POSB356

Health-related quality of life across King's and MiToS stages among Amyotrophic Lateral Sclerosis patients: results from a real-world point-in-time survey

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OBJECTIVE

- To assess the impact of disease progression on HRQoL through EQ-5D administered to patients and caregivers at different stages of ALS on the King's and MiToS staging systems.

CONCLUSIONS

- Across the King's staging, the steepest decline in HRQoL was observed between stages 3 and 4. This coincides with the introduction of feeding and/or ventilation assistance due to nutritional and respiratory failure.
- In contrast, across the MiToS staging, the steepest decline in HRQoL was observed between stages 1 and 2, following loss of independent function in two domains. From this stage onwards, patient's EQ-5D index scores indicated a HRQoL state close to or worse than death.
- For MiToS, where complete loss of function in an additional domain is required to progress to the subsequent stage, a steeper HRQoL decline was observed across stages than for King's.
- As patients' disease states progressed, their caregivers also experienced a gradual decline in HRQoL.
- These results demonstrate that disease progression, as assessed by two independent staging systems, has an adverse impact on HRQoL, highlighting the potential benefit of interventions to maintain patients at earlier stages.

Virtual ISPOR Europe 2021
November 30 - December 3, 2021

Introduction

- Amyotrophic lateral sclerosis (ALS) is a rare, degenerative neuromuscular disease, leading to progressive loss of muscle function, and ultimately death.[1]
- The King's staging and Milano-Torino Staging (MiToS) systems are used for evaluating clinical progression.
- King's staging assesses any impact based on the number of affected regions, whereas MiToS assesses complete loss of independence in four key domains (bulbar, gross motor, fine motor, and respiratory function).[2] Both staging criteria are derived or can be mapped from Revised Amyotrophic Lateral Sclerosis Functional Rating (ALSFRS-R) scores.
- While outcome measures such ALSFRS-R measure physical function, enabling assessment of clinical outcomes, wellbeing as perceived by patients may be assessed.
- The EQ-5D-5L is one of the most widely used measures assessing five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[3]
- The EQ-5D can be used to determine the impact of the disease on the HRQoL of patients and caregivers. Real-world data quantifying patient perceived well-being at different ALS disease stages is limited.[4]

Methods

- Data were drawn from the Adelphi ALS Disease Specific Programme™ (DSP), a point-in-time survey of de-identified neurologists and patients with ALS in France, Germany, Italy, Spain, the UK, and the USA. The data were collected between July 2020 and March 2021.
- The DSP methodology has been previously published[5] and was conducted according to the relevant regulations.
- Neurologists were asked to complete a questionnaire reporting recently consulted patients' demographics and clinical characteristics, including King's and MiToS stages.
- These same patients (and their caregivers, where applicable) were invited to complete questionnaires reporting on disease burden and HRQoL measures, including the EQ-5D-5L.
- Correlation of cross-walked EQ-5D index scores (UK tariffs) and visual analogue scale (VAS) scores with King's and MiToS stage was assessed through linear regression; adjusted for age, sex, Body Mass Index (BMI), and number of comorbidities.
- Bivariate comparisons across disease stages were conducted using Kruskal-Wallis tests.

Results

- 142 neurologists recorded data for 880 patients with ALS. Complete EQ-5D-5L data were provided by 163 patients, and EQ-5D VAS data were provided by 172 patients (or their caregivers, by proxy).
- Across the sample, the mean age was 61.7 years. 61.8% were male and 90.2% were white/Caucasian. The mean time since ALS diagnosis was 19.4 months (**Table 1**).
- Statistically significant negative correlations (all p<0.001) were observed between disease stage and patient EQ-5D Index and VAS scores between certain stages (**Figures 1-4**).
- Across the King's stages, statistically significant differences were observed for each individual EQ-5D dimension except for anxiety/depression (**Figure 5**). Across the MiToS stages, statistically significant differences were observed for all individual EQ-5D dimensions (**Figure 6**).
- Statistically significant negative correlations (p<0.05) were observed between disease stage and caregiver EQ-5D Index scores (**Figures 7 & 8**)

Strengths

- Two clinical staging systems were considered.
- Both patient and caregiver perspective was sought.
- The real-world study design enables capture of HRQoL data for ALS patients in general, independent of any therapeutic intervention or management strategy.

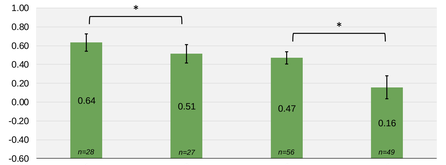
Limitations

- The DSP is not based on a truly random sample of physicians and patients. While minimal inclusion criteria governed the selection of the participating physicians, participation is influenced by the willingness to complete the survey.
- The DSP is a point-in-time survey and as such different individuals (with different value judgements) make up the groups for each disease stage, rather than a fixed cohort of patients and caregivers being followed over time.

Table 1. Patient demographics

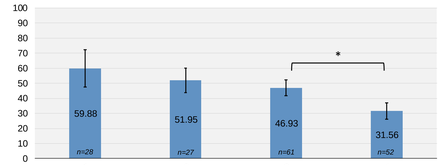
	All Patients (n=880)	Patients with EQ-5D-5L (n=163)	Patients with EQ-5D-VAS (n=172)
Age (years), mean (SD)	61.7 (11.1)	60.7 (11.5)	60.8 (11.5)
Sex - male, n (%)	544 (61.8)	98 (60.1)	104 (60.5)
Ethnicity - White/Caucasian, n (%)	793 (90.2)	152 (93.8)	161 (94.2)
	(n=854)	*(n=160)*	*(n=169)*
Time since ALS diagnosis (months), mean (SD)	19.4 (22.1)	22.4 (30.3)	22.3 (29.6)
King's stage, n (%)	*(n=857)*	*(n=160)*	*(n=169)*
Stage 1	125 (14.6)	28 (17.5)	29 (17.2)
Stage 2	151 (17.6)	27 (16.9)	27 (16.0)
Stage 3	303 (35.4)	56 (35.0)	61 (36.1)
Stage 4	278 (32.4)	49 (30.6)	52 (30.8)
MiToS stage, n (%)	*(n=880)*	*(n=163)*	*(n=172)*
Stage 0	600 (68.2)	115 (70.6)	122 (70.9)
Stage 1	104 (11.8)	17 (10.4)	18 (10.5)
Stage 2	71 (8.1)	10 (6.1)	10 (5.8)
Stage 3	40 (4.5)	8 (4.9)	8 (4.7)
Stage 4	65 (7.4)	13 (8.0)	14 (8.1)

Figure 1. EQ-5D-5L index scores by King's stage



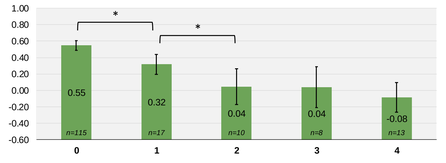
Marginal means with standard errors shown.
Significant negative correlation between King's staging and EQ-5D-5L score; r_s= 0.318, p<0.001, n=160.
* p<0.05

Figure 2. EQ-5D-VAS scores by King's stage



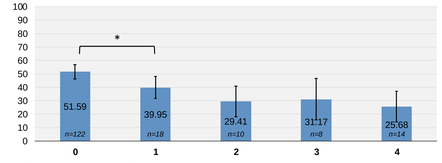
Marginal means with standard errors shown.
Significant negative correlation between King's staging and EQ-5D-VAS score; r_s= 0.226, p<0.001, n=169.
* p<0.05

Figure 3. EQ-5D-5L index scores by MiToS stage



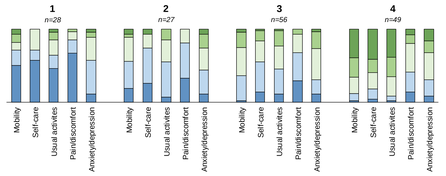
Marginal means with standard errors shown.
Significant negative correlation between MiToS staging and EQ-5D-5L score; r_s= 0.461, p<0.001, n=163.
* p<0.05

Figure 4. EQ-5D-VAS scores by MiToS stage



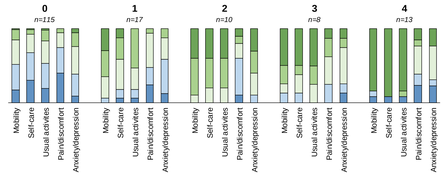
Marginal means with standard errors shown.
Significant negative correlation between MiToS staging and EQ-5D-VAS score; r_s= 0.202, p<0.001, n=172.
* p<0.05

Figure 5. EQ-5D-5L dimensions by King's stage



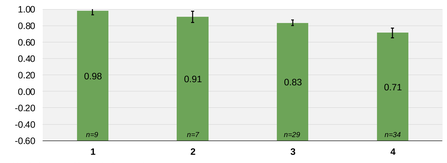
Mobility: *p*<0.001; Self-care: *p*<0.001; Usual activities: *p*<0.001; Pain/discomfort: *p*<0.001; Anxiety/depression: *p*=0.077

Figure 6. EQ-5D-5L dimensions by MiToS stage



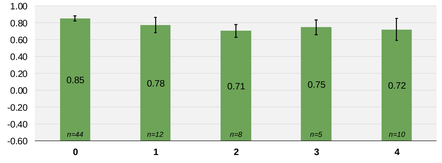
Mobility: *p*<0.001; Self-care: *p*<0.001; Usual activities: *p*<0.001; Pain/discomfort: *p*<0.001; Anxiety/depression: *p*=0.036

Figure 7. Caregiver EQ-5D-5L index score by King's stage



Marginal means with standard errors shown.
Significant negative correlation between King's staging and Caregiver EQ-5D-5L score; r_s= 0.141, p=0.002, n=79
* p<0.05

Figure 8. Caregiver EQ-5D-5L index score by MiToS stage



Marginal means with standard errors shown.
Significant negative correlation between MiToS staging and Caregiver EQ-5D-5L score; r_s= 0.100, p=0.030, n=79.
* p<0.05

References: 1. Masrori P et al. Amyotrophic Lateral Sclerosis: A clinical review. *European Journal of Neurology.* 27: 1918-1929. *2.* Ton Fang et al. Comparison of the King's and MiToS staging systems for ALS. *Amyotroph Lateral Scler Frontotemporal Degener.* 2017; 18: 227-232. 3. EuroQol Research Foundation. *EQ-5D-5L User Guide, 2019.* Available from: https://euroqol.org/publications/user-guides. 4. Emrani Z et al. Health-related quality of life measured using the EQ-5D-5L: population norms for the capital of Iran. *Health Qual Life Outcomes* 2020; 18: 108. 5. Anderson P et al. Real-world physician and patient behavior across countries: Disease-Specific Programmes - a means to understand. *Curr. Med. Res. Opin.* 2008; 24: 3063-3072.

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