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Preoperative measurement of pulmonary vascular resistance in complete transposition of the great arteries

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Abstract

Transposition of the great arteries is frequently complicated by the early onset of pulmonary vascular disease. It is difficult to measure pulmonary blood flow by the Fick principle because the pulmonary arteriovenous oxygen content difference is small and bronchial blood flow is increased in this condition. In eight patients (mean age 7·7 years, range 3 months to 29 years) with transposition of the great arteries mass spectrometry was used to measure oxygen uptake and predict pulmonary end capillary blood oxygen content. The effects of the bronchial circulation were studied by computer modelling. There was close agreement between pulmonary end capillary and pulmonary vein blood oxygen contents but the resultant percentage difference in arteriovenous content difference was significant (mean (SE of difference)) (14·5(3·8)%). The effect of the bronchial circulation was to give spuriously high estimates of pulmonary blood flow. The error was greatest when oxygen consumption was low and aortic blood was very desaturated.

Rapidly progressive pulmonary vascular disease is an important complication of transposition of the great arteries.[1–3] It may occur as early as the first year of life,[4–6] whether or not the ventricular septum is intact[6–8] and despite the presence of pulmonary stenosis[5 9] or adequate banding of the pulmonary artery.[2 10] Assessment of severity is helpful in determining the nature and timing of operation. Measurement of pulmonary vascular resistance may not be reliable in these children because the high pulmonary artery saturation results in a low arteriovenous oxygen content difference.[9 10] Accurate determination of this difference is necessary for application of the Fick principle.[10–12] Furthermore, bronchial artery hypertrophy has been shown angiographically[9] and histologically,[1] and an increased bronchial blood flow may affect the measurements.[9] This paper reports our approach to the preoperative measurement of pulmonary blood flow in these children. We also discuss how reliable such measurements are likely to be. This assessment was based in part on computer modelling of the pulmonary and bronchial circulation.

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Patients and methods

We report nine haemodynamic studies in eight patients. There were five male patients and three female patients, mean age 7·7 years, range three months to 29 years. All had transposition of the great arteries with communications between the circulations at atrial or ventricular level. Table 1 shows the full details. No patient had a ductus arteriosus at the time of the study. In all oxygen saturation was higher in the pulmonary artery than in the aorta. Patient 1 was studied on two occasions, three months apart, because of fears that pulmonary vascular disease had developed while he was awaiting operation. Flow was measured at diagnostic cardiac catheterisation while the patients were intubated and ventilated. Full details of the methods have been published elsewhere.[13–15]

In summary, fluid filled catheters were introduced percutaneously into the femoral artery and vein and positioned in the aorta and pulmonary artery respectively. For the measurements of pulmonary blood flow, oxygen consumption was measured by mass spectrometry (MGA 200), by the steady state, argon dilution principle.[13] Blood P_{O_2}, pH, and base excess were measured on a Corning 165 blood gas analyser and used to calculate blood oxygen contents.[16] We assumed that the solubility of free oxygen in blood was 0·03 ml/mm Hg/l. End tidal P_{CO_2} was measured with the mass spectrometer and used to calculate the alveolar P_{O_2} from the alveolar air equation. This value was then used to calculate the oxygen content of pulmonary end capillary blood, which replaced the oxygen content of the pulmonary vein in the Fick equation. Whenever possible, we also sampled the pulmonary vein to check the validity of our assumption that the oxygen contents of the

Table 1 Additional diagnoses in patients with complete transposition of the great arteries

No	*Age (yr)*	*Sex*	*Diagnoses*
1	3/12	M	VSD/PS
2	7/12	M	ASD
3	8/12	M	ASD/VSD
4	21/12	F	VSD/PAB/Coarc/DA
5	26/12	F	VSD/PAB
6	10	M	PAB/TR
7	17	M	PAB/VSD
8	29	F	VSD

ASD, atrial septal defect; Coarc, coarctation; DA, ductus arteriosus (closed surgically before the study); PAB, pulmonary artery band; PS, pulmonary stenosis; TR, tricuspid regurgitation; VSD, ventricular septal defect.

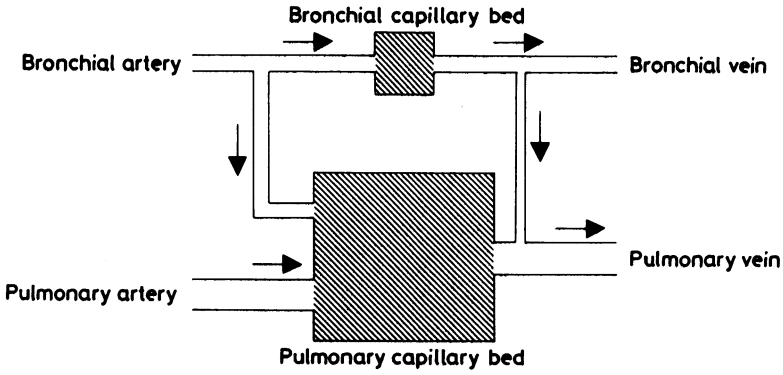

Figure 1 The blood supply to the lungs, as modelled in this paper. The bronchial arterial tree supplies both alveolar and bronchial capillaries; the bronchial capillaries drain into both bronchial and pulmonary veins.

pulmonary vein and pulmonary end capillary are similar.

COMPUTER MODEL

Bronchial artery blood flow cannot easily be measured in humans. The model (fig 1) therefore arbitrarily allocates values which increase from zero in steps of 100 ml/min per m^2. The oxygen content of bronchial artery blood equals that of aortic blood. Because it is desaturated, this stream of blood may be able to take up oxygen, particularly if it perfuses alveolar capillaries through precapillary anastomoses with the pulmonary circulation. This bronchial blood oxygen uptake would be indistinguishable from uptake of oxygen by blood in the pulmonary circulation. Therefore in the Fick equation used in the calculation of pulmonary artery blood flow, the numerator (pulmonary blood oxygen uptake) is overestimated. The effects of this can be modelled if the oxygen content of bronchial venous blood is known. In healthy individuals, approximately one third of the bronchial circulation drains into the right atrium via the bronchial veins, and two thirds drains into the left atrium via the pulmonary veins.[17] In neither route can bronchial venous oxygen content be measured, nor can it be assumed to be equal to that of vena caval blood. Bronchial venous blood cannot be more oxygenated than pulmonary end capillary blood whatever route it takes, so the two are assumed to be equal. If any bronchial venous blood is less saturated than pulmonary end capillary blood, then the uptake of oxygen by the bronchial circulation will be overestimated.

The steps in the calculation are as follows. An arbitrary value of bronchial blood flow (QBr) is allocated by the program. If the blood oxygen contents of pulmonary artery, aortic, and pulmonary end capillary blood are respectively $Cpao_2$, $Caoo_2$, $Cc'o_2$, then applying the Fick equation to the bronchial circulation,

$$QBr = Vo_2Br/(Cc'o_2-Caoo_2)$$

where Vo_2Br is the oxygen uptake in the bronchial circulation. After rearranging,

$$Vo_2Br = QBr \times (Cc'o_2-Caoo_2)$$

Total oxygen uptake (Vo_2T) = Vo_2Br + pulmonary capillary oxygen uptake. Application of the Fick equation to the pulmonary circulation gives

$$\text{Pulmonary capillary blood flow} = (Vo_2T-Vo_2Br)/(Cc'o_2-Cpao_2)$$

Therefore, pulmonary capillary blood flow can be calculated for as many different bronchial circulation blood flows as desired.

The model is written in FORTRAN 04 to run on the hospital mainframe computer (Prime 750). A full listing is available from AB. It could easily be adapted to run on a microcomputer.

Results

HAEMODYNAMIC DATA

Table 2, in which the patients are arranged in ascending order of age, shows total oxygen uptake, the calculated oxygen contents of blood in aorta, pulmonary artery, pulmonary vein, and pulmonary end capillary, and the values of pulmonary blood flow and pulmonary vascular resistance.

We compared the calculated oxygen content of pulmonary end capillary blood and the measured oxygen content of pulmonary vein blood. The mean difference between the two was 0·29 ml/dl (SD 0·43) measured in air (n = 5) and 0·27 (SD 0·20) measured in oxygen (n = 7). The difference was statistically significant (p = 0·0004) according to

Table 2 Detailed results of the studies of haemodynamic function in which calculations of pulmonary blood flow (Qp) and pulmonary vascular resistance (PVR) were based on pulmonary end capillary blood not pulmonary venous blood

Patient no	Insp	Vo_2	Blood oxygen content				PAP	Qp	PVR
			Ao	PA	PV	Pc'			
1a	100% O_2	160	24·34	23·00	24·34	24·79	35	9·0	3·3
1b	Air	173	16·03	19·07	20·58	21·04	38	9·0	3·7
	100% O_2	154	—	21·19	22·81	23·16	39	7·8	4·4
2	Air	234	11·11	22·15	24·73	24·72	15	9·1	1·0
	100% O_2	236	15·53	24·36	26·67	26·91	15	9·3	1·0
3	Air	88	15·48	18·40	21·23	21·14	23	3·2	6·4
	100% O_2	88	—	20·95	23·14	23·37	16	3·6	3·6
4	Air	162	18·64	20·38	—	24·23	15	4·2	1·8
	100% O_2	168	20·88	23·60	26·40	26·42	16	5·9	1·1
5	Air	190	17·07	19·10	26·00	26·96	33	2·4	11·9
	100% O_2	160	21·04	23·23	—	29·29	35	2·6	11·4
6	Air	166	16·94	17·31	—	18·81	51	12·3	3·0
	100% O_2	148	19·02	19·13	—	20·78	50	10·0	3·7
7	Air	154	24·31	27·47	—	29·31	17	8·3	1·5
	100% O_2	147	27·08	29·56	31·37	31·52	16	7·5	1·5
8	Air	240	25·45	28·96	30·81	30·93	84	9·4	8·5
	100% O_2	174	28·71	30·31	32·54	33·14	74	4·7	14·3

Oxygen consumption (Vo_2), ml/min per m^2; blood oxygen content, ml/dl; pulmonary artery pressure (PAP), mm Hg; pulmonary blood flow (Qp), l/min per m^2; pulmonary vascular resistance (PVR), mm Hg. $l^{-1}.min.m^2$.
Insp, inspired gas; Ao, aorta; PA, pulmonary artery; PV, pulmonary vein; Pc', pulmonary end capillary.

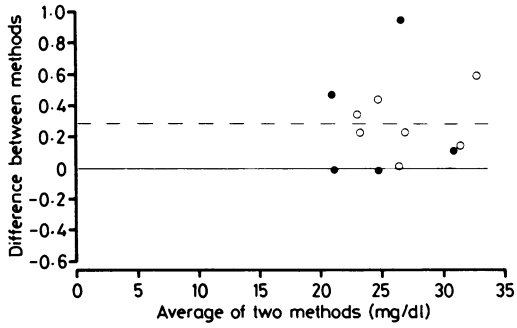

Figure 2 Comparison of oxygen contents of pulmonary venous and pulmonary end capillary blood. This plot shows that estimates of pulmonary end capillary blood oxygen content were systematically slightly greater than measured pulmonary venous blood oxygen content. Closed circles are measurements in air and open circles are measurements in 100% oxygen. The dotted line is the mean of all twelve points.

repeated measures analysis of variance, allowing for missing data.[18] Figure 2 shows the error and bias. If pulmonary end capillary blood was paired with pulmonary artery blood, the mean (SE) of the blood oxygen content differences across the pulmonary circulation was 2·78 (0·52) ml/dl; if pulmonary vein blood was used instead, the corresponding result was 2·47 (0·46) ml/dl. The mean percentage difference between these two sets of values was 14·5 (3·8) (range −3·2 to 33·9%). Figure 3 shows the error and bias.

Figure 4 shows the results of the bronchial circulation modelling. This shows the mean and 95% confidence intervals of the percentage error in pulmonary blood flow caused by unsuspected bronchial blood flow of 0·1–1·0 l/min per m^2. The results for a normal subject are shown for comparison. There is considerable individual variation; for a bronchial flow of 0·5 l/min per m^2, the error could have been as much as 32% or as little as 1·4%. The lower the total oxygen uptake, and the lower the aortic blood oxygen content, the greater the errors that were encountered.

FOLLOW UP DATA

We were able to compare measurements of pulmonary vascular resistance with lung structure in two patients. Patient 5 had Heath Edwards late grade III disease (her pulmonary vascular resistance was 10·5 units in air) and patient 6 had only grade I/II with a pulmonary vascular resistance on air of 3·7 units. Patient 1 had a Mustard's procedure, with closure of the ventricular septal defect and has done well postoperatively. Patients 2, 3, 4, and 7 are awaiting corrective operation. Patient 8 had a palliative Mustard's procedure, and a postoperative study showed a pulmonary vascular resistance of 9·9 units in air.

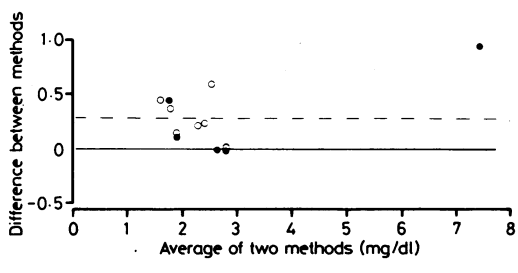

Figure 3 Comparison of differences in the pulmonary arteriovenous oxygen content when pulmonary end capillary blood and pulmonary venous blood are used. This plot shows that, because the arteriovenous oxygen content difference is so small, the minor discrepancies shown in figure 2 result in large discrepancies in the oxygen content differences. Closed circles are measurements in air, open circles are measurements in 100% oxygen. The dotted line is the mean of all twelve points.

Discussion

The conventional solution of the Fick equation for organ blood flow assumes that either the concentration difference or the flow rate or

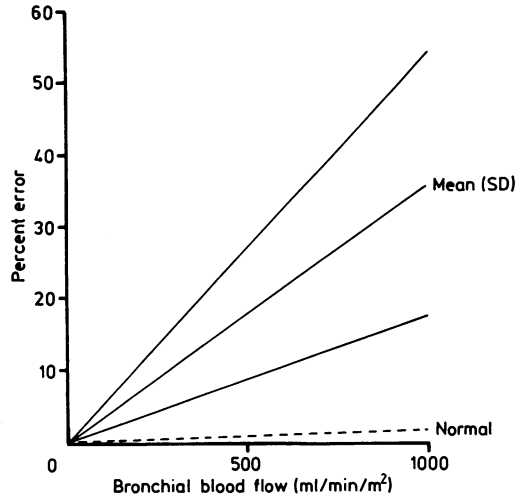

Figure 4 Results of the bronchial circulation model. The mean and 95% confidence intervals for the overestimate of pulmonary blood flow are plotted against bronchial blood flow. The dotted line shows equivalent results for a control.

both are constant while the measurement is made.[9] This is rarely if ever true. The smaller the arteriovenous concentration difference, the greater the error that these assumptions produce.[9] This paper highlights two particular problems in the measurement of pulmonary vascular resistance in transposition of the great arteries, namely the difficulty of ascertaining the true pulmonary vein blood oxygen content and the possible role of the bronchial circulation.

The lungs are drained by four pulmonary veins. Even in the supine position during cardiac catheterisation there are likely to be regional variations in pulmonary gas exchange. This could result in variations in the oxygenation of blood in the four pulmonary veins, of which one only is routinely sampled. Blood flow is pulsatile at all levels of the pulmonary circulation,[19] and hence red cell capillary transit times will vary with the phase of the cardiac and respiratory cycles. This will result in small phasic alterations in blood oxygen content with time. Slow withdrawal of a systemic blood sample would partially overcome these effects if there were no intracardiac shunts. But this procedure is open to the criticism that it produces a time average sample at a point not a volume average at the area of sampling.[9] In transposition the choices are either to use a sample from a single pulmonary vein or to use the alveolar air equation to predict pulmonary end capillary oxygen content. This latter approach assumes a uniform distribution of ventilation to perfusion ratios within the lung, but, particularly if the patient is ventilated on 100% oxygen, even large inequalities will not significantly affect the calculated oxygen content. This equation thus provides a way of partially overcoming regional differences but takes no account of the anatomical intrapulmonary shunt. There is good agreement between the end capillary and pulmonary vein blood, as found in other patients with congenital heart disease.[15] However, even a minor systematic difference between the two, results in big differences in calculated flow if the

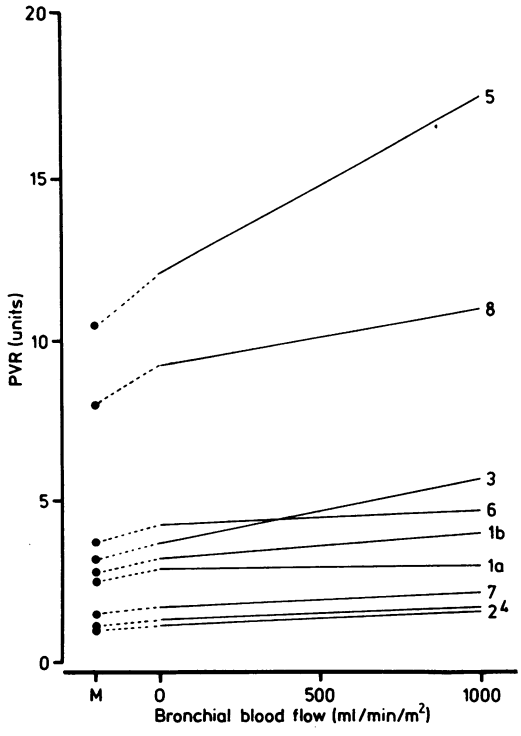

Figure 5 Lowest pulmonary vascular resistance (PVR, mm Hg.l $^{-1}$.min.m^2) plotted against bronchial blood flow QBr, ml/min/m^2. M is the actual measurement made in pulmonary end capillary blood. The difficulties of getting a true pulmonary vein sample were estimated as likely to understimate true PVR by 15% (see text; plotted as QBr = 0·0). The remaining points are based on the additional effects of the bronchial circulation, which were modelled as described.

arteriovenous blood oxygen content difference is small.

The nature of bronchial blood flow in this condition may also lead to inaccuracy. Normally, bronchial artery blood is nearly fully saturated and can take up far less oxygen than pulmonary artery blood. In transposition this is not the case. Normal bronchial blood flow has been estimated as 50–100 ml/min per m^2.[20] Our computer model has shown that even modest increases in bronchial blood flow can result in significant overestimation of pulmonary blood flow.

Other workers have confirmed that the Fick method overestimates pulmonary blood flow.[11 12] Dye dilution or thermodilution with pulmonary artery sampling will not be affected by bronchial blood flow,[11] but such measurements are difficult to interpret in infants with intracardiac shunting. Pulmonary blood flow has been measured from angiograms[12 21 22] but only in infants with no ventricular septal defect. The dose of contrast necessary precludes repeated measurements to assess any response to vasodilators. It is therefore likely that the Fick method will continue to be used and we believe it provides useful information if correctly interpreted. The follow up data, although incomplete, nevertheless support the view that resistance measurements may be valuable. High values were found with severe pulmonary vascular disease (patient 5) or a high resistance after palliative operation (patient 8), when the more normal pattern of oxygen saturations allows greater certainty about the measurements. Low values were found with only mild pulmonary vascular disease (patient 6) or a good outcome after operation (patient 1).

These data suggest that the measured lowest pulmonary vascular resistance is the "best case". The "worst case" is found by modelling the effects of the bronchial blood circulation and adding 15% for the effects of the problems of pulmonary venous sampling. Figure 5 shows this approach in our patients. Pulmonary vascular resistance is plotted against bronchial blood flow, to show the "best" and "worst" cases. In many patients the decision to operate can be reached without recourse to these calculations. In patients where there is doubt, we believe that such calculations may be helpful, permitting the importance (or otherwise) of the uncertainties in the conventional calculations to be modelled. In our laboratory, a lowest resistance of 6·5 units was associated with inoperable pulmonary vascular disease.[23] So if the "best case" is significantly greater than 6·5 units, then only palliative procedures should be offered; if the "worst case" is less than 6·5 units, then corrective operation can be considered. If the possible range of resistance spans 6·5 units, then a lung biopsy is needed to assess the disease.

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