Pulmonary haemodynamics after single-lung transplantation for end-stage pulmonary parenchymal disease


ABSTRACT: In a prospective study, we investigated the effect of single-lung transplantation (SLT) on pulmonary haemodynamics and the relationship between pulmonary hypertension (PH) and the fraction of perfusion to the transplant in patients with end-stage pulmonary parenchymal disease. Twenty-four SLT recipients were included in the study, 19 with chronic obstructive pulmonary disease (COPD), two with sarcoidosis and three with fibrosing alveolitis. Spirometry, determination of arterial blood gas values, perfusion scintigraphy and right heart catheterization were performed before and 1, 6, 12 and 24 months after transplantation. Patients with a mean pulmonary artery pressure (Ppa) ≥20 mmHg before transplantation were defined as having PH (PH group, 15 patients) and the remainder (9 patients) constituted the non-PH group.

In the PH group, Ppa and pulmonary vascular resistance (PVR) were significantly decreased after transplantation: 28±2 to 18±1 mmHg and 288 to 161±11 dynes·s·cm⁻⁵, respectively (mean± SEM). In the non-PH group, the haemodynamic parameters were unchanged after transplantation. Over the 2 year follow-up period, no significant change was found in Ppa and PVR, nor any difference between the PH and non-PH group. There was no significant difference between the two groups in terms of pulmonary perfusion to the graft.

In conclusion, patients with pulmonary hypertension obtain pulmonary haemodynamics within the normal range after single-lung transplantation. Presence or absence of pulmonary hypertension before transplantation does not influence perfusion to the graft. These findings persist up to 2 yrs, despite the coexistence of an "end-stage" native lung and a lung transplant.


In patients with end-stage pulmonary parenchymal disease, single-lung transplantation (SLT) is established as a treatment with acceptable survival [1], and satisfactory medium term pulmonary function [2, 3].

End-stage pulmonary parenchymal diseases are associated with increased pulmonary artery pressure (Ppa) in the majority of patients [4–6]. In these patients, SLT improves pulmonary haemodynamic abnormalities in the early postoperative period [7, 8], but scarce data are available during follow-up in patients with moderately increased Ppa [9]. On the other hand, in patients with primary pulmonary hypertension (PH) and other causes of severe PH, SLT has recently been associated with normalized pulmonary haemodynamics persisting for 4 yrs [10]. The impact of PH on survival and functional status in SLT is, however, controversial [8, 10].

After SLT for pulmonary parenchymal disease, the mean fraction of perfusion to the transplanted lung is 70–80%, but with individual values ranging 50–95% [2, 3, 11, 12]. The relationship between PH before transplantation and the fraction of perfusion to the allograft has not previously been studied.

We have, therefore, conducted a prospective study to evaluate the effect of SLT on pulmonary haemodynamics in patients with pulmonary parenchymal disease. The investigations were performed during a 2 year follow-up period after transplantation, and include the relationship between PH and the relative perfusion to the transplant.

Patients and methods

Between March 1990 and March 1994, 27 patients with end-stage pulmonary parenchymal disease underwent single-lung transplantation. The operative technique, immunosuppression and follow-up have been described previously [13, 14]. Three patients died early postoperatively. The diagnosis, functional characteristics before transplantation and causes of death are summarized in table 1. No follow-up assessments are available in these patients and, as a result, they have not been included in the study. The 24 survivors (mean age 50 yrs, range 40–60 yrs) with a mean observation time after transplantation of 30 months (range 13–61 months) are the basis of this report. Demographic data are shown in table 2.
The pretransplant assessment included spirometry, determination of arterial blood gas values, pulmonary perfusion scintigraphy and right heart catheterization. After transplantation, the same tests were repeated after 1, 6, 12 and 24 months. In the late follow-up period, six recipients died. The causes of death were: acute pancreatitis (patient No. 3, 58 months after transplantation); malignant melanoma (patient No. 8, 8 months); obliterative bronchiolitis (patient No. 9, 14 months); bronchial stenosis (patient No. 16, 9 months); obliterative bronchiolitis and intra-abdominal bleeding after liver biopsy (patient No. 19, 10 months); and massive haemorrhage (patient No. 26, 2 months). Three patients were retransplanted on the contralateral side because of bronchiolitis obliterans syndrome [15], 11, 19 and 39 months after the first transplantation, and were excluded from further follow-up. The number of patients at the different follow-up times are, thus, as follows: before and 1 month after transplantation, 24 patients; after 6 months, 19 patients; after 1 year, 18 patients; and after 2 yrs, 10 patients (7 patients had an observation time of between 12 and 24 months, leaving 10 with a 24 month follow-up).

Patients with a mean pulmonary artery pressure (P_{pa}) of \( \geq 20 \) mmHg before transplantation were defined as having pulmonary hypertension [16], constituting the PH group. Patients with a \( P_{pa} < 20 \) mmHg were defined as the non-PH group.

### Pulmonary function tests

Dynamic lung volumes were measured using an automated pulmonary function unit (Gould 2400; Sensormedics, Bilthoven, The Netherlands). At least three satisfactory trials were performed. The highest forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were recorded.

### Quantitative perfusion scintigraphy

Macroaggregated albumin (IFE MAA; Institutt for Energiteknikk, Norway) was labelled with \(^{99m}\)Tc and an intravenous dose of 180 MBq in approximately 1 mL was administered during 1 min, with the patient in the supine position, breathing in and out slowly and deeply. With the camera in the dorsal position, the imaging was started immediately after the injection, and continued until a picture with 500,000 counts was obtained. Thereafter, using the same acquisition time as in the dorsal view, scintigrams from the anterior and from the four oblique views were taken. The perfusion of each lung was expressed as a percentage of the total counts in both lungs, using the arithmetic mean of the counts in the anterior and posterior view.

### Statistical analysis

A mixed model analysis of variance (ANOVA) [17] with repeated measurements was used to analyse the data. In the tables, the results are presented as estimated mean \( \pm \)SEM in each group before transplantation and after...
transplantation (corrected for time). A two-sample t-test was used to compare the values before transplantation between the PH and non-PH group. A p-value for the difference between groups is given. All the tests are two-sided, and a p-value of less than 0.05 is regarded as statistically significant.

### Results

Fifteen patients (12 with chronic obstructive pulmonary disease (COPD), two with sarcoidosis, and one with fibrosing alveolitis (FA)) had PH before transplantation and constituted the PH group, while nine patients (seven with COPD and two with FA) made up the non-PH group (Table 3). All of the individual $P_{pa}$ values in the observation period are presented in Table 3. Ten patients were followed for 2 yrs, and at 24 months they had a $P_{pa}$ of 17±1 mmHg.

Pulmonary haemodynamics in the PH and non-PH group before and after transplantation at 1, 6 and 12 months are presented in Table 4. $P_{pa}$ and PVR were significantly greater in the PH group compared to non-PH group before transplantation (Table 5). The $P_{a,O2}$ was lower in the PH group ($p<0.05$), while FVC, FEV1, and $P_{a,CO2}$ were not significantly different between the two groups (Table 5).

After transplantation $P_{pa}$ and PVR were significantly decreased in the PH group (Table 5). Using the mixed model ANOVA and including all
the observations (1, 6, 12 and 24 months after transplantation). The pulmonary function, \( P_a \), PVR, and the perfusion to transplanted side in the two groups were analysed (table 5). There was no significant difference between the PH group and the non-PH group in any of these parameters, and there was no change during the observation period after the transplantation.

Figure 1 shows that half of the total perfusion before transplantation was directed to the lung that was replaced by the allograft. After transplantation, the percentage of total perfusion to the graft increased to approximately 70% both in the PH and non-PH group. The correlation between \( P_a \) (dependent variable) and \( P_a \) before transplantation had an estimated change in \( P_a \) of 17 mmHg after 2 yrs (10 patients) and \( P_a \) was 18 mmHg [9], i.e. similar to the present results. In severe PH because of pulmonary vascular disease, SLT has become a feasible therapeutic option with normalized pulmonary haemodynamics in the long-term follow-up. [10, 18, 19]. These results persisted up to 4 yrs [10], and the haemodynamic results were similar to those in the present study. After 2 yrs (11 patients) and 4 yrs (6 patients) \( P_a \) was 21 mmHg, compared to a \( P_a \) of 17 mmHg after 2 yrs (10 patients) in the present study. A normal \( P_a \) persisting for 2–4 yrs after transplantation despite PH before transplantation indicates that a successful SLT is accompanied by normalized pulmonary haemodynamics in the long-term follow-up.

After SLT for severe pulmonary hypertension, there was a mismatch between ventilation and perfusion distributed to the transplant, approximately 50 and 80%, respectively. Even with this mismatch, the functional status was satisfactory [10]. In the non-PH group in the present study, the lungs had only a slightly elevated PVR before transplantation and, theoretically, the opposite mismatch might appear; perfusion might be distributed evenly between the native and transplanted

<table>
<thead>
<tr>
<th>Before transplantation</th>
<th>After transplantation</th>
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<tbody>
<tr>
<td></td>
<td>Non-PH</td>
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<tr>
<td>( P_aO_2 ), kPa</td>
<td>7.8±0.5</td>
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<tr>
<td>( P_aCO_2 ), kPa</td>
<td>6.1±0.5</td>
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<td>FVC, L</td>
<td>2.18±0.4</td>
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<td>FEV1L</td>
<td>0.82±0.15</td>
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<td>PVR, dynes·s(^{-1})·cm(^{-5})</td>
<td>177±26</td>
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<td>( P_a ), mmHg</td>
<td>16±1</td>
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<tr>
<td>Perfusion %</td>
<td>48±5</td>
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</tbody>
</table>

Values are presented as mean±SEM in each group before transplantation, estimated mean values±SEM (measurements at 1, 6, 12 and 24 months) and the \( P \) values for comparison between the two groups. \( P_aO_2 \): arterial oxygen tension; \( P_aCO_2 \): arterial carbon dioxide tension; FVC: forced vital capacity; FEV1: forced expiratory volume in one second; \( P_a \): mean pulmonary artery pressure; PVR: pulmonary vascular resistance. Perfusion: perfusion to side of transplantation as a percentage of total perfusion; ANOVA: analysis of variance. *: p<0.05, **: p<0.01 vs non-PH; ‡: p<0.05 vs before transplantation.

There was no correlation between perfusion to the transplanted side (dependent variable) and \( P_a \) and PVR (p=0.172 and p=0.86, respectively).

**Discussion**

In the present study, the patients with PH had mild-to-moderately increased \( P_a \) values prior to transplant. Their pulmonary haemodynamics were within the normal range after SLT, and remained so after 2 yrs. The patient group with normal \( P_a \) before transplantation had unchanged haemodynamics after transplantation. Furthermore, the percentage of pulmonary perfusion to the transplanted side was not significantly different in the two groups.

There are no previous reports of serial measurements of pulmonary haemodynamics after SLT for pulmonary parenchymal disease. In one report, however, with a single follow-up measurement in five patients with pulmonary fibrosis and PH (mean observation time 18 months, range 2–29 months), the \( P_a \) was 18 mmHg [9], i.e. similar to the present results. In severe PH because of pulmonary vascular disease, SLT has become a feasible therapeutic option with normalized pulmonary haemodynamics and satisfactory functional improvement during follow-up [10, 18, 19]. These results persisted up to 4 yrs [10], and the haemodynamic results were similar to those in the present study. After 2 yrs (11 patients) and 4 yrs (6 patients) \( P_a \) was 21 mmHg, compared to a \( P_a \) of 17 mmHg after 2 yrs (10 patients) in the present study. A normal \( P_a \) persisting for 2–4 yrs after transplantation despite PH before transplantation indicates that a successful SLT is accompanied by normalized pulmonary haemodynamics in the long-term follow-up.

After SLT for severe pulmonary hypertension, there was a mismatch between ventilation and perfusion distributed to the transplant, approximately 50 and 80%, respectively. Even with this mismatch, the functional status was satisfactory [10]. In the non-PH group in the present study, the lungs had only a slightly elevated PVR before transplantation and, theoretically, the opposite mismatch might appear; perfusion might be distributed evenly between the native and transplanted.
lungs, while ventilation would be directed mainly to the transplanted lung. However, the present study revealed a similar percentage of perfusion to the graft as in previous reports and, in addition, demonstrated that the perfusion to the transplanted lung was not significantly different between patients with and without PH before transplantation. Furthermore, this pattern persisted for at least 2 yrs.

Pulmonary artery pressure in pulmonary parenchymal disease has previously been shown to be inversely correlated with $P_{pa,O_2}$ [16, 20–22]. The correlation between FEV1 and $P_{pa}$ is controversial; in one study, no correlation was found [23], whilst another long-term study reported a weak inverse correlation [16]. In the present study, in accordance with these results, a significant inverse correlation was found between $P_{pa,O_2}$ and $P_{pa}$, but no correlation between FEV1 and $P_{pa}$.

SLT is the most effective way of utilizing available donor organs. However, in one study a $P_{pa}$ greater than 30 mmHg before transplantation was reported to be associated with lower 1 year survival, prolonged intensive care unit stay and less symptomatic improvement. Accordingly, the authors raised the question of whether SLT may be suboptimal therapy in patients with PH [8]. In another study of SLT for severe PH, the survival and functional results were good, but the PH patients were not compared with non-PH patients [10]. The three patients in the present study with early postoperative death had a $P_{pa}$ greater than 30 mmHg, but their causes of death are difficult to associate with PH. The other six deaths had a $P_{pa}$ below 30 mmHg, and three were in the PH and three the non-PH group. Some controversy, therefore, still exists about the impact of PH on the outcome of SLT. Further long-term studies of the effects of PH in SLT appear to be warranted.

In conclusion, the occurrence of mild-to-moderate pulmonary hypertension before transplantation is not associated with elevated pressures in the pulmonary circulation after transplantation and does not influence perfusion to the graft. The present findings indicate that the coexistence of a lung graft with normal function and an end-stage diseased native lung has no negative impact on the pulmonary haemodynamics in long-term follow-up.

References