Evolution of resting lung function in the first year after cardiac transplantation


ABSTRACT: The aim of our study was to characterize the time course and magnitude of the changes in lung function in the first year after cardiac transplantation.

Resting pulmonary function tests (spirometry, lung volumes and transfer factor) were performed in 14 patients prior to and at 1, 3 and 12 months after surgery. Resting central haemodynamics were also measured serially in the first year post-transplantation.

Before transplantation, patients had impaired resting lung function with marked decrease in transfer factor (T L,CO). Although resting central haemodynamics improved markedly within the first week after cardiac transplantation, lung function (forced expiratory volume in one second (FEV1)) was significantly improved only at three months post-transplantation. T L,CO, however, decreased further early after cardiac transplantation. By 12 months, FEV1 and forced vital capacity had increased significantly by 31 and 33%, respectively, while total lung capacity increased by 22%. On the other hand, T L,CO did not increase significantly and remained well below normal at 12 months after cardiac transplantation, at a value equal to 68% of predicted.

We conclude that the resting abnormalities in lung function of most patients with heart failure are reversible after cardiac transplantation, except for T L,CO which remains below normal values. Recovery of lung function, however, lags behind the improvement in cardiac function.


Restrictive ventilatory defects and decreased transfer factor of the lungs for carbon monoxide (T L,CO) have been described at rest in patients with chronic heart failure [1–4]. During exercise, rapid shallow breathing is characteristic [5], together with increased ventilation for a given metabolic demand, e.g. carbon dioxide output [6]. These changes are related to the severity of heart failure and contribute to decreased exercise tolerance [5–8]. Cardiac transplantation provides a unique opportunity for evaluating the effect of improved cardiac performance on pulmonary function. Studies on the changes in pulmonary function after cardiac transplantation have not reported the early and late changes post-surgery [9–12]. In order to study the temporal relationship between the improvement in central haemodynamics and the changes in lung function after cardiac transplantation, pulmonary function tests and resting central haemodynamics were performed in 14 patients, before transplantation and serially in the first 12 months post-surgery.

Methods

Patient population

Fourteen consecutive patients, undergoing cardiac transplantation at our institution and surviving the first operative year, were studied prior to and in the first year following cardiac transplantation. All patients were male. At the time of transplantation, the mean age was 47±12 yrs (range 23–58 yrs). Patients mean height and weight were 1.73±0.06 m and 76±10 kg, respectively. The aetiology of heart disease leading to transplantation was coronary artery disease in six patients, cardiomyopathy in seven and valvular heart disease in one. Ten patients had smoked prior to transplantation, however six had stopped at least 2 yrs before the operation. No patient had severe chronic obstructive lung disease prior to transplantation, nor did any patient receive bronchodilator agents during the study period. The immunosuppressive regimen consisted of prednisone and cyclosporine in all
patients. The dose of cyclosporine was on average 600, 400 and 300 mg·day⁻¹ at 1, 3 and 12 months, respectively. Azathioprine was added in five patients at 1 month, in six at 3 months, and in seven at 12 months post transplantation.

Pulmonary function

Pulmonary function tests were performed on average 60 days before transplantation (10–380 days), and were repeated at 1, 3 and 12 months after transplantation. Pulmonary function testing performed on a given day included measurement of forced expiratory volumes, lung volumes and transfer factor. Spirometric indices were calculated from the best of three satisfactory breaths. All pulmonary function test results, except the forced expiratory volume in one second/forced vital capacity (FEV₁/FVC) ratio and the peak flow rate, were expressed as a percentage of the predicted value based on age, height, and sex. FEV₁ and FVC, were obtained by spirometry (dry rolling seal) and evaluated utilizing the predicted values of Knudson et al. [13]. The predicted values of Goldman and Becklake [14] were used for the helium dilution determination of lung volumes, which included total lung capacity (TLC) and residual volume (RV). The TL,CO was determined using the single breath carbon monoxide technique, and values were corrected for haemoglobin concentration [15]. The transfer factor was corrected for alveolar volume (carbon monoxide transfer coefficient (KCO)) by dividing TL,CO by TLC. The predicted values for the TL,CO and KCO were those of Miller et al. [16].

Resting haemodynamics

Resting supine haemodynamics were measured after a routine endomyocardial biopsy performed through the right internal jugular vein, using a flow directed balloon-tipped catheter, as described previously [17], prior to and at 1–2 weeks and 3 and 12 months after transplantation. Central haemodynamics were measured in the following sequence: pulmonary artery phasic and mean pressures, mean pulmonary capillary wedge pressure, and mean right atrial pressure. Thermodilution cardiac outputs were measured in duplicate or triplicate to obtain values in agreement by 10%.

Data analysis

Descriptive data are listed as means ± standard deviation. Serial data were assessed using a repeated measures analysis of variance. Correlations were determined using Pearson’s correlation coefficient. A p-value of less than 0.05 was considered significant.

Results

Resting haemodynamics

Pre- and post-operative resting haemodynamic results are reported in table 1. Right and left atrial pressures and cardiac output returned to near normal within 1–2 weeks after cardiac transplantation, and remained so in the first year.

Pulmonary function

Prior to transplantation, pulmonary function test results were abnormal in many patients. The transfer factor was

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<th>Table 1. – Resting central haemodynamics before, and at 1–2 weeks, and 3 and 12 months following cardiac transplantation</th>
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Data are presented as mean±sp: CI: cardiac index; PRA: mean pulmonary artery pressure; Ppcw: mean pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance; PRA: mean right atrial pressure. *p<0.05 versus pre-transplantation.

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<th>Table 2. – Resting pulmonary function tests before and at 1, 3 and 12 months following cardiac transplantation</th>
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Data are presented as mean±sp: FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; KCO: transfer factor corrected for alveolar volume; PEFR: peak expiratory flow rate; RV: residual volume; TLC: total lung capacity; TL,CO: transfer factor of the lung for carbon monoxide; % pred: percentage of predicted value. *: p<0.05 vs Pre; **: p<0.05 vs Pre and 1 month; ***: p<0.05 vs Pre, 1 and 3 months; †: p<0.05 vs 3 months; ‡: p<0.05 vs 1 and 3 months.
LUNG FUNCTION AFTER CARDIAC TRANSPLANTATION 961

low and abnormal (<75% of predicted when corrected for haemoglobin) in 13 of the 14 patients. A mild restrictive defect (TLC <75% pred) was also observed in three of the 14 patients. Only two patients had significant airway obstruction (FEV1/FVC <70%). After transplantation, there was an increase in forced expired volume. FEV1 and FVC increased significantly by 3 months post-transplantation and increased further by 12 months (table 2). Similarly, the peak expiratory flow rate increased significantly by 12 months post-transplantation. Total lung capacity also increased significantly by 12 months post-transplantation (table 2), due to increased inspiratory capacity (fig. 1).

Before transplantation patients had a low TL,CO (table 2). Despite general improvement in lung function, the TL,CO, however, decreased early post-transplantation and returned only to within pre-transplant values at 12 months, well below predicted values (table 2). The increase in TL,CO from 1 to 12 months after cardiac transplantation was not related to the increase in TLC. Similarly, the TL,CO measured at 12 months did not correlate with any pre-transplant or 12 month post-transplant haemodynamic measurements or daily dose of cyclosporine (p>0.05).

However, a significant correlation was observed between the pre-transplant and 12 months post-transplant TL,CO values (r=0.71; p<0.01) (fig. 2).

Discussion

Patients awaiting cardiac transplantation have abnormal resting pulmonary function. Although not usually severe, because cardiac transplantation would otherwise be contraindicated, some reduction in FVC, FEV1, TLC and TL,CO has been described [9–12, 18, 19]. These abnormalities are due primarily to reduced cardiac function leading to an increase in cardiac size, pleural effusions and pulmonary congestion. Accordingly, with normalization of cardiac size and central haemodynamics after cardiac transplantation, abnormalities in pulmonary function test have been reported to improve [9–12]. The present results provide further insight into the time course of the early changes in pulmonary function after cardiac transplantation. Such serial observations have allowed us to evaluate the temporal relationship between improved central haemodynamics and lung function.

Although normalization of central haemodynamics occurs early after transplantation, lung function continued to improve up to 12 months post-surgery. This delay between the improvement in central haemodynamics and return to normal lung volumes may, in part, be due to the effect of the surgical incision, the cardiopulmonary bypass, and the slow reversal of pulmonary changes from long-standing pulmonary congestion. A significant decrease in lung compliance and volumes has been reported after coronary artery bypass surgery [20, 21]. These changes are believed to be due, in part, to the operative trauma on the chest wall. The sternotomy may cause alterations in chest wall mechanics and pain to the patient that could persist up to 3–4 months post-surgery. Similarly, although the greatest improvement in pulmonary function after an acute episode of heart failure occurs within the first few days, it may take months for the pulmonary function to return to normal in some patients [22].

In the present study, despite a delay, the recovery of most parameters of lung function appeared to be complete by 12 months post-transplantation, with mean FEV1, FVC and TLC values well within the normal range at that time. The increase of inspiratory capacity after transplantation is possibly the result of increased lung compliance from the relief of pulmonary congestion. However, the increased peak expiratory flow rate observed at 12 months after transplantation suggests that increased inspiratory capacity could also be due to increased patient effort following increased respiratory muscle strength. Increased peak flow rates have not been previously reported after cardiac transplantation.

Despite improvement in lung volume, like others [9–12, 23, 24], we observed a persistently low TL,CO after cardiac transplantation. The TL,CO decreased from pre-operative values in the first month post-transplantation but returned.

Fig. 1. – Lung volumes before (Pre) and at 1, 3, and 12 months after (Post) transplantation. Values are means±SEM. Total lung capacity (TLC) and inspiratory capacity (IC) significantly different from pre, 1 and 3 months post-transplantation, *: p<0.05. FRC: functional residual capacity. : IC; : FRC.

Fig. 2. – Correlation between transfer factor of the lungs for carbon monoxide (TL,CO) before (pre) and 12 months after (post) cardiac transplantation. % pred: percentage of predicted values.

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to pre-transplant values by 12 months. Even when corrected for alveolar volume, the transfer factor-TLC ratio (Kco) remained well below the predicted value. The early decrease in TL,CO may be the result of decreased pulmonary capillary blood volume, and the effect of extracorporeal circulation. Reduced values for TL,CO have been reported early after coronary artery bypass surgery and may persist up to 4 months post surgery [21]. These changes are, in part, the result of pulmonary vascular injury from lung ischaemia and, possibly, the release of endotoxin and tumour necrosis factor [25] during cardiopulmonary bypass. TL,CO might remain low thereafter independently from the change in lung volume, due to irreversible changes from chronic pulmonary congestion, interstitial damage from subclinical respiratory infections in these immunocompromised patients and, possibly, as a result of the gradual effect of cyclosporine toxicity, as suggested previously [17–23]. In addition, since the transfer factor of the lung for carbon monoxide depends not only on the area and thickness of the blood-gas barrier but also on the volume of blood in the pulmonary capillaries, alterations in the pulmonary circulation, as a result of cardiac denervation, could reduce the transfer factor. However, the correlation observed between pre-transplant and 12 month post-transplant TL,CO values suggests an important contribution of the pulmonary vascular changes as a result of possibly long-standing pulmonary congestion prior to transplantation.

In the present study, marked improvement in resting lung function was observed within the first 3 months after cardiac transplantation. These early changes, however, lagged behind the normalization of cardiac function, suggesting a slow recovery of the pulmonary system. Increased forced expired volume and total lung capacity after transplantation are possibly mediated by improved lung compliance, respiratory muscle strength and patient effort. Unlike the other pulmonary function tests, TL,CO did not improve after transplantation, even when corrected for alveolar volume, possibly due to irreversible pulmonary vascular changes from prolonged pulmonary congestion prior to transplantation.

References