Pulmonary Perfusion Abnormalities and Ventilation-Perfusion Imbalance in Children after Total Repair of Tetralogy of Fallot

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SUMMARY The pulmonary perfusion of 25 children who had total surgical correction of tetralogy of Fallot was evaluated by radionuclide perfusion scans. In addition, 18 had 133Xe ventilation studies. Eighteen of the children previously had palliative systemic-pulmonary shunts; 14 had aortic-pulmonary shunts (Waterston or Potts-Smith) and four had Blalock-Taussig shunts. Seven children had single stage total corrections.

An asymmetric perfusion pattern was found in 13 of 18 children who previously had systemic-pulmonary shunts, including 12 of 14 with previous aortic-pulmonary shunts (P < 0.05). The most common finding was relative hypoperfusion of the lung which had received the palliative shunt (P < 0.001). The distribution of ventilation remained relatively symmetric, even when perfusion was markedly abnormal, and this resulted in ventilation-perfusion imbalance in several patients. Asymmetric perfusion was significantly less common in patients who had undergone single stage corrections (P < 0.05).

The findings document the frequent occurrence of residual abnormalities of pulmonary perfusion and ventilation-perfusion imbalance in patients who have palliative aortic-pulmonary shunts prior to total repair, and support the position that single stage correction is preferable to aortic-pulmonary shunting in the surgical management of tetralogy of Fallot.

Palliative Systemic-Pulmonary Surgical Shunts are often employed to alleviate hypoxia in infants and young children with tetralogy of Fallot. Systemic-pulmonary anastomoses which have been employed at the Washington University Medical Center include the descending aorta to left pulmonary artery anastomosis of Potts and Smith, the ascending aorta to right pulmonary artery operation of Waterston, and the subclavian to pulmonary artery operation of Blalock and Taussig. When the children are older these shunts are taken down and a total surgical repair is performed. An alternative to this two-stage surgical approach is primary total surgical repair. This approach has also been used at this medical center. A group of patients who have had systemic-pulmonary anastomoses prior to total repair and several who have had single-stage repairs have been evaluated postoperatively by radionuclide studies of ventilation and perfusion. This report describes the findings of these radionuclide studies and examines the possible causes of the asymmetric pulmonary perfusion which was frequently present.

Methods

Twenty-five children who had total repair of tetralogy of Fallot were studied after parental consent was obtained. Eighteen children previously had palliative systemic-pulmonary shunts; seven had Potts-Smith shunts, seven had Waterstons, and four had a Blalock-Taussig shunt. These shunts were taken down at the time of corrective surgery. The age of the patients at the time of their initial palliative surgery ranged from one month to five years (table 1). Seven of the 18 patients were three years of age or older when they underwent their first operation. Three children required a second palliative operation; one had a clotted Potts shunt replaced by a Waterston and two had clotted Waterston shunts replaced by Blalock-Taussig shunts. Angiograms revealed definite alterations in the pulmonary perfusion of these patients after the initial palliative shunt, and angiograms done prior to total repair revealed that the changes persisted. Therefore, these patients were classified according to their initial palliative procedure. The average time between palliative surgery and total repair was six years (table 1). During the course of the study, over 80% of the Washington University Medical Center patients who had aortic-pulmonary shunts were evaluated. Seven patients had single stage corrective surgery. Two had single stage repairs when less than one year old, and five were three years of age or older. One patient who had mild cyanosis as an infant was first operated upon at age 12.

The interval between corrective surgery and the radionuclide studies averaged 19 months (range 1-55). In patients who had aortic-pulmonary palliative shunts, the average interval was 22 months (range 4-43). Several of our initial studies included only a perfusion scan and a chest radiograph, but 18 of the children also had a 133Xe ventilation study. The 133Xe study was performed with the patient seated in front of a gamma camera (Searle Radiographics — HP) which was interfaced to a small digital computer (PDP-12). For four to six minutes the patients breathed 133Xe in air (1 mCi/L) through a plastic mouthpiece connected to a simple rebreathing system. The studies were performed during tidal respiration; no breath holding or other special maneuvers were performed. After the rebreathing period, the patients breathed room air (washout). Children aged three and under were studied by delivery of the 133Xe gas through a standard nasal prongs set as previously described. Sequential polaroid images of 133Xe washin and washout were obtained and digitized data were collected. The relative distribution of ventilation was assessed by comparing the summed 133Xe counts which accumulated in each lung during washin. Perfusion lung scans were performed after the intravenous injection of 99mTc labeled macroaggregated albumin (MAA). The
patients received their injection. While in the supine position, but sat erect while a four view lung scan was obtained. Digitized perfusion data were collected in both the anterior and posterior projections and the counts appearing in each lung were compared to determine the relative distribution of perfusion.

Acceptable normal variations in the distribution of pulmonary perfusion and ventilation were derived from our previously reported studies in normal adult volunteers. Perfusion and ventilation are normally slightly asymmetric in distribution. The right lung receives an average of 52% of perfusion (± 3% SD), while the left lung receives 48 ± 3%. Ventilation is distributed 53 ± 2% to the right lung and 47 ± 2% to the left. Since we did not want variations of normal to be designated as asymmetric perfusion, we chose ± 3% from the mean as the normal limits in this study. Thus, the minimum relative perfusion considered normal for the right lung is 43%, while 39% is acceptable in the left lung. Using these limits, the probability of including a normal variant in the abnormal population is approximately 1%. We set more arbitrary limits to divide the abnormal population into those with mild, moderate, or severely diminished perfusion. If perfusion was decreased, but the lung contained more than 30% of total perfusion, the deficit was considered mild; if relative perfusion was more than 20% but less than 30%, the deficit was moderate; if a lung contained less than 20% of total perfusion the deficit was termed severe. The Chi-square test (Yates corrected) was used to establish the significance of differences in the frequency of abnormal relative pulmonary perfusion in various portions of the patient population.

A separate algorithm used the digital ventilation and perfusion data to calculate relative V/P ratios for each lung. The relative pulmonary distribution of 133Xe after 42 seconds of tidal breathing and the relative distribution of 99mTc-labeled perfusion particles were displayed simultaneously as grey-scale images on the computer output oscilloscope. The position of these images was then modified by the operator until they were superimposed. The algorithm then divided the relative tidal distribution of 133Xe by the relative distribution of 99mTc labeled MAA after both were normalized to regional lung volume. The distribution of 133Xe after rebreathing was used to represent the distribution of lung volume. Thus, the distribution of tidal volume per unit volume represented ventilation (V) and the distribution of perfusion per unit lung volume represented perfusion (P). These relative V/P ratios are not strictly comparable to physiologic V/Q ratios, but provide information similar to that obtained in radionuclide studies which use a single vital capacity breath of 133Xe to represent the distribution of ventilation. A normal V/P ratio for each whole lung is 1.1 (± 0.2 SD). When the lung is divided into an upper, middle and lower zone, an apical to base gradient is apparent. Normal V/P ratios are 1.7 ± 0.50 in the upper zone, 0.92 ± 0.10 in the midzone, and 0.88 ± 0.17 in the lower zones. Three standard deviations from the mean was again used as the limits of normal.

Perfusion lung scans had not been performed prior to initial operative interventions (several of which were eight to ten years prior to the current study), and perfusion scans are not a valid reflection of relative pulmonary perfusion when a functioning left-to-right surgical shunt is in place. Thus pulmonary angiograms were used to assess relative pulmonary perfusion prior to initial and corrective surgery. Angiograms are less sensitive than perfusion lung scans for detecting asymmetric relative perfusion; 60:40 asymmetry is needed before differences can be appreciated. Thus minimally asymmetric perfusion cannot be excluded in initial or precorrection studies which appeared angiographically symmetric. The angiograms also provided anatomic information essential for determining the etiology of the asymmetric perfusion found after total correction. Pre-existing anatomic lesions which could permanently alter pulmonary perfusion (e.g. pulmonary artery atresia, peripheral coarctations) were noted, as were changes in pulmonary artery anatomy which occurred after palliative
shunting. In addition, prior to total repair of patients with palliative systemic-pulmonary shunts, the ratio of resistance in the pulmonary vascular circuit of the shunted lung to that in the systemic vascular circuit (PVR/SVR ratio) was calculated by measuring the mean pressure and O₂ content of the four cardiac chambers. This provided information about the status of the pulmonary vascular system of the lung perfused by the palliative shunt.

The clinical record of each patient was also reviewed. Particular attention was given to the description of operative procedures and findings. Recent outpatient records and physical examination at the time of the radionuclide study confirmed the clinical status of the patients.

Results

The radionuclide studies revealed asymmetric pulmonary perfusion in 13 of 18 children (72%) who previously had systemic-pulmonary shunts (table 1), including 12 of 14 who previously had aortic-pulmonary shunts (P < 0.05). There were no radiographic or ventilation abnormalities that could account for this asymmetry. One patient who previously had a Potts shunt had mildly increased perfusion to the lung which had received the shunt. The other 12 patients with asymmetric patterns showed relative hypoperfusion in the previously shunted lung (P < 0.001). Right lung hypoperfusion was frequent in children with previous Waterston shunts (6/7) and left lung hypoperfusion was common when a Potts shunt had been present (5/7) (fig. 1). One patient who had a previous right Blalock-Taussig shunt had mildly decreased perfusion to the right lung. Moderate or severe perfusion deficits were present in four of seven patients with a previous Potts shunt and in two of seven patients who had Waterston shunts prior to total repair.

Since perfusion deficits occurred frequently in patients with previous aortic-pulmonary shunts and since there was hypoperfusion of the previously shunted lung in 11 of the patients, a causative relationship between palliative aortic-pulmonary shunts and residual perfusion abnormalities seemed likely. Pulmonary angiograms performed prior to surgical intervention revealed asymmetric perfusion in three of these 11 patients. The frequency of asymmetric perfusion was significantly higher (10/11, P < 0.01) when these same patients were studied prior to total repair.

Pre-existing anatomic abnormalities could not account

![Figure 1](http://circ.ahajournals.org/)

**Figure 1** The posterior perfusion images of six patients with previous central shunts are shown. The three patients in A had Potts shunts and the three patients in B had Waterston shunts. The patient numbers (table 1) are given in the right lower corner of each image. The hypoperfusion is on the side of the previous shunt in each case.

![Figure 2](http://circ.ahajournals.org/)

**Figure 2** The pulmonary angiogram of patient 4 (table 1) is shown (A). A Potts shunt was perfusing the left lung at this time. The study shows overcirculation of the left lung with proximal dilatation and rapid tapering of pulmonary vessels. The PVR/SVR ratio was normal. Also shown are the chest radiograph (B), ⁹⁹mTc washin image (C), and the perfusion image (D) obtained after total repair. There is marked discrepancy between left lung perfusion and ventilation. The V/P ratio of the left upper lung zone in this patient was 6.5:1.
for the findings. Two patients had a pre-existing stricture of one pulmonary artery; one patient (#2, table 2) had a 10% stricture of the left pulmonary artery and the other (#3, table 1) had a 50% stenosis of the left pulmonary artery. In most patients who had palliative aortic-pulmonary shunts, valvular and infundibular pulmonic stenosis co-existed with a nearly equal degree of severity. Valvular stenosis did predominate in five patients and infundibular stenosis was the dominant abnormality in one.

Several types of abnormalities were found which related the pulmonary perfusion deficits after total repair to previous aortic-pulmonary shunts. Eleven patients had angiographic evidence of relatively increased perfusion to the lung receiving the surgical shunt, and five of these patients had an elevated PVR/SVR ratio prior to total repair (mean ratio 0.50, range 0.29-0.85, normal upper limit 0.20). Three of these patients had Potts shunts, one had a Waterston shunt, and one had a Blalock-Taussig shunt. The highest PVR/SVR ratios (0.85, 0.74) occurred in two patients with large Potts shunts. These two patients and the patient with the Waterston shunt (#2, 3, 9, table 1) had hypoperfusion of the shunted lung after total repair. The two patients with Potts shunts also had surgical complications that will be described below. Six other patients with angiographic evidence of overcirculation in a lung receiving a palliative shunt had normal PVR/SVR ratios. Three of these patients had aortic-pulmonary shunts and demonstrated hypoperfusion of the shunted lung after repair (fig. 2), while three patients with slight overcirculation from Blalock-Taussig shunts had symmetric perfusion patterns. The pulmonary angiograms of four patients revealed decreased perfusion of the shunted lung prior to total repair. In each case, the pulmonary artery was kinked and stenosed at the site of its insertion into the aorta. Changes in pulmonary artery anatomy after palliative shunting could be documented by comparing initial and pre-repair angiograms (fig. 3). All patients with this finding had relative hypoperfusion of the previously shunted lung on the radionuclide study performed after total repair. There were significant postoperative complications after total repair in two patients with central shunts (#2, #3, table 1). Both had Potts shunts which were difficult to take down. Immediately after repair each patient developed a large pleural effusion and marked congestion of the left lung. The patients became stable within seven to ten days and no further intervention was made. Radionuclide studies were obtained at this time in both patients and showed virtually no perfusion of the left lung. Repeat radionuclide studies over one year later, when both patients were asymptomatic, showed no significant change.

Extensive patch reconstruction of the right ventricular outflow tract was performed prior to total repair in eight patients who had palliative central shunts. Five had asymmetric perfusion patterns after total repair, but in each instance there was relative hypoperfusion of the lung which had received the shunt (three right, two left).

An asymmetric perfusion pattern was present in only two of seven patients (28%) who had single stage corrective surgery (table 2). This is not significantly greater than the frequency of asymmetry seen preoperatively in these patients, and is significantly lower than the frequency of asymmetric perfusion found after total repair in patients with previous aortic-pulmonary shunts (P < 0.05). One of two children who had single stage correction when less than one year of age had mildly asymmetric perfusion (fig. 4). Four of five children who underwent single stage repair when aged three or older had symmetric perfusion patterns. In contrast, four of seven children who first underwent palliative surgery at

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age three or older had asymmetric perfusion after total repair. In one case (fig. 2) the asymmetry was severe.

The relative distribution of ventilation after total repair was normal in six patients who had single stage correction and in nine of 12 patients studied who previously had a central shunt. In two patients with previous Potts shunts (#3, #4, table 1) ventilation was shifted away from a markedly hyperperfused left lung. However, the degree of shift was too small to compensate for the hyperperfusion and markedly elevated whole lung and regional V-P ratios resulted (fig. 2). One patient (#9, table 1) with a previous Waterston shunt had a minimally abnormal distribution of ventilation (i.e., just over 59% relative ventilation of the right lung). However, mild hypoperfusion of the right lung was present and this led to a mild V-P imbalance.

All patients were asymptomatic at the time of their radionuclide study. There were no complaints of congestive failure or cyanotic episodes. All patients denied exercise intolerance. Five of the eight children who had extensive patch reconstruction of the right ventricular outflow tract had grade one or two diastolic murmurs of pulmonary insufficiency. Three of these patients had symmetric perfusion, and two had decreased perfusion to the right lung which had received an aortic-pulmonary shunt.

Discussion

Puyau and Meckstroth compared lung scan findings and pulmonary angiograms in patients with tetralogy of Fallot and showed that scans accurately reflect the relative distribution of pulmonary blood flow prior to surgery and in patients who have total repairs. Draulans-Noë and Evenblij used perfusion scanning to evaluate 38 patients with tetralogy of Fallot who had undergone complete repair after having a palliative shunt. The authors were surprised to find relatively diminished perfusion to the previously shunted lung in 20 patients (53%). This was most common in patients who previously had a large Potts shunt. The authors did not quantitate the perfusion deficits. The current study confirms the high frequency of residual abnormalities of pulmonary perfusion in patients who have had an aortic-pulmonary shunt prior to total repair, and demonstrates that approximately 40% of these patients have moderate to severe perfusion deficits. Draulans-Noë and Evenblij also reported nine patients with increased perfusion in the lung which had received a shunt. We could not confirm this finding. Only one patient in the current study had this pattern and the increase was barely beyond the limits of normal variation. The lower frequency of this finding in our study may be related to the fact that we studied fewer patients who had Blalock shunts. Seven of the nine patients with increased perfusion in Draulans-Noë's study had previous Blalock-Taussig shunts.

The results of the current study demonstrate a relationship between palliative aortic-pulmonary shunts and residual abnormalities of pulmonary perfusion. This group of patients had a significantly higher frequency of postrepair asymmetric perfusion (12/14) than patients with single stage repairs (2/7) \( P < 0.05 \) or patients with single stage repairs combined with those who had Blalock-Taussig operations (3/11) \( P < 0.025 \). Several reasons for the higher frequency of postcorrection abnormalities after a Potts or Waterston procedure were apparent:

1) Patients with pulmonary overcirculation from the surgical shunt could develop elevated vascular resistance in the shunted lung, which could result in relative hypoperfusion of that lung after total correction. Persistent pulmonary hypertension after palliative shunting has been previously reported and is usually secondary to pulmonary arteriolar disease caused by the effects of elevated pressure and flow in the shunted lung. Potts shunts have been cited as causative factors in some reports, but Waterston and Blalock-Taussig shunts have also been associated with this complication. Only two patients in the current series had PVR/SVR ratios which were markedly elevated (0.85, 0.74) prior to total correction, and both had Potts shunts. Several patients in the current study who had angiographic evidence of pulmonary overcirculation from a surgical shunt showed a postrepair shift of perfusion away from the shunted lung even though there was no evidence of elevated pulmonary vascular resistance.

2) Some patients developed strictures where the pulmonary artery was kinked upward at the site of its attachment to the aorta. This proximal obstruction to flow resulted in relative hypoperfusion of the involved lung after total correction, even though attempts were made to surgically correct the deformity at the time of total repair.

3) Finally, operative damage of the pulmonary artery when the palliative shunt was taken down seemed to be an important factor in two of our patients. Operative damage may have been equally important in other cases but there is no direct evidence to support this.

Pre-existing lesions could not account for the asymmetric pulmonary perfusion. Only two patients had significant vessel stenoses prior to palliative shunts. Conway has shown that asymmetric perfusion may occur secondary to a streaming effect caused by the anatomy of the stenotic pulmonary outflow tract. Infundibular stenosis favors right lung perfusion while valvular stenosis leads to increased left lung perfusion. In our population, these lesions were com-
monly coexistent and the baseline perfusion of the majority of patients was relatively symmetric.

Puyau has suggested that flow changes occur secondary to surgical reconstruction of the right ventricular outflow tract during repair, and that these flow changes favor perfusion of the right lung. In the current study, the frequency of asymmetric perfusion in patients with outflow reconstruction did not differ from the rest of the population. When these patients also had a previous aortic-pulmonary shunt, relative hypoperfusion was found in the lung which had received the shunt. Therefore, although reconstruction of the pulmonary outflow tract may alter flow and favor right lung perfusion, changes caused by previous aortic-pulmonary shunts predominated when both were present.

Previous studies have not assessed ventilation or ventilation-perfusion balance in patients after repair of tetralogy of Fallot. Only three of 12 patients with central shunts had an abnormal distribution of ventilation and each of these patients had markedly asymmetric perfusion. The abnormal distribution of ventilation was most likely a secondary response to this altered perfusion pattern. However, the perfusion was diminished to such a degree that the shift of ventilation did not completely compensate and V/P imbalance resulted. These three patients and the others investigated in the current study were asymptomatic. Since the primary purpose of a palliative surgical shunt is to reverse the hypoxemia of the patient, one could argue that the operation served its purpose and that there was no significant adverse effect to these patients. However, one might also predict that these patients will be predisposed to pulmonary difficulties later in life. Lack of coordination of ventilation and perfusion is the most common cause of hypoxemia and becomes clinically important when other areas of lung cannot compensate by increasing ventilation to normally perfused areas. Should these patients develop pulmonary disease in their better lung, their ability to compensate V/P imbalance would be limited. Of course, this concern presumes that the abnormalities we have demonstrated are irreversible. Long-term studies of these patients will be needed to establish the true significance of the perfusion abnormalities and V/P imbalance to their pulmonary health.

Ruzyllo et al. have reported that the results of total repair are hemodynamically less satisfactory if a systemic-pulmonary shunt has been present prior to total repair. The current study supports this position by demonstrating the high probability of residual abnormalities of perfusion and V/P imbalance when an aortic-pulmonary shunt has been present. Furthermore, the results demonstrate that these problems occur less commonly when a single stage surgical approach is employed. Starr, Bonchek and others have demonstrated the feasibility of single stage repair in infants. The results of the current study support the position that single stage repair is preferable to aortic-pulmonary palliative shunting in the surgical management of tetralogy of Fallot.

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