Right and Left Heart Size and Function in Infants with Symptomatic Coarctation

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SUMMARY Right and left heart volumes, ejection fractions and ventricular outputs were determined from biplane cineangiograms in infants with symptomatic coarctation of the aorta and correlated with clinical and hemodynamic alterations. Patients were divided into two age groups: group 1, ages 3.5 to 14 days and group 2, 5 weeks to 7½ months. Infants in group 1 had severe depressions of left ventricular ejection fraction and output associated with normal left ventricular size. The massive cardiomegaly in these infants results from right heart enlargement secondary to left-to-right atrial shunting, and pulmonary hypertensive right heart failure, and possibly a more distensible right than left ventricle. Infants in group 2 also have right to left heart enlargement. Group 2 patients differ from group 1 infants in having less impairment of left heart pump function and significant left ventricular myocardial hypertrophy. Echocardiographic measurements of left ventricular pump function are normal or increased in postoperative patients. Thus alterations of left ventricular function in infants with symptomatic coarctation appear to be largely afterload related and do not indicate permanent impairment of left ventricular contractile function.

IN INFANTS with symptomatic coarctation of the aorta, invariably there is cardiac enlargement which usually is massive and associated with an abnormal vascular pattern on the chest film suggesting either pulmonary venous congestion or increased pulmonary flow. These infants show signs of severe congestive heart failure, and qualitative assessment of angiograms indicates poor left ventricular function. Despite these well-known findings, the localization and quantitation of abnormalities of cardiac chamber size and ventricular function in this syndrome have not been reported. The purpose of this investigation was to determine right and left heart volumes, ejection fractions, and ventricular outputs in infants with symptomatic coarctation of the aorta and to attempt to correlate these findings with clinical and hemodynamic alterations.

Materials and Methods

All data were obtained during routine diagnostic cardiac catheterization. The patients were separated into two age groups whose clinical courses were quite different. Group 1 consisted of a perinatal group of ten infants who presented with severe congestive heart failure and underwent cardiac catheterization between ages 3.5 and 14 days. Nine of the ten infants had resection of the coarctation performed shortly after the catheterization. All but one patient survived the operation and are currently doing well. One infant was treated medically and continues to do well.

Group 2 consisted of seven infants whose ages ranged from five weeks to seven-and-a-half months. These patients presented with symptoms suggestive of mild chronic congestive heart failure. Five of the seven patients had resection of the coarctation performed within a few days of the catheterization, and all survived the operation. One patient died two months later of unknown causes. One patient had the coarctation resected six months after catheterization, and one patient continues to do well on medical therapy.

One patient is included both in group 1 and group 2. This patient was initially studied at ten days of age and underwent resection of a coarctation shortly following this catheterization. At two-and-a-half months he was readmitted with a recurrence of the coarctation. The changes that took place between the two studies are discussed below.

All patients had a short juxta ductal coarctation. There were no patients with severe hypoplasia of the aortic arch as determined by arch measurements which were within 75% of the diameter of the ascending aorta. Patients with significant aortic or mitral valve disease by clinical, echocardiographic, or catheterization findings were excluded from this study. A number of patients may have had bicuspid aortic valves, but significant left ventricular to aortic pressure differences were excluded either at catheterization or by the subsequent absence of a systolic murmur on follow-up. Patients in group 1 had a small degree of left-to-right ductal shunting at catheterization. There was no evidence of an oxygen stepup at the pulmonary artery level in these patients, and the ductal shunting on angiography was considered small. There was no ductal shunting in patients in group 2. Two patients in group 1 had small ventricular septal defects at initial catheterization. These defects were judged to be small by selective cineangiography in which the lesion appeared to be less than one-fourth of the aortic diameter and also by the finding of a left ventricular volume within normal limits.

There was detectable shunting at the atrial level by oxygen measurements and cineangiography in nine out of ten patients in group 1. Only two of seven patients in group 2 had atrial level shunting.

Vital statistics and hemodynamic data are presented in table 1 for the two groups. Group 1 differed from group 2 in having higher heart rates, right atrial mean pressures, right ventricular end-diastolic pressures, right ventricular peak pressures and left atrial mean pressures, and lower left ventricular peak pressures.

Right and left heart volume data were obtained by previously published methodology and compared to normal values.1 2 These data are presented in terms of percent of predicted normal for patient size. Oxygen determinations for shunt measurements were made with reflectance oximetry.

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Results

Figure 1 shows the severe degree of cardiomegaly on X-ray that was present in all patients in group 1. It was not possible to determine from routine chest films which chambers were involved in the enlargement.

Figure 2 shows the cardiothoracic ratio for patients in group 1 versus group 2. All patients in group 1 were well above 0.60 with an average value of 0.70 versus 0.62 for patients in group 2. Although there was considerable overlap, this difference was statistically significant ($P < 0.04$).

Figure 3 shows left ventricular end-diastolic volume and left ventricular systolic output derived from the cineangiographic measurements for patients in group 1 and group 2. The normal values are indicated by the shaded areas. Left ventricular end-diastolic volume was normal or less than normal in all patients in group 1 with an average value of 81.6% of normal. This value is not significantly different from normal. In contrast, patients in group 2 show values which are normal or well above normal with an average value of 136% of normal. This value is significantly different from normal and significantly greater than that found for patients in the perinatal group, table 2.

Left ventricular systolic output is severely depressed in the perinatal group averaging only 39% of normal. In contrast, LVSO averages 93% for the older infants and is not significantly different from normal, but is significantly different from the perinatal value.

Figure 4 shows right ventricular end-diastolic volume and systolic output plotted for the same patient groups. There were two patients in both groups whose right ventricular cineradiographs were inadequate for volume analysis. Right ventricular end-diastolic volume is increased in all but one patient in each group. The values are significantly increased from normal but not significantly different from each other.

Right ventricular systolic output is either normal or increased in all patients studied. These values are not different from each other. The one patient in group 2 with a very large value for right ventricular end-diastolic volume and systolic output had a large atrial shunt at the time of catheterization.

Figure 5 shows right ventricular end-diastolic volume as a percentage of normal plotted against the Qp/Qs ratio deter-

![Figure 1. Posteroanterior chest film of a nine-day-old infant who presented with severe congestive heart failure secondary to an isolated coarctation. The thymic shadow contributes to the cardiac silhouette on the upper right. Cardiothoracic ratio is 0.69.](http://circ.ahajournals.org/doi/fig/10.1161/01.CIR.56.4.642)

![Figure 2. Cardiothoracic ratio for the perinatal vs the older infants. Values are significantly different ($P < 0.04$).](http://circ.ahajournals.org/doi/fig/10.1161/01.CIR.56.4.642)
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Table 2. Coarctation In Infancy: Volume Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>X ± SD</th>
<th>Range</th>
<th>N</th>
<th>P value group 1 vs normal</th>
<th>X ± SD</th>
<th>Range</th>
<th>N</th>
<th>P value group 2 vs normal</th>
<th>P value group 1 vs group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. LVEDV (%)</td>
<td>81 ± 22</td>
<td>44-113</td>
<td>10</td>
<td>NS</td>
<td>136 ± 52</td>
<td>73-229</td>
<td>7</td>
<td>&lt;0.02</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>2. LVEF</td>
<td>0.35 ± 0.09</td>
<td>0.28-0.58</td>
<td>10</td>
<td>&lt;0.001</td>
<td>0.50 ± 0.07</td>
<td>0.38-0.60</td>
<td>7</td>
<td>&lt;0.004</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>3. LVSO (%)</td>
<td>39 ± 12</td>
<td>21-54</td>
<td>10</td>
<td>&lt;0.001</td>
<td>93 ± 36</td>
<td>53-137</td>
<td>7</td>
<td>NS</td>
<td>&lt;0.007</td>
</tr>
<tr>
<td>4. RVEDV (%)</td>
<td>102 ± 51</td>
<td>84-259</td>
<td>9</td>
<td>&lt;0.001</td>
<td>166 ± 63</td>
<td>91-271</td>
<td>6</td>
<td>&lt;0.002</td>
<td>NS</td>
</tr>
<tr>
<td>5. RVF</td>
<td>0.47 ± 0.09</td>
<td>0.34-0.63</td>
<td>9</td>
<td>&lt;0.003</td>
<td>0.55 ± 0.13</td>
<td>0.41-0.75</td>
<td>6</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>6. RVSO (%)</td>
<td>125 ± 32</td>
<td>77-185</td>
<td>9</td>
<td>&lt;0.03</td>
<td>133 ± 68</td>
<td>73-257</td>
<td>6</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>7. LVM (%)</td>
<td>107 ± 8</td>
<td>100-117</td>
<td>4</td>
<td>NS</td>
<td>222 ± 97</td>
<td>127-413</td>
<td>7</td>
<td>&lt;0.001</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>8. LAMax (%)</td>
<td>96 ± 34</td>
<td>69-139</td>
<td>5</td>
<td>NS</td>
<td>157 ± 49</td>
<td>93-242</td>
<td>6</td>
<td>&lt;0.001</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>9. RAMax</td>
<td>183 ± 53</td>
<td>107-231</td>
<td>4</td>
<td>&lt;0.003</td>
<td>141 ± 56</td>
<td>93-221</td>
<td>4</td>
<td>&lt;0.02</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: LVEDV = left ventricular end-diastolic volume as % of predicted normal; LVEF = LV ejection fraction; LVSO = LV systolic output at % of normal; RVEDV = right ventricular end-diastolic volume; RVEF = RV ejection fraction; RVSO = RV systolic output; LVM = LV wall mass; LAMax = left atrial maximal volume; RAMax = right atrial maximal volume.

The ejection fractions for the right and left ventricles are given in FIGURE 3. The RV ejection fraction averaged 0.47 in the perinatal group, which is significantly less than the normal value of 0.65. In the older infant group, RVEF averaged 0.55 and was not significantly different from normal nor from the perinatal group. The one patient who had two studies because of a recoarctation showed a significant increase in the RV ejection fraction from a value well below normal to a value within normal limits.

The left ventricular ejection fraction was severely depressed in the perinatal group averaging 0.35, a value significantly lower than normal. This value was also depressed in the older infant group but was significantly higher than that for the perinatal group. Again, the patient who was studied on two occasions showed a significant increase in the LV ejection fraction.

FIGURE 7 shows values for left ventricular wall mass and left ventricular ejection fraction. Wall mass could be determined in four patients in group 1 and seven patients in group 2. Wall mass was within normal limits in group 1, but was significantly increased for patients in group 2. The one patient with two studies showed a significant increase in left ventricular wall mass in the two-and-a-half months between studies. The values for LV ejection fraction are shown for this same group of patients. The LV ejection fraction was significantly greater in the older infant group than in the perinatal group, and the one patient who had two studies showed a significant increase in ejection fraction between the two studies.

In FIGURE 8, left atrial maximum volume (LAMax) and right atrial maximum volume (RAMax) are shown in patients in whom these variables could be determined. LAMax averaged 96% in group 1 and was not significantly different from normal. This variable averaged 157% of normal in the older infant age group and was significantly different from normal and from the perinatal group. Average values for right atrial maximum volume were increased for both

FIGURE 4. Right ventricular end-diastolic volume and systolic output for the perinatal vs the older infant group.
groups, although this increase in group 2 was due largely to one very high value.

RAMax is plotted as a function of Qp/Qs in figure 9. This variable was increased in six of nine patients in whom it could be calculated. Four patients with large increases in right atrial maximum volume had significant atrial shunts, whereas four of five patients with normal or only slightly increased right atrial maximum volume had no detectable shunting.

Figure 10 shows left ventricular shortening fractions obtained from echocardiograms in patients in whom this information was available. The perinatal group is shown in the left panel and the older infant group in the right panel. Shortening fractions obtained from the midportion of the lateral view of the left ventricle on cineangiograms are indicated in parentheses. These correlated well with the echocardiographic examinations as shown. Two patients had examinations performed before and following operation. These data show significant increases in the shortening fraction from values which were below normal preoperatively to normal or above normal postoperative values.

Discussion

Symptomatic isolated coarctation in infancy usually is secondary to a juxtaglucal posterior aortic shelf which becomes obstructive when the aortic end of the ductus arteriosus constricts. The studies of Rudolph and coworkers and Talner and Berman have demonstrated convincingly this sequence of events. Postnatal development of the aortic obstruction accounts for the sequence of events which begins with a neonate who has a normal physical exam and normal femoral pulses and then progresses rapidly to severe low output heart failure usually between the ages of 3 and 14 days when the aortic end of the ductus arteriosus constricts. The probable pathophysiologic events occurring after the ductal constriction are depicted in figure 11. There is an abrupt increase in the afterload which the left ventricle (LV) pumps against, with a resultant decrease in LV output and subsequently in renal blood flow. Fluid retention occurs, contributing to overall right heart enlargement and pulmonary venous congestion. Left ventricular and left atrial diastolic pressures increase with subsequent opening of the foramen ovale and left-to-right atrial shunting. The left atrium and left ventricle probably do not enlarge significantly because of the “let off” of volume at the atrial level secondary to the shunt. The increase in pulmonary venous pressure is a major contributing factor to the development of pulmonary arterial hypertension. The elevated pulmonary arterial pressure contributes importantly to the poor right ventricular pump function which is expressed as a low ejection fraction.

This sequence of events would account for the majority of the findings which we report in the perinatal group: atrial left-to-right shunting, pulmonary hypertension, right heart enlargement, poor RV pump function, normal or small left heart, poor LV pump function, and diminished LV output. There are some minor discrepancies, however, when one correlates the perinatal catheterization data with this proposed
pathophysiological sequence. There were several infants in the perinatal group who had large right ventricles despite oximetry and cine evidence for small atrial shunts. Possible explanations for this apparent dichotomy include underestimation of the atrial shunt, pulmonary hypertensive right ventricular failure, and a more distensible right than left heart in the perinatal heart which is subjected to volume and pressure loading. The latter explanation is based on the fact that right ventricular geometry probably is more adapted for low pressure pumping than the left ventricle. Thus in coarctation, when both ventricles are subjected to volume loading (fluid retention secondary to decreased renal flow) as well as an increased afterload (pulmonary hypertension-RV, aortic constriction-LV), the right ventricle may dilate to a much greater degree than the left ventricle.

The older infant group requires added explanation. These patients showed normal or increased left ventricular size, an improved LV ejection fraction and output compared to the younger infants, and comparable right heart enlargement. The reason that these patients did not present with severe heart failure in infancy perhaps is related to a less severe acute obstruction with ductal constriction or a more gradual ductal constriction with time enough for myocardial adaptation. The fetal lamb,7 neonatal kitten8,9 and rat10 have a diminished myocardial force generating capacity/cross sectional area of cardiac tissue. In addition decreased right and left ventricular sympathetic nerve endings have been reported in neonatal rat,11 rabbit,12 and lamb.13 Thus the capacity of the newborn heart to adapt to hemodynamic overloads is limited in certain mammals, and this limitation may well apply to human neonates with coarctation who would thus be ill equipped to cope with a sudden increase in afterload and might be expected to show a decreased left ventricular ejection fraction under such conditions. The excellent correlation of an increase in LV muscle mass with an improvement in LV ejection fraction and output in group 2 patients indicates that myocardial hypertrophy was undoubtedly a major factor in their delayed presentation in only mild heart failure at an average age of three months. Older children with significant coarctation have normal left ventricular volumes and increased left ventricular wall mass and ejection fraction14 — findings which support the adaptive response of myocardial hypertrophy which can normalize pump function measurements in the presence of an increased resistance to LV outflow.

Figure 8. Left and right atrial maximum volume for the two age groups.

Figure 9. Right atrial maximum volume as a function of Qp/Qs ratio.

Figure 10. Left ventricular shortening fraction obtained by echocardiogram before and following operation. Figures in parentheses indicate cineangiographic measurements of shortening fraction obtained from lateral view.
The presence of right heart enlargement in the older infants can be explained by an atrial shunt in only one patient. In this group, again the right ventricle may be enlarged due to a more distensible right than left ventricle in this age group. Experimental studies have demonstrated such differences in ventricular distensibility in neonatal lambs.\(^\text{15}\)  

The possibility of depressed myocardial contractile function in these patients is another consideration. An acute increase in afterload is known to decrease the ejection fraction and circumferential fiber shortening velocity (VCF).\(^\text{16, 17}\) Thus the normal or increased echocardiographic left ventricular shortening fractions postoperatively suggest that the preoperative depressions of LV pump function may be largely afterload-related. We are concerned that the three month old infant with the largest left ventricle in this study (229% of normal) coupled with the lowest LV ejection fraction (0.38) had an associated cardiomyopathy, perhaps endocardial fibroelastosis. He had no difficulty at operation, however, and four months following operation he had normal or increased echo values for LV shortening fraction (55%), VCF (2.08), and a low value for LVPEP/ET (0.18). His cardiothoracic ratio is now 0.54 versus 0.70 preoperatively. Thus a permanent alteration in left ventricular contractile function does not appear to be a significant factor even in infants whose function appears most abnormal preoperatively.

The data derived from this study have led us to draw the following conclusions: 1) Symptomatic infants with isolated coarctation in the first two weeks of life have severe depressions of left ventricular ejection fraction and output. These alterations appear to be largely afterload-related and do not indicate permanent impairment of left ventricular contractile function. 2) The massive cardiomegaly in these infants is right heart enlargement secondary to left-to-right foramen ovale shunting, pulmonary hypertensive right heart failure, and possibly to a more distensible right than left ventricle. 3) Infants who present with a milder degree of heart failure beyond one month of age have right, and to a lesser degree left, heart enlargement. 4) Myocardial hypertrophy is a major determinant of normalization of pump function abnormalities in older infants with coarctation.

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LUNG HYPOPLASIA IN CONGENITAL PVS/De Troyer, Yernault, Englert

SUMMARY The pulmonary function of ten adult patients with congenital pulmonary valvar stenosis was investigated. The patients clearly showed smaller lungs than healthy control subjects of equivalent age and height; lung elastic recoil pressure was normal at any given percentage of measured total lung capacity, indicating that postnatal parenchymal damage is not the cause of the small lungs. The lung diffusing capacity for carbon monoxide was reduced, reflecting the anatomical alterations of the pulmonary vascular bed. Finally, the maximal flow-static recoil curves showed a fixed (not dynamic) reduction of airway dimensions: the critical transmural pressure in the collapsible flow-limiting segment (Ptm) was normal, but the conductance of the S segment was lowered. These abnormalities most likely reflect inadequate development of the lung and suggest that pulmonary blood pressure may be an important determinant of lung growth in the postnatal period.

THE POSTNATAL DEVELOPMENT OF THE LUNG

has been the subject of extensive research in the last 20 years. Investigators generally agree that most of the alveoli appear in the postnatal period, but the age at which alveolar multiplication ceases is still debated. Earlier data supported the view that alveolar multiplication stopped at the age of eight years, or even by the end of the first year of life. In contrast, recent morphometric investigations seem to indicate that alveolar multiplication goes on throughout childhood, and does not cease completely before somatic growth stops. This latter view is supported by recent studies of lung mechanics during growth.

Moreover, the factors affecting lung growth in the postnatal period are not well understood, as discussed by Thurbeck in a recent and extensive review. Until now, the amount of blood flow through the lung has not been considered an important determinant of parenchymal development. This conclusion was based only on morphologic findings made in a few cases of congenital lobar overinflation. Human lung growth in conditions of abnormal pulmonary blood flow and pressure has not been studied. The present work reports the investigation of lung mechanics in ten patients with congenital pulmonary valvar stenosis in order to elucidate the role of pulmonary hemodynamics in lung growth during the postnatal period.

Lung Hypoplasia in Congenital Pulmonary Valve Stenosis

ANDRE DE TROYER, M.D., JEAN-CLAUDE YERNault, M.D., AND MARC ENGLERT, M.D.

Material and Methods

Lung mechanics were measured in ten adult nonsmoking patients with congenital pulmonary valvar stenosis, four men and six women whose ages ranged from 16 to 34 years (mean ± SEM: 22 ± 2 years). The results were compared with those obtained in ten healthy young subjects of equivalent age and height, who had no clinical, radiographic or functional evidence of respiratory disease. All patients had a well-documented congenital pulmonary valvar stenosis; the valvar stenosis was mild in one subject, moderate in three and severe in six, based on the criteria used by Johnson and co-workers. None of the patients had a history of lung disease; all patients but one had a normal cardiothoracic index on chest X-ray. In three patients, the pulmonary valvar stenosis was associated with a small right-to-left shunt, due to a ventricular septal defect in one case, and to a patent foramen ovale in two cases.

The techniques used for pulmonary function studies have been described in detail elsewhere. All pulmonary function tests were carried out with the patient in the sitting position. Vital capacity (VC), total lung capacity (TLC), and forced expiratory volume in 1 sec (FEV1) were recorded by spirometry, in conjunction with measurement of functional residual capacity (FRC) and of residual volume (RV) by the helium dilution technique. Lung diffusing capacity for carbon monoxide (DLco) and Krogh's constant (Kco) were measured by the single-breath method.

Airway resistance (Raw) and plethysmographic FRC were measured in a constant volume body plethysmograph. Plethysmographic TLC was calculated by adding the plethysmographic FRC to the inspiratory capacity obtained.
Right and left heart size and function in infants with symptomatic coarctation.
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