Preoperative and postoperative pulmonary function tests in patients with atrial septal defect and their relation to pulmonary artery pressure and pulmonary:systemic flow ratio

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SUMMARY Pulmonary diffusing properties and lung volumes were investigated in 44 patients with atrial septal defect, and in 30 of them preoperative and postoperative data were obtained. The patients were divided into three groups according to mean pulmonary artery pressure: ≤ 15 mm Hg (group 1), 16–29 mm Hg (group 2), and ≥ 30 mm Hg (group 3). Patients in groups 1 and 2 had a high carbon monoxide transfer test which became normal after surgical correction of their septal defect. In group 3, the carbon monoxide transfer test was normal both before and after operation. As mean pulmonary artery pressure increased there was a progressive reduction in both forced expiratory volume in one second and vital capacity. Patients in group 3 had a low forced expiratory volume in one second, a low vital capacity, and a reduced forced expiratory volume in one second:vital capacity ratio. These abnormalities were not corrected by surgical closure of the septal defect.

Formulas were derived from the lung function data, to predict the mean pulmonary artery pressure and the pulmonary:systemic flow ratio. The values predicted when these two formulas were applied to data obtained for patients in this study correlated well with measured values.

In most studies the carbon monoxide transfer test (T_LCO) has been found to be increased in patients with atrial septal defect.^{1–6} It has been suggested that this change is due to an increase in capillary blood volume.^{7,8} A study by De Troyer *et al* showed that patients with atrial septal defect complicated by pulmonary hypertension had reduced lung volumes and increased airway resistance.⁶

There have been few studies measuring T_LCO and lung volumes after surgical correction of atrial septal defects. Bucci *et al* reported seven patients with atrial septal defect in whom T_LCO and capillary blood volume returned to normal after operation.⁹ The present study was designed to investigate the effects on pulmonary function of surgical closure and also to determine whether pulmonary function tests could be used to predict mean pulmonary artery pressure

or the pulmonary:systemic flow ratio in patients with atrial septal defect.

Patients and methods

Forty four consecutive patients (aged 11–60 years) with atrial septal defect presenting over a three year period were studied; 43 had ostium secundum defects and one had an ostium primum defect. All patients with additional cardiac lesions were excluded, and no subject had evidence of primary pulmonary disease. In each case right heart catheterisation was performed to confirm the diagnosis, the mean pulmonary artery pressure was measured, and the pulmonary:systemic flow ratio was calculated by oximetry.¹⁰

The pulmonary function tests were all carried out with the patient in the sitting position. Lung volumes were measured with a conventional water-sealed spirometer (Gould-Goddard expirograph type 16000). The total lung capacity was measured with the same apparatus, by means of a steady-state

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helium dilution method. The results were compared with predicted values.¹¹⁻¹⁴ The Morgan transfer test model C, a single-breath technique, was used to measure the lung carbon monoxide uptake. The predicted values for T_LCO are those of Morgan.¹⁵ In all cases, the interval between pulmonary function testing and cardiac catheterisation was less than six weeks. A control group of 50 subjects who were attending a gastroenterology outpatient clinic had the same pulmonary function measurements taken during the same period of time.

Of the 44 patients in the study, 30 had pulmonary function tests repeated after surgical correction of their atrial septal defect. The remaining 14 patients included five who did not have operation (three had small shunts and two had severe pulmonary hypertension) and nine in whom repeat pulmonary function tests were not performed.

The observed and predicted values for lung volumes and T_LCO were compared by the paired *t* test. Statistical analysis by multiple linear regression was used to investigate the relation between pulmonary function tests and data obtained at cardiac catheterisation.

Results

The 44 patients in the study were divided into three groups according to their mean pulmonary artery pressure: group 1 (≤ 15 mm Hg), group 2 (16–29 mm Hg), and group 3 (≥ 30 mm Hg). These groups are similar to those studied by De Troyer *et al.*⁶ Their age, smoking habits (a "smoker" had smoked five or more cigarettes each day for at least the two previous years), and haemodynamic characteristics are shown in Table 1. The frequency of smoking in each of the three groups was similar.

Table 2 gives preoperative pulmonary volumes and T_LCO values. There was a progressive reduction in forced expiratory volume in one second and vital capacity as mean pulmonary artery pressure increased; in groups 2 and 3 values were significantly (paired *t* test) lower than predicted. There were significant inverse correlations of forced expiratory volume in one second ($r = -0.45$; $p < 0.01$) and vital

capacity ($r = -0.32$; $p < 0.05$) with mean pulmonary artery pressure. The ratio of forced expiratory volume in one second:vital capacity also correlated inversely ($r = -0.52$; $p < 0.001$) with mean pulmonary artery pressure (Fig. 1). The total lung capacity did not differ significantly from predicted values in any of the groups. There was a striking increase in T_LCO in groups 1 and 2 ($p < 0.001$), whereas patients with a mean pulmonary artery pressure of ≥ 30 mm Hg had a normal value. The T_LCO showed a significant inverse correlation ($r = -0.52$; $p < 0.001$) with mean pulmonary artery pressure (Fig. 2), and Fig. 3 shows that mean pulmonary artery pressure increased with age ($r = 0.66$; $p < 0.001$).

Table 3 shows the pulmonary volumes and T_LCO measured after surgical correction of the atrial septal defect and the interval between operation and lung function testing in 30 patients. The reduced forced expiratory volume in one second and vital capacity associated with a mean pulmonary artery pressure ≥ 30 mm Hg did not become normal after operation; they remained significantly lower than predicted ($p < 0.01$). The pronounced increase in T_LCO noted in groups 1 and 2 before operation became normal postoperatively.

Backward stepwise multiple linear regression showed that mean pulmonary artery pressure correlated positively with age (Fig. 3) and inversely with T_LCO (Fig. 2). A formula was derived from these variables to predict the mean pulmonary artery pressure (P_{pa}):

$$\text{Predicted } P_{pa} = k_1 \times \text{age} + \frac{k_2}{T_LCO} - k_3$$

with age in years, T_LCO as percentage of predicted, and k_1 , 0.483, k_2 , 3246, and k_3 , 19.1. This regression was highly significant ($p < 0.001$, $R^2 = 63\%$) and allowed good prediction in most cases (Fig. 4). Within the measured range of mean pulmonary artery pressure (10–45 mm Hg) the predicted values are even more reliable. The addition of forced expiratory volume in one second and vital capacity to the formula did not improve the degree of prediction of mean pulmonary artery pressure.

Backward stepwise multiple linear regression

Table 1 Data on 44 patients studied with atrial septal defect (mean (SD))

	Age (years)	Smokers (%)	P_{pa} (mm Hg)	P:S flow ratio
Group 1 (n = 16)	21.7 (9.1)	31.3	12.6 (2.3)	2.72 (0.67)
Group 2 (n = 13)	32.3 (12.6)	30.8	20.7 (2.6)	3.47 (1.13)
Group 3 (n = 15)	47.4 (6.2)	33.3	39.3 (11.5)	2.75 (1.11)

P_{pa} , mean pulmonary artery pressure.

P:S flow ratio, ratio between pulmonary and systemic blood flows.

Table 2 Preoperative pulmonary volumes and diffusing properties in 44 patients with atrial septal defect (mean (SD))

	FEV ₁ (l)	VC (l)	FEV ₁ /VC (%)	TLC (l)	T _L CO (ml/min/mm Hg)
Group 1 (n=16)	2.81 (0.71) (2.86 (0.44))*	3.44 (0.91) (3.76 (0.60))	82.5 (7.2)† (76.2 (0.8))	4.96 (0.94) (4.79 (0.98))	33.8 (6.1)‡ (26.1 (4.1))
Group 2 (n=13)	2.39 (0.83)† (2.77 (0.54))	3.02 (1.13)† (3.65 (0.72))	79.5 (6.5) (75.9 (0.6))	4.59 (1.40) (4.88 (1.05))	35.7 (6.5)‡ (26.4 (4.4))
Group 3 (n=15)	1.74 (0.73)‡ (2.83 (0.57))	2.54 (0.87)‡ (3.72 (0.76))	67.7 (9.2)† (75.9 (1.1))	4.62 (1.27) (4.58 (0.90))	27.0 (6.9) (24.9 (4.1))

FEV₁, forced expiratory volume in one second; VC, vital capacity; TLC, total lung capacity; T_LCO, carbon monoxide transfer test.

*Figures in parentheses are predicted values (mean (SD)). †Significantly different from predicted (p<0.01). ‡Significantly different from predicted (p<0.001).

showed that the pulmonary:systemic flow ratio did not correlate with the age of the patient, the forced expiratory volume in one second, or the vital capacity when these were expressed as a percentage of predicted values ($r = -0.16$, $r = -0.15$, $r = -0.14$ respectively). There was, however, a significant correlation between pulmonary:systemic flow ratio and T_LCO expressed as percentage of predicted ($r = 0.45$, $p < 0.005$) (Fig. 5). It was interesting to note that a pulmonary:systemic flow ratio of 4 or 5 produced T_LCO values rising to 160–170% of predicted, since similar T_LCO measurements have been obtained in normal subjects on maximum exertion, when cardiac output is four or five times that of normal.¹⁶ T_LCO was used to derive a formula to predict the ratio between pulmonary and systemic blood flow (P:S flow ratio): Predicted $\log_{10}$ P:S flow ratio = $k_a \log_{10}$ T_LCO - k_b ; where T_LCO is percentage of predicted, k_a , 1.015; and k_b , 1.673. Again, this regression was highly significant ($p < 0.001$, $R^2 = 40\%$) (Fig. 6). When this formula was used to predict a pulmonary:systemic flow ratio of > 2 , or < 2 , the prediction was correct in 38 of the 44 cases studied. The horizontal

and vertical lines in Fig. 6 correspond to a pulmonary:systemic flow ratio of 2, predicted and measured respectively.

The size of the shunt in patients with atrial septal defect is also reflected by the pulmonary artery oxygen saturation. It is noteworthy that T_LCO, expressed as percentage of predicted, correlated significantly ($r = 0.60$; $p < 0.001$) with the pulmonary arterial oxygen saturation (Fig. 7).

The pulmonary volumes and T_LCO measured in the control group did not differ significantly from predicted values.

Discussion

The increase in T_LCO in some patients with atrial septal defect is well established,¹⁻⁶ and occurs as a consequence of an increase in capillary blood volume.^{7,8} In the study by De Troyer *et al* of 24 patients with atrial septal defect, T_LCO was not increased in patients with mean pulmonary artery pressure > 25 mm Hg.⁶ The finding of a normal or low T_LCO in the presence of pulmonary hypertension has also been

Fig. 1 Ratio of forced expiratory volume in one second to vital capacity (FEV₁:VC %) versus measured mean pulmonary artery pressure (P_{pa}) in 44 patients with atrial septal defect.

Fig. 2 Carbon monoxide transfer test (T_LCO) as percentage of predicted versus measured mean pulmonary artery pressure (P_{pa}) in 44 patients with atrial septal defect.

Fig. 3 Relation between age and measured mean pulmonary artery pressure (P_{pa}) in 44 patients with atrial septal defect.

described by Burgess.⁵ The results from our larger study therefore accord with those of most other investigators, in that patients with a mean pulmonary artery pressure ≥ 30 mm Hg had a normal T_LCO . It has been suggested^{5,9} that the chronic increase in pulmonary blood flow results in the opening of previously closed pulmonary capillaries and possibly distension of open capillaries and that this increases capillary blood volume and T_LCO . The presence of pulmonary hypertension, however, and an increased pulmonary vascular resistance limits the increase in capillary blood volume and T_LCO . Bucci *et al* have suggested that there is some active regulation of the resistance of the prepulmonary and postpulmonary capillary vessels which affects capillary blood volume.⁹

There was a progressive fall in both forced expiratory volume in one second and vital capacity as mean pulmonary artery pressure increased. In patients with a mean pulmonary artery pressure of ≥ 30

Fig. 4 Measured versus predicted mean pulmonary artery pressure (P_{pa}) from $k_1 \times \text{age} + k_2/T_LCO - k_3$. T_LCO is carbon monoxide transfer test.

mm Hg, the forced expiratory volume in one second:vital capacity ratio was significantly lower than predicted. As there was no significant difference in the percentage of smokers in each group, the changes are unlikely to be the consequence of smoking habits. These findings are consistent with those of De Troyer *et al* who described reduced lung volumes and increased airway resistance in patients with mean pulmonary artery pressure > 25 mm Hg.⁶ They reported a progressive decrease in lung compliance with increasing pulmonary hypertension, due to vascular engorgement. Their results also suggested that the obstruction to airflow was mainly localised in the small peripheral bronchioles. It has been postulated¹⁷ that competition for space between vessels and airways within the bronchovascular sheaths increases the resistance of the small airways. Other studies in children with heart disease¹⁸ and in adults¹⁹ support this theory.

Bucci *et al* reported seven patients with atrial septal defect in whom T_LCO and capillary blood volume decreased to within normal limits after surgical cor-

Table 3 Preoperative and postoperative pulmonary volumes and diffusing properties in 30 patients with atrial septal defect (mean (SD))

	FEV_1 (l)	VC (l)	T_LCO (ml/min/mm Hg)	Months after operation
Group 1 (n=11):				
Preoperative	2.85 (0.62)	3.55 (0.80)	34.3 (5.3)†	
Postoperative	3.02 (0.79)	3.46 (0.75)	27.9 (5.4)	42
	(2.81 (0.44))*	(3.69 (0.58))	(26.5 (4.6))	
Group 2 (n=9):				
Preoperative	2.43 (0.90)	3.14 (1.28)	35.0 (7.6)‡	
Postoperative	2.57 (1.13)	3.41 (1.55)	27.6 (7.6)	39
	(2.81 (0.55))	(3.70 (0.74))	(25.8 (4.5))	
Group 3 (n=10):				
Preoperative	1.89 (0.84)†	2.73 (0.98)†	29.8 (6.5)	
Postoperative	1.96 (0.72)†	2.80 (0.99)†	24.9 (7.1)	33
	(2.92 (0.60))	(3.84 (0.80))	(25.4 (4.2))	

Abbreviations are given in footnote to Table 2.

*Figures in parentheses are predicted values (mean (SD)). † Significantly different from predicted ($p < 0.01$). ‡ Significantly different from predicted ($p < 0.001$).

Fig. 5 Carbon monoxide transfer test (T_{LCO}) as percentage of predicted versus pulmonary:systemic flow ratio (P:S flow ratio) in 44 patients with atrial septal defect.

resection of their cardiac abnormality.⁹ Auchincloss *et al*² reported two cases in which T_{LCO} became normal after closure of the defect. In our study, 30 patients had T_{LCO} measured before and after operation. In the 20 cases with mean pulmonary artery pressure < 30 mm Hg the high T_{LCO} values became normal after surgical correction; in the remainder with mean pulmonary artery pressure $\geq$ 30 mm Hg, T_{LCO} was within normal limits before and after operation. These results suggest that the re-establishment of normal haemodynamic conditions is followed by a return towards normal of the pulmonary capillary bed. It is of interest that in patients with mean pulmonary artery pressure $\geq$ 30 mm Hg, the low forced expiratory volume in one second and vital capacity did not return to normal after surgical correction of

Fig. 6 Measured versus predicted ratio between pulmonary and systemic blood flow (P:S flow ratio). Predicted $\log_{10}$ P:S flow ratio = $k_a \times \log_{10} T_{LCO} - k_b$. T_{LCO} is carbon monoxide transfer test.

Fig. 7 Carbon monoxide transfer test (T_{LCO}) as percentage of predicted versus pulmonary arterial oxygen saturation in 44 patients with atrial septal defect.

the atrial septal defect. This suggests that there is some permanent irreversible change in the small airways and lung parenchyma as a consequence of long-standing increased pulmonary blood flow.

The formula derived to predict mean pulmonary artery pressure involved two variables—age (years) and T_{LCO} (percentage of predicted). The regression was highly significant and allowed good prediction of mean pulmonary artery pressure particularly within the measured range of 10–45 mm Hg. The ratio of pulmonary to systemic flow is generally considered to be the best overall indication of the haemodynamic importance of an atrial septal defect. Although a value of 2 or more is usually considered to indicate an important defect, the measurement is itself subject to error. When $\log_{10} T_{LCO}$ (as percentage of predicted) was used to predict $\log_{10}$ pulmonary:systemic flow ratio, the regression was highly significant. When the formula was used to predict whether the pulmonary:systemic flow ratio was > 2 or < 2 the prediction was correct in 86% of patients. The pulmonary arterial oxygen saturation, which reflects shunt size, also correlated with T_{LCO} expressed as a percentage of that predicted.

In recent years radionuclide angiography²⁰ and echocardiography²¹ have provided information in patients with atrial septal defect that previously could be obtained only by invasive techniques. It has been suggested that routine preoperative catheterisation may be unnecessary when typical clinical features of an uncomplicated atrial septal defect are confirmed by cross sectional echocardiography and, when indicated, other non-invasive tests.^{22, 23} It is possible that the techniques we describe for predicting mean pulmonary artery pressure and the pulmonary:systemic flow ratio could provide useful additional information in the assessment and follow up of patients with atrial septal defect and thereby

increase confidence in management decisions made without cardiac catheterisation. At this stage, however, the formulas have only been tested on the population from which the predictions were derived.

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