The Use of Home Spirometry in Detecting Acute Lung Rejection and Infection Following Heart-Lung Transplantation*

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The value of home spirometry in detecting acute lung rejection and opportunistic infections was studied in 15 heart-lung transplant recipients over a six-month period. The patients measured their FEV₁ and FVC twice daily at home using a portable turbine spirometer. The records were then reviewed in relation to the results of transbronchial lung biopsy carried out during occurrences of respiratory symptoms and during routine posttransplant assessment. FEV₁ and FVC fell by a mean (±SD) of 10.4 ± 6.9 percent and 9.3 ± 7.9 percent, respectively, during 20 episodes of lung rejection. The corresponding figures during opportunistic infections were 12.8 ± 10.1 percent and 12.5 ± 14.3 percent. No such change was observed during routine normal biopsies. Regular home spirometry offered early detection of these complications allowing early transbronchial lung biopsy as well as assessing efficacy of their therapy. Above all, measurements can be made daily, which is unique in the assessment of solid organ transplants.

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TBB = transbronchial lung biopsy; HLT = heart-lung transplant

The benefits of lung transplantation are compromised by two common acute complications: acute lung rejection, and opportunistic infection. The lungs are a common site for these disorders. Chronic lung rejection appears to cause obliterative bronchiolitis, which has been reported to cause disability and death in up to 50 percent of long-term heart-lung transplant (HLT) recipients.

Various clinical investigations have been used to monitor the lungs for acute rejection and infection. They include chest radiology, measurement of 99m-Tc-DTPA clearance of the lung, pulmonary function testing, and more recently transbronchial lung biopsy (TBB). Transbronchial lung biopsy is currently the most sensitive and specific test for lung rejection and allows the distinction between infection and rejection to be made. However, it required fiberoptic bronchoscopy which, while easily repeated, is not a procedure that can be undertaken daily.

Previously we reported the value of laboratory lung function testing, in particular forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC), in detecting acute lung rejection and infection, thereby facilitating a decision as to when TBB should be performed. As regular daily spirometry at home is now possible using a battery-operated spirometer, we decided to monitor pulmonary function in this way so as to allow early detection of rejection and infection. The results of a prospective study of this monitoring form the basis of this report.

**Patients and Methods**

**Spirometer**

The pocket-sized spirometer (Micro-medical Ltd, Rochester, Kent, England) (Fig 1), the prototype of which has been fully described in a previous report, measures the FEV₁ and FVC by means of a turbine volume transducer. The turbine drives a low-inertia vane that, during forced expiration, reflects infrared light from an enclosed source onto a sensor to generate electrical pulses. These are then proportionately computed into FEV₁ and FVC. The accuracy of the spirometer is within 2 percent.

The subject blows through the mouthpiece and by means of a switch, the FEV₁ or FVC is read off a digital display unit. The measurements are registered in liters at body temperature and pressure saturated with water vapor (BTPS).

The spirometers are factory calibrated. However, the calibration was checked regularly by connecting the spirometer in a series with a Vitalograph spirometer (Vitalograph U.K. Ltd, Kent, England) and comparing the two measurements of spirometric volumes.

**Patients**

Fifteen HLT recipients, six male and nine female, 12 to 51 years old, were prospectively studied over a period of six months. They were supplied with the pocket-sized turbine spirometer, taught how to use this instrument, and requested to record the best of three attempts twice daily at home. The record was reviewed by the physician during each clinic visit and the data were entered into a data file on a microcomputer (Tandon).
and total lung capacity (TLC) were carried out in each patient at routine assessments and when they had respiratory symptoms.

Acute lung rejection was diagnosed by histologic findings from the transbronchial biopsy specimen. Characteristically there are perivascular infiltrates consisting of large pyroninophilic, ie, immunoblastic, lymphocytes. The diagnosis was confirmed if in the absence of infection the patient's symptoms, signs, roentgenogram, or lung function improved with augmented immunosuppression. Opportunistic and bacterial lung infections were diagnosed histologically, serologically, and by culture of tissue or lavage specimens.  

**Analysis**

The records of home spirometry and histologic findings of transbronchial biopsy specimens over the six-month period were reviewed. All the values of FEV₁ and FVC recorded every day by each patient were plotted against time and dates of TBB, both routine and on the occurrences of histologically diagnosed pulmonary rejection or infection, using a microcomputer (Tandon) (Fig 2).

The change in FEV₁ or FVC with rejection or infection was defined as the difference in the immediately preceding stable recording and that recorded on a day before the time of the TBB. The normal value for each patient was defined by the stable spirometric value corresponding to the time of routine TBB that showed normal appearances histologically.

Significance of changes in spirometry was tested using the unpaired Student t test.

**Results**

A total of 38 transbronchial biopsies were carried out in the 15 HLT recipients during the period under review. Twenty (52.6 percent) of these showed acute lung rejection. Nine (23.7 percent) demonstrated evidence of infection, of which six were cytomegalovirus (CMV) pneumonia, two were bacterial bronchitis, and one was herpes simplex pneumonitis. The remaining nine biopsy specimens had a normal appearance histologically.

The mean (+SD) values of FEV₁ and FVC as recorded at home by the patients at the time of the acute rejection episodes were 2.27 ± 1.2 L and 2.72 ± 1.3 L, respectively. Corresponding values dur-
Table 1—Mean (± SD) Spirometric Values During Lung Biopsies*

<table>
<thead>
<tr>
<th></th>
<th>FEV₁, L</th>
<th>FVC, L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rejection (n=20)</td>
<td>2.27±1.2</td>
<td>2.75±1.3</td>
</tr>
<tr>
<td>Infection (n=9)</td>
<td>1.64±0.6</td>
<td>2.08±1</td>
</tr>
<tr>
<td>Normal (n=9)</td>
<td>2.65±0.7</td>
<td>3.14±0.9</td>
</tr>
</tbody>
</table>

*FEV₁ indicates forced expiratory volume in 1 s; FVC, forced vital capacity. Compared with values during normal biopsies, the values during infection differed significantly (p<0.01) but those during rejection did not reach statistical significance (p = 0.39)

ing infection episodes and also during normal biopsies are shown in Table 1.

A mean (± SD) fall of 0.23±0.2 L occurred in the FEV₁ during rejection, representing 10.4±6.9 percent decrease from the prerejection values. During the infection episodes, similar decreases were sustained in the FEV₁ and FVC, the former falling by a mean 12.8±10.1 percent (Table 2). The individual changes in FEV₁ during acute rejection are shown in Figure 3 and those during infection are shown in Figure 4.

All the patients had a transbronchial biopsy within one week of the onset of decline in FEV₁ at home. The mean duration between onset of decline in FEV₁ and transbronchial biopsy during the rejection episodes was 3.25±2 days. Similarly biopsy specimens confirming infection were carried out a mean 3.4±2 days from the period the FEV₁ started to fall.

In nine patients the daily FEV₁ did not vary. However, six of the 15 patients had a total of 22 occasions when temporary falls in FEV₁ occurred without development of symptoms. The mean fall in FEV₁ at these times was 8.4±3.5 percent rising back to normal spontaneously within a mean of 1.9±1 days.

**DISCUSSION**

A fall in FEV₁ and vital capacity (VC) led to transbronchial biopsy on 29 occasions for either infection or rejection. All the patients had symptoms at this time. On nine other occasions, the FEV₁ and VC were unchanged at a time of routine TBB and the histologic findings of the lung were normal. These patients did not have symptoms. The battery-operated pocket spirometer performed in these 15 patients without fault during the study and there was no change in calibration. From our experience we recommend that HLT recipients be instructed to record FEV₁ and VC daily and to contact the hospital when a fall of 10 percent or more occurs after a period of stable

Table 2—Mean (± SD) Decreases in Spirometry During Rejection and Infection*

<table>
<thead>
<tr>
<th></th>
<th>FEV₁, L</th>
<th>FVC, L</th>
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<tbody>
<tr>
<td>Rejection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in liters</td>
<td>0.23±0.2</td>
<td>0.24±0.2</td>
</tr>
<tr>
<td>% change</td>
<td>10.4±6.9</td>
<td>9.36±7.9</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in liters</td>
<td>0.24±0.2</td>
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<tr>
<td>% change</td>
<td>12.8±10.1</td>
<td>12.49±14.3</td>
</tr>
</tbody>
</table>

*FEV₁ indicates forced expiratory volume in 1 s; FVC, forced vital capacity. Similar changes in FEV₁ and FVC occurred with both infection and rejection. In individual cases, however, the difference is not significant enough to distinguish between the two complications.

Figure 3. Individual FEV₁ recordings in the 20 episodes of rejection. B indicates before rejection; D, during rejection. In all cases, a fall in FEV₁ was sustained.

Figure 4. Recordings of FEV₁ before (B) and during (D) the nine episodes of opportunistic infection. There was a decline in FEV₁ with infection in all cases.
spirometry and persists for longer than two days.

In both acute rejection\textsuperscript{10-12} and opportunistic infection\textsuperscript{13,14} of the lungs, inflammatory cell infiltrates are found predominantly in the lung periphery. This is likely to affect compliance and this, we suspect, causes the comparable fall in both FEV\textsubscript{1} and VC with these complications.\textsuperscript{6,9} Indeed, TLC also falls.\textsuperscript{6,9} Change in Dco is more variable.

There were 22 occasions in six of the 15 patients where temporary falls in FEV\textsubscript{1} occurred without the development of symptoms. The fall was less than in the histologically diagnosed infections and rejection and lasted for a shorter period despite no treatment being given. The cause of these changes is uncertain. It is unlikely to be technical as there was no evidence of calibration drift of the turbine spirometer. Rejection or infection sufficiently severe to alter lung mechanics is more likely to cause sustained falls in FEV\textsubscript{1} and VC if treatment is not given. Alternatively, the fluctuation of FEV\textsubscript{1} in particular, could reflect bronchial hyperresponsiveness. Bronchial hyperresponsiveness to methacholine\textsuperscript{15,16} and histamine\textsuperscript{17} is common in HLT recipients and appears to be unrelated to the presence of rejection.\textsuperscript{18} Indeed, a marked diurnal variation has been seen in some HLT recipients similar to that in asthma sufferers.\textsuperscript{19} As a result of these recent observations we now ask patients to record FEV\textsubscript{1} and VC on rising from bed in the morning so as to avoid the diurnal variation.

Treatment of both infection or rejection is associated with a return of spirometry to normal\textsuperscript{9,11} (Fig 2). Spirometry can therefore be used to monitor efficacy of treatment. Chronic rejection, characterized by obliterator bronchiolitis,\textsuperscript{20,21} is associated with an irreversible fall in spirometry, severe airflow obstruction being predominant.\textsuperscript{22} Daily records show a progressive fall in FEV\textsubscript{1} without response to augmented immunosuppression (Fig 5). In this particular patient the diagnosis of chronic rejection was confirmed by histologic examination of an open lung biopsy specimen.

Home spirometry affords a means of early detection of pulmonary complications in HLT recipients facilitating the decision to undertake TBB.

REFERENCES

Plan to Attend ACCP's

56th Annual Scientific Assembly
Toronto, Ontario, Canada

October 22-26, 1990

Dis 1985; 152:1182-91