Quantitative cineangiographic analysis of ventricular volume and mass in patients with single ventricle: relation to ventricular morphologies

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ABSTRACT With the use of biplane selective ventriculography, the ventricular volume, ejection fraction, and ventricular mass were evaluated in 28 patients with a single ventricle, and those with the left ventricular type (LV type, 12 patients) and right ventricular type (RV type, 16 patients) were compared. There were no significant differences in terms of age, hemoglobin, systemic oxygen saturation, or pulmonary-to-systemic flow ratio in the two groups. No patients with atrioventricular valve regurgitation were included. The ventricular cavity volume was calculated by the area-length method. The ventricular mass volume was determined as the shell volume created by subtracting the ventricular cavity volume from the total ventricular volume calculated by adding the free wall thickness to the chamber dimensions. The ventricular mass volume was converted to mass by multiplying by the gravity of the heart muscle. There was no significant difference between patients with the LV type and RV type of single ventricle with respect to the end-diastolic ventricular volume (188 ± 53 and 179 ± 61 ml/m² in LV and RV types, respectively), end-systolic volume (88 ± 31 and 84 ± 27 ml/m²), or ejection fraction (0.54 ± 0.06 and 0.52 ± 0.06). The following four indexes of the ventricular mass were significantly (p < .001) lower in patients with the RV type of single ventricle: ventricular wall thickness (3.9 ± 1.2 mm in RV type vs 6.9 ± 1.9 mm in LV type), ratio of the ventricular wall thickness to the transverse diameter of the ventricle (6.8 ± 1.9% vs 12.1 ± 2.4%), ventricular mass (87 ± 35 vs 160 ± 47 g/m²), and ratio of ventricular mass to end-diastolic volume (0.48 ± 0.11 vs 0.88 ± 0.17 g/ml). There was a positive linear correlation between the ventricular mass index and the pulmonary-to-systemic blood flow ratio in patients with LV type (r = .71, p < .01) but no correlation was seen in those with RV type. These results suggest that there is inadequate ventricular hypertrophy (insufficient ventricular mass to ventricular volume) in patients with the RV type of single ventricle compared with that in those with the LV type and this may lead to abnormal contractile state and poor adaptation of ventricular function in patients with the RV type of single ventricle.


FOR SINGLE VENTRICLE in which the dominant chamber has a right (RV type), left (LV type), or indeterminate morphology, various surgical approaches have been applied, including both palliative1–3 and definitive procedures.4–9 Moodie et al.,10 11 however, reported that unoperated patients with a single ventricle of the RV type apparently have a grim prognosis, and that their long-term prognosis is not actually improved by palliative procedures. Furthermore, the results of definitive surgery for this type of single ventricle are still discouraging.12 13 The cause of these less than satisfactory results may partly be the higher incidence of associated anomalies in patients with single right ventricle.14 15 Ventricular dysfunction may be a more important cause of this difficulty in clinical management, but this has not yet been proven.

After documenting frequent late deaths from congestive heart failure after the Blalock-Taussig shunt operation in patients with single right ventricle, we hypothesized that this type of single ventricle may result in poor functional adaptation to volume overload. Although analysis of ventricular cavity size and extent of myocardial hypertrophy is essential in the evaluation of ventricular function of a single ventricle, there has been little information published on quan-
tative analysis of ventricular hypertrophy or the comparison of these variables in patients with LV type and those with RV type single ventricle. The purposes of this study were to describe the ventricular volume and mass of single ventricles and to elucidate the relationship of these variables to ventricular morphology in patients with this defect.

Methods

Patients. Twenty-eight children with a single ventricle were investigated in this study. The anatomic findings and previous treatments that the patients received are summarized in table 1. Twelve patients had a single left ventricle characterized by a smooth trabecular architecture on the angiogram. In 16 patients, including three with mitral atresia, the main ventricular chamber had a rough trabecular architecture compared with the single left ventricle on the angiogram. With regard to the morphology of the atroioventricular valve, two atroioventricular valves were more common in patients with the LV type of single ventricle (83%), whereas common atroioventricular valve was more frequent in those with the RV type (69%). All but four patients with the LV type of single ventricle had varying degrees of pulmonary outflow obstruction. Two of four without pulmonary stenosis had undergone previous pulmonary artery banding. Forty-two percent of the patients with LV type and 38% of those with the RV type of single ventricle had previously undergone a Blalock-Taussig shunt operation. No patients with atroioventricular valve regurgitation on the ventriculogram were included in this study so that ventricular function could be compared in the two groups under similar hemodynamic and volume overload conditions. A comparison of the basic clinical findings in the groups is shown in table 2. The ages at the time of investigation ranged from 7 months to 17 years in the LV type group and from 3 months to 14 years in the RV type group. There were no significant differences between the groups in terms of age, hemoglobin, systemic oxygen saturation, or pulmonary-to-systemic flow ratio obtained at cardiac catheterization.

Angiocardiographic studies. All patients underwent cardiac catheterization and biplane 35 mm cineangiocardiography (Philips PolyaDiagnost C) under anesthesia with ketamine hydrochloride. After pressure measurement and oximetry, ventriculograms were filmed in the posterior-anterior and lateral projections at 60 or 90 frames/sec after injection of contrast medium (diatrizoate 76%, 1.0 to 1.2 ml/kg body weight) into the main ventricular chamber. Immediately after the ventriculogram was obtained a steel sphere of 30 mm diameter was filmed, for calibration purposes, at the spatial location that the ventricle had occupied.

Measurements. The border of the ventricular cavity in both projections was traced manually at end-diastole and end-systole during the sinus rhythm on the recorded selective ventriculogram (figure 1). The largest ventricular projection was assumed to represent end-diastole and the smallest end-systole. The ventricular cavity area and the length of the long axis were measured. In addition, on the each posteroanterior projection the outer margin of the free ventricular wall was outlined at end-diastole. The middle third segment of the left cardiac border (and that of the right cardiac border in patients with dextrocardia) was traced (figure 1), since this region is most clearly outlined on the ventriculogram. The ventricular wall thickness was determined as an average of 30 to 50 wall thickness measurements of this segment. These measurements were processed with a digitizer (NEC PC-8875) connected to a computer (NEC PC-9801).

Calculation of ventricular volume. The ventricular volume was calculated according to the area-length method by calibration with a steel sphere 30 mm in diameter. No regression equation was applied. The ventricular volume was expressed as the indexed value for the body surface area.

Ventricular mass calculation. The ventricular mass volume was determined as the shell volume created by subtracting the ventricular cavity volume from the total ventricular volume (the cavity volume plus mass volume) calculated by adding the ventricular wall thickness to the chamber dimensions. The formula used was as follows: \( VMV = \frac{4}{3} \left( \frac{da}{2} + h \right) \times \left( \frac{dl}{2} + h \right) \times \left( \frac{1}{2} + h \right) - \frac{4}{3} \frac{da}{2} \times \frac{dl}{2} \times \frac{1}{2} \)

where \( VMV = \) ventricular mass volume; \( da = \) transverse diameter calculated from the posteroanterior projection; \( dl = \) transverse diameter calculated from the lateral projection; \( h = \) end-diastolic wall thickness; \( l = \) maximum length of the long axis, whether on the posteroanterior or lateral projection.

**Table 1**

<table>
<thead>
<tr>
<th>Main ventricular chamber (n)</th>
<th>AV valves</th>
<th>Pulmonary outflow</th>
<th>Palliations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Common</td>
<td>Double inlet</td>
<td>AV Atresia</td>
</tr>
<tr>
<td>LV type (12)</td>
<td>2 (17%)</td>
<td>10 (83%)</td>
<td>0</td>
</tr>
<tr>
<td>RV type (16)</td>
<td>11 (69%)</td>
<td>2 (13%)</td>
<td>3</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Main ventricular chamber</th>
<th>Age (years)</th>
<th>Hb (g/dl)</th>
<th>SaO₂ (%)</th>
<th>Qp/Qs</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV type</td>
<td>6.4 ± 1.1</td>
<td>15.4 ± 4.1</td>
<td>81 ± 6</td>
<td>1.16 ± 0.46</td>
</tr>
<tr>
<td>RV type</td>
<td>5.7 ± 1.1</td>
<td>16.3 ± 2.1</td>
<td>77 ± 9</td>
<td>0.85 ± 0.40</td>
</tr>
</tbody>
</table>

Hb = hemoglobin concentrations; Qp/Qs = pulmonary-to-systemic flow ratio; SaO₂ = systemic oxygen saturation.
FIGURE 1. Posteroanterior angiocardiograms from a patient with LV type (left) and a patient with RV type (right) single ventricle, illustrating the ventricular cavity border (dashed line) and the outer cardiac border (arrow) used to calculate the ventricular volume, wall thickness, and mass. The ventricular wall thickness was 4.7 mm in the patient with LV type and 3.8 mm in the patient with RV type single ventricle.

The ventricular mass volume was converted to the ventricular mass by multiplying by the specific gravity of the heart muscle (1.05). Ventricular mass was expressed as the ventricular mass index (VMI) corrected for the body surface area and the ratio of ventricular mass to end-diastolic volume (VM/EDV).

Statistical analysis. Data are expressed as the mean ± SD. Statistically significant differences in the ventricular function data from the two groups were determined by unpaired t test. The relationship between ventricular mass and the pulmonary-to-systemic flow ratio were evaluated by linear regression analysis.

Results

The ventricular volume and mass data are listed in table 3.

Ventricular volume and ejection fraction. The end-diastolic volume ranged from 93 to 279 ml/m$^2$ (188 ± 53 ml/m$^2$) in patients with LV type single ventricle and from 63 to 270 ml/m$^2$ (179 ± 61 ml/m$^2$) in those with the RV type. The end-systolic volume index ranged from 41 to 152 ml/m$^2$ (88 ± 31 ml/m$^2$) in patients with LV type single ventricle and from 41 to 152 ml/m$^2$ (84 ± 27 ml/m$^2$) in those with the RV type. There were no significant differences in these volume indexes in the two groups. The ejection fraction was depressed (0.54 ± 0.06, LV type; 0.52 ± 0.06, RV type) in both groups and there was no significant difference between them.

Ventricular wall thickness. Ventricular wall thickness ranged from 4.5 to 11.3 mm (6.9 ± 1.9 mm) in patients with LV type single ventricle, and from 2.1 to 6.5 mm (3.9 ± 1.2 mm) in those with the RV type; this difference was significant (p < .001). The ratio of ventricular wall thickness to the transverse diameter of the ventricle calculated from the posteroanterior projection

<table>
<thead>
<tr>
<th>Main ventricular chamber</th>
<th>EDVI (ml/m$^2$)</th>
<th>ESVI (ml/m$^2$)</th>
<th>EF (%)</th>
<th>VWT/TDVC (%)</th>
<th>VMI (g/m$^2$)</th>
<th>VM/EDV (g/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV type</td>
<td>188 ± 53</td>
<td>88 ± 31</td>
<td>0.54 ± 0.06</td>
<td>12.1 ± 2.4</td>
<td>160 ± 47</td>
<td>0.88 ± 0.17</td>
</tr>
<tr>
<td>RV type</td>
<td>179 ± 61</td>
<td>84 ± 27</td>
<td>0.52 ± 0.06</td>
<td>6.8 ± 1.9</td>
<td>87 ± 35</td>
<td>0.48 ± 0.11</td>
</tr>
<tr>
<td>p value</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

EDVI = end-diastolic volume index; EF = ejection fraction; ESVI = end-systolic volume index; VWT/TDVC = ratio of ventricular wall thickness to transverse diameter of ventricular cavity.
was also significantly (p < .001) smaller in patients with RV type single ventricle (4.7% to 13.0%, 6.8 ± 1.9%) than in those with the LV type (7.4% to 15.5%, 12.1 ± 2.4%) (figure 2). Eleven of 12 patients with the LV type single ventricle had a ratio of greater than 10%. Conversely, 15 of 16 patients with the RV type defect had a ratio of less than 8%.

Ventricular mass. VMI ranged from 85 to 260 g/m² (160 ± 47 g/m²) in the LV type group and from 33 to 152 g/m² (87 ± 35 g/m²) in the RV type group, a significant difference (p < .001; figure 3). VM/EDV ranged from 0.57 to 1.14 g/ml (0.88 ± 0.17 g/ml) in patients with LV type single ventricle and from 0.35 to 0.79 g/ml (0.48 ± 0.11 g/ml) in those with the RV type, and VM/EDV was also significantly (p < .001) smaller in the RV type group (figure 4). The value of 0.7 g/ml for VM/EDV clearly distinguished between the two types of single ventricle in all but two patients (one in each group). The difference in ventricular mass in the two groups was enhanced by the comparison of mass with end-diastolic volume.

Relationship between ventricular mass and pulmonary-to-systemic flow ratio. There was a positive linear correlation between VMI and the pulmonary-to-systemic flow ratio in patients with LV type single ventricle (r = .71, p < .01), while no significant correlation was found in those with the RV type (r = .35; figure 5).

Discussion

There have been many reports of ventricular dysfunction in patients with tricuspid atresia17-20 or single left ventricle,21 and recently some reports that ventricular mass may affect the outcome of the Fontan procedure for single right ventricle.13, 22 However, the evaluation of ventricular mass or function has not been attempted in comparable patient groups with single left and right ventricles.

In this study, it was shown that there was no significant difference in the ventricular volume characteristics in patients with the two types of single ventricle, a finding that is consistent with previous studies.23, 24 The ventricular mass value, however, including the wall thickness, was significantly smaller in the RV type than in the LV type group. VM/EDV and the wall thickness–to–chamber diameter ratio in patients with RV type single ventricle were also significantly reduced compared with those in patients with the LV type. Thus, low ventricular mass and insufficient mass relative to chamber volume have been demonstrated in patients with RV type single ventricle. These data also suggest that ventricular contractile state and function may be different in patients with the two types of single ventricle, even though they have similar ventricular volumes and pump function.
There was no significant difference between the two groups in terms of the age at investigation, systemic oxygen saturation, or hemoglobin values. There was also no significant difference in the pulmonary-to-systemic flow ratio or in the end-diastolic volume. The degree of volume overload is directly related to the pulmonary blood flow\textsuperscript{17}; therefore, the two groups in this study were compared under similar hemodynamic and ventricular volume overload conditions. The difference in ventricular mass and VM/EDV thus appear to be mainly related to the morphologic difference between the two types of single ventricle.

The methodologic validity of the measurement of ventricular mass in this study may be controversial. Accuracy of ventricular mass data is subject to limitations due to the chamber shape and nonuniformity of wall thickness. However, the shape of the main chamber of a single ventricle observed angiographically and echocardiographically in this study appeared to be elliptical or spherical, and this was true in patients with LV and RV type of single ventricle. Regarding the uniformity of wall thickness, we also performed two-dimensional echocardiographic studies. Figure 6 illustrates short-axis echocardiograms from the two patients whose ventriculograms are shown in figure 1. The ventricular wall, excluding the papillary muscle and trabeculae, has almost uniform thickness in patients with both types of single ventricle. Asymmetrical ventricular hypertrophy was not detected in any of the 22 patients undergoing the echocardiographic study. In addition, we measured the wall thickness of an adequate lateral free wall of the main chamber on the cineangiogram. For the above reasons, we concluded that ventricular mass could be calculated in patients with single ventricle by basically the same method with the use of a shell model in left ventricle.\textsuperscript{16}

Confirmation of the method for measurement of the wall thickness from the cineangiogram is possible with other, more direct, methods such as echocardiography and autopsy. We evaluated wall thickness by two-dimensional echocardiography in eight patients with each type of single ventricle and obtained a significant linear correlation between the cineangiographic (y) and echocardiographic (x) measurements: $y(\text{mm}) = 0.984x - 0.166$ ($r = .99, p < .001$). We also measured wall thickness in one postmortem heart with single right ventricle. The heart was kept in saline for 12 hr after autopsy and a ventriculogram was prepared. Figure 7 shows the cineangiogram of this heart filled with contrast medium. On this ventriculogram the lateral and anterior wall thickness measured 4.6 and 4.9 mm, respectively. The wall thickness actually measured 4.3 mm for the midlateral wall and 4.6 mm for the midanterior wall, respectively. These findings show only a minimal difference between the two measurements. These data confirm that ventricular wall thickness can be evaluated from the cineangiogram of a single ventricle. Despite some methodologic limitations and assumptions necessary for use of this technique, our
FIGURE 6. Short-axis view echocardiograms from the two patients whose ventriculograms are shown in figure 1. Echocardiographic measurement of lateral wall thicknesses (arrow) was 4.8 mm in the patient with LV type single ventricle (left) and 4.1 mm in the patient with the RV type (right).

FIGURE 7. Posteroanterior projection from the ventriculogram of one postmortem heart with RV type single ventricle. The lateral wall thickness (arrow) was 4.6 mm angiographically and 4.3 mm by direct measurement.
data presumably represent the true ventricular wall thickness and mass of a single ventricle.

VM/EDV has been suggested as a useful variable for the evaluation of functional adaptation of the volume-loaded ventricle in various situations, but mainly in the assessment of patients with acquired heart diseases. 25–27 This concept has also been introduced in the study of congenital heart disease by Jarmakani et al. 28 VM/EDV was 0.88 g/ml in patients with the LV type of single ventricle and was similar to that in the normal left ventricle (1.01 g/ml), as reported by Onnasch et al. 29 and that in patients with tricuspid atresia (1.01 g/ml), as reported by Nishioka et al. 18 On the other hand, VM/EDV in our study was remarkably low in patients with the RV type of single ventricle compared with that in patients with the LV type. Thus, poor adaptation to volume overload may be present in patients with RV type single ventricle. These results indicate that in the presence of the RV type defect there is inadequate ventricular hypertrophy in response to volume overload (insufficient ventricular mass relative to chamber volume). Ventricular hypertrophy is a major compensatory mechanism for increased volume and pressure overload. 25 Systemic-pulmonary arterial shunts and atroventricular valve regurgitation significantly increase the ventricular volume by increasing volume overload, and the latter especially may lead to an unfavorable outcome. It is common after the Fontan procedure for patients to have hemodynamic derangement, such as low pulsatile pulmonary flow, elevated right heart pressure, and systemic venous congestion. The low VM/EDV in patients with the RV type of single ventricle, suggesting increased ventricular wall stress, may carry a risk of afterload mismatch, 26, 30 with possible deterioration and decompensation as a result of the additional volume load or the hemodynamic derangement.

The poor natural history and results of surgical treatment of the RV type of single ventricle 10–13 may be mainly related to these findings of poor adaptation of ventricular function to stress. In our earlier study, patients with RV type single ventricle and low VM/EDV were shown to have an increased risk of late death due to congestive heart failure after a Blalock-Taussig shunt operation. Application of the systemic-to-pulmonary artery shunt operation has to be considered carefully for such patients with the RV type of low ventricular mass.

In conclusion, our data demonstrate that ventricular wall thickness and mass are significantly less in patients with the RV type than in those with the LV type of single ventricle, although neither the ventricular vol-

References


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