Maximal Expiratory Flow Patterns After Single-Lung Transplantation in Patients With and Without Chronic Airways Obstruction*

Yuri Villaran, MD, FCCP†; Michael E. Sekela, MD, FCCP‡; and Nausherwan K. Burki, MD, PhD, FCCP

Background: A biphasic-plateau pattern in the maximal expiratory flow-volume (MEFV) curve has been described after single-lung transplantation (SLT) in patients with chronic airways obstruction (CAO). It has been theorized that this pattern is either related to stenosis at the anastomotic or subanastomotic site, or the sum of the airflow contribution from the native lung with airways obstruction and transplanted lung.

Subjects and methods: We analyzed data in 16 patients with CAO who had undergone transplantations (5 men, 11 women; mean age [± SD], 53.8 ± 4.9 years), and 9 patients with pulmonary vascular disease (PVD) without airways obstruction who had undergone transplantations (2 men, 7 women; mean age, 35.4 ± 11.4 years).

Results: In the patients with PVD, there were no significant changes in static or dynamic lung volumes or in the MEFV curve after SLT. In the patients with CAO, indexes of airways obstruction improved significantly after SLT, and the typical biphasic-plateau pattern developed in the MEFV curve. In one patient with CAO who required pneumonectomy of the native lung after SLT, the biphasic pattern was absent.

Conclusions: These results support the view that this MEFV pattern is a result of airflow from the native and transplanted lungs in patients with CAO. In addition, the results show that in patients with no prior airways obstruction, SLT does not alter static or dynamic lung volumes or maximal expiratory flow rate.

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Key words: airways resistance; flow-volume curves; lung transplantation; pulmonary time constants

Abbreviations: FRC = functional residual capacity; MEFV = maximal expiratory flow-volume; PVD = pulmonary vascular disease; RV = residual volume; SLT = single-lung transplantation; TLC = total lung capacity; Vmax75% = maximal flow at 75% of TLC; Vmax50% = maximal flow at 50% of TLC

After single-lung transplantation (SLT) in patients with chronic airways obstruction, the maximal expiratory flow-volume (MEFV) curve is characterized by a distinct biphasic pattern.¹⁻³ Initially, it was suggested that this pattern reflected stenosis at the bronchial anastomosis.¹ However, a subsequent study suggested, on the basis of theoretical analysis, that the biphasic pattern was not related to anastomotic stenosis, but was related to flow limitation immediately downstream from the anastomotic site.² A more recent analysis³ suggests that these patterns reflect the expected contributions of the increased airways resistance in the native lung and the normal airways resistance in the transplanted lung. Interestingly, even though SLT is now an established treatment modality in many types of end-stage lung disease, most studies of posttransplant function have focused on COPD patients, and there is only one report of the effects of SLT on static and dynamic lung volumes in patients with pulmonary vascular disease (PVD) without airways obstruction;⁴ there are no reports of expiratory flow patterns in such patients after lung transplantation.

In our lung transplant program, we have had the unusual opportunity to examine a patient with chronic airways obstruction, before and after SLT, and after subsequent pneumonectomy of the re-
Materials and Methods

During a period of 39 months, 18 patients with COPD and 11 patients with PVD causing severe pulmonary hypertension underwent SLT at our institution; complete data for this study were available in 16 of the COPD patients and 9 of the PVD patients.

As part of the routine preoperative assessment, each patient underwent full medical history, physical examination, and comprehensive cardiac and pulmonary function tests. The static and dynamic lung volumes and flow values used for the present analysis, both before and after transplant, were measured during clinically stable periods in each patient when there was no clinical evidence of pulmonary infection or exacerbation of the underlying cardiopulmonary condition. All pretransplant studies were performed within 1 month before transplantation, and all posttransplant values were measured within 6 months of transplantation. Subsequent measured maximal expiratory flow patterns were reviewed in all patients to date.

SLT was performed by standard techniques using a telescoping bronchial anastomosis of the transplanted lung. Static lung volumes were measured by the helium dilution technique. Spirometry was performed by standard techniques; simultaneous recordings of volume-time and flow-volume plots were made. On each occasion, at least three valid forced expiratory spirograms were recorded, according to recommended acceptability criteria. From the tracings, the highest FVC and FEV1 were recorded; in addition, the peak expiratory flow rate and the expiratory flow rates after transplantation (Table 1); in three, this was associated with α1-antitrypsin deficiency. In the PVD group, 5 subjects had primary pulmonary hypertension, 1 subject had chronic pulmonary embolism, and 3 subjects had congenital heart disease with Eisenmenger's syndrome. In the COPD group, 13 of the 16 subjects received a left lung transplant and the others received a right lung transplant; in the PVD group, 2 of the 9 subjects received a left lung transplant, and the others received a right lung transplant.

Table 1 shows the baseline static and dynamic lung volume data in each group; as expected, the COPD group had cigarette smoke–induced airways obstruction; in three, this was associated with α1-antitrypsin deficiency. In the PVD group, 5 subjects had primary pulmonary hypertension, 1 subject had chronic pulmonary embolism, and 3 subjects had congenital heart disease with Eisenmenger's syndrome. In the COPD group, 13 of the 16 subjects received a left lung transplant and the others received a right lung transplant; in the PVD group, 2 of the 9 subjects received a left lung transplant, and the others received a right lung transplant.

Table 1—Pulmonary Function Tests*

<table>
<thead>
<tr>
<th>Test</th>
<th>COPD Patients (n = 16)</th>
<th>PVD Patients (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After SLT</td>
</tr>
<tr>
<td>FVC, L</td>
<td>1.5 ± 1.0</td>
<td>2.3 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>(40 ± 22%)</td>
<td>(61 ± 17%)</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>0.5 ± 0.2</td>
<td>1.3 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>(16 ± 5%)</td>
<td>(43 ± 7%)</td>
</tr>
<tr>
<td>TLC, L</td>
<td>5.3 ± 1.5</td>
<td>4.9 ± 1.2</td>
</tr>
<tr>
<td></td>
<td>(59 ± 16%)</td>
<td>(87 ± 16%)</td>
</tr>
<tr>
<td>FRC, L</td>
<td>4.2 ± 1.7</td>
<td>3.1 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>(150 ± 44%)</td>
<td>(101 ± 29%)</td>
</tr>
<tr>
<td>RV, L</td>
<td>4.1 ± 1.6</td>
<td>2.6 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>(205 ± 62%)</td>
<td>(130 ± 47%)</td>
</tr>
<tr>
<td>Peak flow, L/s</td>
<td>1.7 ± 1.0</td>
<td>2.8 ± 1.1</td>
</tr>
<tr>
<td>Vmax75%, L/s</td>
<td>0.4 ± 0.2</td>
<td>1.5 ± 0.8</td>
</tr>
<tr>
<td>Vmax50%, L/s</td>
<td>0.2 ± 0.1</td>
<td>0.8 ± 0.3</td>
</tr>
</tbody>
</table>

*Values are mean ± SD. Numbers in parentheses are percent predicted values.
†Value indicates significance of difference from baseline, paired t test; NS = not significant, p > 0.05.
‡Significantly different from baseline value of COPD patients, p < 0.05, unpaired t test.
biphasic shape and plateau in the MEFV trace (Fig 1). However, in the 59-year-old man previously mentioned, after SLT and pneumonectomy of the native lung, the MEFV tracing did not show this pattern (Fig 2).

In the PVD group, baseline static and dynamic lung volumes were moderately reduced, but maximal expiratory flow rates were within normal limits (Table 1), and the lung volumes and flow rates did not change significantly ($p > 0.5$) after transplantation. Furthermore, the shapes of the MEFV traces remained within normal limits (Fig 3).

All subjects underwent repeated bronchoscopic examinations, both for specific indications and as part of the standard posttransplant surveillance protocol. Stenosis at the anastomotic site was ruled out by direct bronchoscopic visualization in all subjects included in the present report.

Progressive bronchiolitis obliterans was diagnosed in 7 of the 16 COPD patients after SLT, on the basis of standard criteria from histopathologic findings on transbronchial lung biopsy and progressive airways obstruction. All these patients had initially shown the typical expiratory biphasic pattern after SLT. With development of increasing airways obstruction, the biphasic pattern disappeared and took on the appearance of the typical MEFV curve associated with airways obstruction (Fig 4).

**DISCUSSION**

SLT is now generally considered an acceptable option for patients requiring lung transplantation for COPD or PVD. Complications affecting airflow after transplantation are not uncommon; these include narrowing at the anastomotic site as well as the development of bronchiolitis obliterans. Therefore, knowledge of the usual MEFV patterns after SLT is important. A number of studies have evaluated maximal and tidal expiratory flow patterns after SLT in patients with chronic airways obstruction; however, there are no reports of longitudinal changes in these patterns with time after SLT. A similar systematic examination of MEFV curves has not been reported in patients without airflow obstruction. Similarly, although a few studies have reported the effects of SLT on static lung volumes in COPD, there is only one report of static and dynamic lung volume measurements after SLT in three patients with PVD.

The present study has produced two major findings. SLT per se does not alter the pattern of maximum expiratory airflow in patients with initially normal expiratory airways resistance. The typical biphasic pattern with plateau in the MEFV curve, seen in the majority of patients with chronic airways obstruction after SLT, is not caused by changes at the anastomotic site in the major bronchus, but is a result of the combination of airflows from the native and transplanted lungs.

The effects of SLT on static and dynamic lung volumes in patients with PVD have been previously reported in one study of three patients. In only two of these patients were results available > 6 weeks after SLT: spirometric values remained unchanged, and the TLC decreased; residual volume (RV) and functional residual capacity (FRC) values were not

**Figure 1.** MEFV curves in four representative patients with COPD. Top: baseline studies. Bottom: post-SLT values.
reported. Our results show that the static and dynamic lung volumes and flow rates are not significantly changed after SLT. This would imply that respiratory mechanics, in terms of respiratory muscle strength (which is a determinant of maximal flow rates and RV) and total lung elastic recoil (which determines maximal flow rates, TLC, RV, and FRC), are unaltered by the surgical procedure in these patients. These results are not surprising inasmuch as these patients did not have intrinsic lung or chest wall mechanical abnormality. After SLT, in spite of the telescoping bronchoscopic anastomotic procedure used, none of these subjects developed any increase in bronchial airways resistance.

The present study found a significant decrease in RV after transplantation in the patients with chronic airways obstruction, with no significant changes in the FRC or TLC. There are few previous reports of systematic measurements of static lung volumes after SLT in patients with chronic airways obstruction. Bavaria et al. reported only the RV measurement, Cheriyan et al. only the TLC, Chacon et al. the TLC and RV, and Murciano et al. TLC, RV, and FRC. These studies also reported a significant decrease in RV after transplantation in the patients with chronic airways obstruction.

Figure 2. MEFV curves in a subject with COPD at baseline (left, A) and after SLT and pneumonectomy of the native lung (right, B).

Figure 3. MEFV curves in four representative patients with PVD. Top: baseline studies. Bottom: post-SLT values.
crease in RV after SLT. Only one prior study has reported FRC values after SLT: Murciano et al noted a significant decrease in FRC after SLT, whereas in the present study the decrease was not significant. Cheriyan et al only reported the TLC values; their findings, and those of Murciano et al, are similar to the present study, showing there was no significant change in the TLC after SLT, although in all three studies, the TLC decreased slightly. In contrast, Chacon et al found a significant decrease in TLC after SLT. However, their patients had markedly increased TLC before transplantation (mean, 148% predicted), indicating severe emphysema. In contrast, in the present study, the TLC was within the accepted normal range, implying that emphysema was not a major factor in the airways obstruction. It is to be noted that TLC was measured by a dilution technique, whereas in the previous studies it was measured either by body plethysmography or radiographic planimetry, both of which techniques would be expected to yield higher TLC values. The results of the previous and present studies, taken together, indicate that those static lung volumes that are affected by increased airways resistance or decreased lung elastic recoil, such as the FRC and RV, decrease significantly after SLT, whereas large changes in TLC would not be expected to occur after SLT unless the patient has significant emphysema.

Baseline FEV\textsubscript{1} values in the COPD patients (mean FEV\textsubscript{1}, 0.5 L; 16% predicted) were very comparable to previous reports (mean FEV\textsubscript{1}, 0.4 to 0.6 L; 15.5 to 17% predicted). The changes in FEV\textsubscript{1} and FVC after SLT in the COPD patients in the present study were also very similar to those reported previously, ie, there was a significant improvement in FVC, FEV\textsubscript{1}, and FEV\textsubscript{1}/FVC after SLT.

The characteristic shape of the forced expiratory spirogram after SLT noted in the present study in patients with airways obstruction was first described in one patient by Neagos et al. They reported a biphasic expiratory flow pattern, with an initial high flow rate and a terminal low flow rate, separated by a plateau flow. They attributed it to obstruction at the anastomotic site as well as severe airflow obstruction in the native lung. This pattern was confirmed and further analyzed by Herlihy et al, who suggested that the characteristic pattern was not caused by obstruction at the anastomotic site, but that the flow limitation was immediately below the anastomotic site. The suggestion that the shape of the MEFV curve is related to the flow-limiting effects of the anastomotic site is unlikely to be true as in the present study, patients with PVD and no airways obstruction did not demonstrate this shape in the flow-volume curve, in spite of undergoing an exactly similar unilateral surgical anastomosis of the main bronchus. Furthermore, in the case of the subject with airways obstruction (who underwent a pneumonectomy of his native lung after SLT), the biphasic, plateau shape in the flow-volume trace disappeared. These results support the analysis of Murciano et al.
that the characteristic shape of the MEFV curve is most likely caused by the different time constants and airways resistances of the transplanted and native lungs. Peak airflow is effort dependent, and primarily determined by respiratory muscle strength and the caliber of the large airways—trachea and major bronchi. Subsequent flow is determined primarily by the transplanted lung, which has a shorter time constant. This portion of the tracing therefore shows the plateau appearance as maximal flow is limited and becomes effort independent. The final portion of the tracing shows an abrupt decrease in flow as the contribution from the native lung with severe airways obstruction comes into play. Bronchiolitis obliterans increases the airways resistance primarily in the transplanted lung, and the change in the shape of the curve in subjects who developed bronchiolitis obliterans (Fig 4) is consistent with the above analysis. Thus, in these patients, as airways resistance in the transplanted lung increases, the maximal flow in the early portion of the MEFV curve decreases, leading to a disappearance of the biphasic nature of the curve.

In conclusion, our data show that in patients with PVD and initially normal maximal expiratory airflow rates, SLT does not alter static or dynamic lung volumes or the shape of the MEFV curve. In patients with chronic airways obstruction, indexes of airways obstruction, such as the RV and spirometric values, improve significantly, whereas changes in TLC reflect the underlying disease process, with little change in TLC in the absence of significant emphysema. In these patients, the characteristic biphasic, plateau shape seen in the MEFV trace after SLT is not related to the bronchial anastomotic site, but is most likely caused by the combination of flows from the transplanted and native lungs. Development of bronchiolitis obliterans results in the disappearance of the characteristic biphasic expiratory flow curve because of the increased airways resistance in the transplanted lung.