Right Ventricular Volume Characteristics Before and After Palliative and Reparative Operation in Tetralogy of Fallot

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SUMMARY   Right heart volume data were obtained in 63 patients with tetralogy of Fallot. The patients were divided into three groups: 1) preoperative tetralogy (N=34); 2) post shunt procedure (N=14); 3A) post repair without outflow patch (N=10); 3B) post repair with an outflow patch (N=8). In Group 1 right ventricular end-diastolic volume (RVEDV), RV ejection fraction (EF), and RV systolic output (SO) were all mildly depressed. In post shunt patients, RVEDV was normal but RVEF remained depressed. RVEDV and RVSO increased following a shunt procedure, and these variables were larger in patients with a large versus a small shunt. In Group 3A RVEDV, RVEF, and RVSO were normal. In contrast in patients in Group 3B, RVEDV was increased averaging 177 ± 15% of normal, RVEF was depressed averaging 0.45 ± 0.04, and RVSO was normal. RV size and pump function are abnormal in patients whose operation requires an outflow tract patch and the factors which may contribute to these abnormalities include a higher RV peak pressure, pulmonary incompetence, and a larger noncontractile outflow tract. Longitudinal studies relating these variables to clinical performance and exercise testing will be important in assessment of the importance of these abnormalities.

ALTHOUGH TREATMENT for suspected right ventricular (RV) failure is common after tetralogy of Fallot repair, very little information is available on the direct measurement of RV performance in these patients. Such measurements may become increasingly important in the evaluation of current methods of treatment for both the infant and the older child with tetralogy of Fallot. The purpose of this investigation, therefore, was to analyze biplane cineangiocardiograms in patients before and after surgery for tetralogy of Fallot to determine right ventricular end-diastolic and end-systolic volumes, ejection fraction, systolic output, and maximum right atrial volume and to attempt to correlate these findings with clinical course and other pertinent hemodynamic data.

Methods

All patients studied at Vanderbilt Hospital from July 1971 to October 1975 with the diagnosis of tetralogy of Fallot and adequate biplane cineangiocardiograms for analysis were included. Tetralogy of Fallot was defined as the condition in which there is a large ventricular septal defect with equal right and left ventricular peak systolic pressures associated with right ventricular outflow tract obstruction, and bidirectional shunting. There were three basic patient groups.

Group 1 consisted of patients prior to any surgical procedure. There were 34 studies performed on 32 patients in this group whose ages ranged from 3 days to 12 years with an average age of 2.1 ± 0.4 yr (mean ± SEM). Sixteen patients were less than one year of age and 24 were less than two years. Arterial oxygen saturation (O_2 SAT) ranged from 67–98% at rest and averaged 80 ± 2%. Only four patients had arterial O_2 SATs at rest ≥ 90%, and all four had a de-

crease in O_2 SAT with crying. Hematocrits ranged from 36–73% with an average of 47 ± 2%, table 1.

Group 2 included 14 studies in 13 patients who were studied at varying intervals following a shunt procedure to increase pulmonary blood flow. Seven patients had Waterston shunts, five patients had Blalock-Taussig shunts, and one patient had both shunts. The shunts were performed at ages ranging from 3–18 months and recatheterization was performed from 0.7 to 12 years later (mean 3.9 yr). Ages at restudy ranged from 1.3–14 years and averaged 4.5 ± 0.8 years. Arterial oxygen saturation ranged from 62–91% (mean 83 ± 2%) and hematocrit ranged from 40–78% (mean 50 ± 3%).

Group 3 consisted of 18 patients studied following a reparative operation. Ten patients were repaired without an outflow tract patch and constitute Group 3A. Eight patients required an outflow tract patch of either pericardium or dacron to be placed across the anulus in seven instances and up to the anulus in one patient with an anomalous coronary artery and these patients constitute Group 3B. Three patients in Group 3A and six patients in 3B had a prior shunt procedure.

In table 2 age at operation, time from operation to restudy, right ventricular pressures (RVP) and resting gradients are compared for Group 3A versus 3B. Postoperatively Group 3B patients had a higher peak RVP and a higher gradient from RV to pulmonary artery than Group 3A. Three patients in each group had small residual shunts which were undetectable by oximetry and/or indicator dilution in all but one instance and were detected by cineangiocardiography. The one patient with larger shunt had a small VSD with a 17% left-to-right shunt calculated from a dye curve. Seven of eight patients in Group 3B had pulmonary incompetence by clinical exam, and one patient had mild tricuspid incompetence by clinical exam and by RV cineangiocardiography. None of the patients in 3A had either pulmonary or tricuspid incompetence by clinical exam or at catheterization.

All data were obtained during routine diagnostic cardiac catheterization. Premedication in infants ≤ two years of age was with meperidine 1 mg/kg and hydroxyzine 1 mg/kg in-

TABLE 1. *Patient Groups*

	Group 1 Preoperative (N = 34 studies in 32 pt)	Group 2 Postshunt (N = 14 studies in 13 pt)	Group 3 Postrepair (N = 18 studies in 18 pt)
Age at catheterization	3 days — 12 yr*	1.3 — 14 yr	1.6 — 10.8 yr
	2.1 ± 0.4 yr	4.5 ± 0.8 yr	6.1 ± 0.7 yr
Systemic O_2 sat	67 — 98%	62 — 91%	91 — 97%
	80 ± 2%	83 ± 2%	94 ± 2%
Hematocrit	36 — 73%	40 — 78%	34 — 45%
	47 ± 2%	50 ± 3%	38 ± 2%

*Top line is range, second line is x̄ ± SEM.

tramuscularly given at least 45 minutes prior to the cineangiocardiograms. Occasionally intravenous meperidine (0.25 mg/kg) was required during the procedure. In children > two years, Innovar was used in a dose of 0.025 cc/kg (maximum 1.0 cc IM) for premedication. Rarely additional intravenous Innovar was required during the procedure in a dose of ¼-½ the original dose.

Pressures were obtained prior to cineangiocardiography using NIH catheters with zero referenced to midchest. Oxygen saturations were determined using reflectance oximetry in all patients. Right ventricular (RV) and right atrial (RA) volumes were calculated from biplane cineangiocardiograms following injection into RV, RA, or superior vena cava. Left ventricular (LV) volumes were calculated following RV, PA, left atrial (LA), or LV injections. Ectopic and postectopic beats were excluded from analysis. Methodology for these calculations and normal values for comparison have been published previously.[1-3] Patient volume data are expressed in ml/m² or in terms of a percentage of predicted normal values using body surface area (BSA). Values between 75-125% of predicted normal are within the normal range of variation for these variables.

Results

Preoperative Patients

Right ventricular end-diastolic volume (RVEDV) averaged 88 ± 3% of normal for the entire preoperative group and was significantly different from normal, $P < 0.01$. The preoperative tetralogy group was also compared with normal by relating RVEDV to BSA for both groups. For the normal group, RVEDV (ml) = 69.9 (BSA)$^{1.37}$ and for the tetralogy group RVEDV (ml) = 65.9 (BSA)$^{1.16}$. Both the coefficients ($P < 0.05$) and the exponents ($P < 0.05$) were significantly different by the likelihood ratio test. In nine of

34 studies, RVEDV was < 75% of predicted normal, and none of the 34 studies showed an RVEDV > 125% of normal (fig. 1). Of the nine patients with a low RVEDV, five had a low ejection fraction. There was no significant correlation of RVEDV with age, Hct, arterial O_2 saturation, or LVEDV in this group.

Right ventricular ejection fraction (RVEF) averaged 0.58 ± 0.02 versus a normal value of 0.65 ± 0.01 and was significantly decreased ($P < 0.001$). The lower limit of normal for our laboratory for RVEF (mean − 2 SD) is 0.49 and eight patients had values < 0.49 (fig. 2). Of the eight patients with an ejection fraction < 0.49, three had a low RVEDV. There was no significant correlation of RVEF with RVEDV, Hct, or arterial O_2 saturation in this group.

Right ventricular systolic output (RVSO) averaged 81 ± 6% and was also mildly depressed ($P < 0.001$). Fourteen patients had values < 75% of normal.

The ratios RVEDV/LVEDV, RVEF/LVEF, and RVSO/LVSO averaged 0.98, 0.98, and 0.89 and were not significantly different from normal. Right atrial maximal volume (RaMax) could be calculated in 25 patients and averaged 135 ± 8% of normal ($P < 0.001$). Fourteen patients had RaMax values > 125% of normal (fig. 3).

Post Shunt Patients

RVEDV was normal in this group, averaging 114 ± 6%, and only one of the patients had a small RVEDV (< 75% of normal). RVEDV in shunted patients was significantly greater than that found for preoperative patients ($P < 0.002$).

Four patients with large shunts as judged by clinical course, physical exam, chest film, cardiac catheterization data, and LV volume overload (LVEDV 160-262% of normal) had both pre and post shunt RVEDV data as shown in figure 4. Here RVEDV in ml is plotted as a function of body

TABLE 2. *Comparative Values for Postcorrection Patients with and without an Outflow Patch*

	Group 3A (No outflow patch) N = 10	Group 3B (Outflow patch) N = 8	P value (3A vs 3B)
Age at operation	9 mos — 8 yr*	1.7 — 9.8 yr	NS
	4.1 ± 0.8 yr	5.9 ± 1.0 yr	
Time from operation to restudy	10 mos — 5.2 yr	0.8 — 2.8 yr	NS
	1.4 ± 0.2 yr	1.2 ± 0.2 yr	
Right ventricular peak pressure	30 — 58 mm Hg	34 — 100 mm Hg	<0.01
	46 ± 3 mm Hg	65 ± 8 mm Hg	
Right ventricular end-diastolic pressure	2 — 12 mm Hg	4 — 12 mm Hg	NS
	8 ± 1.1 mm Hg	8 ± 1.0 mm Hg	
Resting gradient (RV — PA)	0 — 26 mm Hg	0 — 50 mm Hg	<0.01
	18 ± 4 mm Hg	29 ± 7 mm Hg	

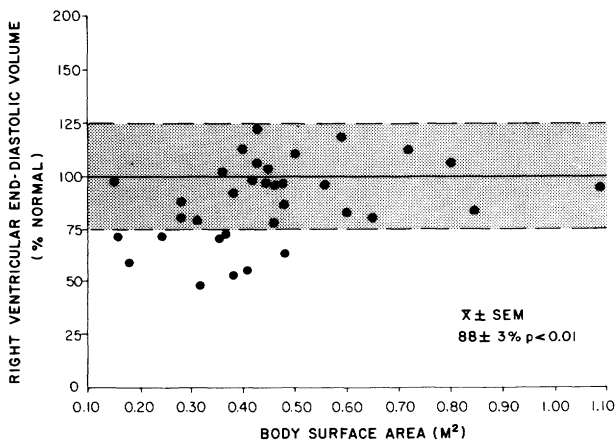*Top line is range, second line is x̄ ± SEM.

FIGURE 1. *Right ventricular end-diastolic volume as a function of body surface area for all preoperative tetralogy patients. The shaded area indicates the normal range.*
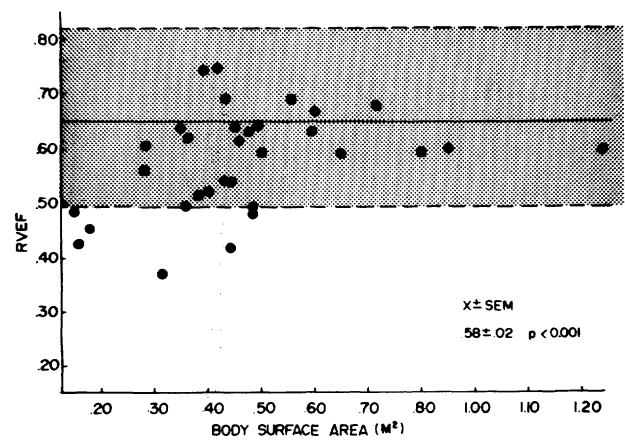

FIGURE 2. *Right ventricular ejection fraction as a function of body surface area for all preoperative tetralogy patients. The shaded area indicates the mean ± two standard deviations for normal.*

surface area. RVEDV clearly increases following a successful shunt procedure with preoperative values being normal or less than normal and postoperative RVEDV being greater than the normal upper limit for RVEDV. There was in this group a negative association of RVEDV with Hct ($r = 0.671$) as well as a positive correlation with arterial O_2 saturation ($r = 0.689$) and LVEDV ($r = 0.848$).

RVEF was mildly depressed in this group also, averaging 0.52 ± 0.02 ($P < 0.001$). This variable was not significantly different from that found for the preoperative group. In regard to individual values, five patients had RVEF < 0.49. Of these five patients, two had increased RVEDV and three had normal values.

RVSO also was mildly depressed averaging 91% of normal ($P < 0.01$). The value was not significantly different from the preoperative value. Only two patients in the shunt group showed RVSO values $< 75\%$ of normal and both had small shunts at the time of the study as reflected by elevated Hct (55 and 59%) and normal LVEDV (96 and 78% of normal).

In the 14 studies, seven showed large shunts and seven relatively small shunts as judged by clinical exam, chest film, Hct, systemic O_2 saturation, LVEDV, and LVSO (table 3, fig. 5). RVEDV and RVSO were significantly larger in the large shunt group as shown in figure 5. The ratios RVEDV/LVEDV and RVSO/LVSO were decreased from normal in the large shunt group but not different from normal in the small shunt group.

RaMax was determined in eight patients and was increased in seven and at the upper limit of normal in one instance from that for the preoperative group (fig. 3).

Post Repair

RVEDV averaged $108 \pm 6\%$ and was not different from normal in Group 3A patients with no outflow patch. This variable, however, was increased from the preoperative value of $88 \pm 3\%$ ($P < 0.05$). One of the ten patients had a slightly increased RVEDV of 138% of normal while all other patients were well within the normal range (fig. 6).

In contrast RVEDV was increased in seven of eight patients with an outflow patch (Group 3B) and averaged $177 \pm 15\%$ of normal ($P < 0.001$) (fig. 6).

RVEF was normal in nine of ten patients in Group 3A and averaged 0.60 ± 0.02 (NS) (fig. 7). This value was not different from the preoperative value of 0.58 ± 0.02. RVEF in Group 3B, however, was decreased in six of eight patients and averaged 0.45 ± 0.04 ($P < 0.01$) (fig. 7). This variable was also significantly decreased from the preoperative value ($P < 0.002$). For the entire post repair group, there was a
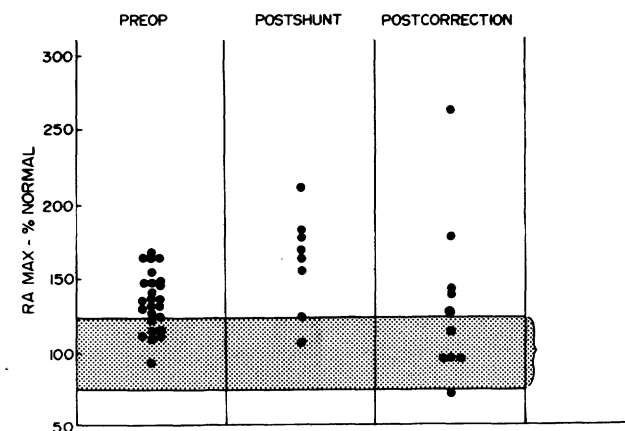
TABLE 3. *Postshunt Tetralogy Patients — Large and Small Shunt Groups ($\bar{x} \pm$ SEM)*

	2A. Small shunt N = 7	2B. Large shunt N = 7	P value (2A vs 2B)
Hct (%)	54 ± 1	45 ± 1	<0.01
Systemic O_2 sat (%)	79 ± 4	87 ± 2	<0.01
LVEDV (%)	97 ± 7	187 ± 18	<0.001
LVSO (%)	73 ± 9	184 ± 14	<0.001
RVEDV (%)	97 ± 4	130 ± 5	<0.001
RVEF	0.53 ± 0.02	0.52 ± 0.03	NS
RVSO (%)	77 ± 4	106 ± 5	<0.01
RVEDV/LVEDV	0.87 ± 0.04	0.65 ± 0.07	<0.01
RVEF/LVEF	1.17 ± 0.14	0.84 ± 0.07	<0.02
RVSO/LVSO	1.04 ± 0.13	0.55 ± 0.04	<0.001

FIGURE 3. *Right atrial maximum volume for preoperative, post shunt, and postcorrection tetralogy patients. The shaded area indicates the normal range.*
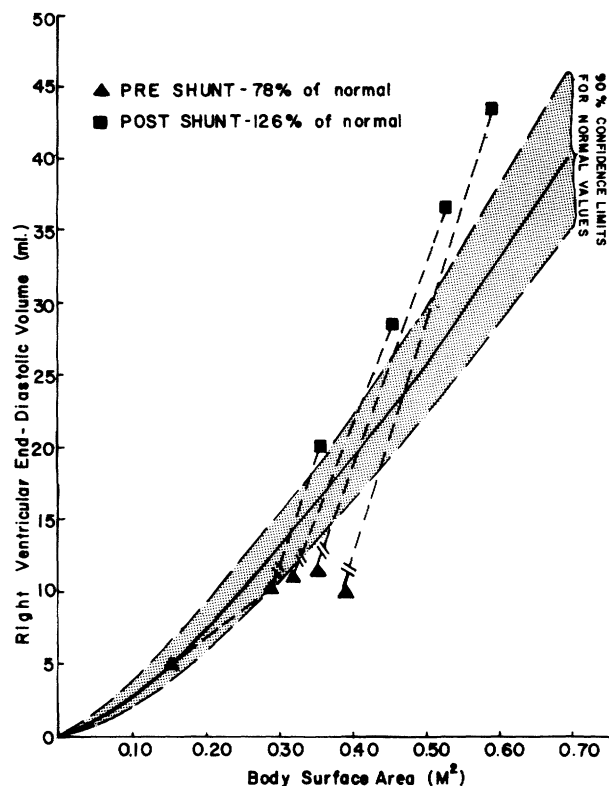
FIGURE 4. *Right ventricular end-diastolic volume in milliliters as a function of body surface area for four patients who had both pre and post shunt determinations of right ventricular end-diastolic volume.*

weak negative association of RVEF with RVEDV ($r = 0.572$).

RVSO was normal in eight of ten patients without a patch, averaging $95 \pm 8\%$. This variable was increased in three of eight patients with a patch and averaged $120 \pm 16\%$, a value which was not different from normal but
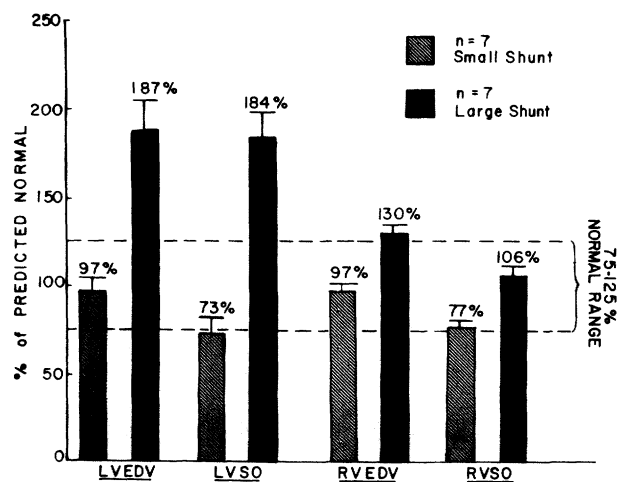
was increased over the preoperative value of 81 ± 6 ($P < 0.001$) (fig. 8).

RaMax was measured in ten patients and increased in two of six patients in Group 3A and in three of four patients in Group 3B (fig. 3).

The ratios RVEDV/LVEDV and RVEF/LVEF were not different from normal in Group 3A, but were significantly abnormal in Group 3B averaging 1.26 ± 0.11 ($P < 0.001$) and 0.73 ± 0.05 ($P < 0.001$). RVSO/LVSO was not different from normal for either group.

An initial attempt was made to separate the post repair patients into two groups according to age at operation. There were only five patients, however, with correction at $\lesssim 2.0$ yr of age and four of these had no patch used in the operation. Such a comparison, therefore, did not seem valid.

The possible influence of a previous shunt procedure on the post repair RV volume variables also was considered. Three of the ten patients in Group 3A had a prior shunt. These patients' RVEDVs were 93, 118, and 115% of normal following correction, and their RVEFs were 0.61, 0.60, and 0.69. Six of eight patients in Group 3B had a prior shunt procedure. Although the numbers are small, there was no obvious difference within each post repair group in RVEDV and RVEF values for patients with or without a previous shunt.

The possible influence of peak RV pressure on RV function following operation also was considered. In Group 3A none of the patients had a resting value for peak RVP > 58 mm Hg. In Group 3B peak RVP was > 60 mm Hg in four of the eight patients. In the four patients with high RVP (mean 84 mm Hg), RVEDV averaged 210% of normal versus 144% of normal for the four patients with low RVP which averaged 46 mm Hg. RVEF averaged 0.45 in both the high and low RVP subgroups. Thus in these small subgroups, RVEDV is larger but the ejection fraction is unchanged in the presence of more severe residual RV outflow obstruction.

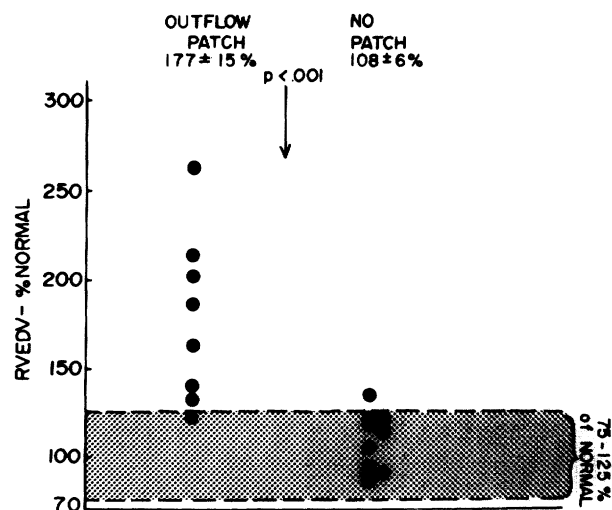Finally, the possible influence of pulmonary valvular in-

FIGURE 5. *Left ventricular end-diastolic volume, left ventricular systolic output, right ventricular end-diastolic volume and right ventricular systolic output for tetralogy patients following a shunt procedure. The patients designated as the small shunt group had clinical as well as catheterization findings of small shunts.*

FIGURE 6. *Right ventricular end-diastolic volume for patients following reparative operation. The patients are separated into those without an outflow patch and those with an outflow patch which was required in the reparative procedure.*
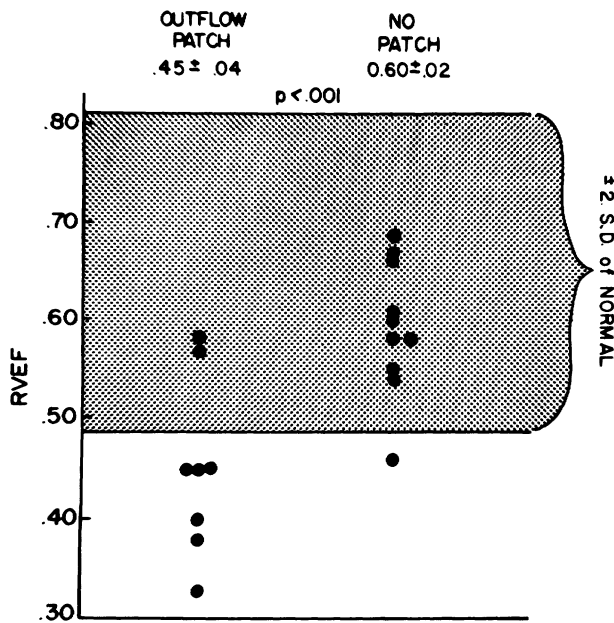
FIGURE 7. *Right ventricular ejection fraction for both post repair groups.*

FIGURE 8. *Right ventricular systolic output for both post repair groups.*

competence on RV size and function was considered. None of the patients in Group 3A had a significant diastolic murmur (I/VI) or evidence of filling of the body of the RV with pulmonary artery injections of contrast media. In Group 3B, six of eight patients had a pulmonary incompetence (PI) murmur of grade II–III/VI. All six patients had at least moderate RV body filling with pulmonary artery injection. Because of these small numbers and our inability to quantitate PI further, no conclusions could be made concerning this hemodynamic abnormality and RV size and function.

Discussion

In this investigation preoperative patients with tetralogy of Fallot were found to have mild depressions of RV end-diastolic volume, ejection fraction, and systolic output. Similar findings have been reported previously for both the left ventricle[4] and the right ventricle[5] in tetralogy patients. In the presence of a low end-diastolic volume, a subnormal ejection fraction does not necessarily indicate abnormal ventricular function since initial load (preload) is an important determinant of ejection fraction at least in acute experimental conditions.

In patients studied following a successful shunt procedure, RVEDV increases commensurate with the increase in pulmonary blood flow. This finding is in agreement with data we have obtained in patients with an isolated ventricular septal defect (VSD) in whom RVEDV was increased when pulmonary blood flow was increased.[6] This increase in RVEDV, which is less than the corresponding increase in LVEDV, is explicable in terms of the significant amount of diastolic and isovolumic LV to RV shunting which has been demonstrated in patients with both an isolated VSD[7] and tetralogy of Fallot.[8] These findings, together with the low end-diastolic volumes in preoperative patients, indicate the importance of pulmonary blood flow as a determinant of both right and left ventricular volumes in patients with a VSD.
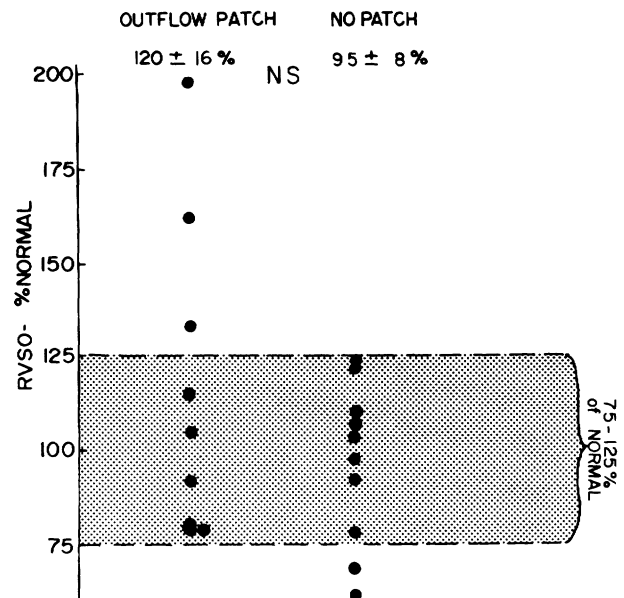
The RV ejection fraction in the shunted patients remained abnormally low despite a normal value for RVEDV. A low ejection fraction usually indicates a depression of RV function if the afterload for the RV is either normal or decreased. Quantitation of afterload for the RV is not possible by current methodology. Patients with isolated pulmonary stenosis have a normal or even increased RV ejection fraction,[2] and thus a chronic pressure overload per se does not cause a depression of RVEF. Patients with transposition of the great arteries, however, usually have a depressed RVEF,[9-11] suggesting that the combination of cyanosis and RV pressure overload can result in abnormal RV function. The possibility of a disturbance in the normal relationship between RV oxygen demands and oxygen supply being associated with such an abnormality in RV function[12] seems worthy of further investigation.

The increased right atrial volume seen in preoperative patients probably reflects the right ventricular pressure overload with resultant altered filling pressures for the RV. Although the RA size was in general lower following repair, some of this decrease in size may be related to the excision of RA tissue during bypass.

In patients studied following repair, two distinct groups were apparent. The presence of a noncontractile patch in the RV outflow tract with resultant significant pulmonary incompetence is associated with an abnormally large RV with a low ejection fraction. In contrast, patients who did not require an outflow patch had normal values for RVEDV and RVEF. There are multiple factors which may be associated with these findings including severity of RV outflow obstruction and cyanosis prior to operation, operative procedure itself, residual RV outflow obstruction, pulmonary incompetence, and the presence of the noncontractile patch itself.

There is no simple way to quantify the severity of the preoperative anatomy in these patients. The patients with severe RV outflow obstruction who required a patch usually had a shunt operation early in life and thus did not have a

long period of extreme cyanosis when compared with the no-patch group. In addition the operative procedure did not differ considerably between the two groups except for the need for the outflow tract patch in Group 3B.

We believe that the differences in RV function between the two groups are related to the combination of the presence of a noncontractile patch, pulmonary incompetence, and the slight difference in residual outflow tract obstruction between the two groups. The relative contribution of these three factors to the functional abnormalities remains difficult to determine.

Experimental animal studies of the effect of pulmonary incompetence on RV function have yielded conflicting results with some investigators showing normal RV function and output while others have shown evidence for depressed function.[13-17] Burnell and co-workers[18] studied seven dogs 4-5 months following pulmonary valvectomy. When compared with a group of five normal dogs, there were no differences in RV pressure, but there was a 50% increase in RV weight/body weight (2.1 g/kg vs 1.4 g/kg), an increase in RVEDV as measured by thermodilution (4.1 ml/kg vs 3.3 ml/kg), and a decrease in RVEF (0.31 vs 0.45). There were no obvious clinical signs of right heart failure in these animals and cardiac output was not different between the two groups. These investigators concluded that overall cardiac performance was relatively well maintained despite these laboratory measurements of abnormal RV size and pump function.

Burnell and co-workers[19] also have studied patients with thermodilution volume determinations 1-3 years following reparative operation for tetralogy. RVEDV in eight patients averaged 153 ml/m² versus a normal value of 103 ml/m² and RVEF was 0.33 versus a normal value for their lab of 0.47. The thermodilution method generally overestimates volume, but these directional differences in normal versus tetralogy patients undoubtedly are significant. Three of the eight postoperative patients with abnormal RV size and EF had neither clinical nor angiographic evidence for pulmonary incompetence. Residual gradients did not exceed 32 mm Hg in their patients and peak RV pressure ranged from 28-55 mm Hg. No data were given regarding the use of outflow tract patches in these patients.

The deleterious effect of RV a pressure overload in combination with a RV volume overload is well known. In our patients peak RVP was higher in the group with an outflow patch, and within this small group RV size was larger but RVEF the same in the high versus the low pressure group.

The possible relationship between abnormalities of RV size and ejection fraction and overall cardiovascular performance remains unclear. Most patients have a remarkable clinical improvement following tetralogy repair and usually show a normal response to mild exercise.[20-26] Bristow et al.,[27] however, studied ten patients at 13 months and again at seven years following tetralogy repair using supine exercise with a bicycle ergometer. Seven of the ten patients had an outflow patch. RV end-diastolic pressure was mildly elevated at both studies, and the exercise factor was mildly depressed in five of the ten patients. Epstein et al.[28] studied ten postrepair tetralogy patients, aged 12-36 yr, whose operation was performed 6 months - 4 yr prior to study. Five of the ten patients had clinical signs of significant pulmonary incompetence. Peak RVP at rest ranged from

22-43 mm Hg. The cardiac output response to intense exercise fell below the normal range in nine of the ten patients. Peak RVP increased from a mean of 35 mm Hg at rest to 80 mm Hg with intense exercise in six of the ten patients. The RV to pulmonary artery gradient increased from 17 mm Hg at rest to 43 mm Hg with intense exercise. Thus, these authors found significant impairment of the cardiovascular response to intense upright exercise despite lack of symptoms, near normal hemodynamics at rest, absence of dysrhythmias, absence of residual shunts, and absence of pulmonary hypertension.

The clinical significance of the findings of the present investigation remain unclear at present. Although many patients with tetralogy and markedly reduced pulmonary blood flow have a somewhat small right[5,29] (and left)[4] ventricle, the reduction in end-diastolic volume is usually only moderate in degree with both RVEDV and LVEDV being ⩾ 65% of predicted normal. We do not believe that such a reduction in ventricular size is a contraindication to repair. Rarely relatively severe hypoplasia of the right ventricle occurs which can be associated with an abnormality of the tricuspid valve (overriding tricuspid valve). If the RVEDV (and/or LVEDV) is < 55% of normal, we would at present consider a shunt procedure as a preferable first operation. Obviously, other major considerations such as outflow tract and pulmonary artery size enter into this decision. The data are not available at present in sufficient numbers of patients with both ventricular volume determinations as well as careful postoperative monitoring of right and left atrial pressures with cardiac output to determine if our present considerations regarding ventricular size and operative procedure are correct.

In regard to the effect of an outflow tract patch and pulmonary incompetence on long-term right heart function, the findings of this as well as previous studies indicate significant abnormalities of RV size and pump function. In patients with low RV pressure, these abnormalities are well tolerated. The majority of these patients have such severe abnormalities of the RV outflow tract that the use of a patch as well as the residual pulmonary incompetence are unavoidable consequences. The only alternative procedure at present would be the use of a valved conduit or homograft to reconstruct the outflow tract. Because of the uncertainty regarding possible future complications of this procedure, it does not seem a reasonable alternative for the usual tetralogy patient.

The long-term follow-up of large numbers of post repair tetralogy patients with ventricular volume determinations, exercise studies, and evaluation of their clinical course will be required to determine the significance of residual abnormalities of right heart function as reported herein and elsewhere.[5,19]

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Potential Role of QT Interval Prolongation in Sudden Infant Death Syndrome

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SUMMARY To investigate the possibility that a genetically transmitted cardiac abnormality is involved in the genesis of the sudden infant death syndrome (SIDS), 42 sets of parents who had at least one infant with SIDS were studied by electrocardiography. Prolongation of the QT interval was present in at least one member of 11 (26%) sets of parents. In families in which QT interval prolongation was found in a parent, prolonged QT interval was also present in 39% of the siblings of infants with SIDS, suggesting an autosomal dominant pattern of inheritance. In addition, an infant with "near-miss" SIDS showed marked prolongation of the QT interval. Thus, our data suggest that prolonged QT interval may play a role in a considerable proportion of sudden and unexpected infant deaths. However, definitive confirmation of the relation between QT interval prolongation and SIDS will require large prospective investigations.

SUDDEN INFANT DEATH SYNDROME (SIDS) is the largest single cause of death between one week and one year of age in the United States, accounting for the deaths of approximately 10,000 apparently well infants annually.[1, 2] Although numerous theories have been proposed,[2-5] the primary mechanisms responsible for SIDS are still unknown. Recently, many investigators have incriminated respiratory and cardiac mechanisms such as chronic hypoxemia,[6, 7] prolonged apnea,[8] dysfunction of central nervous system reflexes that are responsible for stabilization of cardiac rate,[9] or cardiac arrhythmias[10, 11] as the cause of SIDS.

We have considered the possibility that prolonged QT interval syndrome,[11-13] a genetically transmitted cardiac condition known to cause sudden death in children[11-13] and in infants,[14-21] is related to SIDS. The present study describes our investigation into the possible relation between prolonged QT interval syndrome and sudden, unexplained death in infancy.

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Right ventricular volume characteristics before and after palliative and reparative operation in tetralogy of Fallot.

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