Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS)

The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function

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Abstract

The ALS Functional Rating Scale (ALSFRS) is a validated rating instrument for monitoring the progression of disability in patients with amyotrophic lateral sclerosis (ALS). One weakness of the ALSFRS as originally designed was that it granted disproportionate weighting to limb and bulbar, as compared to respiratory, dysfunction. We have now validated a revised version of the ALSFRS, which incorporates additional assessments of dyspnea, orthopnea, and the need for ventilatory support. The Revised ALSFRS (ALSFRS-R) retains the properties of the original scale and shows strong internal consistency and construct validity. ALSFRS-R scores correlate significantly with quality of life as measured by the Sickness Impact Profile, indicating that the quality of function is a strong determinant of quality of life in ALS.

1. **Introduction**

The Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS) is a validated questionnaire-based scale that measures physical function in carrying out activities of daily living (ADL) of patients with ALS [1–4]. It has been used in clinical trials [5,6] as well as in clinical practice because of its ease of use and its correlation with both objective measures of disease status and levels of disability. The components of the scale group into four factors or domains that encompass gross motor tasks, fine motor tasks, bulbar functions and respiratory function [1]. The components of the scale, however, are not equally weighted. Where three questions each rate the motor and bulbar abilities only one question rates breathing ability.

In the course of conducting a clinical trial with brain-derived neurotrophic factor (BDNF), a series of queries were developed to evaluate the progression of respiratory dysfunction in ALS. In this report, we investigate the impact of adding three of these evaluation items to replace the breathing scale of the ALSFRS (Table 1). We tested the ability of the revised scale to assess respiratory function without altering the overall properties, utility, or validity of the original instrument. The addition of the respiratory symptom ratings resulted in an improved scale that is more sensitive to change and has better ability to predict survival than the original ALSFRS. This report is a retrospective validation of the revised scale.

2. **Patients and methods**

The 387 placebo-treated patients who were followed as part of the BDNF Phase II–III treatment study sponsored by Amgen–Regeneron Partners constitute the population for this evaluation. The demographic characteristics and the pretreatment measures of ALS status of these patients are summarized in Table 2.

The patients were evaluated monthly for 9 months as part of a therapeutic treatment trial. Monthly evaluations performed during the trial included the ALSFRS, percent

Table 1. (*Continued*)

10. Dyspnea (new)	
4	None
3	Occurs when walking
2	Occurs with one or more of the following: eating, bathing, dressing (ADL)
1	Occurs at rest, difficulty breathing when either sitting or lying
0	Significant difficulty, considering using mechanical respiratory support
11. Orthopnea (new)	
4	None
3	Some difficulty sleeping at night due to shortness of breath, does not routinely use more than two pillows
2	Needs extra pillows in order to sleep (more than two)
1	Can only sleep sitting up
0	Unable to sleep
12. Respiratory insufficiency (new)	
4	None
3	Intermittent use of BiPAP
2	Continuous use of BiPAP during the night
1	Continuous use of BiPAP during the night and day
0	Invasive mechanical ventilation by intubation or tracheostomy

predicted forced vital capacity or FVC% (adjusted for each patient's gender, age, and height), assessment of respiratory events associated with ALS (including ventilatory support), and the Sickness Impact Profile (SIP) [7]. The SIP was measured every 3 months.

2.1. Analytical methods

The internal consistency of the revised scale was assessed by Cronbach's alpha [8] and by factor analysis with varimax (variance maximization) rotation [9].

Construct validity is demonstrated by comparison of the novel rating instrument to an established one. The ALSFRS was originally validated against measures of isometric muscle strength, two other subjective rating scales, and milestones of disease progression [1,2]. None of these measures was performed in the BDNF clinical trial. Hence, the ALSFRS and ALSFRS-R were compared with FVC% [1,2] the SIP, an accepted quality-of-life measure. Construct validity was tested by comparing the pretreatment value of the ALSFRS-R and its subscores, as well as 9-month change scores, with independent measures of pulmonary function (FVC%) and the SIP. Pairwise Pearson or Spearman correlation coefficients are reported for each respective cross-sectional comparison. Prospective comparison of the ALSFRS-R with muscle strength testing and the Schwab and England rating scale [1] will be done in a future evaluation.

Table 2
Demographics and baseline measures

Measurement	Number of patients (%)	Mean	Std err mean
Age (years)	387	55.9	0.6
Gender			
Male	259 (66.9)		
Female	128 (33.1)		
Symptom duration (years)	387	2.1	0.1
ALSFRS	387	30.1	0.3
ALSFRS-R	384	38.0	0.3
FVC (%)	387	87.5	1.0
SIP	321	16.0	0.6

Longitudinal change in the ALSFRS-R was compared with changes in the SIP and pulmonary function (FVC%). Pairwise Pearson correlation coefficients are presented for each respective longitudinal comparison.

Survival data were analyzed using Cox's Proportional Hazards Model [10]. Survival prediction is presented as the fitted values from a logistic regression of survival outcome at 9 months as a function of baseline ALSFRS-R.

Test–retest reliability could not be assessed in this study because monthly intervals were too far apart to assume no change in the measures. Test–retest evaluation should be done with visits timed closer, ideally within 1 week, to confirm that a measure does not change in a time frame when the disease is assumed not to be changing at a detectable level. Test–retest reliability will be evaluated in a future, prospective study.

Cronbach's alpha was calculated using SAS, version 6.12 (SAS Institute, Cary, NC, USA). All other analyses were performed using JMP version 3.1.5 (SAS Institute).

3. Results

3.1. Factor analysis: internal structure of the ALSFRS-R

Factor analysis of the revised scale revealed that the evaluation items cluster into four factors that account for 73% of the total variance, as shown in Table 3. As in the original ALSFRS, these factors correspond to fine motor, gross motor, bulbar, and respiratory function [1]. The

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Measure	Finding	Points
speech	normal	4
	detectable speech disturbance	3
	intelligible with repeating	2
	speech combined with nonvocal communications	1
	loss of useful speech	0
salivation	normal	4
	slight but definite excess of saliva in mouth; may have nighttime drooling	3
	moderately excessive saliva; may have minimal drooling	2
	marked excess of saliva with some drooling	1
	marked drooling; requires constant tissue or handkerchief	0

This is the end of the sample ALFRS questionnaire.
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Overview:

The Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS) is an instrument for evaluating the functional status of patients with Amyotrophic Lateral Sclerosis. It can be used to monitor functional change in a patient over time.

Measures: (1) speech (2) salivation

(3) swallowing

(4) handwriting

(5) cutting food and handling utensils (with or without gastrostomy) (6) dressing and hygiene

(7) turning in bed and adjusting bed clothes

(8) walking

(9) climbing stairs

(10) breathing

This is the end of the sample ALFRS scoring & administration instructions. Please return to page 1 to purchase complete version.