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# Functional Decline is Associated with Hopelessness in Amyotrophic Lateral Sclerosis (ALS)

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## Abstract

**Objective—**To determine the relationships between hopelessness, depression, quality of life, and disease progression in ALS.

**Methods—**Hopelessness and depression were assessed prospectively in a cohort of people with ALS using the Beck Hopelessness scale (BHS) and the ALS Depression Inventory (ADI-12), respectively. ALS Specific Quality of Life and measures of functional status (ALSFRS-R and forced vital capacity) were collected. Associations between changes in psychological health and functional scores were calculated using Spearman correlation coefficients.

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David Schoenfeld: Analysis/interpretation of data; drafting/revising the manuscript.
Hong Yu: Data collection; analysis/interpretation of data.
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Merit Cudkowicz: Study concept/design; analysis/interpretation of data; drafting/revising the manuscript.
Nazem Atassi: Study concept/design; analysis/interpretation of data; drafting/revising the manuscript.

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**Results—**Twenty-five people with ALS had at least 2 visits and were followed for a mean of 11 (± 6) months. People with hopelessness and depression reported worse quality of life ($p<0.01$ for both associations). Decline in function between any two visits measured by ALSFRS-R ($p<0.01$) and FVC ($p=0.02$) correlated with increased hopelessness, but not depression.

**Conclusion—**This study highlights the importance of monitoring hopelessness in ALS, particularly in patients with faster functional decline.

### Keywords

Hopelessness; Depression; Quality of life; Predictor; Disease progression

## Introduction

People with amyotrophic lateral sclerosis (ALS) face enormous physical and emotional challenges. It is therefore expected for ALS to have a psychological impact on patients both at the time of diagnosis and throughout the course of the disease [1–8]. In this study we measured hopelessness and depression prospectively in a cohort of people with ALS and estimated their relationship with the rate of disease progression measured by the ALS functional rating scale-revised (ALSFRS-R) [9] and forced vital capacity (FVC).

## Materials and Methods

### Study participants

Eligible participants had a diagnosis of possible, laboratory-supported probable, probable, or definite ALS [10]. All eligible patients seen at the Massachusetts General Hospital ALS multidisciplinary clinic between March 2009 and September 2010 were asked to participate. New patients who came to our clinic only for a one-time second-opinion visit were excluded. The study protocol was approved by the Institutional Review Board (IRB) at Massachusetts General Hospital.

### Study scales

Several scales were administered at study visits that occurred approximately every three months and coincided with their scheduled clinical visits. Hopelessness was assessed using the Beck Hopelessness Scale (BHS), a self-reported series of 20 true-false questions designed to gauge one’s feelings about the future, loss of motivation, and expectations [11]. Depression was measured using the ALS Depression Inventory (ADI-12) [12], a 12-item scale that has been designed to screen for depression in ALS. Quality of life was analyzed using the ALS-specific Quality of Life Questionnaire (ALSSQOL), a 59-item scale that has been designed to assess QOL in ALS [13]. The ALS Functional Rating Scale-revised (ALSFRS-R) [9] and forced vital capacity (FVC) were also obtained at each study visit. FVC values were expressed as percent of predicted for age, gender, and height.

### Statistical analyses

BHS and ADI-12 scores were analyzed as continuous and dichotomous variables. The cut-offs for the dichotomous forms of BHS and ADI-12 were 4 and 23, respectively [11,12].

Changes in BHS, ADI-12, ALSFRS-R and FVC were calculated at each follow-up visit as the difference between the scores at a given visit and the previous visit. Associations between changes in functional scores between two consecutive visits and BHS and ADI-12 scores were calculated using Spearman correlation coefficients, with variances estimated via bootstrapping at the patient level to account for repeated measures. All analyses were performed in SAS version 9.3 (SAS Institute, Cary, NC), using a significance level of 0.05.

## Results

### Study population

Of 155 eligible patients in our clinic, 36 (23%) agreed to enroll in this longitudinal assessment. Those who chose to participate and those who declined to participate were similar at the time of screening with respect to age, gender, family history of ALS, site of onset, time from symptom onset to diagnosis, time from diagnosis to screening, depression as assessed by ADI-12 scores, antidepressant use and riluzole use (Supplementary Table 1). Among the 36 participants, 25 completed at least 2 and as many as 8 study visits, contributing a total of 79 potential observations for the analyses of associations between changes in mood and function. Participants were followed for a mean of 11 (± 6) months Baseline characteristics of both the overall cohort and the subgroup with follow up data are described in Table 1.

### Prevalence of hopelessness and depression

At baseline, 59% of study participants were classified as having at least a mild degree of hopelessness and 36% were classified as at least mildly depressed by the ADI-12. Baseline hopelessness, depression and quality of life were all significantly associated, with Spearman correlation coefficients ranging from 0.58 to 0.71 in absolute magnitude ($p<0.01$ for all associations) (Supplementary Table 2).

### Correlation between functional decline, hopelessness and depression

Among patients with available follow up data (N=25), on average, participants declined 2.4 (± 3.4) points on the ALSFRS-R and declined 8.5 (± 15.1) percent in FVC in between 2 visits. Decline in function between two study visits as measured by ALSFRS-R (Figure 1A) and FVC (Figure 1B) correlated with worsening in hopelessness (Spearman correlation coefficient=−0.39, 95% confidence interval (CI) −0.66 to −0.11, p value <0.01 and −0.34, 95% CI −0.66 to −0.03, p value=0.02, respectively). Decline in ALSFRS-R and FVC did not correlate with depression (Spearman correlation coefficient=0.17, 95% CI −0.11 to 0.45, p value=0.89 and −0.11, 95% CI −0.36 to 0.15, p value=0.20, respectively).

## Discussion

In this study, we found that functional decline correlated with hopelessness but not depression in people with ALS. Hopelessness has been rarely studied in ALS. While hopelessness and depression often co-exist, they are two different constructs. Hopelessness implies negative expectations about the future, pessimism, lack of enthusiasm, and loss of meaning. It is a predictor of negative health outcomes in several populations [14,15]. Of

note, hopelessness correlates with interest in physician-assisted suicide [16,17] and predicts suicidal intent and suicide better than depression [18,19].

The lack of correlation between functional decline and depression in this study is consistent with prior ALS studies [1,6,8,20–22]. Depression implies lowered mood and loss of pleasure. It has been speculated that, as disease progresses, the factors that contribute most to mood and pleasure shift from those that are dependent on physical function to those that are not (social, spiritual, and existential factors) [6,21,22], thus explaining the lack of an association between functional decline and depression.

## Limitations

This study includes the small sample size and the possibility of sample bias. Our patients were recruited from the ALS clinic of a large academic center. Attendance at a multidisciplinary clinic has been associated with improved outcomes, including better quality of life [23]. Therefore, the prevalence of psychological distress may be different in the general ALS population. In addition, the follow-up duration was relatively short. Another limitation of our study is that we did not include assessments of cognitive dysfunction. It is now wellrecognized that ALS and frontotemporal dementia (FTD) form a spectrum of disease [24]. We cannot exclude that some of the psychological features identified in our study could be symptoms of mild cognitive impairment.

## Conclusion

This study highlights the importance of monitoring hopelessness in ALS, particularly in patients with faster functional decline. While several medications are available to treat depression, how to address hopelessness in ALS has been largely unexplored and warrants further research [23,25].

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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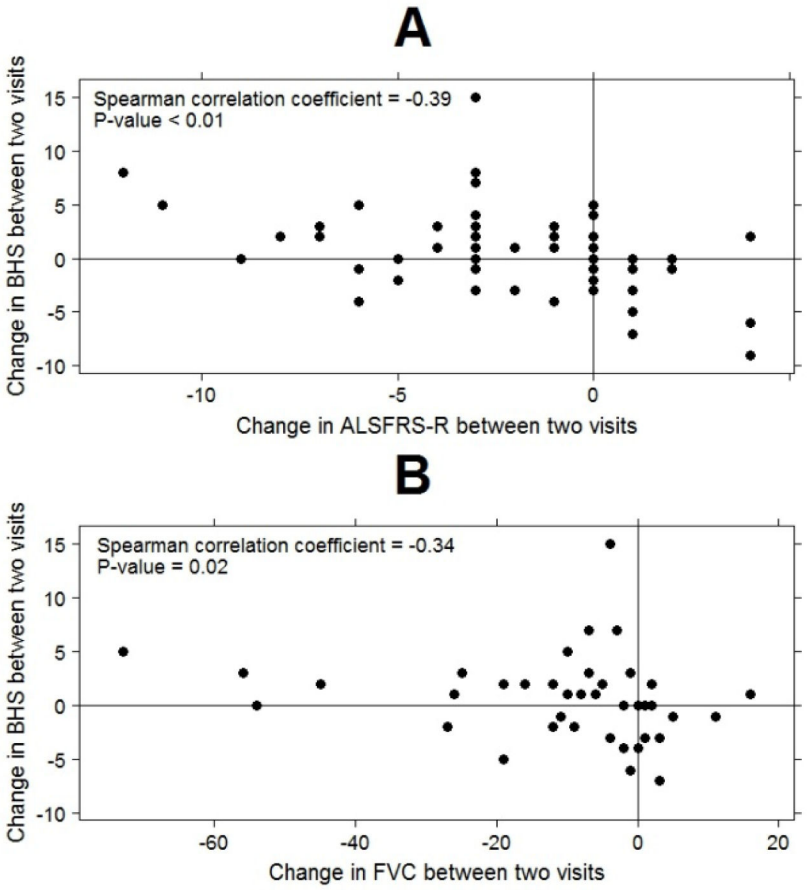


**Figure 1.**

Correlation between changes in function and hopelessness. Worsening ALSFRS-R (A) and FVC (B) between two study visits was associated with worsening hopelessness, as measured by BHS scores.

## Table 1

Baseline clinical and demographic characteristics (ADI-12: ALS Depression Inventory; ALS: Amyotrophic Lateral Sclerosis; ALSFRS-R: ALS Functional Rating specific Scale; ALSSQOL: ALS-specific Quality of Life; BHS: Beck Hopelessness Scale; FVC: Forced Vital Capacity

| | All Participants N=36 | Participants with Available Follow Up Data N=25 |
|---|---|---|
| | Mean (± SD) or N (%) | Mean (± SD) or N (%) |
| Age at baseline (years) | 59.7 (± 11.0) | 59.9 (± 11.7) |
| Gender (% male) | 18 (50.0%) | 11 (44.0%) |
| Race (% white) | 35 (97.2%) | 24 (96.0%) |
| Marital status (% married) | 29 (80.6%) | 20 (80.0%) |
| Any children (%) | 30 (83.3%) | 23 (92.0%) |
| Household income (%) | | |
| <$60,000 | 8 (22.2%) | 6 (24.0%) |
| $60,000–100.000 | 12 (33.3%) | 10 (40.0%) |
| >$100.000 | 8 (22.2%) | 5 (20.0%) |
| Missing or Unknown | 8 (22.2%) | 4 (16.0%) |
| Familial ALS (%) | 4 (11.8%) | 2 (8.3%) |
| Known SOD1 mutation | 1 (25.0%) | 1 (50.0%) |
| Bulbar onset (%) | 10 (27.8%) | 7 (28.0%) |
| Riluzole use (%) | 13 (38.2%) | 8 (34.8%) |
| Antidepressant use (%) * | 8 (22.9%) | 5 (20.8%) |
| Time from symptom onset to diagnosis (months) | 22.7 (± 35.2) | 22.0 (± 38.3) |
| Time from diagnosis to baseline (months) | 24.1 (± 32.8) | 19.8 (± 26.2) |
| ALSFRS-R | 32.5 (± 7.8) | 33.5 (± 7.5) |
| FVC | 81.7 (± 25.3) | 83.7 (± 23.7) |
| ADI-12 | 19.8 (± 6.5) | 19.6 (± 7.2) |
| BHS | | |
| ALSSQOL average score | 6.9 (± 1.5) | 7.0 (± 1.6) |
| ALSSQOL religiosity score | 4.8 (± 3.9) | 5.3 (± 4.0) |

* Antidepressant use is defined as any antidepressant prescribed for the specific purpose of treating depression).