

## Ventricular Performance in Congenital Heart Disease

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**C**ongenital cardiac defects can be associated with a wide variety of conditions of volume and pressure overloading of the right, left, or both ventricles. In certain conditions, overloading of one ventricle is associated with marked underloading of the opposite ventricular chamber. These alterations in hemodynamics can have profound influence on ventricular performance. In more complex conditions, the superimposition of cyanosis on various volume and pressure overloading conditions further complicates the picture and can result in additional effects on myocardial performance. Finally, surgical therapy and the problems associated with the intraoperative ischemia necessary for repair are additional factors leading to alterations in myocardial performance in patients with congenital cardiac defects. The time course over which irreversible changes in myocardial function occur in patients with congenital heart disease remains speculative in most instances and is probably dependent on duration and extent of hemodynamic overload, of cyanosis, and of perioperative myocardial injury. The purpose of this review is to summarize existing data regarding ventricular performance in patients with congenital heart disease before and after surgical intervention.

### Ventricular Response to Volume Loading

In Figure 1, schematic pressure–volume loops for a normal 8-year-old child are shown to illustrate the concepts of acute increase in both preload and afterload. Previously published data have indicated that the average values for hemodynamic variables in such a patient would be an end-diastolic volume of 71 ml/m<sup>2</sup>, ejection fraction of 63%, end-diastolic pressure of 10 mm Hg, and cardiac index of 4.5.<sup>1</sup> The concept of preload reserve is illustrated by an acute increase in venous return such as might occur with intravenous therapy. Although experiments in conscious dogs indicate that end-diastolic volume increase with acute volume loading may be limited to 9–14%,<sup>2,3</sup> a larger increase in end-diastolic volume (Figure 1) might occur in a child in an intensive care

unit with volume increasing by 50%, at which time end-diastolic pressure would increase from approximately 10 to 25 mm Hg. By the Frank Starling mechanism, the heart pumps out whatever volume is presented to it over a moderate range; thus, with heart rate unchanged, cardiac index would increase from 4.5 to 7.9 and ejection fraction would increase from 63% to 75%. Under acute loading conditions, it generally is not possible to increase preload to a much greater extent because of the pericardial restraint and intrinsic myocardial compliance, which cause a marked increase in end-diastolic pressure with further small changes in volume.

The situation, however, is much different in patients who have a chronic volume overload such as occurs with ventricular septal defect. Figure 1 also illustrates data from a typical patient with a large ventricular septal defect, pulmonary hypertension, and pulmonary blood flow more than twice systemic flow. End-diastolic volume is virtually twice that of normal with ejection fraction of 60% and end-diastolic pressure of only 11 mm Hg.<sup>1</sup> Thus, with chronic volume loading, there is a change in operative volume distensibility such that a large increase in diastolic volume is possible with a modest or with no increase in end-diastolic pressure. The time course over which this change occurs is unclear. Ross et al<sup>4</sup> showed a modest rightward shift in the diastolic pressure–volume curve in dogs with 3–6 weeks of ventricular dilatation resulting from an arteriovenous fistula. This change is probably due to alterations in pericardial distensibility as well as alterations in myocardial compliance, which can occur with chronic volume overload.

Previous studies on patients operated on for ventricular septal defect in childhood have revealed residual mild left ventricular dilatation, left ventricular hypertrophy, and depression of ejection fraction. In 1971, we reported 23 patients studied a mean of 2.4 years after surgery that was performed at approximately 5 years of age.<sup>1</sup> Postoperative left ventricular end-diastolic volume averaged 84 ml/m<sup>2</sup> versus a normal value of 71 ml/m<sup>2</sup>, left ventricular wall mass was 110 g/m<sup>2</sup> versus a normal value of 82, and left ventricular ejection fraction was 54% versus a normal value of 63%. All of these values were significantly different from normal. Further study revealed abnor-

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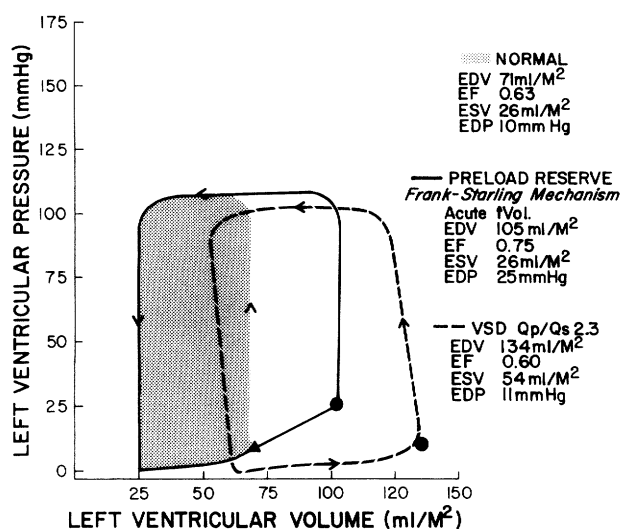


FIGURE 1. Normal pressure-volume relations contrasted with preload reserve and chronic volume overload secondary to large ventricular septal defect (VSD). EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; EDP, end-diastolic pressure.

mal isovolumetric contractile element indexes of myocardial function in a similar group of nine patients with an average age of 7 years studied approximately 1 year after closure of a large ventricular septal defect.<sup>5</sup> In addition, Maron et al<sup>6</sup> demonstrated an abnormal response to intense upright exercise in five of 11 asymptomatic patients studied 3–15 years after closure of ventricular septal defect performed at an average age of 15 years. The magnitude of the abnormality at exercise was directly related to age at surgery.

In contrast to these studies on older children, repair of a large ventricular septal defect during the first 2 years of life results in a decrease of left ventricular volume from 255% of normal to within normal limits with normal ejection fraction and wall mass as demonstrated by postoperative study approximately 1 year after surgery.<sup>7</sup> Comparison of this latter study with the prior study on older children<sup>1</sup> appears to indicate that volume loading in childhood that is not reversed by 5 years of age results in residual cardiac dilatation and functional abnormalities after repair. The results are confounded, however, by the fact that the infants were repaired using cardioplegia and myocardial protection with profound hypothermia.<sup>7</sup> These techniques were not used in the studies on the older patients cited<sup>1,5,6</sup>; thus, it is at least theoretically possible that intraoperative ischemia resulted in the minor degree of left ventricular dilatation and dysfunction reported in those patients. The time course over which irreversible dilatation and ventricular dysfunction occur in childhood with an isolated left ventricular volume overload is not clear. It is clear, however, that if intervention occurs to repair the volume load during the first

TABLE 1. Summary of Data on Ventricular Performance With Ventricular Septal Defect

Left ventricle	
Persistent dilatation, hypertrophy, and mildly decreased pump function in patients operated on during childhood	
Normal size, wall mass, and pump function in patients operated on during the first 2 years of life	
Right ventricle	
Dilated before surgery in most patients (less than left ventricular dilatation)	
No postoperative dysfunction reported	

2 years of life, residual left ventricular dilatation and/or dysfunction is uncommon.

Right ventricular volume overload also occurs with a large ventricular septal defect, although right ventricular dilatation is less than left ventricular dilatation.<sup>8</sup> There are no data to indicate the presence of residual right ventricular enlargement or dysfunction in patients who have had repair of an isolated ventricular septal defect. A summary of postoperative findings with ventricular septal defects are shown in Table 1.

Patients with large atrial septal defects have isolated right ventricular as well as right atrial enlargement. Incomplete regression of right ventricular dilatation has been found in several studies of short-term follow-up of children after atrial septal defect closure.<sup>9–11</sup> We have studied right ventricular volumes and ejection fractions before and after atrial septal defect closure in children using quantitative angiography.<sup>12</sup> Figure 2 shows preoperative right ventricular end-diastolic volumes averaging twice that of normal in 18 patients aged 1 month to 8 years with secundum or sinus venosus atrial septal defects, pulmonary-to-systemic flow ratios of 1.8 or more, and normal pulmonary vascular resistance. Postoperative studies in four similar patients 5–12 years old who were studied 1–4 years after surgery reveal residual right ventricular dilatation averaging approximately 1.5-fold that of normal. Right ventricular ejection fraction was normal before surgery in all patients with only one of four showing a low right ventricular ejection fraction after repair. In addition to these studies in children, Peerman et al<sup>13</sup> found persistent abnormalities of right ventricular diastolic diameter on echocardiography in 77% of 31 adult patients studied as long as 38 months after surgery. After surgery, right ventricular size returned to normal in seven of 17 patients (41%) operated on before age 25 but remained increased after repair in all 14 patients older than 25 years at the time of surgery (Figure 3). Despite this abnormality, 14 consecutive postoperative patients who underwent exercise stress testing and maximal oxygen consumption measurement during exercise had normal values.

Libertshon et al<sup>14</sup> reported abnormal right ventricular exercise ejection fraction persisting after surgery in 14 adult patients studied with radionuclide techniques after repair of atrial septal defects. These

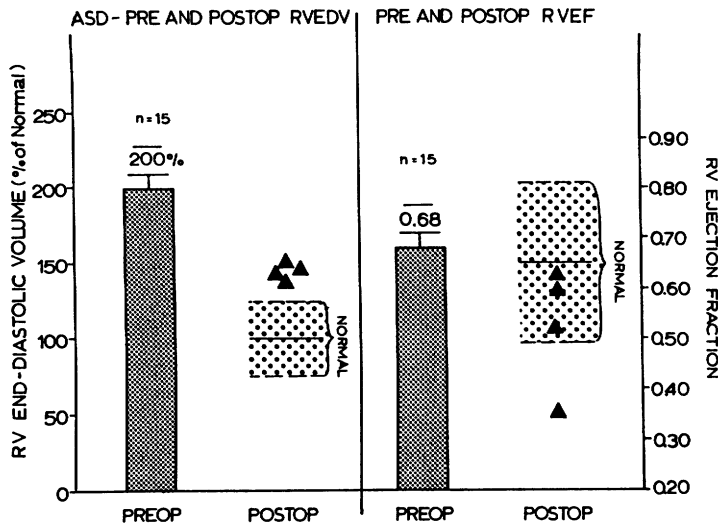


FIGURE 2. Bar graphs of preoperative and postoperative right ventricular (RV) end-diastolic volume (EDV) and ejection fraction (EF) for patients with an isolated atrial septal defect (ASD). Reprinted with permission.<sup>12</sup>

patients were distinguishable from patients with no postoperative abnormalities by being older at the time of surgery and having a greater degree of right ventricular dilatation and a lower preoperative right ventricular ejection fraction. Thus, persistent right ventricular dilatation can occur in patients who have repair of atrial defects delayed until later childhood or adult life. Surgery is currently performed in most patients during the first 5 years of life. Residual right

ventricular dilatation or right ventricular dysfunction has not been reported in a group of patients operated on at this age.

In preoperative patients with more severe right ventricular volume overload secondary to total anomalous pulmonary venous connection, residual right ventricular dilatation can occur, but right ventricular pump dysfunction has not been documented.<sup>15,16</sup>

The question of abnormal left ventricular function after surgery for atrial septal defect has also been raised.<sup>17-19</sup> Abnormalities have been felt to be related, in many instances, to acquired disease or decreased filling of the left ventricle. A small left ventricle could theoretically be caused by chronic underloading of this chamber in the presence of a large left-to-right atrial shunt and altered diastolic filling characteristics due to the large right ventricle with the septum deviating posteriorly. Davies and associates<sup>19</sup> reported seven patients who presented with elevated pulmonary arterial wedge, left ventricular end-diastolic pressure, or both after repair of atrial septal defect. These patients were all adults and were repaired at an age of 21-44 years. They were not thought to have coronary artery disease or hypertensive disease. Residual atrial defects and significant pulmonary arterial hypertension were ruled out, but right ventricular end-diastolic pressure was elevated. Thus, diastolic pressure abnormalities of the left ventricle may be due to permanently altered pressure-volume characteristics of a chronically overloaded right ventricle. The diastolic pressure abnormality could be transmitted to the left heart in patients whose right ventricles remain abnormal after surgery.

In the majority of patients with atrial septal defect, the left ventricle is only slightly smaller than normal, and significant left ventricular hypoplasia does not occur in isolated atrial septal defect.<sup>20</sup> In patients operated on while in infancy or childhood, postoperative left ventricle abnormalities have not been re-

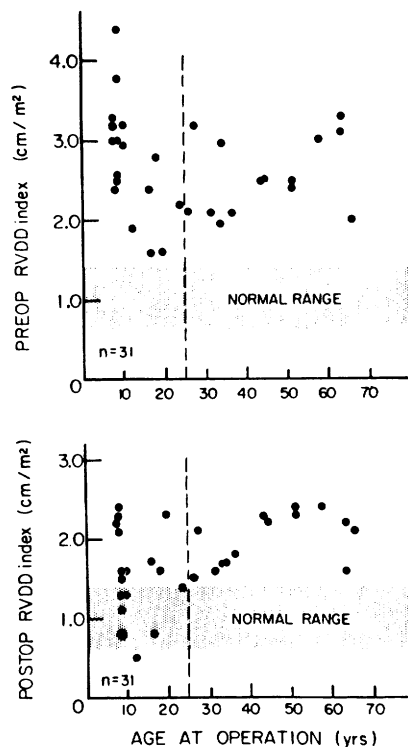


FIGURE 3. Scatterplots of postoperative (POSTOP) right ventricular diastolic diameter (RVDD) index related to age at surgery. Right ventricular size remains increased in all patients operated on after age 25 and in 10 of 17 operated on before age 25. Reprinted with permission.<sup>13</sup> PREOP, preoperative.

**TABLE 2. Summary of Data on Ventricular Performance With Atrial Septal Defect****Right ventricle**

Persistent dilatation, altered compliance, and decreased pump function reported in adults after repair

Risk factors for these abnormalities include older age at repair and poor preoperative function

Repair during the first 5 years usually associated with no residual dilatation or dysfunction

**Left ventricle**

Size at lower limit of normal in many preoperative patients

Pump function abnormalities very rare

Altered left heart filling pressures usually secondary to altered right heart diastolic pressure, which can persist after surgery in patients operated on after childhood

ported.<sup>20,21</sup> A summary of findings in patients with atrial septal defect is shown in Table 2.

**Ventricular Underload**

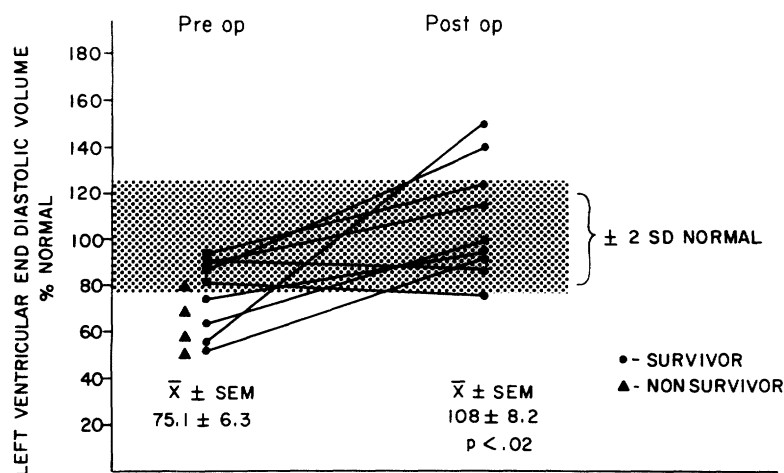
There are a number of congenital defects that have the anatomic and/or hemodynamic conditions for significant underloading of either ventricular chamber. Conditions with the potential for isolated volume underloading of the left ventricle include total anomalous pulmonary venous connection,<sup>15,16,20,22</sup> the unbalanced form of complete atrioventricular canal,<sup>23</sup> and occasional patients with tetralogy of Fallot<sup>24–26</sup> or pulmonary atresia plus ventricular septal defect who have had markedly decreased pulmonary blood flow for a considerable period of time.

The delineation of the lower limit of normal for ventricular volume to proceed with reparative surgery is not clearly defined in all of these conditions. We have studied infants with total anomalous pulmonary venous connection and shown that volumes as low as 50% of normal are compatible with successful repair.<sup>16</sup> Figure 4 shows left ventricular end-diastolic volume in 14 infants with total anomalous pulmonary venous connection. Left ventricular end-diastolic volume is less than normal in seven of 14, with two infants having volumes approximately 50%

of normal. There were four perioperative deaths in these patients; three of seven patients with small volumes died, and one of seven with normal volumes died. Low left ventricular ejection fraction was not a determinant of survival; infants with left ventricular ejection fractions of 28% and 34% lived and had normal ejection fractions 1 year after repair.<sup>16</sup> Thus, volumes as low as 50% of normal do not preclude survival with normal postoperative left ventricular size and function.

There has been considerable debate regarding the prevalence and importance of a small left ventricle in tetralogy of Fallot.<sup>24–26</sup> Left ventricular end-diastolic volume was found to be mildly decreased (average,  $79 \pm 3\%$  of normal) in 25 children age 2–14 years with tetralogy of Fallot.<sup>24</sup> Cyanotic infants 1.5 years old or younger and acyanotic older children 3–15 years old had normal volumes. In a subsequent study concentrated on younger patients, Hammon and associates<sup>26</sup> found 11 of 26 patients less than 2 years old had left ventricular end-diastolic volume values less than 2 SDs from normal (Figure 5). All patients had primary intracardiac repair; there were two deaths in 11 patients with small left ventricles and one death in 15 patients with normal left ventricle size. This study showed that three of four patients with left ventricular end-diastolic volume values less than 60% of normal survived repair. These data indicate that a small left ventricle is a rare cause of mortality after repair of tetralogy of Fallot.

There are limited quantitative data regarding the lower limit of normal left ventricular end-diastolic volume for repair in the right ventricular dominant type of complete atrioventricular canal. Two recent studies characterized the prevalence of associated cardiac abnormalities in patients with complete atrioventricular canal who had normal chromosomes compared with those with Down's syndrome.<sup>27,28</sup> Patients with Down's syndrome had a lower frequency of left-sided anomalies and a suggestive lower prevalence of dominant right ventricles with hypoplastic



**FIGURE 4.** Plots of left ventricular end-diastolic volume before (Pre op) and after (Post op) surgery in patients with total anomalous pulmonary venous connection. Reprinted with permission.<sup>16</sup>

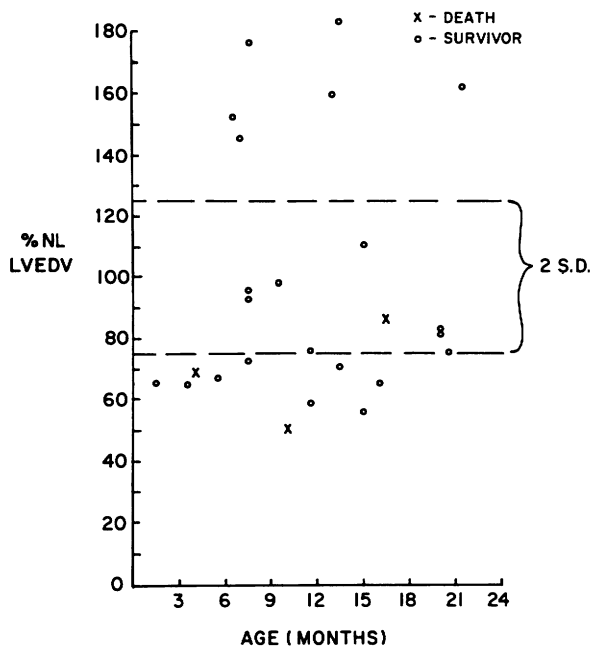


FIGURE 5. Scatterplot of left ventricular end-diastolic volume (LVEDV) in 26 patients less than 2 years old undergoing repair of tetralogy of Fallot. % NL, percent normal; S.D., standard deviation. Reprinted with permission.<sup>26</sup>

left ventricles. Unfortunately, no quantitative studies on left ventricular size were presented.

There have been three reports on angiographic volume studies in patients with endocardial cushion defects.<sup>29-31</sup> Only one of these studies presented data consistent with a right ventricular dominant morphology; two patients had right ventricular end-diastolic volumes of 275% and 251% of normal with left ventricular volumes of 97 and 96% of normal, respectively.<sup>31</sup> Both of these patients died, one with persistent postoperative low output, and the other with a sudden deterioration on day 3 that was considered to be secondary to dehiscence of a mitral valve suture found at autopsy. It seems unlikely that left ventricular volumes that are within normal limits would be a risk factor for surgical mortality. Further data are needed regarding the important question of when left ventricular size is inadequate for biventricular repair in complete atrioventricular canal.

A different situation is encountered in patients with volume underload associated with pressure overload. The classic example is the infant with critical aortic stenosis with a small left ventricle. When does this ventricle reach the stage of being a hypoplastic left ventricle that is incapable of pumping systemic output after surgery? We studied this problem, and our data indicate that no infants survive whose left ventricular volume is less than 50% of normal (Figure 6).<sup>32</sup> Other investigators also have shown a relation between small left ventricle size and mortality.<sup>33-36</sup> Aortic stenosis differs from total anomalous pulmonary venous connection in that the left ventricular myocardium can be quite abnormal in

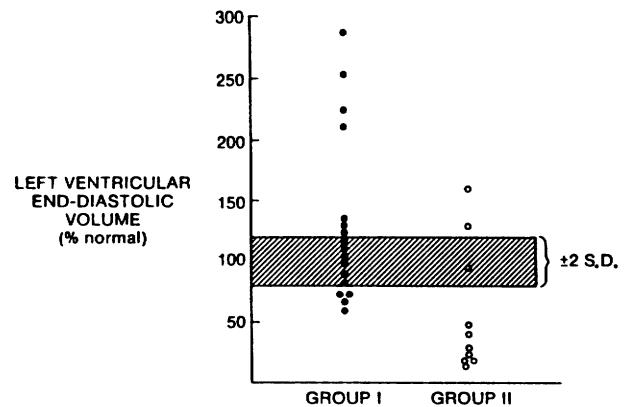


FIGURE 6. Scatterplot of left ventricular end-diastolic volume expressed as percentage of normal values in survivors (group I) and nonsurvivors (group II) with critical aortic stenosis. Shaded area denotes normal values  $\pm 2$  standard deviations (S.D.). Reprinted with permission.<sup>32</sup>

aortic stenosis with significant ischemic damage to the ventricle before surgery. In addition, most infants with aortic stenosis continue to have an excessive impedance to ejection after surgery due to residual outflow obstruction. Nevertheless, patients with volumes as low as 60% of normal have had good results from surgery with long-term survival. From the preceding data regarding the relation between mortality and small left ventricular cavity size, it seems reasonable that volumes approximately 50% of normal approach the lower limit for survival after surgery for various congenital heart defects. There obviously are no clear guidelines in every condition, and some patients may have ventricles approximately 50% of normal in size that can dilate after repair to a size capable of pumping a normal cardiac output after surgery.

Zeevi and associates<sup>37</sup> reported on percutaneous balloon valvotomy as an alternative to surgical valvotomy for critical aortic stenosis. In their retrospective study, there were eight of 16 late survivors with surgical treatment and nine of 16 late survivors with balloon therapy. This relatively new modality can be a reasonable alternative for groups with expertise and experience with catheter interventional therapy in young infants. The small left ventricle remains a significant risk factor for either surgical or catheter therapy.

For patients whose left ventricle is judged too small for direct valvular surgery, infant heart transplantation<sup>38</sup> or the Norwood procedure<sup>39</sup> for hypoplastic left heart syndrome is possible as a more "radical" form of surgical therapy.

A similar situation on the right side of the heart occurs in infants with isolated critical pulmonary stenosis or pulmonary atresia. The lower limit of normal right ventricular size for survival after surgery is also a major concern for both cardiologists and surgeons who deal with this condition. Figure 7 demonstrates preoperative and postoperative right

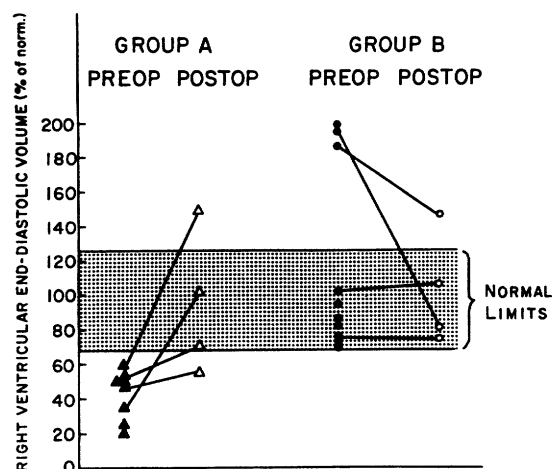


FIGURE 7. Plots of preoperative (PREOP) and postoperative (POSTOP) right ventricular end-diastolic volume in group A and group B patients with critical pulmonary stenosis. Reprinted with permission.<sup>32</sup>

ventricle end-diastolic volumes in 18 patients with critical pulmonary stenosis and intact ventricular septum.<sup>40</sup> In the group of eight patients with small right ventricles (group A), there was one death in a patient with a right ventricular volume of only 21% of normal and an ejection fraction of 33%. The remainder of the patients survived and are clinically well. Postoperative studies were available for four of these patients, and all except one are within normal limits. Four survivors had preoperative volumes between 20% and 45% of normal. Similar increases in volume have been reported by other investigators for hypoplastic right ventricles in pulmonary stenosis or atresia with intact ventricular septum after relief of obstruction.<sup>41–44</sup> The response to relief or partial relief of obstruction is much less predictable in pulmonary atresia because of the frequent occurrence of coronary artery abnormalities as well as myocardial ischemia and fibrosis.<sup>41</sup> There continues to be enthusiasm for early decompression of a hypertensive right ventricle in neonates with pulmonary atresia with the perception that flow through the ventricle will induce growth. There is no general consensus at present on the lower limit of preoperative right ventricular size that makes this approach feasible. It is clear, as indicated above, that some right ventricles with volumes considerably less than 50% of normal can be associated with excellent results after surgery, and patients should not be considered inoperable even if they have very small end-diastolic volumes.

Other congenital conditions that can be associated with right ventricular hypoplasia include the left ventricular dominant form of atrioventricular canal,<sup>29,30</sup> congenitally corrected transposition of the great arteries,<sup>45</sup> complete transposition of the great arteries, tricuspid stenosis or atresia, and overriding or straddling tricuspid valve. There have been insufficient patients described with these rare conditions

TABLE 3. Ventricular Volume Underloading in Congenital Heart Disease

Without associated pressure overload

Left ventricle: Total anomalous pulmonary venous connection (TAPVC), tetralogy of Fallot, unbalanced atrioventricular canal

Postoperative survival possible with preoperative volumes of approximately 50% of normal in TAPVC, tetralogy of Fallot

Data on atrioventricular canal not clarified

Right ventricle: Unbalanced atrioventricular canal, congenitally corrected transposition, complete transposition, tricuspid stenosis or atresia, overriding or straddling tricuspid valve

Many conditions not repairable

Lower limit of size for postoperative survival not clarified

With associated pressure overload

Left ventricle: Aortic stenosis

Small size in 20–40%

Postoperative survival unlikely with preoperative volumes of less than 50% of normal

Right ventricle: Pulmonary stenosis, pulmonary atresia

Postoperative survival possible with preoperative volumes of 20–50% of normal

Lower limit of normal volume for survival unclear, but pulmonary atresia patients much less predictable

to determine the effect of small preoperative volumes on postoperative survival. A summary of data on ventricular underloading in congenital heart disease is shown in Table 3.

### Pressure Overload

Infants with coarctation of the aorta have the classic demonstration of afterload mismatch<sup>46</sup> that occurs most often at 10–14 days of age when the aortic end of the ductus arteriosus constricts and a previously well infant is suddenly faced with a severe increase in left ventricular afterload.<sup>47</sup> This results in a decrease in left ventricular ejection fraction and output, increased left ventricular end-diastolic pressure and left atrial pressure, and a sizeable left-to-right shunt at the atrial level. Figure 8 demonstrates pressure-volume relations in an infant with isolated coarctation compared with normal perinatal values. Pulmonary hypertension occurs secondary to pulmonary vasoconstriction, in part induced by the left atrial hypertension. Cardiac output decreases with decreased renal perfusion and oliguria. Infants then present with marked right heart enlargement, a normal-to-small left ventricle, and a low left ventricular ejection fraction.<sup>48,49</sup> Surgical repair of the coarctation results in the return of virtually all volume and pressure abnormalities to normal with the majority of patients having no residual left ventricular dysfunction.<sup>48,49</sup> The apparent paradox of severe left ventricular afterload excess resulting in a small or normal left ventricle and a large right ventricle occurs with or without a large ventricular septal defect.<sup>49</sup> This unexpected finding is explainable on the basis of left-to-right atrial shunting and in some patients by

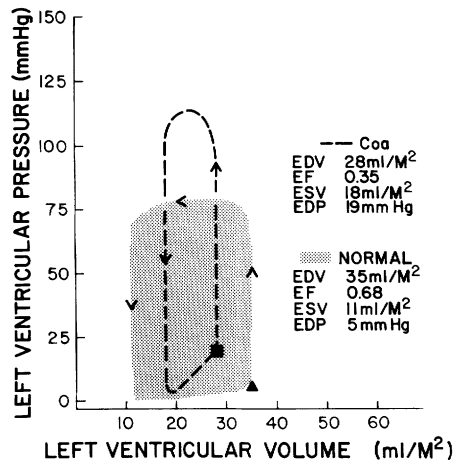


FIGURE 8. Pressure-volume relations in an infant with isolated coarctation (Coa) compared with normal perinatal values. Reprinted with permission.<sup>53</sup> EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; EDP, end-diastolic pressure.

associated right-to-left ductal shunting. In this acute situation, there usually is insufficient time for hypertrophy to occur to normalize left ventricular wall stress and permit hemodynamic improvement.

Aortic stenosis is another situation in which abnormal impedance to ejection can be present in the young infant as described above. In the critically ill infant, volumes range from hypoplastic to massive enlargement with ejection fractions ranging from markedly decreased to within normal limits. Patients who do not present with symptoms as an infant but are recognized as children or adolescents with a significant gradient and left ventricular hypertrophy virtually always have compensated pressure overload with marked increase in wall thickness such that end-systolic wall stress is normalized and contractile function is normal.<sup>50,51</sup> These patients usually have slightly smaller-than-normal left ventricular volumes with increased ejection fractions and normal outputs, as depicted in Figure 9.<sup>52,53</sup> In this figure, chronic left ventricular pressure overload due to aortic stenosis is contrasted with a theoretical afterload reserve, that is, pressure generated by the left ventricle on the first beat after a sudden marked increase in afterload from a normal end-diastolic volume. Under these conditions, peak pressure is almost doubled, but ejection fraction and stroke volume are considerably reduced. With compensated aortic stenosis, hypertrophy occurs to normalize wall stress, and stroke volume is maintained despite a slightly decreased end-diastolic volume. End-diastolic pressure is mildly increased, indicating a small decrease in operative volume distensibility. This type of compensation is not usually obtained in the neonate. The reasons for lack of compensation are not known, but speculations include the frequent occurrence of myocardial ischemia in the neonate with critical aortic stenosis and the relatively immature myocardium, which is

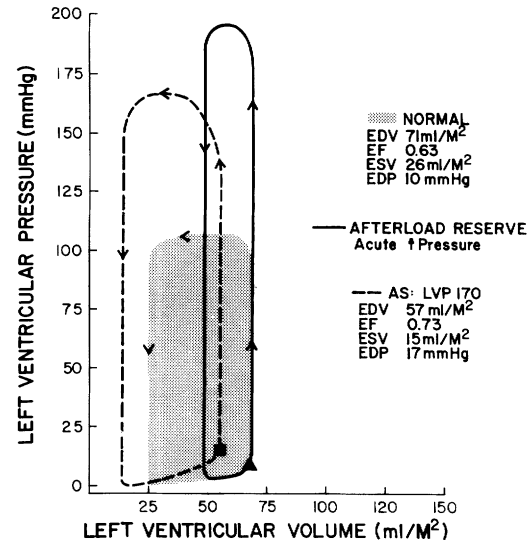


FIGURE 9. Schematic pressure-volume loops for a normal 10-year-old, illustrating concepts of acute and chronic pressure overload. AS, aortic stenosis; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; EDP, end-diastolic pressure; LVP, left ventricular pressure.

less able to hypertrophy in response to this type of afterload excess.

The possibility of subendocardial ischemia occurring in children with aortic stenosis has been evaluated using the ratio of diastolic pressure time index multiplied by the arterial oxygen content to systolic pressure-time index ratio.<sup>54</sup> An abnormally low value for this ratio has been associated with electrocardiographic abnormalities, but correlations with left ventricular functional alterations have not been proven. It is rare for a child to present with significant left ventricular pump dysfunction due to aortic stenosis in childhood or adolescence. Compensation can continue well into adult life, as has been documented previously. With successful surgical intervention in childhood, there is little indication for significant postoperative abnormalities of pump performance of the left ventricle unless severe stenosis recurs or severe aortic regurgitation develops. Unfortunately, stenosis almost invariably recurs, and valve replacement is eventually required in virtually all patients after initial valvulotomy.

A complete discussion of the factors associated with the onset of congestive failure in adults with aortic stenosis is beyond the scope of this review. These factors undoubtedly include progression of obstruction, myocardial fibrosis secondary to ischemic episodes, acquired heart disease, and inability for hypertrophy to compensate for excessive obstruction (afterload mismatch).<sup>55</sup>

Patients with pulmonary stenosis have a similar situation on the right side of the heart. Infants can present with critical pulmonary stenosis, usually with a small right ventricle and significant right-to-left atrial shunting. With successful intervention as described above, their outcome is usually an excellent

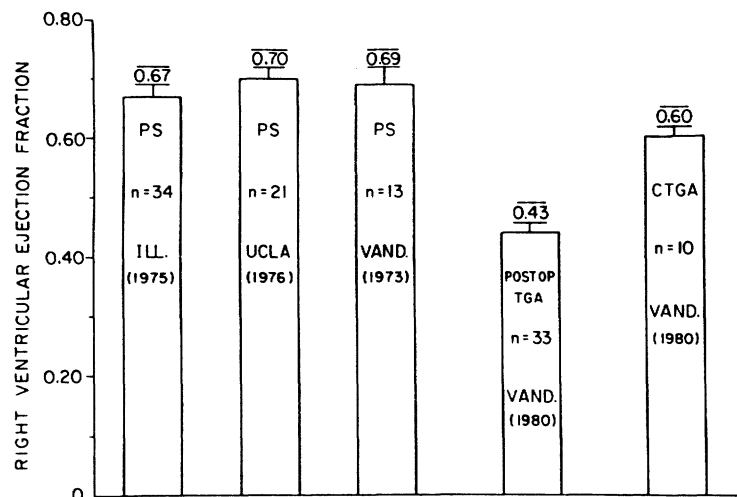


FIGURE 10. Bar graphs of right ventricular ejection fraction compared for patients with isolated pulmonary stenosis (PS), postoperative interatrial repair of transposition of the great arteries (POST OP TGA), and congenitally corrected transposition of the great arteries (CTGA). Reprinted with permission.<sup>58</sup>

one with normal right ventricular size and function with continued growth. Children and adolescents presenting with pulmonary stenosis usually present with compensated ventricular hypertrophy with right ventricular end-diastolic volume at the lower limit of normal or slightly small with increased ejection fraction and normal right ventricular output.<sup>11,56-58</sup> Figure 10 shows right ventricular ejection fraction for three groups of patients with compensated severe pulmonary stenosis studied at three different institutions. Ages ranged from 4 days to 22 years, and peak right ventricular pressure averaged more than 90 mm Hg. The values for ejection fraction were all normal or supranormal, despite systemic or suprasystemic pressure in the right ventricle. Virtually all patients who have had valvulotomy or successful balloon valvuloplasty in childhood have normal right ventricular systolic function.

There are rare instances of right ventricular dysfunction in patients with pulmonary stenosis. These patients are usually those who have had severe pressure overload for a long period of time. It is probable that they develop significant myocardial fibrosis in this situation and will continue to have significantly abnormal systolic and diastolic function after intervention. Fortunately, such patients are rare, and many are able to function reasonably well, despite a mild increase in right-sided filling pressure. A summary of data on ventricular performance with pressure overload is given in Table 4.

### Cyanotic Conditions

Patients with complete transposition of the great arteries represent a unique anatomic condition in which the right ventricle is connected to the aorta. The use for more than 20 years of the Mustard and Senning atrial repairs for transposition has resulted in a large number of patients who continue to have the right ventricle connected to the aorta after surgery. Data from a number of different institutions have indicated depressed resting right ventricular ejection fraction in patients after atrial repair of

transposition of the great arteries.<sup>58-63</sup> Figure 10 shows that there was an average resting right ventricular ejection fraction of 43% for 33 post-atrial repair patients with transposition of the great arteries. This value is significantly less than normal values for the right<sup>11</sup> or left ventricle.<sup>64</sup> In addition, it is also significantly less than right ventricular ejection fractions of patients with pulmonary stenosis and systemic or suprasystemic pressure.<sup>11,56-58</sup> If closure of a ventricular septal defect was performed at the time of atrial repair, ventricular function was even more depressed. In addition to resting right ventricular function, right ventricular response to exercise is abnormal in the majority of patients after atrial repair,<sup>53</sup> as is response to afterload stress in the form of methoxamine challenge at postoperative catheter-

TABLE 4. Summary of Data on Ventricular Performance With Pressure Overload

Left ventricle
Infant with afterload mismatch
Coarctation
Normal or small left ventricle with low ejection fraction
Left-to-right atrial shunt
Postsurgical function normal
Aortic stenosis
Left ventricle decreased, normal, or increased
Ejection fraction usually low; improves with decrease in obstruction
Older child or adolescent with aortic stenosis
Wall mass increases to normalize wall stress
Left ventricle size small and ejection fraction increased
Diastolic pressure elevated
Symptoms are uncommon unless obstruction severe
Right ventricle-pulmonary stenosis
Children and adolescents have normal to small right ventricle size
Ejection fraction usually increased
Diastolic pressure mildly elevated
Symptoms are uncommon unless obstruction severe



ization.<sup>62,65,66</sup> Despite laboratory abnormalities of right ventricular function, however, many patients remain free of cardiovascular symptoms. The prevalence of clinically important right ventricular dysfunction 10–20 years after repair is unclear, but reports indicate that it may be increasing with time and approach 10–20%. The reason for the right ventricular dysfunction is undoubtedly multifactorial; possible contributory factors include preoperative myocardial damage caused by the cyanosis before surgery, perioperative damage occurring due to inadequate myocardial protection during repair, and the inability for the right ventricle, which is geometrically configured more as a volume pump, to be as effective and efficient a pump as a normal left ventricle. Evidence that duration or degree of cyanosis before surgery influences long-term ventricular function is not available. Most children with minimal cyanosis have surgery delayed, and vice versa. Thus, severe cyanosis leads to early surgery, and there are very few patients with severe cyanosis who have had late surgery. Our data do not show a difference in postoperative resting right ventricular ejection fraction in patients with Senning repair before compared with after 3 months of age.<sup>62</sup> We have reported a lower right ventricular ejection fraction in patients operated on before 1974 versus those operated on from 1974 to 1984.<sup>62</sup> The reason for this difference could be inadequate intraoperative myocardial protection in the earlier group. Thus, the reasons cited above for postoperative right ventricular dysfunction in patients after atrial repair remain largely speculative.

There are a number of patients with congenitally corrected transposition who have the right ventricle connected to the aorta and have no or minimal associated defects. Most of these patients have normal right ventricular function when studied in childhood or early adult life.<sup>67–72</sup> There is an increasing prevalence of right ventricular dysfunction with advancing years.<sup>67,71</sup> This is frequently associated with systemic atrioventricular valvular insufficiency and/or heart block. Despite these findings, a number of patients live into their 60s with the right ventricle subjected to systemic pressure without ventricular dysfunction. It remains unclear as to the factors related to compensation in these patients versus the more common situation of right ventricular failure with advancing adult years.

A number of patients with complete transposition with atrial repair have been reported to have left ventricular dysfunction.<sup>68</sup> This abnormality is probably related, in most instances, to preoperative or perioperative myocardial damage. In addition to systolic dysfunction, abnormal right ventricular dysfunction contributing to left ventricular diastolic dysfunction also occurs, as a result of ventricular interdependence. This problem is clinically uncommon.

The most common present therapy for complete transposition is the arterial switch operation with coronary translocation performed within the first few weeks of life. Early results indicate normal left ventric-

**TABLE 5. Summary of Data on Ventricular Performance With Transposition of the Great Arteries**

Complete transposition	
Atrial switch operation (Mustard or Senning)	
Right ventricle	
Abnormal resting function in approximately 50% of patients repaired within past 10 years; abnormalities more prevalent in patient operated on earlier, in patient with combined ventricular septal defect repair, or with exercise testing or afterload stress	
Clinical right ventricle failure late: 10–20%; may become more prevalent with time	
Left ventricle	
Abnormal function may be underdiagnosed because of usual low afterload	
Prevalence may be 10–20%	
Arterial switch operation (only 1–5-year follow-up at most centers)	
Right ventricle—normal	
Left ventricle—normal	
Exceptions—ventricular septal defect repair, two-stage operation, older age at surgery	
Congenitally corrected transposition	
Right ventricle (systemic ventricle)	
Usually normal function in childhood	
Progressive deterioration of function as young adults common, particularly with atrioventricular valve regurgitation and/or heart block	
Left ventricle (pulmonary ventricle)—function usually normal	

ular function in the vast majority of patients, with follow-up extending in a number of instances from 2 to 4 years after surgery.<sup>73</sup> Patients who have shown systemic ventricular dysfunction have frequently been older at the time of surgery and/or had ventricular septal defect repair carried out. Arterial switch combined with ventricular septal defect repair is associated with a longer ischemic time, and postoperative dysfunction may be related to intraoperative ischemia. Table 5 summarizes data on ventricular performance in patients with transposition of the great arteries.

### Tetralogy of Fallot

After tetralogy of Fallot repair, patients have a reasonably normal clinical course unless there are residual hemodynamic abnormalities. Left ventricular dysfunction was reported a number of years ago after repair of tetralogy of Fallot.<sup>74,75</sup> Recent data, however, indicate that most patients repaired during the past 20 years have normal left ventricular function.<sup>58,76–80</sup> Prior reports of abnormal left ventricular function probably were related to inadequate myocardial protection during surgery, although proof of this hypothesis is not possible.

In contrast, right ventricular function abnormalities are common after tetralogy of Fallot repair.<sup>80,81</sup> These are usually present in patients with residual right ventricular outflow obstruction. Figure 11 illustrates right ventricular end-diastolic volume determined at cardiac catheterization 1 year or later after

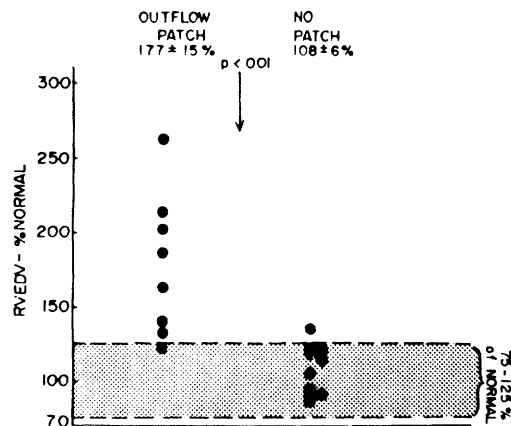


FIGURE 11. Scatterplot of right ventricular end-diastolic volume (RVEDV) in postrepair tetralogy patients with and without transannular outflow patch. Reprinted with permission.<sup>81</sup>

surgery in patients who required transannular outflow tract patches and patients who required no patches. There is considerable right ventricular dilatation, as would be expected in these patients with significant pulmonary regurgitation.<sup>81</sup> Figure 12 shows ejection fraction data from these same groups of patients. There are low ejection fractions in a majority of patients with outflow patch repair but normal ejection fractions in patients with a more favorable anatomy who did not require a patch repair.

The overall cardiac response to exercise after tetralogy repair has been reported by a number of investigators. Abnormal right ventricular response to exercise is common and is probably related to pulmonary regurgitation, dyskinetic right ventricular outflow tract after ventriculotomy, and, possibly, right ventricular outflow obstruction that increases with exercise.<sup>80,82-88</sup>

Surgery at a younger age is probably associated with a better result in regard to right ventricular size and function, but data to substantiate this point have not been obtained. Improved response to afterload

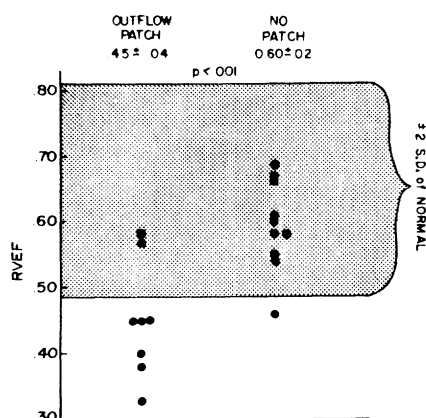


FIGURE 12. Scatterplot of right ventricular ejection fraction (RVEF) in postrepair tetralogy patients with and without transannular outflow patch. Reprinted with permission.<sup>81</sup>

stress in patients repaired earlier in life has been shown.<sup>89</sup> This result may have been due to improved intraoperative myocardial protection in the younger group.

Postoperative patients with moderate or severe right ventricular enlargement, severe pulmonary regurgitation, and right ventricular dysfunction can benefit from placement of a valve-containing pulmonary or aortic homograft.<sup>90-92</sup> This operation is usually followed by decreased heart size, improved exercise tolerance, and halted progressive right ventricular dysfunction.

There are a number of patients with complex cardiac conditions associated with ventricular septal defect whose surgery involves placement of a conduit or homograft from the right ventricle to the pulmonary artery. These include truncus arteriosus, pulmonary atresia with ventricular septal defect, and transposition of the great arteries with ventricular septal defect and pulmonary stenosis. These conditions are similar to tetralogy in having a ventricular septal defect and right ventricular hypertension before surgery and the potential for a dyskinetic right ventricle as well as pulmonary stenosis and/or regurgitation after surgery. Left ventricular function abnormalities have been determined in a number of these patients after repair, as illustrated in Figure 13. These abnormalities of ejection fraction are common in patients whose surgery is performed in late childhood or adolescence and uncommon with infant repair.<sup>93</sup>

Left ventricular contractile dysfunction was found in eight of 11 transposition patients after conduit repair who were studied 0.7 to 14 years after surgery using heart rate-corrected velocity of circumferential fiber shortening velocity plotted as a function of end-systolic wall stress<sup>94</sup> (Figure 14). These data theoretically assess ventricular contractile function independent of preload or afterload.<sup>95</sup> It is possible that preoperative myocardial damage plus intraoperative damage are responsible for these abnormalities, as discussed previously. Data to support this speculation are not available.

Right ventricular dysfunction is also common in this age group (Figure 13).<sup>93</sup> Most of these patients have some residual right ventricular obstruction at the conduit or pulmonary artery site; thus, increased impedance to ejection is undoubtedly in part responsible for an impaired ejection fraction occurring after surgery. It is probable that a combination of outflow obstruction, myocardial fibrosis, and inadequate hypertrophy leads to afterload excess, which results in a depressed right ventricular ejection fraction. A summary of data regarding ventricular function in postoperative tetralogy and post-conduit repair patients is shown in Table 6.

#### Tricuspid Atresia or Other Single-Ventricle Anatomy

The final group of patients to be discussed are those with tricuspid atresia or another type of single-ventricle anatomy. Preoperative abnormalities of

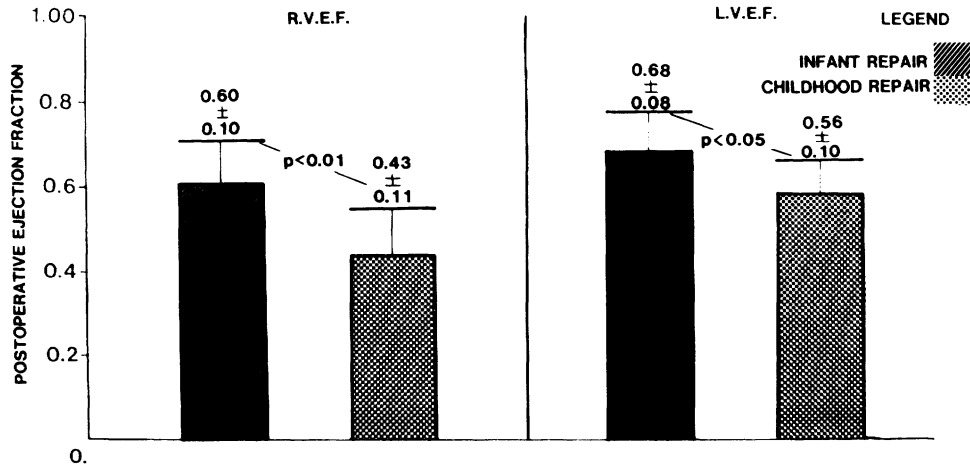


FIGURE 13. Bar graphs of right (R.V.E.F.) and left ventricular ejection fractions (L.V.E.F.) for patients with infant vs. childhood right ventricle-to-pulmonary artery conduit repairs. Reprinted with permission.<sup>93</sup>

ventricular function are common in these patients and, again, are probably related to longstanding volume overload, chronic cyanosis, and intermittent episodes of myocardial hypoxemia with resultant myocardial damage.<sup>96-99</sup>

Patients with tricuspid atresia and palliative aorto-pulmonary shunts show left ventricular volumes and wall mass more than twice normal values, borderline low or reduced ejection fractions, and increased afterload as estimated by end-systolic wall stress ( $56 \pm 5$  g/cm<sup>2</sup> versus a normal value of  $43 \pm 3$  g/cm<sup>2</sup>).<sup>100</sup> Estimates of contractile function with load-independent indexes for these patients are shown in Figure 15. In this figure, circumferential fiber shortening velocity is plotted as a function of meridional end-systolic stress for 23 palliated patients from 1.8 to 15

years old. There were nine of 23 patients with depressed left ventricular contractile function (low circumferential fiber shortening velocity for a given meridional end-systolic stress). Of particular note, eight of 12 patients more than 5 years old (average age, 8 years) had abnormal contractile function, whereas only one of 11 patients less than 5 years old (average age, 3.4 years) had abnormal function. This finding emphasizes the importance of duration of volume overload and cyanosis on ventricular dysfunction.

After surgical intervention by the Fontan procedure, a number of these patients continued to show myocardial dysfunction.<sup>100-106</sup> Theoretically, the

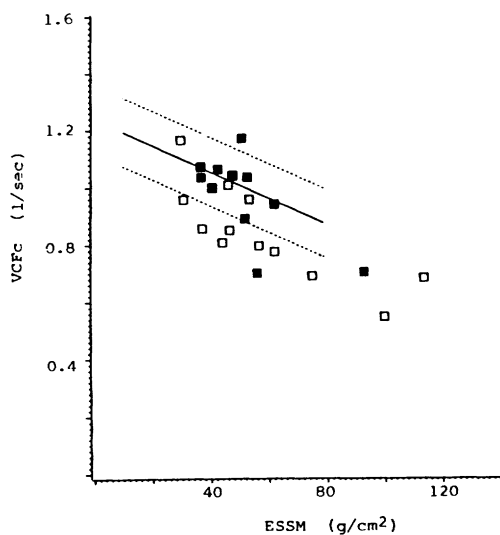


FIGURE 14. Scatterplot of rate-corrected velocity of circumferential fiber shortening (VCFc) vs. meridional end-systolic stress (ESSM) in transposition patients after Rastelli repair. Reprinted with permission.<sup>94</sup> Normal values from Colan et al.<sup>95</sup>

TABLE 6. Summary of Data on Ventricular Performance in Tetralogy of Fallot and Pulmonary Atresia Plus Ventricular Septal Defect After Repair

#### Tetralogy

##### Right ventricle

Increased end-diastolic volume and decreased ejection fraction common when transannular patch required for repair; residual obstruction or pulmonary hypertension poorly tolerated

Patients with significant right ventricular dysfunction and pulmonary regurgitation usually benefit from homograft therapy

##### Left ventricle

Patients with repair 15-25 years earlier may have left ventricular dysfunction

Function usually normal in patients repaired in past 10-15 years

#### Pulmonary atresia plus ventricular septal defect (and similar lesions)

##### Right ventricle

Dysfunction common in patients with repair after childhood  
Residual or recurrent obstruction poorly tolerated

##### Left ventricle

Dysfunction much more common than in tetralogy patients  
Patients with repair in infancy usually show normal function

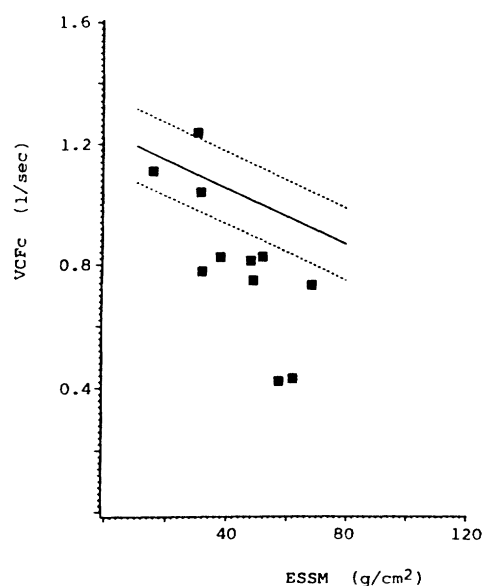


FIGURE 15. Scatterplot of rate-corrected velocity of circumferential fiber shortening (VCFc) as a function of meridional end-systolic stress (ESSM) for patients with tricuspid atresia after palliative shunts. Patients older than 5 years are indicated by open symbols. Reprinted with permission.<sup>100</sup>

Fontan operation, which results in the elimination of cyanosis and volume overloading, could ameliorate or at least prevent progression of ventricular dysfunction. Many of these patients undoubtedly have significant myocardial dysfunction before surgery that is not alleviated by surgery. There is some indication for improved myocardial performance, however, with time after a successful Fontan operation.<sup>106,107</sup>

The degree of myocardial hypertrophy in tricuspid atresia may also be an important determinant of outcome after Fontan. Both Kirklin et al,<sup>108</sup> using a qualitative method, and Sellem et al,<sup>109</sup> using quantitative angiography, related the degree of hypertrophy to outcome of the Fontan procedure and indicated that excessive hypertrophy can occur and is associated with an increase in both mortality and morbidity. Both groups speculated that abnormal postoperative diastolic function was in part related to suboptimal subendocardial perioperative reperfusion and could be the cause of the increased morbidity and mortality in these patients. These data as well as those of other studies indicating the deleterious effects of excessive volume loading<sup>96-98,100</sup> in patients with single-ventricle anatomy have resulted in attempts to avoid or ameliorate these problems by the early use of the classic Glenn shunt (superior vena cava-to-right pulmonary artery shunt) or the bidirectional Glenn shunt. Data regarding improved morbidity and mortality with this approach are not available at the present time.

Patients with other types of single-ventricle anatomy frequently have myocardial dysfunction before and after surgery.<sup>110,111</sup> There is evidence to suggest that those with primary right ventricular anatomy are

TABLE 7. Summary of Data on Ventricular Performance With Tricuspid Atresia and Single Ventricle

Tricuspid atresia
Abnormal function common in older patients
Risk factors for abnormal function: chronic volume overload and cyanosis
After Fontan operation, contractile function can improve
Single ventricle
Findings similar to tricuspid atresia
Patients with right ventricular type of single ventricle may have more severe ventricular dysfunction

more prone to ventricular dysfunction before and after surgical intervention.<sup>110,111</sup> Again, the chronic volume overload, chronic cyanosis, and perioperative myocardial damage during the time of intraoperative ischemia, remain the most probable causes for ventricular dysfunction with chronic cyanotic congenital heart disease. A summary of data regarding ventricular function in tricuspid atresia and single ventricle is shown in Table 7.

### Speculation

As mentioned, myocardial damage in patients with congenital defects may occur at times of stress when oxygen demand exceeds supply. There is some experimental evidence for this concept, including pacing studies carried out by Friedli et al<sup>112</sup> on tetralogy patients. These authors showed myocardial lactate production in five of nine cyanotic patients whose arterial oxygen saturation fell during pacing. Further evidence for myocardial injury in cyanotic patients was provided by Boucek et al,<sup>113</sup> who found elevated creatine kinase-MB activity in 29 of 32 infants with transposition of the great arteries (mean aortic oxygen saturation, 62%) and in 19 of 31 infants with right ventricular outflow tract obstruction (mean oxygen saturation, 75%).

An additional cause of postoperative ventricular dysfunction is inadequate myocardial protection during the ischemic time required for surgical repair. Studies by Bull et al,<sup>114</sup> Hammon et al,<sup>115</sup> del Nido et al,<sup>116</sup> Yamaguchi et al,<sup>117</sup> and Sawa et al<sup>118</sup> have suggested that myocardial damage can occur in this setting, particularly in cyanotic patients and during prolonged ischemic times needed for more complicated operations.

These studies, as well as others cited in this review, have led me to speculate that improved methods for myocardial protection and earlier age at surgery should improve postoperative ventricular function in patients currently undergoing reparative surgery for congenital heart defects.

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