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# Trends of quality of life changes in amyotrophic lateral sclerosis patients

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ABSTRACT

*Background:* Amyotrophic lateral sclerosis (ALS) is an incurable progressive neurodegenerative disease and thus the assessment of quality of life (QOL) changes and factors that may influence its course is valuable in the meantime.
*Objectives:* The present study aimed to assess the deterioration rate of QOL and influencing factors in different subgroups of Iranian ALS patients.
*Methods:* 132 patients were evaluated in this prospective multicenter observational study. QOL was measured using ALS Assessment Questionnaire (ALSAQ-40) during 1 year follow up and its progression rate was assessed in different subgroups of patients according to age, sex, stage of disease, riluzole consumption, onset type. Also physical disability and functional disability were measured using MMT and ALSFRS-R scores respectively and their progression rates were compared with ALSAQ-40 changes.
*Results:* Significant deterioration of the scores of ALSAQ-40 during study was consistent in all of its domains ($p = 0.000$). There was a significant negative correlation between ALSFRS-R and MMT changes and ALSAQ-40 change ($p = 0.000$) and this was consistently observed in all domains of ALSAQ-40 ($p = 0.00$). ALSAQ-40 deterioration rate was shown to be significantly lower in severe/terminal stages compared to mild/moderate stages ($p = 0.00$). Significantly higher deterioration rate was observed in bulbar onset versus limb onset patients [$F(1,130) = 4.52$, $p = 0.04$] but no significant difference was observed among other subgroups according to age, sex and riluzole consumption.
*Conclusion:* All domains of QOL significantly deteriorate during ALS course and there is a significant correlation between their changes and progression of physical and functional disabilities. Rate of degradation of QOL may be different at different stages of the disease. QOL worsens independent of factors such as sex, age and consumption of riluzole; but onset type (bulbar versus limb) is an imperative factor in quality of life changes during the disease course.



## 1. Introduction

Amyotrophic lateral Sclerosis (ALS) is a degenerative disease of upper and lower motor neurons. The course of the disease is rapidly progressive and causes disability in the variable domains, including physical mobility, respiration, nutrition, communication and emotional aspects [1].

Unfortunately, most people with ALS die within 5 years of the onset after facing progressive weakness. At present, there is no cure and the only available drug (riluzole) prolongs the life of only a few months; therefore, the quality of life (QOL) changes are very useful in the meantime [2]. The interest in studying QOL of ALS patients has increased as recent studies have shown that alleviating symptoms and improving the QOL can affect the course of the disease and survival [2–4]. Besides, it is not obvious yet whether physical disabilities of patients and their QOL follow the same course line or not. [5].

In the present study we intended to assess the course of QOL in Iranian patients through a prospective multicenter study. We have focused on the deterioration rate of the QOL in different categories of patients and evaluated the effect of other variables on this subject.

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## 2. Patients and methods

This prospective, multicenter, observational study (patients enrolled from August 2009 through March 2010) tracked the outcomes of 132 Persian ALS patients and follow-up visits were performed after 6 and 12 months. These patients were selected from Iran ALS registry who survived 1 year from the onset of observation and had complete follow-up [6].

The research team was established in 2006 comprising of >60 neurologists from 28 provinces of Iran. All included patients fulfilled the El Escorial criteria for probable and definite ALS [7]. Demographic data, disease onset, the presence of positive family history and riluzole consumption were recorded. The known effects of riluzole were described to the patients and as it was not covered by insurance patients decided whether to consume it or not. Also ALS health state scale (ALSHSS) was used at the first visit to categorize people into 4 groups (mild, moderate, severe and terminal) [8] Furthermore, different scores such as Manual Muscle Test scoring (MMT) (0−130) [9], revised ALS Functional Rating Scale (ALSFRS-R) [10] and ALS Assessment Questionnaire (ALSAQ-40) [11] were utilized to measure patients' status at the start of study and in periods of 6 and 12 months.

### 2.1. Scales

#### 2.1.1. ALSHSS

Clinical status at the start of the study was measure by ALSHSS. ALS health state scale [8]. The ALSHSS categorizes patients into 4 subgroups of severity: state I (mild): deficit is seen in only one of 3 regions (i.e. speech, arm and leg) and the patient is functionally independent in speech, upper extremity activities of daily living and ambulation. State II (moderate): deficit is seen in all 3 regions or moderate to severe deficit in one region while the other 2 regions are normal or mildly affected. State III (severe): the patient needs assistance in 2 or 3 regions: speech is dysarthric, and/or patient needs assistance to walk, and/or with upper extremity activities of daily living. State IV (terminal): non-functional use of at least 2 regions and moderate or non- functional use of the third region.

#### 2.1.2. Manual muscle testing (MMT)

MMT was recorded by means of the 6-point Medical Research Council (MRC) scale (range 0–5). Strength was evaluated bilaterally for 6 upper- and 7 lower-extremity muscle groups (total of 26 groups). MRC scores for the 26 muscle groups were summed to produce a combined score of global strength (range 0–130). Also, we defined a new variable as MMT decline (MMT month 12 minus MMT month 0) [9].

#### 2.1.3. ALSFRS-R

For functional score we used Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R). The scale comprises 12 items which are categorized in four domains including bulbar, fine motor, gross motor and respiratory function. Each item is scored 0 to 4 and the total score is between 0 and 48; higher numbers indicate less disability [10].

#### 2.1.4. ALSAQ-40

Quality of life was assessed using ALSAQ-40. The 40-Item Amyotrophic Lateral Sclerosis Assessment Questionnaire is specifically designed to evaluate the quality of life of ALS patients. Forty questions each with five choices constitute this questionnaire which are categorized in five domains including physical aspects and mobility, activities in daily living and independence, eating and drinking, communication, and emotional aspects. ALSAQ-40 evaluates the patient's condition in two recent weeks. ALSAQ-40 was designed in 1999 by Jenkinson et al. and its internal reliability was confirmed in two separate studies [11]. Reliability and validity of the Persian version of ALSAQ-40 was approved in another study and therefore we used this version to evaluate the course of quality of life [12].

In the current study, QOL changes were evaluated during the time of the study and it was related to the predictor variables including age, sex, onset site and ALSHSS.

### 2.2. Statistical analysis

The IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp. was used to analyze the data. Continuous data are presented as mean ± standard deviation (SD). $p$-Values below 0.05 were regarded as significant. Kolmogorov-Smirnov Z test was used to determine the normal distribution of all continuous variables.

To compare trend changes between ALSFRS-R and ALSAQ-40, we calculated the correlation between ALSFRS-R changes (ALSFRS-R month 6 – ALSFRS-R baseline in addition to ALSFRS-R month 12 – ALSFRS-R month 6) and ALSAQ-40 changes (ALSAQ-40 month 6 – ALSAQ-40 baseline as well as ALSAQ-40 month 12 – ALSAQ-40 month 6); likewise, we measured the correlation.

Likewise, we measured the correlation between ALSAQ-40 domains and ALSFRS-R as well as MMT.

A mixed between-within subjects analysis of variance was conducted to assess the impact of sex, age, riluzole consumption, ALSHSS, and onset site on QOL scores across 3 time periods (month 0, month 6, and month 12).

#### 2.2.1. Bonferroni correction

In this study, since 3 measurement scales (i.e. ALSAQ, ALSFRS, and MMT) were used; accordingly, to prevent multiple comparison error, we performed the Bonferroni correction. This correction sets the significance cut-off at $\alpha/n$. As a result, for our study, we set the new $p$-value as $0.05/3 = 0.017$.

## 3. Results

Totally 132 patients were recruited. Mean age of patients was 52.9 ± 12.5; 80 (60.6%) were males. According to ALSHSS, 27 (20.5%) were classified as mild, and 68 (51.5%), 31 (23.5%), 6 (4.5%) were classified as moderate, severe, and terminal, respectively. Moreover, 109 (82.6%) had limb-onset type and 23 (17.4%) had bulbar onset.

#### 3.1.1. ALSAQ-40 domains

The changes in 5 subdomains are depicted in Table 1 and Fig. 1.

#### 3.1.2. ALSAQ-40 and ALSFRS-R changes

There was a significant negative correlation between ALSFRS-R change and ALSAQ-40 change ($r = -0.40, p < 0.001$) (Fig. 2). Regarding the domains, there was a negative significant correlation between all domains and ALSFRS-R: physical aspects and mobility ($r = 0.71$, $p < 0.01$), activities in daily living and independence ($r = 0.82$, $p < 0.01$), eating and drinking ($r = 0.64$, $p < 0.01$), communication ($r = 0.79$, $p < 0.01$), and emotional aspects ($r = 0.83$, $p < 0.01$).

#### 3.1.3. ALSAQ-40 and MMT

There was a significant negative correlation between MMT change and ALSAQ-40 change ($r = -0.39, p < 0.001$) (Fig. 2). Regarding the domains, there was a negative significant correlation between all subdomains and MMT: physical aspects and mobility ($r = -0.34$, $p < 0.01$), activities in daily living and independence ($r = -0.38$, $p < 0.01$), eating and drinking ($r = -0.23$, $p < 0.01$), communication ($r = -0.30$, $p < 0.01$), and emotional aspects ($r = -0.24$, $p < 0.01$).