

Abnormalities of Right Ventricular Function Following Mustard's Operation for Transposition of the Great Arteries

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SUMMARY

Postoperative data were obtained at cardiac catheterization in twelve patients studied 6–29 months following Mustard's operation for transposition of the great arteries (TGA) to assess the incidence and severity of abnormalities of right ventricular (RV) function. Age at operation was 5–13 months in seven patients (infant group) and 19–25 months in the remaining five patients. RV end-diastolic volume (EDV) decreased in all patients following surgery and averaged 123% of normal in the postoperative group (NS). RV ejection fraction (EF) was depressed postoperatively averaging 0.45 (69% of normal, $P < 0.001$) as was RV systolic output (78% of normal, $P < 0.01$). LVEDV averaged 65% of normal ($P < 0.001$), LVEF 0.67 (103% of normal, NS), and LV systolic output 67% of normal ($P < 0.001$) following operation. Left atrial (systemic venous) volume was decreased in all postoperative patients averaging only 39% of normal ($P < 0.001$). A high incidence (>50%) of partial baffle obstruction was found and LV systolic output showed a significant negative correlation with baffle gradients. The low output postoperatively may be related to decreased LV filling pressure, a small LV reservoir, and thus a small atrial "booster pump." Pressure-velocity indices of RV contractile function in four patients showed a poor correlation with pump function. Long-term follow-up will be required to determine the clinical significance of the abnormalities of venous return and ventricular function.

ALTHOUGH the short term results of Mustard's operation¹ for transposition of the great arteries (TGA) without associated intracardiac defects have been extremely gratifying in most patients, two recent reports have demonstrated abnormalities of right ventricular (RV) function in the majority of preoperative patients with isolated TGA²⁻³ and one of these reports also showed abnormal RV function in five of six postoperative patients.² The purpose of this investigation, therefore, was to attempt to determine the incidence and severity of abnormalities of RV function in twelve patients studied following successful intra-atrial baffle repair for TGA.

Patient Population and Methods

From July 1971 to July 1974, 17 patients have undergone intra-atrial baffle repair at Vanderbilt Medical Center for TGA with either an intact ventricular septum or a small ventricular septal defect (VSD). All patients have survived the

operation, but there have been two late deaths at 10 and 16 months postoperatively. Both deaths occurred in patients with systemic venous baffle obstruction. One of the patients (C.M.) who died also had severely abnormal RV function while the other patient did not have postoperative RV studies. Complete postoperative catheterization data including right and left ventricular volume studies have been obtained to date in 14 studies in 12 of these patients and form the basis for this report (table 1). At the time of surgery, the patients ranged in age from 5–25 months ($\bar{x} \pm \text{SD} = 15.1 \pm 6.7$ months), and their weights ranged from 5.1–9.9 kg (8.1 ± 1.5 kg). Seven patients had the operation performed at ages ranging from 5–13 months with weights from 5–8.9 kg. In this infant group, hypothermia with partial bypass and total circulatory arrest was used. The remaining five patients had the operation performed at ages 19–25 months with weights from 9.4–9.9 kg using conventional cardiopulmonary bypass. Preoperative left ventricular pressure (LVP) averaged 47 ± 6 mm Hg with LVP/RVP = 0.45 ± 0.07 . Two patients had small VSDs which were seen with selective cineangiograms but which were not closed at operation; thus, no patient had a ventriculotomy. Recatheterization was performed from 6–29 months (13.5 ± 5.7 months) following operation. Ten of the twelve patients were asymptomatic at the time of restudy. Two patients had intermittent edema, but despite this abnormality, their activity and exercise tolerance were described as normal by their parents. Only one patient (C.M.) was on cardiac glycosides at the time of recatheterization. Systemic O_2 saturation increased from $66 \pm 6\%$ preoperatively to $93 \pm 2\%$ postoperatively. Five of the twelve patients had residual shunts, and in four of these patients, the shunts were small and detectable only by indicator dilution studies or selective cineangiography.

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Table 1

Vital Statistics and Postoperative Hemodynamic Data

Pt	Wt at op (kg)	Age at op (mos)	Age at recath (mos)	Preop O ₂ sat (%)	Postop O ₂ sat (%)	Shunts		RVP (mm Hg)	LVP (mm Hg)	PAP (mm Hg)
						L-R	R-L			
1. R.B.	6.6	5	20	66	90	0	0	130/10	16/5	7/5
2. P.H.	6.8	9	15	70	93	0	0	115/4	27/5	--
3. V.B.	7.2	10	21	59	94	<20%*	6%*	110/5	26/6	--
4. L.Co.	8.9	10	17	65	99	0	0	95/5	29/4	25/19
5. B.C.	7.6	11	19	62	96	0	0	100/11	35/10	28/12
6. K.R.	7.0	11	23	76	91	<20%†	0	125/7	25/3	24/6
7a) T.B.	5.1	13	26	76	92	<20%†	0	85/3	17/5	9/6
b) T.B.			32		91	<20%†	0	80/3	18/2	--
8. C.M.	9.8	19	31	68	89	0	0	100/11	35/10	25/12
9. S.N.	9.5	20	31	66	95	0	0	110/3	30/4	20/10
10. T.G.	9.4	24	39	54	96	0	0	105/7	20/2	20/8
11a) P.M.	9.5	24	41	69	92	47%*	41%*	125/9	44/7	37/10
b) P.M.					88	45%*	32%*	140/12	44/12	35/14
12. L.Ca.	9.9	25	54	65	93	<20%*	6%*	105/12	36/2	26/10
Mean	8.1	15.1	26	66	93	--	--	109/7.6	29/5.5	23/10
± SD	± 1.5	± 6.7	± 11	± 6	± 2	--	--	± 14/± 3.2	± 8/± 2.9	± 9/± 2.6

*Baffle shunt.

†Small VSD.

Abbreviations: O₂ sat = systemic oxygen saturation; RVP = peak/end-diastolic right ventricular pressure; PAP = pulmonary artery pressure.

One patient (P.M.) had a moderately large bidirectional shunt in the superior limb of the baffle (table 1). In two patients small right-to-left shunts were found when injection of dye or contrast medium was made in superior vena cava (SVC) but not when injection was into inferior vena cava (IVC). Two patients (T.B. and K.R.) had small ventricular septal defects detectable only by selective cineangiograms at repeat cardiac catheterization which purposefully were not closed at operation because of their size and lack of hemodynamic effect.

All patients were in sinus rhythm at restudy, and none had a past history or electrocardiographic evidence for dysrhythmias. Right ventricular pressure (RVP) averaged $109 \pm 14/7.6 \pm 3.2$ mm Hg and LVP averaged $29 \pm 8/5.5 \pm 2.9$ mm Hg. No patient had significant pulmonary stenosis (PS): peak left ventricular to pulmonary artery pressure differences ranged from 0–10 mm Hg in ten of 12 patients while the remaining two patients had PS excluded at preoperative catheterization and postoperative LV pressures were 26 and 27 mm Hg.

All data were obtained at the time of routine diagnostic cardiac catheterization. Patients under two years old were sedated with meperidine 1 mg/kg and hydroxyzine 1 mg/kg given intramuscularly one hour or more prior to data collection. Additional intravenous meperidine 0.5 mg/kg occasionally was required. Patients two years or older were sedated with the neuroleptic combination of droperidol and fentanyl (Innovar) 0.025 cc/kg.⁴ Systemic venous and left heart pressure measurements were obtained prior to contrast medium injection with 5 F or 6 F NIH catheters attached to P23Db Statham transducers with mid-chest used for zero reference level. SVC to left atrium (LA) and IVC to LA gradients were obtained by pullback or simultaneous measurements in 11 of 12 patients. Cardiogreen indicator dilution curves were obtained in eight of 12 patients for shunt analysis or cardiac output determination. Injection was into SVC or IVC and withdrawal was from femoral artery through a short polyethylene catheter. Deter-

minations of O₂ saturation were obtained for shunt detection and quantitation by reflectometry (AO oximeter) prior to contrast medium injection.

Right ventricular pressures were obtained in the majority of patients following left heart cineangiography. These data were obtained only after at least 15 minutes had elapsed since the left heart cineangiogram, to allow time for the return of hemodynamics (aortic pressure, heart rate, and left heart pressure) to baseline. In an attempt to validate the cineangiographic measurements of RV volumes and output in patients with TGA, a repeat indicator dilution curve was obtained immediately prior to the RV cineangiogram in seven patients to allow a direct comparison of indicator dilution output with RV cineangiographic output derived from RV volume calculations. This comparison is shown in figure 1 where RV cineangiographic output is plotted as a function of indicator dilution output. There is close agreement between the two measurements ($r = 0.977$).

In four patients high fidelity pressure recording of RVP and dp/dt were obtained with a catheter-tipped micromanometer (Millar, 5F) and a Hewlett-Packard differentiator. The micromanometer has a frequency response that is flat to > 100 Hz. The differentiator has a frequency response which is a linear function of frequency to > 100 Hz when calibrated with a triangular wave input. Estimates of RV contractile element velocity and V_{max} were calculated with both total and developed pressure using the same equations and assumptions as have been used for the left ventricle. This methodology has been described previously.⁵

Right and left ventricular end-diastolic (EDV) and end-systolic volumes (ESV) and left atrial (systemic atrial) volumes were calculated from biplane cineangiocardiograms using previously described methods.⁶⁻⁷ All ectopic and postectopic beats were excluded from analysis. Comparisons were made with published normal values.⁶⁻⁷ In all but two patients, preoperative volumes were available for comparison. Statistical analysis of differences from preoperative values and differences from normal was per-

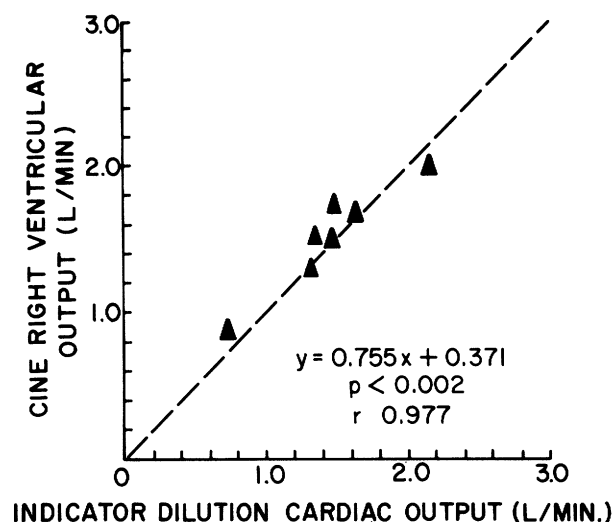


Figure 1

Right ventricular output derived from cineangiographic volume measurements as a function of indicator dilution cardiac output in postoperative transposition patients. Cine output = 0.755 (indicator dilution output) + 0.371 ($r = 0.977$).

formed using Student's *t*-test with a *P* value ≤ 0.05 considered significant.

Because of the high incidence of partial systemic venous baffle obstruction, an attempt was made to correlate caval to LA gradients with RV and LV volumes and outputs using regression analysis.

Results

Volume Determinations

Right ventricular end-diastolic volume (RVEDV) expressed as percent of normal is shown for pre and postoperative studies in figure 2. As in subsequent figures, the patients whose operations were performed

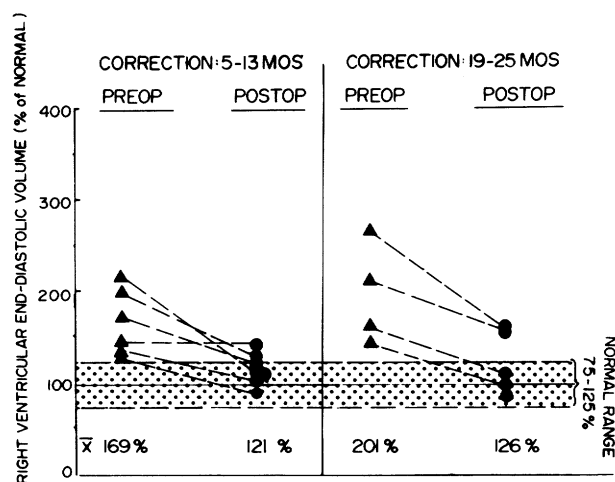


Figure 2

Right ventricular end-diastolic volume before and after Mustard's repair for transposition.

from 5–13 months (hypothermia with circulatory arrest) are plotted separately from those patients whose operations were performed from 19–25 months. All but one patient showed a decrease in RVEDV following operation with the changes in volume being of similar magnitude for both groups. Five of the twelve patients had persistent elevations of RVEDV ranging from 132–165% of normal. The average value of RVEDV for all 12 patients was 123% of normal, which is not significantly increased from normal.

Figure 3 shows RV ejection fraction (EF) for the same patients. This variable is below normal in eight of 12 patients and at the lower limit of normal in one additional patient. The average value for all 12 patients was 0.45 (69% of normal) which was significantly less than the normal value of 0.65 ($P < 0.001$). There were only small changes in the EF from pre to postoperative studies although each individual value for the EF decreased. The decreases ranged from 0.01 to 0.10 (mean 0.04) with six of the ten decreases being 0.04 or less.

In nine of ten patients with both pre and postoperative studies, RVEDV decreased. In six of these nine patients, the ejection fraction was essentially unchanged (-0.01 to -0.04) while in the remaining three patients, the EF decreased by 0.07 to 0.10. The one patient with an unchanged RVEDV showed a significant decrease in the ejection fraction from 0.49 to 0.42. These data are reflected in figure 4 which shows right ventricular systolic output (RVSO). All patients with pre and postoperative studies show a decrease in this variable. The preoperative values for the older patients are higher than those for the infants, but the postoperative values do not differ. The average postoperative RVSO for all patients was 78%,

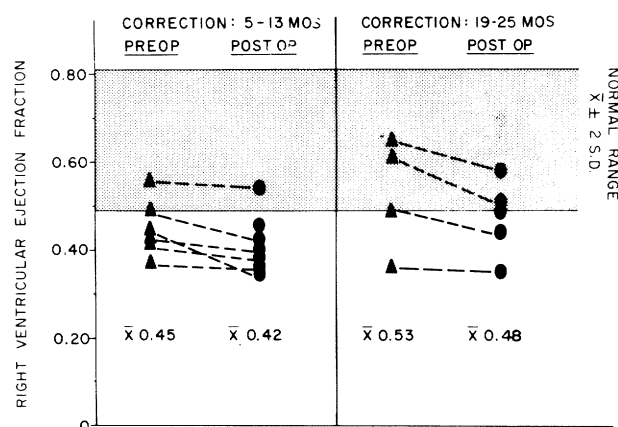


Figure 3

Right ventricular ejection fraction before and after Mustard's repair for transposition.

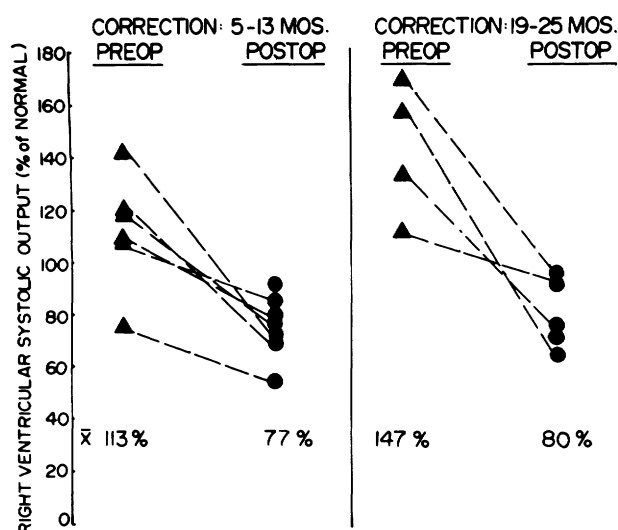


Figure 4

Right ventricular systolic output before and after Mustard's repair for transposition.

a value significantly less than normal ($P < 0.01$).

Left ventricular end-diastolic volume (LVEDV) is shown in figure 5. This variable decreased following operation in all patients with similar changes seen in both age groups. The average preoperative value for all patients was 128% of normal, and the postoperative value was significantly less than normal averaging only 65% of normal ($P < 0.001$).

The LVEF was normal in all patients both pre and postoperatively but decreased from a high normal value of 0.72 preoperatively to 0.67 postoperatively.

The findings for the LVSO were similar to the data obtained for LVEDV. LVSO averaged 138% of nor-

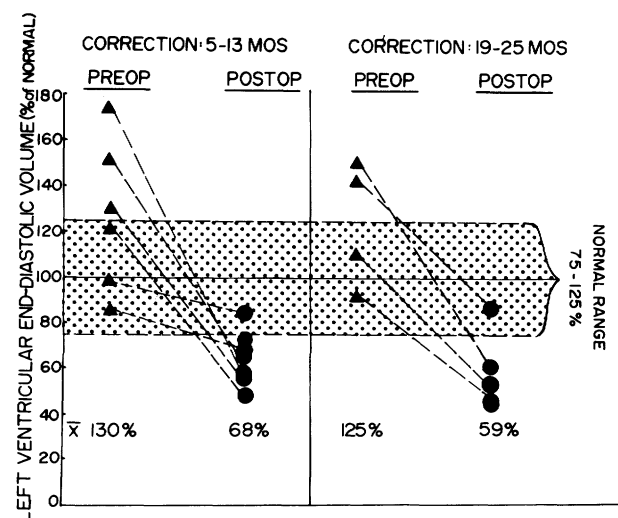


Figure 5

Left ventricular end-diastolic volume before and after Mustard's repair for transposition.

mal preoperatively and was decreased below normal to 67% following operation ($P < 0.001$).

Right ventricular EDV was greater than LVEDV in all patients with RVEDV/LVEDV averaging 1.75 versus a normal value of 1.00 and a value of 1.46 previously observed for preoperative TGA patients.³

Left atrial maximal volume (LAMax) is shown as a function of age in figure 6. This variable was decreased in all eleven patients in whom it could be determined, and averaged only $39 \pm 12\%$ of normal ($P < 0.001$). There was no significant correlation between LAMax and LV output.

RV Pressure Velocity Indices

Four of the patients studied postoperatively had high fidelity RV pressures and dp/dt measured just prior to RV cineangiography. Three of these patients had definitely decreased ejection fractions, and one had a value for RVEF at the lower limit of normal. In figure 7, values for peak VCE, Vmax index using total pressure, and maximal positive dp/dt are shown for these four patients. The shaded areas indicate normal left ventricular values. Despite abnormal pump function as manifest by the low ejection fraction, values for the velocity variables are within the normal range or increased.

Baffle Obstruction: Relation to Volume Data

Six of twelve (50%) patients had mean pressure differences greater than 5 mm Hg between SVC and the systemic venous atrium (left atrium [LA]) and six of eleven (55%) patients had mean pressure differences greater than 5 mm Hg from IVC to LA (fig. 8). In one patient catheterized from the arm, the IVC could not be entered, but LA cineangiogram

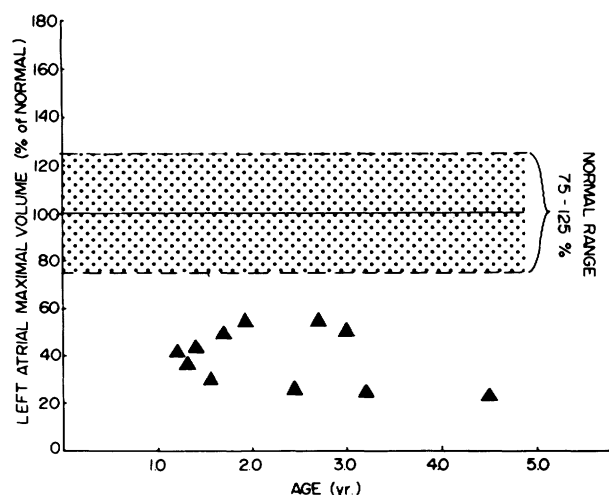


Figure 6

Left atrial maximal volume as a function of age for postoperative transposition patients.

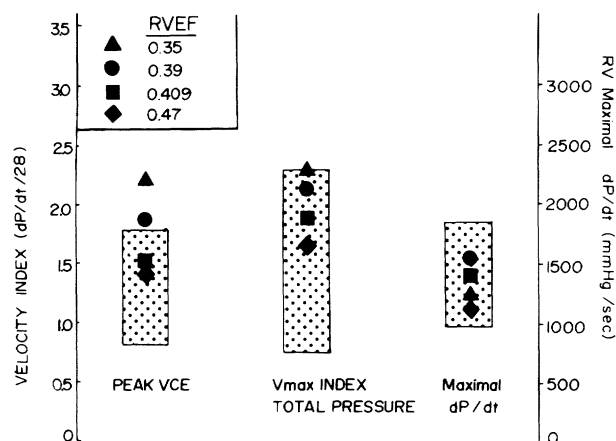


Figure 7

Right ventricular contractility indices for postoperative transposition patients.

revealed a narrowed baffle between IVC and LA. SVC to LA gradients ranged from 0–14 mm Hg (mean, 6.1 ± 4.2), and IVC to LA gradients ranged from 0–11 mm Hg (4.6 ± 3.7). Six of twelve patients had both SVC-LA and IVC-LA gradients greater than 5 mm Hg, and two of these six had intermittent edema. In both patients with edema, the SVC was virtually completely obstructed, and the lower limb of the baffle was narrowed.

The possible effect of age and size at surgery on baffle gradients can be assessed in figure 8. Three of seven infants (43%) had significant gradients recorded, while three of five older children (60%) had significant gradients recorded.

The possible effect of baffle material used also is illustrated in figure 8. Nine of twelve patients had a

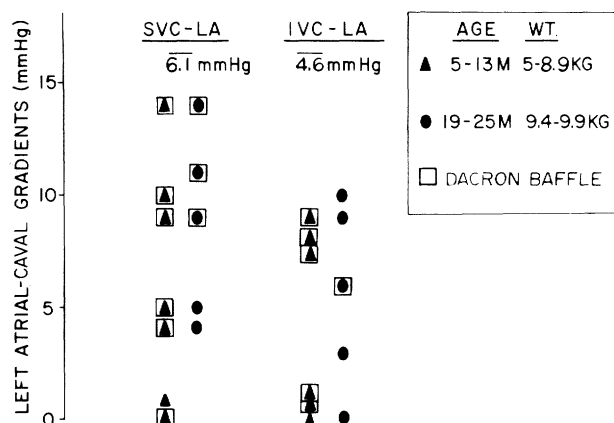


Figure 8

Gradients from left (systemic venous) atrium to superior vena cava (SVC) and inferior vena cava (IVC) in postoperative transposition patients.

dacron baffle and six of these nine (67%) had significant obstruction. None of the three patients with a pericardial baffle had significant obstruction. In addition, none of the twelve patients had evidence of significant obstruction of the pulmonary venous atrium by chest X-ray, pulmonary artery pressure (table 1), or cineangiocardiology.

The relationship between combined SVC-LA and IVC-LA gradients to left ventricular output is shown in figure 9. There is a significant relationship between the two variables showing that the highest gradients are associated with the lowest LV outputs. A weak relationship was found between LVEDV and caval gradients ($r = 0.460$).

Discussion

The majority of patients in this study showed evidence for abnormal right ventricular function as indicated by a normal or increased RVEDV, a depressed ejection fraction, and a low RV output. These data are in agreement with two previous reports of similar findings in preoperative TGA patients.^{2, 3} In addition, Jarmakani and Canent² found a depressed RVEF in five of six postoperative TGA patients who were operated upon between two and three years of age. Our data suggest that the operation itself did not impair RV function since there was little change in ejection fraction following operation. Furthermore, there was no clearcut evidence for a progressive deterioration of RV function with time since the infant group showed as much or greater depression of RV ejection fraction as the older age group. The cause of the abnormal RV function remains unclear; reversal of hypoxemia does not reverse the functional impairment. On a purely

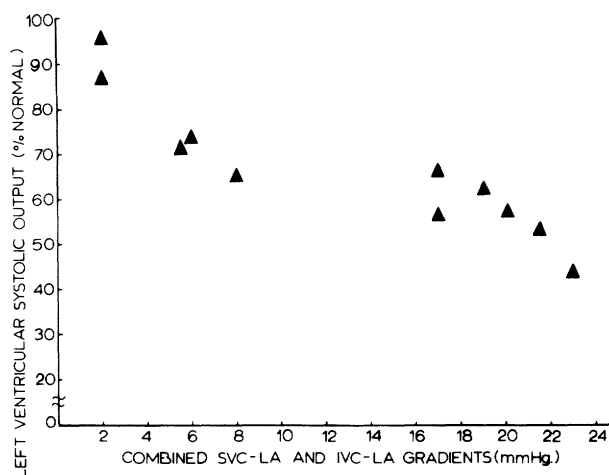


Figure 9

Left ventricular systolic output as a function of combined SVC-LA and IVC-LA gradients in postoperative transposition patients. $LVSO = -1.67 (\text{gradient}) + 87.73$, $r = 0.805$, $SEE \pm 7.09$.

speculative basis, one would consider long term relative myocardial ischemia with resultant permanent histological changes as a possible factor. Pressure overload of an anatomical right ventricle is probably not a major factor since patients with isolated severe valvular pulmonary stenosis without transposition have normal RV volumes and ejection fractions.⁷

Despite the obvious problems in the assumptions involved, we also considered RV function in terms of pressure-velocity indices of performance. It is not possible to measure true contractile element velocity either in the intact heart or in isolated cardiac tissue. Nevertheless, numerous investigators have demonstrated that measurements of dp/dt and derived velocity variables can reflect accurately changes in LV contractile state when preload and afterload are not markedly altered. In TGA where the RV pumps against systemic resistance, these measurements were performed using normal LV values for comparison. Despite severe depression of RV pump function, these velocity variables were normal or increased. Such a marked discrepancy between pump function measurements and velocity determinations was reported recently for the LV by Peterson et al.⁸ These findings indicate that normal cardiac function cannot be predicted reliably from normal pressures, dp/dt , and velocity variables, and that assessment of pump function is required for a complete evaluation of ventricular performance.

The findings for the left heart consisted of a small LVEDV, a normal LVEF, a low systolic output, and a small left atrium. There was a significant correlation between combined caval gradients and LVEDV and LV output. It is interesting to speculate on the relationship of the caval obstruction and the low output. It is possible that the caval obstruction produces a chronically diminished venous return with a low LV filling pressure. Parr et al.⁹ have shown diminished cardiac indices in infants studied in the early postoperative period following a Mustard procedure. These authors speculated that a small left atrium could impair LV output by loss of the reservoir function of the atrium with resultant limitation of diastolic flow into the atrium. Such a correlation between a small atrial volume and output has been shown experimentally.^{10, 11} With the usual intra-atrial sites for obstruction, the postoperative functional left atrium becomes a small chamber with limited capacity to serve as a booster pump to augment late diastolic filling of the left ventricle. Whether or not the small left atrium is an important contributing factor to the low LV output cannot be determined from our data.

Left heart volumes and output before and after Mustard's operation have been reported previously in four patients studied an average of one year following

surgery which was performed between two and three years of age. These patients did not have significant caval-atrial gradients and showed a decrease in LVEDV and output to normal but not subnormal values following operation.¹²

It is not possible to assess over-all LV function reliably. The ejection fraction is normal, but resistance to ejection is low, and thus impaired performance might be masked by this low impedance to ejection.

In regard to the possible effect of baffle obstruction on RV function, we can only speculate. Since the pulmonary and systemic circuits are in series following operation, the outputs of the two ventricles will be equal if there are no shunts and no valvular incompetence. Thus, if the baffle obstruction plays a role in the diminished LV output, it also is important in the diminished RV output. If systemic venous return were to return to normal, then one might expect RVEDV to increase and remain above normal since RV pump function is diminished and the Frank-Starling mechanism would be required to pump the augmented inflow.

The relationship of the altered hemodynamics and RV function to clinical status remains unclear at present. The majority of patients are asymptomatic despite clearcut abnormalities of right ventricular function and systemic venous return. We suspect that these patients have a diminished cardiovascular reserve and may have a lowered tolerance for stressful situations such as severe infections or prolonged strenuous activities. We have no proof for these speculations at present.

From the data presented, we have made the following conclusions: 1) Right ventricular pump function is impaired in TGA prior to correction and does not return to normal following successful operation. 2) Pressure-velocity indices do not reflect accurately the functional performance of the right ventricle in TGA. 3) Low left ventricular output postoperatively may be related to baffle obstruction with a resultant small left atrial reservoir and decreased LV filling. 4) Long term follow-up studies will be required to assess the clinical significance of both impaired RV performance and intracardiac baffle obstruction.

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