Cardiac Performance in Infants After Repair of Total Anomalous Pulmonary Venous Connection

Grant V. S. Parr, M.D., John W. Kirklin, M.D., Albert D. Pacifico, M.D., Eugene H. Blackstone, M.D., and Poul Lauridsen, M.D.

ABSTRACT Hemodynamic and metabolic data were obtained from 9 infants aged 4 months or younger early after repair of total anomalous pulmonary venous connection (TAPVC) in an effort to determine the cause of continuing mortality. A review by Barratt-Boyes [2] of recent experience from a number of centers shows that hospital mortality from repair of total anomalous pulmonary venous connection during the first 6 months of life is still 31% (16 of 51 patients). By contrast, in such centers the risk of repair of ventricular septal defect or tetralogy of Fallot, for example, is less than 10% in the same age group.

Immediately after repair the stroke index in all infants was lower than the mean for the entire study, but a significant positive trend with increasing postoperative time was noted in all early survivors. The cardiac and stroke indexes in the 2 patients who died early were significantly below normal but were similar to values obtained early after repair in a variety of other congenital heart diseases in infants of similar age. Abnormal phasic fluctuations in the left atrial pressures of these patients undergoing TAPVC repair indicated that the left atrium was small in relation to ventricular stroke volume (inadequate reservoir function). Thus, ventricular filling and cardiac performance may have been impaired.

We have studied the hemodynamic and metabolic states of a group of 9 infants following repair of total anomalous pulmonary venous connection (TAPVC) in an effort to determine the cause of a continuing mortality in infants undergoing this type of repair. We conclude that most deaths are the result of low and ineffective cardiac output, and that this in turn may be related to the small size of the left atrium in some of these patients.

Materials and Methods

PATIENTS

In the one-year period from July, 1972, to July, 1973, 11 patients 4 months of age and younger underwent repair of TAPVC. Two of these, both
2 weeks old, died within an hour after repair with clinical evidence of low cardiac output; they were not included in this study because cardiac output was not measured. The study group thus included 9 patients. Individual age, weight, body surface area, and type of pulmonary venous connection are shown in Table 1.

In the study group the mortality was 3 of 9 patients or 33.3%. Two patients, B. W. and C. Y., died of low cardiac output 20 and 16 hours, respectively, after repair. One patient, J. H., died on the ninth postoperative day after developing marked jaundice. (He is considered an early survivor in this paper.) Postmortem examination revealed a good repair but complete hepatic necrosis.

Patient M. M. developed stenosis of the anastomosis between the common pulmonary venous sinus and the left atrium after discharge from the hospital. She was successfully reoperated upon 3½ months later. She and the other 5 infants remain well.

TECHNIQUES OF REPAIR

Anesthesia included the use of halothane in all patients. Surface cooling to provide a nasopharyngeal temperature of 30°C., profound hypothermia (nasopharyngeal temperature 20°C.), and total circulatory arrest (about 45 minutes) with limited cardiopulmonary bypass were employed in all patients. Two venous cannulas were used in some patients [10]. Repair was performed through a median sternotomy with the heart mobilized to the left. The common venous sinus and left atrium were opened widely, the interatrial communication was closed by suture, and the common venous sinus was anastomosed to the left atrium. The abnormal venous connection was doubly ligated in all cases. Any patent ductus arteriosus was ligated prior to establishment of circulatory arrest.

<table>
<thead>
<tr>
<th>Patient &amp; Age</th>
<th>Weight (gm.)</th>
<th>BSA (m.²)</th>
<th>TAPVC Diagnosis</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>G. H., 3 mo.</td>
<td>5,440</td>
<td>0.321</td>
<td>Infra diaphragmatic to portal vein</td>
<td>Well</td>
</tr>
<tr>
<td>B. W., 2 days</td>
<td>3,280</td>
<td>0.255</td>
<td>Infra diaphragmatic with patent ductus</td>
<td>Died POD 1</td>
</tr>
<tr>
<td>L. H., 2 mo.</td>
<td>3,060</td>
<td>0.217</td>
<td>Left vertical vein</td>
<td>Well</td>
</tr>
<tr>
<td>C. G., 3 mo.</td>
<td>4,870</td>
<td>0.295</td>
<td>Azygos vein</td>
<td>Well</td>
</tr>
<tr>
<td>J. S., 1 mo.</td>
<td>3,960</td>
<td>0.254</td>
<td>Left vertical vein</td>
<td>Well</td>
</tr>
<tr>
<td>M. M., 2 mo.</td>
<td>4,190</td>
<td>0.268</td>
<td>Left vertical vein with patent ductus</td>
<td>Well</td>
</tr>
<tr>
<td>J. H., 2 wk.</td>
<td>3,170</td>
<td>0.217</td>
<td>Infra diaphragmatic with patent ductus</td>
<td>Died POD 9*</td>
</tr>
<tr>
<td>R. N., 2 mo.</td>
<td>3,260</td>
<td>0.247</td>
<td>Left vertical vein</td>
<td>Well</td>
</tr>
<tr>
<td>C. Y., 4 mo.</td>
<td>4,870</td>
<td>0.314</td>
<td>Left vertical vein</td>
<td>Died POD 1</td>
</tr>
</tbody>
</table>

*Died of hepatic necrosis.
BSA = body surface area; POD = postoperative day.
POSTOPERATIVE CARE

Postoperatively, blood was infused as required to keep mean left atrial pressure between 11 and 14 mm. Hg. Other measures were used as needed, including the infusion of epinephrine or isoproterenol or both (7 patients), digoxin (5 patients), and furosemide (6 patients). The patients remained intubated for 1 to 6 days postoperatively. Spontaneous breathing with continuous positive airway pressure alone was used in only 1 patient [17]. A volume ventilator was used initially followed by spontaneous breathing with continuous positive airway pressure in 6 patients. The 2 patients who died early postoperatively were maintained on volume ventilators. No patients received a tracheostomy. The fraction of inspired oxygen was varied between 72 and 40% while the patient was intubated in order to maintain an arterial Po\(_2\) above 70 mm. Hg. Mean arterial Po\(_2\) was 151.84 for all patients; the lowest Po\(_2\) was 41 mm. Hg subsequent to the initial resuscitation from cardiac arrest in patient C. Y. Mean Pco\(_2\) was 37.22 mm. Hg with a range between 24.0 and 57.0 mm. Hg. When bleeding became greater than was deemed acceptable, reoperation was performed 1\(1/2\) to 4\(1/2\) hours postoperatively (3 patients).

STUDY METHODS

Prior to sternotomy, a 20-gauge Teflon needle* was inserted into the brachial artery. At the conclusion of cardiopulmonary bypass, vinyl catheters† 0.028 inch in internal diameter were placed in the right and left atria and in some patients into the pulmonary artery.

Cardiac output was determined by the indicator dilution technique, using in each instance the mean of duplicate or triplicate measurements. The concentration of the indicator (indocyanine green) was 0.625 mg. per milliliter. One milliliter of indicator solution was injected rapidly by hand through the catheter into the right atrium or pulmonary artery. Blood was simultaneously withdrawn at a rate of 7.64 ml. per minute from the brachial artery through a cuvette densitometer‡ by a constant-rate pump.§ Five to 7 ml. of blood was withdrawn for each indicator dilution curve, and the blood was not reinfused. Cardiac output calculations were performed on a digital computer using the adaptation of the Stewart-Hamilton formula devised by Sekelj, Tait, and Nathanson [15]. Each curve was examined, and those without a good exponential decay of the indicator were rejected. Cardiac output was normalized by the body surface area (BSA), expressing it as cardiac index. The BSA (in square meters) was calculated from Boyd’s modification of the DuBois equation.

Pressure measurements were referenced to zero pressure at midchest level with the patients in a supine position. Strain gauges|| were calibrated at

†No. 6129, Becton, Dickinson and Co., Rutherford, N.J.
‡No. G250, Waters Co., Rochester, Minn.
||P23-DE and P23-BB, Statham Laboratories, Inc., Hato Rey, P.R.
frequent intervals using a mercury manometer. A continuous flushing system* insured patency of all catheters. Mean end-expiratory atrial pressures were derived after pressure variations in the atria due to the cardiac cycle had been electronically filtered. Phasic atrial pressures were recorded on a strip chart recorder without electronic filtering.

Immediately after withdrawal, heparinized arterial and venous blood was analyzed on automated assemblies† for pH, Po2, Pco2, hemoglobin, and oxygen saturation.

Oxygen consumption (Vo2) per square meter BSA was calculated by the formula:

\[ Vo_2 = CI \times [(Sao_2 - Svo_2) \times Hgb \times 1.34 + 0.0032 \times (Pao_2 - Pvo_2)] \]

in which

- CI = cardiac index (L/min/m²)
- Sao2 = arterial oxygen saturation
- Svo2 = venous oxygen saturation
- Pao2 = arterial partial pressure of oxygen (mm Hg)
- Pvo2 = venous partial pressure of oxygen (mm Hg)
- Hgb = hemoglobin

The data were analyzed by standard statistical techniques for means, standard deviation, and standard error of the mean. Unless otherwise specified, the data are presented as mean ±1 standard deviation. Linear and polynomial curve fitting was employed to examine changes in hemodynamic variables with time [1, 19]. For regression analyses the BMD02R stepwise regression computer program (forward stepwise with elimination) was employed [6]. All regressions are presented as the intercept and the regression coefficient ±1 standard error.

Results

The mean cardiac index for all patients averaged over the entire study period was 2.06 ± 0.695 L/min/m². Mean cardiac index in the 7 patients who survived early postoperatively was 1.87 ± 0.434 during the first 6 hours postoperatively and 2.32 ± 0.517 during the entire study period. As suggested by these numbers, in all surviving patients a trend of increasing cardiac index with postoperative time was noted which was statistically significant (p < 0.05) in 4 (Fig. 1). The mean cardiac index for the 2 patients who died early postoperatively was 1.27 ± 0.071 during the first 6 hours postoperatively. A trend of decreasing cardiac index with postoperative time was present but nonsignificant in each.

The mean stroke index for all patients averaged over all the study

*Intra-Flo CFS03F, Sorenson Research Corp., Salt Lake City, Utah.
†Model 313 and Model 182, Instrumentation Laboratories, Inc., Watertown, Mass.
period was $13.21 \pm 5.000 \text{ ml} \cdot \text{m}^{-2}$. In the 7 early survivors, mean stroke index was $10.59 \pm 2.780$ during the first 6 postoperative hours and $14.99 \pm 4.091$ during the entire study. In these patients, a significant ($p < 0.05$) positive trend with postoperative time was present. The 2 had a mean stroke index of $7.45 \pm 1.471$ during the first 6 hours, and no significant change of stroke index with postoperative time was noted in either (Fig. 2).

Cardiac index was significantly correlated with the mixed venous oxygen
saturation, the mixed venous PO₂, the arterial pH, and the arterial blood base excess (−1·base deficit); however, the variability was great with all of these (Fig. 3). An inverse correlation of cardiac index with heart rate was significant, but the variability was also great (Fig. 4).

Mean values for the systolic, diastolic, and mean arterial pressures were 90.70 ± 11.36, 51.90 ± 5.51, and 70.71 ± 7.49, respectively. Cardiac index did not correlate significantly at the 0.05 level with any of these pressures.
Mean oxygen consumption in the 7 patients in whom it was studied was 134.43 ± 27.501 ml·min⁻¹·m⁻², and this value was significantly correlated with the measured cardiac index. Again, great variability was noted (Fig. 5).

The mean right atrial pressure for all patients averaged over all times was 8.7 ± 1.62 mm Hg, whereas mean left atrial pressure was 13.1 ± 2.24 mm Hg. However, in all patients the phasic left atrial pressure fluctuated widely, with a rapid Y-descent early in diastole and a rapid increase (V wave) at the onset of systole (Fig. 6). In 1 patient mean left atrial pressure was 19 mm Hg.

FIG. 4. The cardiac index of each patient at each study is plotted against the heart rate measured at the same time. The regression equation is: CI = 3.792 - (0.010 ± 0.038) heart rate; r = -0.287; p < 0.01.

FIG. 5. The oxygen consumption of each patient at each study is plotted against the cardiac index measured at the same time. The regression equation is: oxygen consumption = 58.092 + (32.130 ± 7.888) cardiac index; r = 0.457; p < 0.01.
Comment

The accuracy, reproducibility, and limitations of the indicator dilution technique using indocyanine green in measuring cardiac output in adults have been well documented. The use of this technique in infants requires that dye concentration be no greater than 3 mg. per liter in the patient's blood [16] and that appearance time be greater than 5 seconds [14]. Our technique satisfied these criteria. The coefficient of variation for the duplicate and triplicate dye curves in these patients was 9.86%. To validate the technique used in these infants, we measured cardiac index by this technique over the complete range of cardiac indexes observed in this study using 2 puppies, weighing 6.0 and 10.5 kg., on right heart bypass. The mean difference between pump flow into the pulmonary artery and measured cardiac index was \(0.025 \pm 0.438 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}\). This value by paired t-test was not significantly different from zero.
TABLE 2. CARDIAC INDEX IN InfANTS WITH CONGENITAL HEART DISEASE AND IN NORMAL INFANTS

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of Patients</th>
<th>Mean ± SE (L. • min⁻¹ • m⁻²)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAPVC in early postop. period</td>
<td>9</td>
<td>2.06 ± 0.232</td>
<td>. .</td>
</tr>
<tr>
<td>(age ≤ 4 mo.) (present series)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital heart disease other than TAPVC</td>
<td>17</td>
<td>2.03 ± 0.188</td>
<td>n.s.</td>
</tr>
<tr>
<td>(first 72 hr. postop.) (age ≤ 6 mo.) (UAB)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal newborn infants (mean age 26.2 hr.)</td>
<td>23</td>
<td>4.06 ± 0.18</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(Emmanouilides et al. [7])</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal infants &amp; children (age &lt; 48 mo.) (Jegier et al. [8])</td>
<td>22</td>
<td>4.15 ± 0.25</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*p for differences from TAPVC group.

SE = standard error about the mean; n.s. = not significant; UAB = University of Alabama School of Medicine, Birmingham.

The values for cardiac index and stroke index in our patients must be interpreted in light of the fact that pharmacological support was used when indicated. Therefore, low values represent not only poor cardiac performance but inadequate cardiac reserve as well. Along this line, the mean left atrial pressure of 13.1 mm. Hg was determined by our therapy (see Materials and Methods).

The mean cardiac index of 2.06 for all patients averaged over all periods was not significantly different from the value of 2.03 which we have observed in 17 other infants aged 6 months or younger early after intracardiac repair of a variety of congenital heart diseases other than TAPVC (Table 2). Although few data are available about normal cardiac indexes for infants in this age range, the mean cardiac index was significantly below the 4.06 found in 23 neonates studied by Emmanouilides and colleagues [7]. It was also significantly below the 4.15 found in 22 normal infants and children less than 48 months old studied by Jegier and colleagues [8].

Cardiac index was correlated with oxygen consumption at a coefficient of only 0.457. We have the impression that this correlation is higher in adults and that postoperatively adults autoregulate so that oxygen consumption is reduced and mixed venous oxygen levels are only moderately depressed with a reduction of cardiac output. These infants increased their oxygen extraction markedly, such that the mean mixed venous Po₂ was 30.3 ± 5.96 mm. Hg (normal = 39.4) [5]. The mixed venous oxygen level was as low as 18 mm. Hg in a few patients, indicating a severe degree of tissue hypoxia. In this circumstance myocardial oxygen levels in particular could be expected to be low, which might further depress cardiac performance to a fatally low level.
TABLE 3. STROKE INDEX IN INFANTS WITH CONGENITAL HEART DISEASE AND IN NORMAL INFANTS

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of Patients</th>
<th>Stroke Index (ml. · m⁻²)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAPVC in early postop. period</td>
<td>9</td>
<td>13.21 ± 1.667</td>
<td>...</td>
</tr>
<tr>
<td>(age ≤ 4 mo.) (present series)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital heart disease other than TAPVC</td>
<td>17</td>
<td>13.46 ± 1.353</td>
<td>n.s.</td>
</tr>
<tr>
<td>(first 72 hr. postop.) (UAB)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal infants &amp; children</td>
<td>22</td>
<td>37.9 ± 2.43</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(age &lt; 48 mo.) (Jegier et al. [8])</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p for differences from TAPVC group. Abbreviations same as for Table 2.

The mean stroke index of 13.21 was not significantly different from that of the 13.462 which we have observed in 17 other infants 6 months of age or younger early after repair of congenital heart disease (Table 3). It was significantly below the mean of 37.9 found in the 22 normal infants 48 months of age and younger studied by Jegier [8].

The small stroke volume in these patients may have been due in part to the small, noncompliant left atrium often present in infants with this malformation, or to a small and noncompliant left ventricle. We have no data from this study relative to the latter possibility. The marked phasic pressure fluctuations seen in the left atrial pressure tracings are indicative of the poor reservoir function of such an atrium. During diastole the small volume of blood (in relation to ventricular stroke volume) held in this chamber empties rapidly into the ventricle, and the pressure drops precipitously. During systole it fills rapidly, generating abnormally high pressures. We have observed similar pressure tracings from the small systemic venous atrium created by the baffle employed for interatrial transposition of venous return in transposition of the great arteries [12]. Peters, Donovan, and Kawai [13] have reported similar atrial pressure tracings in calves after implantation of artificial hearts, and these marked pressure fluctuations were related to the small size of the atrium.

A small atrium may impair cardiac output. In 1963, Trusler and colleagues [18] found in dogs that reduction of atrial volume by more than 50% reduced cardiac output by about 40%. In a study of the performance of the artificial heart, Brighton and colleagues [3] showed that cardiac output was diminished by small or absent atria, especially with high heart rates or prolonged systole. Although there was an inverse correlation of stroke index and heart rate in these patients (r = -0.575, p < 0.001), it was not possible...
Cardiac Performance After Repair of TAPVC

to determine if rapid heart rates were detrimental to the stroke index in those patients with TAPVC.

Prior to repair of TAPVC, the left ventricle fills through the patent foramen ovale from the large right atrium which has good reservoir function. After repair, the left ventricle fills only from the left atrium, which has poor reservoir function. The resultant reduction of cardiac output may keep hospital mortality rates at present levels in sick, small infants with this malformation unless alternative methods of treatment are evolved. Enlargement of the interatrial communication by balloon septostomy and medical treatment for some months, as suggested by Mullins and colleagues [11], may not enlarge the left atrium; also, they noted a 44% mortality (4 of 9 patients) with this plan in infants less than 6 months of age. Alternatively, enlargement of the left atrium at the time of repair has been suggested for years [4, 9]. In fact, it may be difficult to do this effectively. In repairing a stenosis at the site of the pulmonary venous anastomosis of patient M. M., 3½ months after the initial operation, we noted that the left atrium remained small (its volume was about 1.5 ml.). Enlargement of the atrium with a Dacron-velour patch approximately doubled this volume. Nevertheless, after repair a marked drop in left atrial pressure was still noted in early diastole. Peak left atrial pressure was 15 to 17 mm. Hg, and left ventricular end-diastolic pressure was 8 to 10 mm. Hg. Cardiac index was 2.32 L. • min.⁻¹ • m.⁻²

References


Discussion

Dr. Quentin R. Stiles: (Los Angeles, Calif.): At the Children’s Hospital in Los Angeles we have operated upon 38 patients with total anomalous pulmonary venous connection. Of these, 22 were under 6 months of age. Our overall mortality has been 11 deaths, or 29%. The group under 6 months of age suffered a 36% mortality rate. This is not very different from Dr. Parr’s figures.

We have been tempted to use deep hypothermia with circulatory arrest to make the operation easier in a dry field, as described by the authors. We have not done so, however, because of our uncertainty of how to avoid brain damage, which may take years to become apparent. Instead we use normothermia or mild hypothermia and keep the pump running. Bleeding from the pulmonary venous side during the anastomosis is a nuisance but not an overwhelming problem.

In our experience a factor of significant prognostic importance is the anatomical type of anomalous connection present. Patients with the supracardiac or intracardiac varieties suffered a mortality of 20% and 15% respectively, whereas those with the intracardiac type, in which the common pulmonary venous trunk goes down through the diaphragm to join the portal system, experienced a 57% mortality. This is due to the fact that these children develop severe pulmonary congestion at a very early age. Both children with the mixed type died; this was due to their multiple congenital anomalies.

Dr. Parr’s paper establishes that a probable cause for failure of operative repair in some of these children is inadequate size of the left atrial reservoir. Unfortunately, there is very little we can do to remedy that. Another factor responsible for the high mortality in this disease is the rapid deterioration of these children once they begin to get into trouble from pulmonary congestion. An
educational process which would provide earlier diagnosis and lead to an operation before the baby becomes moribund probably would do much to improve the mortality statistics.

DR. PARR: I wish to thank Dr. Stiles for his comments. I would agree that it is not important whether the bypass technique of normothermia and high flow versus profound hypothermia and total circulatory arrest is employed. The similarity of the results by different bypass techniques might indicate that there is some anatomical problem with this defect itself which requires further surgical correction.

NOTICE FROM THE SOUTHERN THORACIC SURGICAL ASSOCIATION

The Twenty-first Annual Meeting of the Southern Thoracic Surgical Association will be held at the Williamsburg Inn and Lodge, Williamsburg, Va., November 7–9, 1974. Reservations may be made by writing to the Reservations Manager, The Williamsburg Inn and Lodge, Williamsburg, Va. 23185.

Application for membership in the Southern Thoracic Surgical Association, on forms provided by the Association, should be sent directly to George R. Daicoff, M.D. (Chairman of the Membership Committee), University of Florida College of Medicine, Gainesville, Fla. 32601. The deadline for application to membership is September 1, 1974.

Papers that are accepted for the program will be considered for publication in The Annals and must be submitted to the Editor by October 15, 1974.

James W. Brooks, M.D.
Secretary-Treasurer