

PAPER

A cross sectional study on determinants of quality of life in ALS

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Background: Understanding the determinants of quality of life (QoL) in amyotrophic lateral sclerosis (ALS) has become increasingly important with the recent emphasis on the comprehensive management of patients.

Objective: To evaluate the determinants of QoL in ALS using two scales with different theoretical constructs: the Schedule for the Evaluation of QoL-Direct Weighting (SEIQoL-DW), which evaluates subjective aspects of QoL, and the McGill QoL Questionnaire (MQOL), which evaluates both health related and non-health related factors of QoL.

Methods: Eighty consecutive patients with ALS underwent a battery of tests evaluating QoL and a series of physical, emotional, psychological, and socioeconomic predictor variables. A stepwise linear regression model was used to compare QoL scores and explicatory variables.

Results: SEIQoL-DW score was related to social support, depression, religiosity, and socioeconomic status. Total MQOL score was related to social support, socioeconomic status, and clinical status. MQOL single item score (MQOL-SIS) was related to social support, depression, social withdrawal, and socioeconomic status. SEIQoL-DW score was not related to total MQOL score. Conversely, a significant correlation was found between SEIQoL-DW and MQOL-SIS.

Conclusions: With both QoL scales, the most important explicatory variable of QoL was the self perceived quality of social support. Physical status was not relevant in determining QoL. This study indicates that health related QoL measures are not adequate to assess QoL in patients with ALS, because their appreciation of QoL mainly relies on psychological, supportive, and spiritual factors. Therapeutic interventions should consider the psychological needs of patients and pay greater attention to caregivers' issues.

The understanding of factors related to quality of life (QoL) in chronic neurological disorders is becoming increasingly important, with the recent emphasis on the comprehensive management of patients' conditions.¹ This is particularly true in amyotrophic lateral sclerosis (ALS), a disease characterised by a progressive impairment of motor functions up to a complete loss of autonomy, which in most patients is associated with the total preservation of mental state.

The understanding of factors related to QoL in ALS may have major implications, both in the care of patients and in the clinical research setting. QoL in ALS has been evaluated with different instruments, because there is no consensus on which scales are more suitable for measuring QoL in these patients. Some studies have used generic measures of health status, such as the Short Form 36 (SF-36),² and the Sickness Impact Profile (SIP).³ More recently, an ALS specific health status measure—the ALS Assessment Questionnaire (ALSAQ-40)—has been developed and validated.⁴ Other studies have used non-health related QoL scales.^{3–7} The use of health related QoL (HR-QoL) scales, such as SIP and SF-36, in patients with ALS has been criticised because they are more distressing, and they seem to have a limited validity in this population of patients.^{3–5} Conversely, non-health related measures of QoL might be more useful in a chronic and progressive disorder such as ALS.⁵

Few papers have been devoted to the analysis of QoL determinants in ALS. In general, physical status seems to be poorly correlated with QoL,^{3–9} whereas psychological, existential, and support factors appear to play a more important role in determining QoL in ALS.^{3–7,9}

The goal of our present study was to evaluate the determinants of QoL in a series of patients with ALS using two QoL scales with different theoretical constructs.

PATIENTS AND METHODS

Eighty consecutive patients with definite, probable, or laboratory supported probable ALS according to El Escorial revised criteria¹⁰ were recruited through the Turin ALS centre from July 2001 to March 2002. Our study was approved by the local institutional review board. All patients signed a written informed consent form.

QoL was evaluated with two instruments, with different theoretical constructs:

- (1) The Schedule for the Evaluation of Quality of Life-Direct Weighting (SEIQoL-DW).¹¹ This is a participant generated measure that allows an estimation of the QoL subjectively perceived by the patient. In the SEIQoL-DW,

Abbreviations: ALS, amyotrophic lateral sclerosis; ALSAQ-40, ALS Assessment Questionnaire; ALS-FRS, Amyotrophic Lateral Sclerosis-Functional Rating Scale; BHS, Beck Hopelessness Scale; HR-QoL, health related quality of life; IIR, Idler Index of Religiosity (-Pr, private; -Pu, public); MMSE, Mini-Mental Status Examination; MQOL, McGill Quality of Life Questionnaire (-EW, existential well being; Ph, physical symptoms; -Ps, psychological symptoms; -PW, physical well being; -SIS, single item score; -Su, support); PLACS, Pathological Laughing and Crying Scale; PSQ, Psychosocial Questionnaire; QoL, quality of life; SEIQoL-DW, Schedule for the Evaluation of QoL-Direct Weighting; SF-36, Short Form 36; SIP, Sickness Impact Profile; SSQ, Social Support Questionnaire (-S, satisfaction); SWS, Social Withdrawal Scale (-F, family and friends); Tot-MQOL, total McGill Quality of Life Questionnaire; ZDS, Zung Depression Scale

the patients propose the five areas of their lives that they consider most relevant for their QoL, indicating the relative importance of each area, and then they are asked to rate each area. This measure has been shown to be reliable,⁸ and not distressing,⁵ in patients with ALS.

- (2) The McGill Quality of Life Questionnaire (MQOL).^{12, 13} This is a 16 item questionnaire, with each question rated from 0 (not at all) to 10 (extremely). MQOL includes five domains, two of which are health related (physical well being (MQOL-PW) and physical symptoms (MQOL-Ph)), and three are non-health related (existential well being (MQOL-EW), psychological symptoms (MQOL-Ps), and support (MQOL-Su)). For each domain, the score is the mean of the values of the relative items. A total rate (Tot-MQOL) is obtained as the mean value of the score of the five domains. Moreover, the patient is also asked to indicate his/her self perceived QoL in the past two days in a single item scale (MQOL-SIS), rated from 0 (very bad) to 10 (excellent). MQOL-SIS was administered before the completion of the MQOL scale. MQOL has been effectively used in patients with ALS,^{6, 7} and in patients with other life threatening illnesses,^{13, 14} and has good validity.¹³ It was also well accepted by patients with various types of chronic disorders.¹³

QoL was related to the following predictor variables:

- (1) Demographic variables: for each patient we recorded sex, age, and disease duration at the time of the interview, in addition to marital status and education level (< 5 years, 6–11 years, or > 11 years).
- (2) Clinical status: clinical status was evaluated using the Amyotrophic Lateral Sclerosis-Functional Rating Scale (ALS-FRS) and manual muscle testing, rated with the Medical Research Council scale. In addition, the type of onset (bulbar versus spinal), presence of pain and cramps, and use of enteral nutrition or non-invasive ventilation at the time of the interview was considered.
- (3) Mental status: mental status was evaluated with Mini-Mental Status Examination (MMSE),¹⁵ and the Pathological Laughing and Crying Scale (PLACS).¹⁶ This second scale measures the occurrence and severity of emotional incontinence, a symptom related to fronto-temporal syndrome in ALS.¹⁷
- (4) Depression and hopelessness: depression was measured with the Zung Depression Scale (ZDS),¹⁸ a self administered scale with 20 items, each rated from 1 to 4, obtaining a total score ranging from 20 to 80. A score over 50 indicates depression. Hopelessness was measured with the Beck Hopelessness Scale (BHS)¹⁹; a score between 8 and 13 indicates moderate hopelessness, and greater than 14 indicates severe hopelessness. BHS measures the outlook about the future.²⁰
- (5) Social support: The level and quality of self perceived social support was evaluated with the six item short form of the Social Support Questionnaire (SSQ).²¹ This scale allows the patients to determine (a) the number of persons available to help them, and (b) their satisfaction for the care they receive by the listed persons (indicated for each item from 1 (very satisfied) to 6 (very dissatisfied)) (SSQ-S).
- (6) Social attitudes: the social attitude of the patients was evaluated with the Social Withdrawal Scale (SWS),²² an instrument with 24 items, each rated from 1 (none at all) to 6 (completely agree). The scale has four domains, each including six items (withdrawal from community and wider world, withdrawal from family and close friends (SWS-F), emotional withdrawal, and physical withdrawal).

- (7) Religiosity: the level of religiosity was assessed with the Idler Index of Religiosity (IIR).²³ This is a four item instrument that measures two key dimensions of religiosity, organisational (public, IIR-Pu), and subjective (private, IIR-Pr) religiosity. The IIR-Pu score ranges from 2 to 10, and the IIR-Pr score from 2 to 7. The total score ranges from 4 (least religious) to 17 (most religious).
- (8) Social status: social status was evaluated with a four item, internally generated, Psychosocial Questionnaire (PSQ).

To avoid the possible differential interference of the answers on a scale over the others, we decided to administer the scales in the same order to each patient: MMSE, SSQ, SEIQoL, MQOL, PSQ, PLACS, ZDS, SWS, BHS, and IIR. The time taken for participants to complete the battery was generally between 50 and 60 minutes. Participants were given breaks when necessary between the administration of the measures to avoid fatigue.

Statistical methods

Each QoL scale was compared with explicatory variables using a stepwise linear regression model (least square, forward). All calculations were performed with the SAS Statistical Package, version 6.12.²⁴ A p value of 0.10 was the cutoff for inclusion and a p value < 0.05 was considered significant. Because multiple evaluations were performed, the Bonferroni correction was applied.

RESULTS

In total, 80 patients with ALS were enrolled (49 men and 31 women), with a mean age of 59.8 years (SD, 12.6; range, 26–81), and a mean duration of the disease at the time of the interview of 2.1 years (SD, 1.7; range, 1–7.8).

QoL scales

The mean SEIQoL-DW score was 73.3 (SD, 22.8; range, 1–98). The mean Tot-MQOL score was 6.3 (SD, 0.9; range, 4.2–8.4). The mean values for the five MQOL domains were: MQOL-PW, 5.8 (SD, 2.7; range, 1–10); MQOL-EW, 7.1 (SD, 1.7; range, 1–10); MQOL-Ps, 5.7 (SD, 2.7; range 1–10); MQOL-Ph, 6.5 (SD 2.5, range 1–10); and MQOL-Su, 7.4 (SD, 1.6; range, 3–10). The MQOL-SIS had a mean score of 5.5 (SD, 2.6; range, 1–10).

Predictor variables

Table 1 reports the mean values and ranges of the predictor variables. In total, 20 patients had a ZDS score over 50, indicating overt depression; seven patients had a BHS score over 13 (severe hopelessness), and 13 had a score between 8 and 13 (moderate hopelessness). Seven of the eight depressed patients, and 12 other patients, were receiving antidepressant medication at the time of the interview, all selective serotonin reuptake inhibitors.

Explanatory variables of QoL

- (1) SEIQoL-DW: the model that maximised the predicted value of the SEIQoL-DW score included SSQ-S ($p = 0.0021$), ZDS ($p = 0.03$), IIR-Pr ($p = 0.04$), and PSQ ($p = 0.05$). This model explained 44% of the variance of SEIQoL-DW.
- (2) Tot-MQOL: the model that maximised the predicted value of the Tot-MQOL score included SSQ-S ($p = 0.003$), PSQ ($p = 0.012$), and ALS-FRS ($p = 0.04$). This model explained 47% of the variance of Tot-MQOL. As for the five domains of MQOL, in multivariate analysis MQOL-PW was related to ZDS ($p = 0.0001$) and ALS-FRS ($p = 0.02$); MQOL-Ph was related to ALS-FRS ($p = 0.01$); MQOL-EW was related to SSQ-S

Table 1 Predictor variables scores

Variable	Mean	SD	Range
ALS-FRS	26.6	9.5	3–38
MMSE*	27.9	1.9	21.7–31
IIR-Pu	5.8	2.4	2–10
IIR-Pr	5.2	1.6	1–7
ZDS	43.4	10	29–66
BHS	5.8	4.5	0–17
SSQ-N	2.6	1.2	0–6
SSQ-S	6.3	3.1	4–10
SWS-C	19.6	4.5	8–29
SWS-F	15	6.4	6–31
SWS-E	14.2	6.9	0–31
SWS-P	21.6	11.3	0–36
PSQ	3.0	2.8	0–8

*Data corrected according to educational level. ALS-FRS, Amyotrophic Lateral Sclerosis-Functional Rating Scale; MMSE, Mini-Mental State Examination; IIR-Pu, Idler Index of Religiosity-public score; IIR-Pr, Idler Index of Religiosity-private score; ZDS, Zung Depression Scale; BHS, Beck Hopelessness Scale; SSQ-N, Social Support Questionnaire-number of persons available; SSQ-S, Social Support Questionnaire-satisfaction; SWS-C, Social Withdrawal Scale-community; SWS-F, Social Withdrawal Scale-family; SWS-E, Social Withdrawal Scale-emotional; SWS-P, Social Withdrawal Scale-physical withdrawal; PSQ, Psychosocial Questionnaire.

($p = 0.001$) and ZDS ($p = 0.006$); MQOL-Ps was related to ZDS ($p = 0.0001$), SWS-F ($p = 0.0002$), and SSQ-S ($p = 0.004$); and MQOL-Su was related to SSQ-S ($p = 0.003$) and BHS ($p = 0.02$).

(3) MQOL-SIS: the model that maximised the predicted value of the MQOL-SIS score included SSQ-S ($p = 0.009$), ZDS ($p = 0.015$), SWS-F ($p = 0.02$), and PSQ ($p = 0.04$). This model explained 52% of the variance of MQOL-SIS. In multivariate analysis, MQOL-SIS was related to the following domains of MQOL: MQOL-EW ($p = 0.0001$), MQOL-Su ($p = 0.008$), and MQOL-Ps ($p = 0.008$).

Comparison between SEIQoL-DW, Tot-MQOL, and MQOL-SIS

The SEIQoL-DW score was not significantly related to the Tot-MQOL score ($r = 0.11$; $p = \text{NS}$) (fig 1), but it was related to MQOL-EW ($r = 0.34$; $p = 0.002$). Conversely, a very good correlation was found between SEIQoL-DW and MQOL-SIS ($r = 0.33$; $p = 0.003$) (fig 2).

DISCUSSION

In modern medical literature, QoL does not have a straightforward, shared definition. Classically, QoL has been conceptualised as perceived health status, encompassing broad categories of well being, such as impairment, duration of life, functional status, in addition to perceptions and opportunities.²⁵ This concept corresponds to the so called HR-QoL. HR-QoL, measured with different scales, such as Euro-QoL, SIP, ALSAQ-40, and SIP/ALS-19,^{4 7 25 26} was significantly related to the severity of ALS. However, the presence of an association with clinical status does not necessarily indicate that HR-QoL scales are good indicators of QoL in ALS. In fact, although the severity of functional impairment, measured with the Barthel Index, in a series of patients with ALS was significantly correlated with psychological distress, evaluated with the 12 item General Health Questionnaire, it explained only a small amount of the variance.²⁷ Moreover, it has been shown that in ALS physical functioning and strength do not correlate with self rated QoL;^{3 7-9} conversely, existential and support factors may play a central role in determining QoL in ALS.⁷ In samples of patients with chronic, life threatening disorders, the hypothesis that the existential domain is

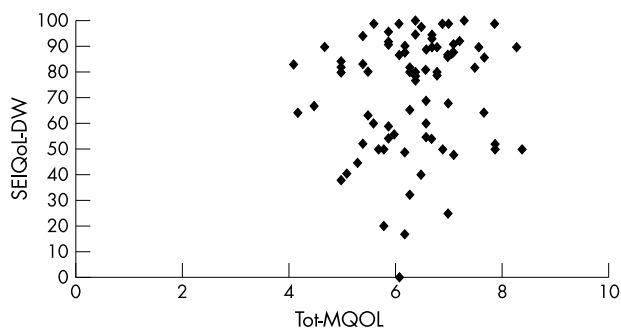


Figure 1 Correlation between the Schedule for the Evaluation of QoL-Direct Weighting (SEIQoL-DW) and the total McGill QoL Questionnaire (Tot-MQOL) ($p = \text{NS}$).

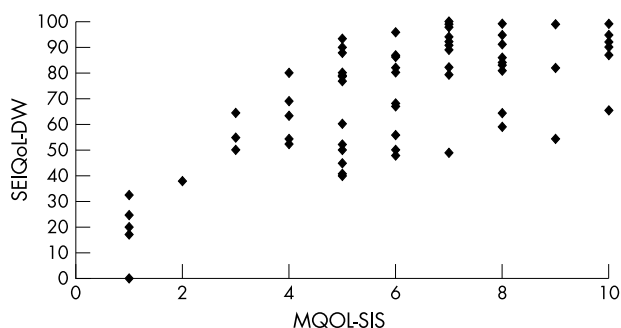


Figure 2 Correlation between Schedule for the Evaluation of QoL-Direct Weighting (SEIQoL-DW) score and the McGill QoL Questionnaire single item score (MQOL-SIS) ($p = 0.003$).

important has been supported by the observation that the existential subscale of MQOL was at least as important as any other subscale (including the two health related subscales) in predicting the MQOL-SIS.¹²⁻¹⁴ In this setting, existential includes concerns regarding death, freedom, isolation, and the question of meaning.^{12 13} Under this perspective, QoL is best conceived as subjective well being,¹³ and, rather than being a description of patients' health status and disability, it is a reflection of the way patients perceive and react to their health status and to other, non-medical, aspects of their life.

In our study, we have compared two QoL scales with different theoretical constructs, and we have analysed the determinants of QoL using a battery of possible explicatory variables.

The mean QoL score was relatively high when measured with SEIQoL-DW (73.3 out of a maximum of 100) and Tot-MQOL (6.3 out of a maximum of 10), but slightly lower with the MQOL-SIS (5.5 out of a maximum of 10). The generally high QoL in patients with severe disability indicates that internal forces play a major role in patients coping positively with their disease.²⁸ Considering the five domains of the MQOL, MQOL-Ps and MQOL-PW have the lowest scores, whereas MQOL-Su has the highest, which is consistent with previous observations.⁷

The SEIQoL score was not related to the Tot-MQOL score, but it was strongly related to the existential well being domain of the MQOL, indicating that in patients with ALS SEIQoL-DW does not explore the physical domains of QoL. Similarly, MQOL-SIS was not related to the Tot-MQOL score, but it was related to MQOL-EW, and to a lesser extent to MQOL-Ps and to MQOL-Su. Not surprisingly, SEIQoL-DW and MQOL-SIS were strongly related to each other. These findings support the concept that the existential domain is the most important determinant of QoL in ALS, and that

when the patients are allowed to indicate their QoL with a single, open ended question (as in MQOL-SIS) or with an unstructured interview (as in SEIQoL-DW), the most important considerations in their self appreciation of QoL are their subjective perceptions and not their physical status.

Despite the theoretical differences of the two QoL scales, when considering the explicatory variables of QoL, the best multivariate models for MQOL and SEIQoL-DW were similar. With both instruments, the most important variable was the quality of social support, measured with SSQ, indicating that the quality of care given by the caregiver(s) and the extent that the patients' social network is considered really supportive are of utmost importance for defining the patients' feelings of well being. Surprisingly, social support has not been studied extensively in ALS. In a study on the role of psychological factors on survival in ALS,²⁹ social support was not included in the final explicatory model. In a study on QoL in ALS, social support was the second most important explicatory variable of QoL, after suffering.³⁰ In another study on resilience and distress among patients with ALS, satisfaction with social relationships, finances, and recreational activities was inversely correlated with depression, anxiety, hopelessness, and desire for hastened death.³¹ Finally, in a study on hopelessness in ALS, satisfaction about social support was not a significant predictor of hopelessness.²⁰ The withdrawal from family and friends subscale of the SWS showed a significant association with MQOL-SIS, confirming the importance of social support in affecting QoL in patients with ALS. In fact, relationships with family members and close friends are influenced by how the patient feels about interacting with the significant others.²²

Depression also plays a major role in determining QoL in ALS, although in our series only a fifth of patients had scores indicating a clear cut level of depression according to ZDS, a prevalence lower than that found in a previous survey (44%), which used the Center for Epidemiologic Study Depression Scale,⁶ but similar to those found in another study (25%), based on the Beck Depression Inventory.³¹ These differences may be explained by the different rating scales used to investigate depression, by the cross sectional design of the various studies, which makes the findings strongly dependent on the characteristics of the studied populations, and by the different prevalence of use of antidepressant drugs in various series. In our survey, depression was associated with all non-health related domains of the MQOL and also with MQOL-SIS. Moreover, one fifth of patients had a significant level of hopelessness on BHS, a figure slightly lower than those reported in two recent studies.²⁰⁻³¹ However, the mean BHS score (5.8) was similar to that found in other studies on patients with ALS.²⁰⁻²⁹⁻³¹ In a recent paper, a BHS score of 9 or higher, evaluated in the last month of life in a series of patients with ALS, but not depression, social support, suffering, pain, religiousness, or QoL, was a significant predictor of interest in assisted suicide.³²

The third most important factor in determining QoL was socioeconomic status, which was evaluated indirectly using an internally generated questionnaire assessing patients' satisfaction in their life conditions and opportunities. Even in a highly socialised health system such as the Italian one, low socioeconomic status may hamper the possibility of obtaining health services and, consequently, of achieving a high quality standard of care; moreover, low family income may represent a serious problem when 24 hour care becomes necessary.

The fourth factor related to QoL was the patients' level of religiosity, in particular their private religiosity (that is, patients' self assessment of their depth of religiousness and how much strength and comfort they receive from religion).²³ In a previous study, the total IIS was significantly related to

MQOL-SIS, MQOL-EW, and MQOL-Su in univariate analysis.⁷ In a subsequent follow up study, the same group found that total IIS, IIS-Pr, and IIS-Pu were not related to MQOL at entry, but a significant association developed with time.³³ It has also been shown that religious well being may positively impact on QoL measured with SIP, and that it is not dependent on the clinical stage of ALS.³⁴ Moreover, a high level of spirituality or religiosity appears to influence the tendency to accept percutaneous endoscopic gastrostomy, non-invasive ventilation, and tracheotomy, and also to improve attitudes towards the dying process,³⁵ and may have a positive impact against the request for euthanasia or physician assisted suicide.³¹⁻³⁶⁻³⁷ Religiosity may be important for the individual's psychological, social, and physical well being and QoL, because it may create meaning and coherence when an individual's world is devastated by a distressing and progressive disease.³⁴ These findings strongly support the idea of including spiritual assistants in the multidisciplinary ALS team.³⁸

Similar to other studies,³⁻⁷⁻⁹⁻³⁰ the physical status of the patients was not included in the final model when considering SEIQoL or MQOL-SIS, but it was included when considering the Tot-MQOL score, because this scale specifically contains two health related domains.

Our study indicates that HR-QoL measures are not fully adequate for investigating QoL in ALS, because patients' appreciation of QoL mainly relies on psychological, spiritual, and support factors. MQOL appears to be a good scale for patients with ALS, because it encompasses both physical and non-physical domains. SEIQoL-DW also appears to be very useful and not distressing and, although it assesses primarily the existential domain of QoL, it gives valuable information about patients' adjustment to the disorder.

In general, maintaining a good QoL in patients with ALS, in the absence of an effective treatment, is a complex task. However, the understanding of QoL determinants gives some useful clues for planning a more effective care strategy. To improve QoL, the focus of interventions should be the patients' relatives/caregivers, who have the heavy burden of supporting patients in their day by day activities and to relieve their distress. The therapeutic team should be aware of the strengths and deficiencies of the caregivers, and should help them in improving their coping skills. Moreover, the caring neurologist should accurately assess the presence of depression in patients with ALS, paying particular attention to subthreshold symptoms, which may negatively influence patients' QoL and clinical course, and treat these symptoms aggressively. And finally, every effort should be made to remove financial and personal obstacles to the delivery of health services.

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