESV), indexed stroke volume (iSV), indexed cardiac output (iCO), indexed neo-aortic stroke volume (iAo), tricuspid regurgitation (TR), and MRI-derived ejection fraction (MRI EF).

Patients with significant forward flow through the left heart (n = 11) were excluded from this correlation due to the effect of this on volumetry.
Other echocardiographic parameters: diastolic function

The tricuspid valve inflow pattern was also recorded from the standard four-chamber view using pulsed-wave Doppler. The E-wave velocity was measured from this and the e’ measured from the pulsed tissue Doppler trace acquired as described above. The E to e’ (E/e’) ratio was calculated.

Magnetic resonance imaging

Images were acquired on a Philips 1.5 Tesla Achieva scanner (Philips Healthcare, Best, The Netherlands). MRI scans were performed as clinically indicated including short axis steady-state free precession cine stack for volumetry and neo-aortic phase contrast flow. Analysis was performed on a Viewforum EWS Version 2.0 workstation (Philips Healthcare, Best, The Netherlands). RV end-diastolic volume, RV end-systolic volume, ejection fraction, stroke volume, and cardiac output were calculated according to published methodology. Cardiac output and stroke volume calculated from RV volumetry reflect all blood leaving the RV. For time intervals, the ranges obtained from the normal mitral valve annulus and tricuspid valve annulus are almost identical. We have elected to compare the TDI values from HLHS patients with those from the normal tricuspid valve annulus in the calculation of z-scores. The TDI results were correlated with MRI-derived ejection fraction and cardiac output indexed to body surface area. In patients with a cavopulmonary anastomosis it is our routine clinical practice to measure central venous pressure (CVP) at the time of MRI, which, in the absence of pulmonary arterial obstruction, we recorded to reflect filling pressures. Full catheterization data are only obtained selectively if the CVP is raised, either reflecting obstruction to pulmonary blood flow, increased pulmonary vascular resistance, or ventricular dysfunction.

Data analysis

The range of heart rates, highest in the neonatal period and lower in older patients, complicates analysis of echocardiographic time intervals. Previous authors have corrected IVCT and IVRT by dividing the measured value by the square root of the R–R interval: normal ranges have been produced by this method. In this paper time intervals are presented as absolute values, corrected for heart rate, and as z-scores. The additional consideration in HLHS is identifying an appropriate comparison group for time intervals. Normal TDI time intervals and z-scores have been published but these relate to the structurally normal heart. In HLHS the RV pumps systemic arterial blood. The normal RV TDI time intervals relate to a low pressure RV and those from that of the left ventricle (LV) relate to a ventricle pumping systemic pressure and so may be more appropriate, although the morphology and myoarchitecture of the LV is different from the RV. For time intervals, the ranges obtained from the normal mitral valve annulus and tricuspid valve annulus are almost identical. We have elected to compare the TDI values from HLHS patients with those from the normal tricuspid valve annulus in the calculation of z-scores. The TDI results were correlated with MRI-derived ejection fraction and cardiac output indexed to body surface area. In addition, we correlated MRI planimetric area with other measures of systolic function (peak s’ wave velocity and 

Assessment of inter- and intra-observer variability

Inter- and intra-observer variability was assessed using 2-way random intra-class coefficients with absolute agreement on a subsample of 18 randomly selected cases throughout the operative stages. All analyses of echocardiograms were performed by two members of the research
team (JMS/HBR). Each observer was blinded to other analyses. MRI analysis was performed by two observers (HBR/AJB), blinded to each other’s results.

Statistical analysis
Pearson correlations were calculated between variables. Due to potential confounding, correlation with MRI-derived variables was performed as the whole group and without patients with significant tricuspid regurgitation (regurgitant fraction >10%). Patients with significant residual forward flow through the native aorta were also excluded from correlation with MRI derived variables as this also impacts on RV volumetry and neo-aortic flow. Comparison of heart rate-specific $z$-scores for each measure over four time points (pre Stage 1 Norwood, pre-hemi-Fontan, post-hemi-Fontan and post-TCPC) was performed using one way analysis of variance; point estimates at individual time points were via marginal means with 95% confidence intervals. The statistical package was Stata v11 (StataCorp).

Results
A total of 90 echocardiographic studies were performed in 69 patients. Of these, 76 studies were judged to be of sufficient quality to be included in the analysis. Forty-nine (63.6%) studies had been performed under general anaesthesia to allow correlation with MRI findings. Patient characteristics are shown in Table 1. Mean (standard deviation) time intervals, and MPI are shown in Table 2, with MRI results in Table 3. Median MRI ejection fraction was 55.9% (range 35.4–79.3%). Measurement of $E'/e'$ was not possible in all patients (particularly younger patients with high heart rates) due to fusion of the Doppler E and A signals. Measurement of $dV/dT$ was only possible in patients with measurable tricuspid regurgitation. Significant tricuspid regurgitation was noted in six studies (median regurgitant fraction 12%, range 10.1–32.5%). No significant neo-aortic regurgitation was noted in any patient.

Inter- and intra-observer variability
For RV free wall tissue Doppler time intervals, intra-observer intra-class coefficients for IVCT, ET, and IVRT were 0.904, 0.897, and 0.898 and inter-observer 0.821, 0.777, and 0.736 respectively. For MRI, the intra-class coefficients were 0.945, 0.952, 0.926, and 0.885 for right ventricular end-diastolic volume, right ventricular end-systolic volume, right ventricular stroke volume, and right ventricular ejection fraction, respectively.

Presentation of results
Figure 2 shows the values of heart rate-corrected IVCT in HLHS plotted against age including normal reference ranges from the tricuspid valve annulus in the normal heart. Figure 3 demonstrates the clear impact of heart rate on ET in our patient group with normal reference values from the tricuspid valve annulus. At all operative stages the S:D ratio shows no systematic deviation from the normal range for the heart rate. Figure 5A–C demonstrate the heart rate-specific $z$-scores for IVCT, ET, and ST with normal reference ranges from the tricuspid valve annulus. The only statistically significant correlation was between MPI $z$-score and MRI-derived right ventricular ejection fraction (Pearson 0.437, $P < 0.05$). When patients with a tricuspid regurgitant
Correlation of MPI $z$-score and S:D ratio $z$-score with other measures of systolic and diastolic function

MPI $z$-score did not correlate with $dV/dT$, $s'$ velocity $z$-score, CVP, or $E/e'$ ratio. Heart rate-specific S:D ratio $z$-score did not correlate with $dV/dT$, peak $s'$ velocity $z$-score, or $E/e'$ ratio (Table 5). There was a negative correlation between heart rate-specific S:D ratio $z$-score and CVP (Pearson $-0.451$, $P < 0.05$).

### Discussion

Functional assessment of the systemic RV in the context of HLHS is important to guide clinical management, particularly the detection of pre-symptomatic ventricular dysfunction. Systolic dysfunction early in life has been shown to be an important determinant of patient outcome. Objective assessment of RV function in HLHS is difficult and age-related changes in the heart rate may confound measurements and derived indices.

Assessment of myocardial velocities, time intervals, and derived indices by TDI is readily performed in this patient group on a single Doppler trace. Measurement of systolic time by TDI does not depend on the presence of tricuspid regurgitation, in contrast to continuous wave Doppler, thus avoiding selection bias. Our data demonstrate that measurement of TDI time intervals is reproducible in HLHS. At all ages and surgical stages, the HLHS group has heart rate-adjusted IVCT and IVRT, which are prolonged compared with the normal heart, although there is overlap with the normal range (Figure 5A and B). The prolongation of IVCT and IVRT is likely to reflect the abnormal loading conditions of the systemic RV. Such prolongation is seen in other settings such as in anthracycline cardiomyopathy, chronic heart failure, and pulmonary hypertension. It is not clear in HLHS whether the prolonged IVCT and IVRT reflect adaptation or an evolving disease process.

The MPI is, on average, higher in patients with HLHS at all surgical stages, but overlaps with the normal range (Figure 5C) without evident change between surgical stages. The high MPI is due entirely to prolonged IVCT and IVRT given the normal heart rate-
Table 5  Pearson correlation values for MPI z-score and S:D z-score against measures of systolic and diastolic function

<table>
<thead>
<tr>
<th></th>
<th>dV/dT score</th>
<th>Peak s’ velocity z-score</th>
<th>E/e’ ratio</th>
<th>CVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPI z-score</td>
<td>−0.191</td>
<td>−0.217</td>
<td>0.094</td>
<td>0.152</td>
</tr>
<tr>
<td>S:D z-score</td>
<td>−0.284</td>
<td>0.026</td>
<td>−0.159</td>
<td>−0.451*</td>
</tr>
</tbody>
</table>

Central venous pressure (CVP), change in velocity/change in time (dV/dT), E to e’ ratio (E/e’), myocardial performance index (MPI), systolic to diastolic time (S:D).

*P < 0.05.

adjusted ET across surgical stages (Figures 3 and 5A). With respect to S:D ratio, our data confirm that if heart rate is not taken into account, then the S:D ratio is different in HLHS patients at different surgical stages, with the highest values seen in younger patients (Figure 4a). However, heart rate is a major determinant of the S:D ratio and when heart rate-specific z-scores are computed, the heart rate-specific S:D ratio is within normal limits across all surgical stages (Figure 5C). Thus, adjustment of the S:D ratio for heart rate is essential for longitudinal and cross-sectional comparison of data to avoid misinterpretation of differences or changes of this index.

MPI and S:D ratio have been proposed as markers of systolic or diastolic dysfunction in previous studies of HLHS.11–14,22 Our study was designed to include data from MRI and invasive pressure measurements where possible, to provide an objective means of assessing the usefulness of these indices in the functional assessment of patients with HLHS. MPI z-score did not correlate with dV/dT, s’ velocity z-score, MRI-derived indexed right ventricular cardiac output, or indexed neo-aortic forward flow. Furthermore, neither the E/e’ ratio nor CVP correlated with MPI z-score. This is in contrast to the study of Williams et al.11,13,14 where there was a weak positive correlation between MPI and cardiac catheter end-diastolic pressure. There was a positive correlation between MPI z-score and MRI-derived ejection fraction. This positive correlation was surprising because higher MPI values have been associated with worse ventricular function. A possible influence is the presence of significant tricuspid regurgitation (>10%), and when these patients were excluded, there was no significant correlation. Thus, MPI does not appear to be a surrogate for any of the other direct measures of cardiac performance that were measured.

The heart rate-specific S:D ratio z-score did not correlate with dV/dT, peak s’ velocity z-score, or MRI-derived right ventricular indexed cardiac output, neo-aortic forward flow, or MRI-derived ejection fraction. Thus there was no significant correlation with any of the other measures of systolic cardiac performance. This differs from the report of Friedberg et al.12 where a high S:D ratio (uncorrected for heart rate) was seen in patients with subjectively poor RV systolic function. In our patient group, there was no correlation of S:D ratio z-score with E/e’ ratio, but there was a negative correlation with CVP. Our measured CVPs were within a close range (6–15 mmHg), which were all acceptable for a cavopulmonary connection. This merits further investigation in patients with both normal and abnormal filling pressures.

Study limitations
Our study population included children up to the age of 11 years and our results may not be able to be extrapolated to older children or young adults. Although relatively easy to perform, it will not always be possible to obtain analysable traces in all patients. This study was cross-sectional and the utility of echocardiographic indices when applied longitudinally was not investigated.

Conclusions
In children with HLHS, isovolumic contraction and IVRTs are significantly prolonged compared with normal. The values and trends of ejection time, systolic time, and diastolic time are no different from the normal population when age-related changes in heart rate are taken into account. Differences in the S:D time ratio between surgical stages can be accounted for by heart rate alone. MPI is elevated across all surgical stages due to the prolonged IVCT and IVRT. Neither MPI z-score nor S:D z-score significantly correlated with MRI or other echocardiographic indices of systolic or diastolic function with the exception of a negative correlation between CVP and S:D ratio z-score.

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References
Tissue Doppler time intervals


