Increasing Peak Expiratory Flow Time in Amyotrophic Lateral Sclerosis*

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Background: Serial measurements of pulmonary function to indicate decreasing respiratory muscle strength in patients with amyotrophic lateral sclerosis (ALS) is well documented. Quantitative outcome measures include declining FVC, FEV₁, maximal inspired pressure, maximal expired pressure, and maximal voluntary ventilation. Increasing peak expiratory flow time (PEFT) may represent a further sensitive measure of declining respiratory muscle strength in ALS.

Methods: Fifty-five patients with ALS performed flow-volume loops serially after presentation. The percentage change from baseline values for FVC, peak expiratory flow (PEFR), and PEFT were compared using Spearman correlation coefficients. The prolongation of PEFT with serial tests was analyzed using a Kruskal-Wallis with a Dunn multiple comparison test. Bulbar-onset and limb-onset PEFT was compared using the Mann-Whitney test.

Results: PEFT was significantly increased from baseline values at all follow-up tests. However, PEFTs measured at the third, fourth, fifth, and sixth visits, although higher, were not significantly different. Significant negative correlations existed between the increase in PEFT and the decrease in PEFR and FVC. Significant positive correlations existed between the increase in PEFT and days from diagnosis and the decrease in PEFR and decrease in FVC.

Conclusion: PEFT increases significantly and linearly with time in patients with ALS and may begin to plateau with bulbar symptoms. PEFT increases at a faster rate than the rate of decline in both FVC and PEFR. PEFT is a quantitative measure of decreasing pulmonary function in ALS that is easily measured.

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Key words: amyotrophic lateral sclerosis; FVC; peak expiratory flow rate; pulmonary function testing; respiratory muscles

Abbreviations: ALS = amyotrophic lateral sclerosis; ATS = American Thoracic Society; FVL = flow-volume loop; MEP = maximal expired pressure; MIP = maximal inspired pressure; PEFR = peak expiratory flow rate; PEFT = peak expiratory flow time

Declining respiratory muscle strength is a feature of amyotrophic lateral sclerosis (ALS) that results in respiratory impairment1,2 and contributes significantly to morbidity and mortality.3,4 Serial measurement of pulmonary function is used to follow the decline of respiratory muscle strength. The percentage of predicted FVC has been used in disease progression and survival models.5–6 FEV₁, maximal voluntary ventilation, maximal inspired pressure (MIP), and maximal expired pressure (MEP) are commonly measured in patients with ALS to follow disease progression.

Peak expiratory flow time (PEFT) is the time in milliseconds required to attain the peak expiratory flow rate (PEFR) from initiation of a maximal forced expiratory effort. In healthy male patients, PEFT is approximately 100 ms, and in disease states such as COPD may be shortened.7 Measurement of PEFT has not been studied in patients with ALS. This study examines changes in PEFT serially in patients with ALS, and the correlation between PEFT, FVC, PEFR, and days after presentation.

**Materials and Methods**

**Patient Population**

We undertook a retrospective review of 55 patients with ALS who were referred to the London Health Sciences Centre, University Campus from January 2000 to November 2002.
Patient demographics are shown in Table 1. Fifty-five patients were tested at baseline and the first follow-up, 47 patients were tested at the second follow-up, 26 patients were tested at the third follow-up, 17 patients were tested at the fourth follow-up, and 10 patients were tested at the fifth follow-up. The most common ALS-onset symptoms were weakness (47%) and dysarthria (22%). Interestingly, no patients reported respiratory symptoms at onset. Bulbar-onset patients demonstrated significantly lower pulmonary function values than limb-onset patients initially despite similar patient characteristics (Table 1).

### Pulmonary Function Testing

Flow-volume loops (FVLs) were performed in the pulmonary function laboratory using a dry rolling seal spirometer (model 2130; SensorMedics; Yorba Linda, CA). The equipment was calibrated daily according to American Thoracic Society (ATS) recommendations using a 3-L syringe. FVLs were performed in accordance to the guidelines of the ATS.8 The subject inspired recommendations using a 3-L syringe. FVLs were performed in accordance to the guidelines of the ATS.8

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Patients</th>
<th>Bulbar Onset</th>
<th>Limb Onset</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 55)</td>
<td>(n = 20)</td>
<td>(n = 35)</td>
<td></td>
</tr>
<tr>
<td>Male/female gender</td>
<td>34 (62)/21 (38)</td>
<td>11 (55)/9 (45)</td>
<td>23 (66)/12 (34)</td>
<td>0.57</td>
</tr>
<tr>
<td>Age, yr</td>
<td>54 ± 13.2</td>
<td>60.2 ± 12.2</td>
<td>55.7 ± 13.3</td>
<td>0.23</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169 ± 10.2</td>
<td>166 ± 8.5</td>
<td>171 ± 10.8</td>
<td>0.09</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>77.7 ± 17.8</td>
<td>73.3 ± 13.6</td>
<td>80.2 ± 19.6</td>
<td>0.16</td>
</tr>
<tr>
<td>FVC, L</td>
<td>3.7 ± 1.5</td>
<td>3.0 ± 8</td>
<td>4.0 ± 1.7</td>
<td>0.02</td>
</tr>
<tr>
<td>PEFR, L/min</td>
<td>6.6 ± 2.6</td>
<td>5.2 ± 1.8</td>
<td>7.4 ± 2.7</td>
<td>0.002</td>
</tr>
<tr>
<td>PEFT, ms</td>
<td>80 ± 29</td>
<td>90 ± 40</td>
<td>70 ± 20</td>
<td>0.006</td>
</tr>
<tr>
<td>Time from symptom onset to test, d</td>
<td>1,246 ± 1,499</td>
<td>858 ± 1,067</td>
<td>1,468 ± 1,671</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Diagnosis at time of presentation (El Escorial)

- **Definite**
  - Male/female gender: 40 (72.7)
  - Age, yr: 54 ± 13.2
  - Height, cm: 169 ± 10.2
  - Weight, kg: 77.7 ± 17.8
  - FVC, L: 3.7 ± 1.5
  - PEFR, L/min: 6.6 ± 2.6
  - PEFT, ms: 80 ± 29

- **Suspected**
  - Male/female gender: 2 (3.6)
  - Age, yr: 54
  - Height, cm: 169
  - Weight, kg: 77.7
  - FVC, L: 3.7
  - PEFR, L/min: 6.6
  - PEFT, ms: 80

- **Probable**
  - Male/female gender: 13 (23.6)
  - Age, yr: 54
  - Height, cm: 169
  - Weight, kg: 77.7
  - FVC, L: 3.7
  - PEFR, L/min: 6.6
  - PEFT, ms: 80

*Data are presented as No. (%) or mean ± SD.

### Results

The mean change in pulmonary function values with time are summarized in Table 2. The mean monthly increase in PEFT (4.7%) was greater than...
the mean monthly decline in both FVC (1.2%) and PEFR (1.3%). PEFT increased from baseline values linearly over time, while both FVC and PEFR decreased linearly with time (Fig 1). PEFT was significantly increased from baseline values at all follow-up tests (p < 0.001). PEFT also was significantly increased from the second visit on all follow-up visits as well (p < 0.001). PEFT on the third visit was not significantly higher (p > 0.05) than on the fourth visit. However, PEFT on the third visit was significantly higher than the fifth visit and sixth visit (p < 0.001). In contrast, PEFTs measured at the fourth, fifth, and sixth visits were not significantly different (p > 0.05). This may have resulted from increasing bulbar symptoms, differing rates of disease progression, and decreasing sample size resulting from the patients' inability to perform tests. Although the increase in PEFT in bulbar-onset patients was consistently greater at each follow-up interval in the study when compared to limb-onset patients (Fig 1), the differences were not significant (p = 0.23). There were five ALS-related deaths during the study due to respiratory failure. Mean survival from symptom onset was 35 ± 7 months (± SD). All five patients had bulbar disease before death. The mean increase in PEFT from baseline at the last test prior to death was 99%. PEFR and FVC showed mean declines from baseline values of 3% and 26%, respectively.

The correlations between measured pulmonary function values and days from presentations are shown in Table 3. The best correlation was between PEFR and FVC. PEFT demonstrated a good negative correlation to both PEFR and FVC. The correlation between PEFT and days from presentation was fair. The relative variability of repeated measurement for PEFT, FVC, and PEFR (Table 4) was consistently low for all measures.

**DISCUSSION**

This is the first study to examine the utility of PEFT as a measure of declining pulmonary function in a cohort of patients with ALS. Our data indicate that PEFT increases with progression of disease in patients with ALS. The mean monthly increase in PEFT is greater than the mean monthly decline in both PEFR and FVC. The increase in PEFT was equally correlated with both decreasing PEFR and FVC.

PEFR has been defined by the European Respiratory Society as the maximum flow achieved during expiration delivered with maximal force starting from the level of maximal lung inflation.9 The factors determining peak expiratory flow are the force generated by the expiratory muscles, primarily the abdominal muscles and the level of lung inflation. The

![Figure 1](image-url)
force-velocity properties of the expiratory muscles determine the speed with which alveolar pressure or driving force is reached. Hence, PEFR is dependent on the alveolar pressure the subject can generate. PEFR is thought to be limited by the force-velocity characteristics of expiratory muscles instead of the mechanical properties of the lungs and airways. Pathologic states can impair PEFR apart from the conditions that increase airways resistance, such as diseases that affect respiratory muscle function or limit chest expansion. Kreitzer et al noted the relationship between decreased muscle strength and declining PEFR in 32 patients with ALS. As ALS progresses, both FVC and PEFR decline. As well, the force that can be generated by respiratory muscles is affected by the level of lung inflation. This may explain the better correlation between declining FVC and PEFR noted in our study than with other variables. The same factors that result in declining PEFR and FVC in ALS are responsible for increasing PEFT. Increasing PEFT may be limited by bulbar involvement that results in upper airways dysfunction. Unfortunately, patients in our study dropped out when significant bulbar involvement occurred. This may have resulted in a greater portion of patients with slow progressing ALS remaining in the later stages of the study, and the rate of increase in PEFT with time may have been blunted. Like most measures of lung function, PEFT is dependent on patient effort. However, the patient is not required to sustain effort over a period of many seconds. This may represent an advantage especially when significant bulbar involvement is present. In a study of people 9 to 18 years of age, Enright et al found that PEFT was lower in male than female patients and decreased with increasing age and height. PEFT is decreased in obstructive lung disease and increased with higher body mass index. More study is required to determine normal values for PEFT and to examine the relationship of PEFT to both MIP and MEP. Further study of PEFT in ALS subgroups would also be useful.

Decreasing muscle strength and the alteration of chest mechanics with progression of ALS alters the appearance of the FVL. A progressive inability to overcome the elastic recoil of the chest occurs, and a restrictive pattern develops. Bulbar involvement results in altered upper airways function that is often observed on the FVL. These changes are manifest by decreased FVC, FEV1, PEFR, and an increase in PEFT. The decline in pulmonary function in this study was accompanied by a high degree of interpatient variability. This finding has been noted previously.

### Conclusions

Increasing PEFT is an additional measure of declining pulmonary function in patients with ALS that is easily measured.

### References


