

PEDIATRIC CARDIOLOGY**Assessment of the Intrapulmonary Ventilation-Perfusion Distribution After the Fontan Procedure for Complex Cardiac Anomalies: Relation To Pulmonary Hemodynamics**

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In 12 patients who underwent the Fontan procedure for complex cardiac anomalies, lung scanning with xenon-133 was performed to assess the intrapulmonary ventilation-perfusion distribution, and comparison was made with a control group. All data were then analyzed in relation to either pre- or postoperative pulmonary hemodynamic data. In ventilation scans, the intrapulmonary distribution in the right lung was almost normal.

In perfusion scans, an abnormal increased upper to lower lobe perfusion ratio greater than the normal value found in the control group was noted in seven patients (58.3%). There was a significant correlation ($p < 0.02$) between the upper to lower lobe perfusion ratio and postoperative pulmonary vascular resistance. Furthermore, this perfusion ratio correlated inversely with the preoperative ($p < 0.005$) and post-

operative ($p < 0.02$) right pulmonary artery area index, defined as the ratio of cross-sectional area to the normal value. Of five patients with $<90\%$ arterial oxygen saturation, four showed an abnormal distribution of pulmonary blood flow greater than the normal perfusion ratio. No patient had evidence of a pulmonary arteriovenous fistula by the echocardiographic contrast study.

These results suggest that abnormal distribution of pulmonary blood flow to the upper lung segment may develop in patients after the Fontan procedure, and that insufficient size of the pulmonary artery before operation and the consequent postoperative elevation of pulmonary vascular resistance may be responsible for this perfusion abnormality.

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Since the successful application of the Fontan operation for tricuspid atresia (right atrial-pulmonary artery anastomosis) (1-4), various modifications of this operation have been extended to other complex congenital cardiac anomalies (5-8). Although the criteria for patient selection have been well established and operative risk has been reduced, the resulting pulmonary hemodynamics after these right-sided cardiac bypass procedures have not been fully elucidated. In one of the abnormal hemodynamic situations, the pulmonary circulation is exposed to a low pulsatile flow (9,10). The result may be abnormal distribution of pulmonary blood flow

and consequent influence on lung or cardiac function over the long-term after these surgical procedures.

Recently, Cloutier et al. (11) showed abnormal distribution of pulmonary blood flow after the Fontan or Glenn procedure (cardiopulmonary shunt) by using lung scintigraphy with xenon-133 and technetium-99m. However, the mechanism involved and its relation to the hemodynamic background are still unclear. In the present study, therefore, we determined the pulmonary ventilation-perfusion distribution using xenon-133 as the radionuclide tracer, and analyzed the relation between the scintigraphic data and hemodynamic variables of the pulmonary circulation.

Methods

Study patients. Twelve patients with complex cardiac anomalies who had undergone the Fontan procedure were studied. The cardiac anatomy and surgical procedure for

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Table 1. Diagnosis and Operative Procedures in 12 Patients

| Patient No. | Diagnosis | Surgical Procedure | Age at Fontan Procedure (yr) | Previous Palliative Surgery |
|-------------|----------------------------|------------------------|------------------------------|-----------------------------|
| 1 | TA, PS, d-TGA | RA-PA | 12 | Lt B-T |
| 2 | SV, PS, CAVV, Bi SVC | RA-PA, IAR, Lt SVC-PAA | 9 | Lt B-T |
| 3 | TA, PS | RA-PA | 8 | Bi B-T |
| 4 | SV, PS, CAVV, dextrocardia | RA-PA, IAR | 12 | None |
| 5 | TA, PS | RA-SPRV | 3 | None |
| 6 | MA, PS, TA-PVD | RA-PA, IAR | 8 | Rt B-T |
| 7 | MA, PS, d-TGA | RA-PA, IAR | 16 | Rt B-T |
| 8 | TA | RA-SPRV | 4 | PAB |
| 9 | SV, PS, 2AVV | RA-PA, IAR, Lt SVC-PAA | 7 | Lt B-T |
| 10 | SV, PS, CAVV | RA-PA, IAR | 12 | Lt B-T |
| 11 | Pulmonary atresia | RA-PA | 8 | CS |
| 12 | SV, PS, CAVV, I-TGA | RA-PA | 8 | Lt B-T |

Bi = bilateral; B-T = Blalock-Taussig shunt; CAVV = common atrioventricular valve; CS = central shunt; IAR = intraatrial routing; Lt = left; MA = mitral atresia; PAB = pulmonary artery banding; PS = pulmonary stenosis; RA-PA = right atrial to pulmonary artery connection; RA-SPRV = right atrial to subpulmonary right ventricular connection; Rt = right; SV = single ventricle; SVC = superior vena cava; SVC-PAA = superior vena cava to pulmonary artery anastomosis; TA = tricuspid atresia; TAPVD = total anomalous pulmonary venous drainage; TGA = transposition of the great arteries; 2AVV = two atrioventricular valves.

each patient are summarized in Table 1. There were four patients with tricuspid atresia, five with single ventricle, two with mitral atresia and one with pulmonary atresia. Age at the Fontan procedure ranged from 3 to 16 years (mean \pm SD 9.3 ± 3.7). All but Patients 4 and 5 had previously undergone palliative surgery; eight had a Blalock-Taussig shunt, one had pulmonary artery banding and one had a central shunt. All of these were released at the time of the Fontan procedure. The procedures performed were a right atrium to pulmonary artery connection in 10 patients, including 6 with intraatrial routing in the common atrium for converting the systemic venous return to pulmonary flow, and a right atrial to subpulmonary right ventricular connection in 2. In two patients, a persistent left superior vena cava was divided and anastomosed to the left pulmonary artery in an end to side fashion (12).

Radionuclide assessment. Lung scanning was performed 1 to 23 months (mean 9.4 ± 7.7) after the Fontan procedure with a Toshiba gamma camera (GCA-401-5) interfaced to a Toshiba nuclear medical data processor (GMS-55A), according to the method of Ohno et al. (13). For the ventilation scans, the patient was in the sitting position and inhaled a mixture of 25 mCi xenon-133 gas and room air in a xenon-133 gas control system (ANZAI, AZ-701-NTS) from the maximal expiratory level to the maximal inspiratory level (total lung capacity level). Counts for the upper, middle and lower lung segment on both sides were obtained while the patient held his or her breath for several seconds. Counts at the equilibrium state were also obtained after rebreathing in closed circuit. Thereafter, xenon-133 was washed out of the

airway in an open circuit with steady breathing. Terminally at the background level in perfusion scans, 5 mCi of xenon-133 saline solution was rapidly injected intravenously in an arm while the patient held his or her breath at total lung capacity level until the radionuclide count rate reached a plateau on the recorder. A regional count rate analogous to regional perfusion was thus obtained. The data determined for the regional ventilation distribution and perfusion distribution were corrected for the regional lung capacity measurement. The ratios of the upper to lower lung segment in both the ventilation and perfusion distributions were then calculated.

These variables were compared with our control data, which were obtained from 10 healthy volunteers, aged 24 to 32 years (mean 28.0 ± 3.2) by the same methods. In these subjects, there were no signs of cardiopulmonary disease as determined by physical and chest x-ray film examination. The upper to lower lobe ventilation ratio ranged from 0.70 to 0.90 (mean 0.78 ± 0.06) in the right lung and 0.63 to 1 (mean 0.79 ± 0.10) in the left lung; the perfusion ratio ranged from 0.19 to 0.43 (mean 0.32 ± 0.08) in the right lung and 0.21 to 0.43 (mean 0.30 ± 0.07) in the left lung. In the analysis of relations between the distribution of pulmonary blood flow and hemodynamic data, we used the upper to lower lobe perfusion ratio in the sections of the lungs farthest from the heart to exclude any effects of cardiomegaly. The risk of radiation exposure and the necessity of this examination were sufficiently explained, and informed consent to permit the radionuclide investigation was obtained from each patient and volunteer.

Cardiac catheterization and angiography. These procedures were performed 1 to 45 months (mean 15.4 ± 16.0) before the Fontan procedure, and 1 to 21 months (mean 7.8 ± 7.2) after this operation. Cardiac output was measured by the dye dilution method.

On the posteroanterior projection of the pulmonary arteriogram or right atriogram, the diameter of the right pulmonary artery (rPA) proximal to the origin of the first lobar branch was measured, and the cross-sectional area was calculated. The normal cross-sectional area was calculated by the following formula reported by Castellanos and Hernandez (14):

$$\text{Normal rPA area(cm}^2\text{)} = -0.3546 + 2.8798 \times \text{BSA(m}^2\text{)},$$

where BSA = body surface area. The right pulmonary artery area index (rPAAI) was determined as the ratio of the cross-sectional area to the normal value as:

$$\text{rPAAI} = \text{rPA area(cm}^2\text{)}/\text{normal rPA area(cm}^2\text{)}.$$

In only one patient (Patient 2) with situs inversus in thoracic situs, the left-sided pulmonary artery was substituted. No localized pulmonary artery stenosis or obstruction was recognized in any patient on the postoperative pulmonary arteriogram. One patient (Patient 1) was excluded from this statistical analysis because of a residual left to right shunt. No pulmonary arteriovenous fistula was found in any patient by contrast echocardiography.

Statistical analysis. Values were expressed as mean values \pm SD. A paired *t* test was used for comparison of data obtained before and after operation. Linearity of the relation between two variables was assessed by linear regression analysis. A *p* value <0.05 was considered significant.

Results

Ventilation scans. The radioactive images of both lung fields appeared homogeneous in all patients. The upper to lower lobe ventilation ratio in the right lung was 0.85 ± 0.18 and was not significantly different from the control value (0.78 ± 0.06). The ratio in the left lung was 0.91 ± 0.15 and was higher than the control value (0.79 ± 0.01) ($p < 0.05$). There was no significant difference between the upper to lower lobe perfusion ratio in the right and left lungs.

Perfusion scans. In contrast to the ventilation scans, the perfusion scans revealed abnormal distribution of pulmonary blood flow, with an increase in the upper lung segment in a significant number of patients. The upper to lower lobe perfusion ratio varied widely from 0.26 to 1.43 (mean 0.59 ± 0.34) in the right lung and from 0.18 to 1.06 (mean 0.58 ± 0.3) in the left lung compared with 0.3 ± 0.08 and

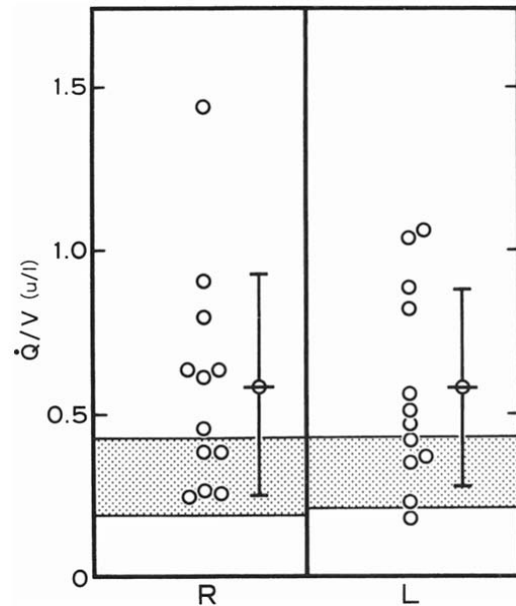


Figure 1. Plot of the upper to lower lobe perfusion ratio (\dot{Q}/V [u/l]) in 12 patients after the Fontan procedure. Shaded area represents the range of control data. L = left lung; R = right lung.

0.3 ± 0.07 , respectively, in the control group (Fig. 1). Of the 12 patients, 7 showed a significantly higher perfusion ratio than the upper limit of the control values. There was no significant difference observed during the period after the Fontan procedure between the seven patients with an abnormally high ratio (at 12.2 ± 7.8 months) and the five with a ratio within normal limits (at 5.4 ± 6.1 months). Two patients who had a right atrial to subpulmonary right ventricular connection showed a slightly abnormal distribution (0.46 and 0.64, respectively, in perfusion ratio in the right lung).

Hemodynamic data (Table 2). The mean pulmonary artery pressure and mean pulmonary venous wedge pressure showed no significant change from preoperative values after the Fontan procedure. In contrast, pulmonary vascular resistance significantly increased postoperatively ($p < 0.01$), with a concomitant decrease in the right pulmonary artery area index ($p < 0.01$) (Fig. 2 and 3).

Correlation of ventilation-perfusion scans and hemodynamic data (Fig. 4). There was a close positive correlation between the upper to lower lobe perfusion ratio and postoperative pulmonary vascular resistance ($p < 0.02$, $r = 0.72$). This tendency was also observed in the relation of the perfusion ratio to preoperative pulmonary vascular resistance, but it was not statistically significant ($p < 0.1$, $r = 0.58$).

There was a significant inverse correlation between the upper to lower lobe perfusion ratio and preoperative ($p < 0.005$, $r = -0.81$) and postoperative right pulmonary artery area index ($p < 0.02$, $r = -0.68$) (Fig. 5). An inverse

Table 2. Pre- and Postoperative Hemodynamic Data in 12 Patients

| Pt. No. | Preoperative Data | | | Postoperative Data | | | | | |
|---------|----------------------|-----------------------------|-------|--------------------|---------------|-----------------------------|--------|-------------------------------------|----------------------|
| | mPAP [mPVWP] (mm Hg) | PVR (units·m ²) | rPAAI | mPAP (mm Hg) | mPAWP (mm Hg) | PVR (units·m ²) | rPAAI | CI (liters/min per m ²) | SaO ₂ (%) |
| 1 | 16 | 1.2 | 0.86 | 17 | 4 | 4.1 | 0.69 | — | 96.0 |
| 2 | 12 | 1.5 | 0.75 | 13 | 5 | 4.2 | 0.37 | 2.16 | 86.1 |
| 3 | 13 | 1.5 | 1.20 | 16 | 6 | 4.7 | 0.55 | 2.13 | 94.1 |
| 4 | 18 | 1.4 | 0.79 | 8 | 5 | 2.3 | 0.52 | 1.76 | 86.5 |
| 5 | 10 | 2.2 | 0.89 | 9 | 7 | 2.0 | 0.53 | 2.00 | 95.4 |
| 6 | 14 | 3.2 | 0.54 | 20 | 11 | 3.7 | 0.36 | 2.45 | 88.4 |
| 7 | [6] | 1.1 | 0.92 | 11 | 5 | 1.3 | 0.62 | 3.83 | 95.1 |
| 8 | 17 | 2.0 | 0.63 | 10 | 3 | 2.3 | 0.80 | 3.07 | 92.6 |
| 9 | [10] | 2.1 | 0.50 | 12 | 6 | 3.6 | 0.38 | 1.66 | 89.8 |
| 10 | 4 | 1.1 | 0.61 | 8 | 3 | 2.3 | 0.51 | 2.18 | 93.6 |
| 11 | [15] | 2.3 | 0.42 | 21 | 7 | 7.1 | 0.24 | 2.10 | 86.0 |
| 12 | 8 | 1.5 | 0.63 | 16 | 11 | 2.7 | 0.59 | 1.86 | 92.7 |
| Mean | 11.9 | 1.8 | 0.73 | 13.4 | 6.1 | 3.4 | 0.51 | 2.29 | 91.4 |
| ±SD | ±4.4 | ±0.6 | ±0.22 | ±4.5* | ±2.6 | ±1.6† | ±0.16† | ±0.64 | ±3.8 |

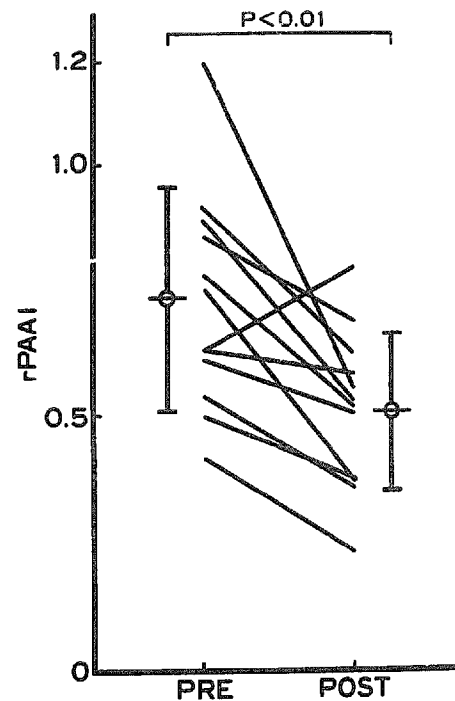
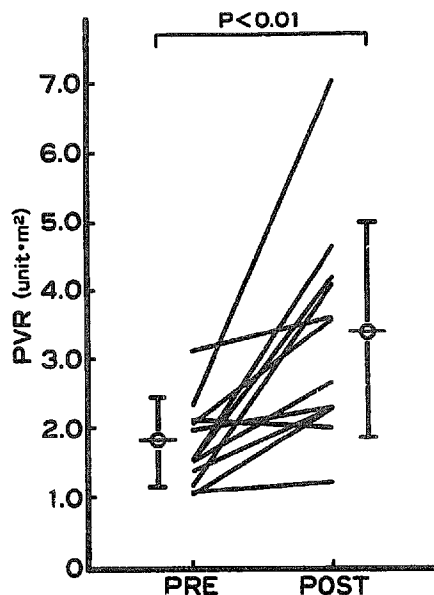
*p = NS; †p < 0.01 (versus preoperative data). CI = cardiac index; mPAP = mean pulmonary artery pressure; mPAWP = mean pulmonary artery wedge pressure; mPVWP = mean pulmonary venous wedge pressure; PVR = pulmonary vascular resistance; rPAAI = right pulmonary artery area index; SaO₂ = systemic arterial oxygen saturation.

correlation was found between the upper to lower lobe perfusion ratio and postoperative arterial oxygen saturation. However, it was not statistically significant (p < 0.2, r = -0.48) (Fig. 6). Four of the five patients with mild hypoxemia (arterial oxygen saturation <90%) had an abnormal perfusion distribution, with an upper to lower lobe perfusion ratio >0.62; one patient had a normal distribution despite a low arterial saturation. In addition, of the seven patients with an arterial oxygen saturation >90%, two

showed an abnormally high upper to lower lobe perfusion ratio. Other variables such as cardiac output, pulmonary artery pressure and pulmonary artery wedge pressure showed no correlation with the upper to lower lobe perfusion ratio.

Figure 3. Plot of right pulmonary artery area index (rPAAI) before (PRE) and after (POST) the Fontan procedure in 12 patients.

Figure 2. Plot of pulmonary vascular resistance (PVR) before (PRE) and after (POST) the Fontan procedure in 12 patients.



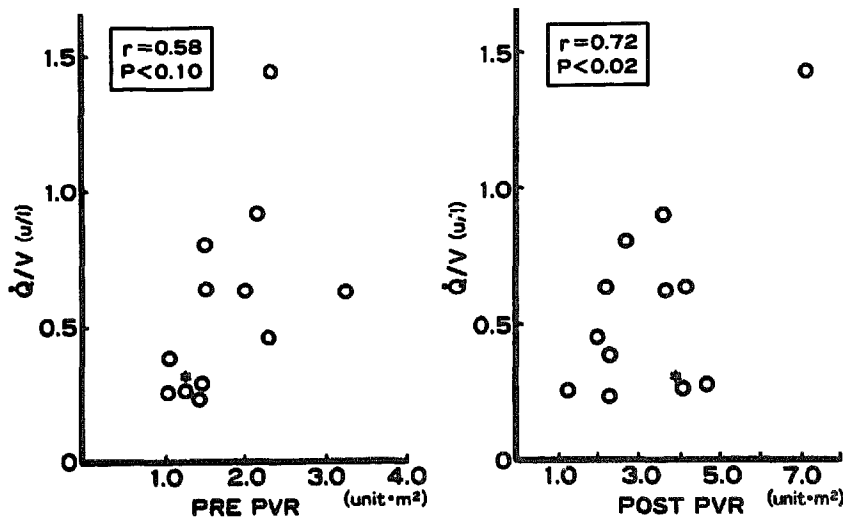


Figure 4. Plot of the relation between the upper to lower lobe perfusion ratio (Q/V [u/l]) and preoperative (PRE) postoperative (POST) pulmonary vascular resistance (PVR). There was a significant correlation postoperatively, but not preoperatively. Asterisk indicates the patient with a left to right shunt.

Discussion

Abnormal lung perfusion distribution in the presence of low pulsatile flow. Along with the increase in right-sided cardiac bypass procedures such as the Glenn shunt, the Fontan procedure and total cavopulmonary shunt operation (15,16) for complex heart anomalies, the influence of low pulsatile pulmonary blood flow on the postoperative prognosis has been an important issue. Although there have been several reports (9,10,17) concerning the abnormal pulmonary circulation in patients after these surgical interventions, the state of the distribution of pulmonary blood flow under low pulsatile flow conditions is still controversial. Several studies (18,19) have revealed that the intrapulmonary blood flow after the Glenn shunt was predominantly to the lower lung segment. In contrast, Pennington et al. (20) reported that the distribution pattern in patients after the Fontan procedure was more homogeneous than that seen after the Glenn shunt. Cloutier et al. (11) observed that the upper to lower lobe perfusion ratio after the Fontan procedure varied widely.

Our data demonstrate that a significant number of patients after the Fontan procedure (7 [58.3%] of 12) had

abnormal shifts of the distribution of pulmonary blood flow to the upper lung segment. No patient had the increased perfusion distribution to the lower lung segment. There was no significant correlation between lung perfusion distribution and postoperative duration. In addition, the distribution of pulmonary blood flow did not significantly correlate with the operative procedure, pulmonary artery pulse pressure or palliative procedures before the Fontan procedure. Despite the limited number of study patients and the short postoperative duration our results suggest that the shift to the upper lung segment may be the major abnormality of pulmonary perfusion distribution after the Fontan procedure.

Influence of pulmonary hemodynamics on lung perfusion distribution. Several pathologic studies (21-23) have revealed that maldistribution of pulmonary blood flow is related to many causes such as alveolar hypoxia (21), increased pulmonary blood flow (22), pulmonary hypertension and elevated pulmonary venous pressure (23). These abnormalities, however, have not been documented in patients who have undergone postoperative cardiac catheterization. Concerning the mechanism of this maldistribution after the Fontan procedure, pulmonary vascular resistance

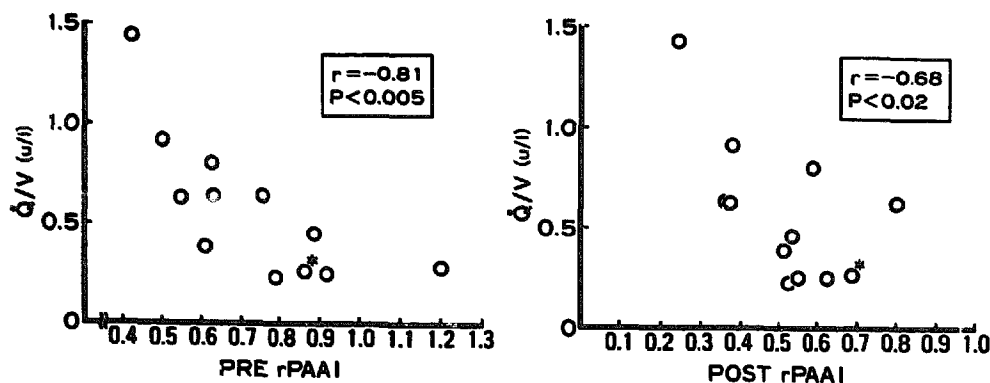


Figure 5. Plot of the relation between the upper to lower lobe perfusion ratio (Q/V [u/l]) and preoperative (PRE) and postoperative (POST) right pulmonary artery area index (rPAAI). There was a significant correlation preoperatively and postoperatively. Asterisk indicates the patient with a left to right shunt.

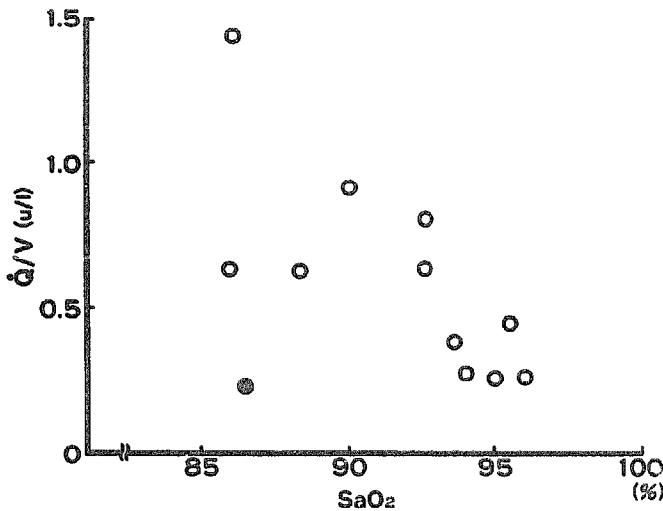


Figure 6. Plot of the relation between the upper to lower lobe perfusion ratio (Q/V (u/l)) and postoperative systemic arterial oxygen saturation (SaO_2). Closed circle indicates Patient 4 with congestive heart failure. Excluding this patient, there was a significant inverse correlation ($p < 0.02$).

may be one of the important factors that affect intrapulmonary perfusion distribution. In our study, as pulmonary vascular resistance increased, pulmonary perfusion tended to shift to the upper lung segment. There are some experimental studies (24-26) demonstrating that vascular resistance under nonpulsatile flow significantly increases compared with that under pulsatile flow. West et al. (27) reported that pulmonary vascular resistance in the lower lung segment was affected mainly because of high hydrostatic and interstitial fluid pressure in this area. An increase in pulmonary vascular resistance, especially in the lower zone, may be an important causative factor for the maldistribution of pulmonary blood flow after the Fontan procedure.

The size of the pulmonary artery may be another significant factor responsible for the abnormal distribution of pulmonary blood flow (28). Nakazawa et al. (29) reported that preoperative pulmonary artery size is an important determinant of postoperative pulmonary blood flow. In our study, the smaller the preoperative right pulmonary artery area index, the greater the flow to the upper lung segment. This result suggests that the development of the pulmonary artery appears to be important for satisfactory pulmonary perfusion after the Fontan procedure. We observed that the actual diameter of the right pulmonary artery did not increase significantly after the Fontan procedure and, consequently, the right pulmonary artery area index decreased. These findings suggest that growth of the pulmonary artery system may not be expected after the Fontan procedure. The preoperative pulmonary vascular state, including the development of the pulmonary vascular bed, may be the important determinant of the distribution of postoperative pulmonary blood flow.

The occurrence of pulmonary arteriovenous fistula may be a serious sequela in the presence of low pulsatile pulmonary flow. It is well recognized that this sequela can occur after the Glenn shunt (30,31). Cloutier et al. (11) suggested that with long perioperative time, patients undergoing the Fontan procedure may be at risk and develop pulmonary arteriovenous fistula. In our study, five patients showed mild hypoxemia, with arterial oxygen saturation $< 90\%$ despite the apparent absence of pulmonary arteriovenous fistula or other right to left shunt. In addition, there was a significant inverse correlation ($p < 0.02$) between the upper to lower body perfusion ratio and arterial oxygen saturation in 11 patients, excluding one patient (Patient 4) who had severe congestive heart failure caused by the deterioration of common atrioventricular valve regurgitation after the Fontan procedure. These results suggest that the abnormal distribution of pulmonary blood flow can cause a ventilation-perfusion mismatch and possible consequent hypoxemia. Further studies are required to elucidate the long-term outcome of this perfusion abnormality in relation to clinical symptoms, as well as to the development of pulmonary arteriovenous fistula.

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