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ORIGINAL ARTICLE

Validation of the DYALS (dysphagia in amyotrophic lateral sclerosis) questionnaire for the evaluation of dysphagia in ALS patients

Luca Diamanti[1] · Paola Borrelli[2] · Raffaele Dubbioso[3] · Margherita Capasso[4] · Claudia Morelli[5] · Christian Lunetta[6,7] · Antonio Petrucci[8] · Gabriele Mora[9] · Paolo Volanti[10] · Maurizio Inghilleri[11] · Lucio Tremolizzo[12] · Jessica Mandrioli[13,14] · Letizia Mazzini[15] · Marcella Vedovello[16] · Gabriele Siciliano[17] · Massimiliano Filosto[18] · Sabrina Matà[19] · Cristina Montomoli[20] · DYALS Study Group

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Abstract

Background Dysphagia is a common symptom during the trajectory of ALS, and it can significantly impact on the quality of life and prognosis of patients. Nowadays, no specific tool for the screening of dysphagia in ALS is validated, and the approach is heterogeneous across the Italian centres.

Objective To validate the DYALS (dysphagia in amyotrophic lateral sclerosis) questionnaire, adapting the DYMUS (dysphagia in multiple sclerosis) questionnaire, for the assessment of dysphagia in ALS patients, in order to uniform the evaluations across the Italian ALS network.

Methods We included 197 patients diagnosed with ALS following the El Escorial criteria, in sixteen Italian ALS centres between 1st December 2019 and 1st July 2020. For each patient, we collected clinical and demographic data and obtained ALSFRS-r score, ALSAQ-5 score, DYMUS score, and EAT-10 score.

Results Across the 197 patients, the ratio M/F was 113/84, and the median age was 64 years (IQR 56–72.5). Bulbar patients were 20%, and spinal patients 80%. The median ALSFRSr total score of patients was 35 (IQR 28–39). DYALS score was statistically higher in bulbar ALS than in spinal ALS (median = 6, IQR 4.5–9 vs median = 1, IQR 0–5, z = 6.253, $p < 0.0001$). DYALS questionnaire showed a high internal consistency (Cronbach's alpha = 0.88). There was a statistically significant correlation between DYALS and EAT-10 (rho = 0.90, $p < 0.0001$).

Conclusions DYALS scale is reliable, manageable, and easily usable for the screening of dysphagia in ALS. It can be shared with all the Italian ALS centres in order to collect uniform data for therapeutic strategies and clinical trials.

Key words Dysphagia · ALS · Screening

Introduction

Dysphagia is a common symptom in patients with amyotrophic lateral sclerosis (ALS), and it can early arise in bulbar onset or more frequently during the trajectory of the disease [1, 2]. In the end-of-life, more than 80% of ALS patients complain dysphagia [3]. However, patients often tend to underestimate dysphagia in the first phases, and caregivers rarely report it during the follow-up visits resulting in a delayed identification [4]. Conversely, the onset of swallowing disturbances should be promptly recognized in order to recommend further specific investigations and identify potential therapeutic approaches minimizing the risk of malnutrition and aspiration [5]. Furthermore, dysphagia can impact on the quality of life resulting in a further psychological burden [6, 7], in particular modifying the social behaviour of patients [8] and interfering negatively with the adherence to the oral therapy [9]. Few instruments are available in order to screen ALS patients for dysphagia [10–12], and the approach is widely heterogeneous across the ALS centres in Italy. Dysphagia in multiple sclerosis (DYMUS) questionnaire has been created and subsequently validated in a large cohort of Italian MS patients as a reliable, manageable, and easy-to-administer tool [13, 14].

The aim of the study is to validate the DYALS (dysphagia in amyotrophic lateral sclerosis) questionnaire, adapting the

✉ Luca Diamanti
luca.diamanti@mondino.it

Extended author information available on the last page of the article

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DYMUS questionnaire, for the screening of dysphagia in ALS patients, and to provide an adequate tool able to uniform the evaluations across the Italian ALS Centres.

Materials and methods

Patient enrolment and data collection

We enrolled patients diagnosed with ALS according to El Escorial criteria [15] and consecutively followed up in sixteen Italian ALS centres between 1st December 2019 and 1st July 2020. Other inclusion criteria were patients aged ≥ 18 years old and patients with ECAS (Edinburgh Cognitive and Behavioural ALS Screen) [16] score ≥ 97 (low grade of education) or ≥ 108 (high grade of education) for patients aged ≤ 60 years old, ≥ 89 (low grade of education) or ≥ 107 (high grade of education) for patients aged ≥ 60 years old. The exclusion criteria were patients affected by other neurological pathologies causing dysphagia; patients using non-invasive ventilation more than 20 h/day or affected by other severe respiratory syndromes; and patients with gastrostomy or tracheostomy.

For all the patients, we collected clinical and demographic data, and obtained ALSFRS-R score, ALSAQ-5 (Amyotrophic Lateral Sclerosis Assessment Questionnaire-5) score, DYMUS score, and EAT-10 score.

DYMUS

DYMUS is a 10-item questionnaire, in which every answer is dichotomous ('yes' or 'no'). The questionnaire was created and validated in a large cohort of MS patients [13, 14], demonstrating high internal consistency. Bergamaschi et al. performed a factor analysis that showed the presence of two subscales: 'dysphagia for solids' and 'dysphagia for liquids'. Both the subscales had high internal consistency [13]. In the present study, we propose to confirm the consistency and the reliability of the questionnaire in a different cohort of neurological patients, affected by ALS, and to make external validation using the gold-standard scales for dysphagia (EAT-10, or ALSFRS-R). A single interviewer has been selected for each centre and trained in the questionnaire's administration and database's data entry.

Ethics approval

The study was approved by institutional ethic committee (N° 20,190,089,507) of the coordinator centre (IRCCS Mondino Foundation) and then by ethic committees of the other centres.

Statistical analysis

The sample size required for validation of the questionnaire was determined on the basis of the 'rule of thumb' (n:p) [17]. This calculation provides for the ratio between the number of subjects (n) and the number of variables or items (p) that make up the questionnaire (specifically, the DYMUS questionnaire consists of 10 items). According to Everitt [18], in order to identify the number of subjects to be recruited in the study, the results of this ratio (n:p) must be at least 10. So to achieve a ratio of 10, at least 100 subjects were recruited (n:p, 100:10 = 10).

The analysis of the collected data was structured as follows: (1) analysis of the questionnaire items through the usual descriptive statistics; (2) analysis of construct validity by means of exploratory factor analysis (EFA) for binary items, based on a matrix of tetrachoric correlation coefficients. The number of dimensions to be extracted (corresponding to the latent factors) was determined according to Kaiser's criterion (eigenvalues greater than 1), Cattell's criterion (scree plot), and Horn's Parallel Analysis. Saturations of questionnaire items on the extracted factors were determined after a Promax rotation, and a score for each dimension was then built; (3) assessment of the reliability of the questionnaire by means of Cronbach's alpha to analyse the internal consistency, taking the value 0.70 as the threshold; (4) external validation of the score obtained by specific analyses (Pearson correlation coefficient, Student T test, ANOVA, and/or corresponding Spearman's rank correlation coefficient, Mann–Whitney or Kruskal–Wallis test non-parametric tests) with the gold standard scale used in clinical practice and the relationships with detected clinical variables; (5) recode of the score in three levels of dysphagia severity (low, intermediate, high) through the use of quartiles to verify the association with clinical characteristics (Kruskal–Wallis test non-parametric tests, Pearson's chi-square test or Fisher's exact test if necessary). Normality distribution for quantitative variables was assessed by the Shapiro–Wilk Test. For all analyses, the statistical significance was set at the level of ≤ 0.05. All analyses were performed using Stata software v15.1 (StataCorp, College Station, USA).

Results

A total of 197 ALS patients were recruited (M/F = 113/84, 57.5% vs 42.5%), of which 35.6% definite, 32% probable, 14.9% probable lab-supported, and 17.5% possible following the El Escorial criteria. The median age was 64 years

Table 1 Factor loadings (N = 197)

	*Factor 1
Item	
1. Difficulty swallowing solid food	0.898
2. Difficulty swallowing liquids	0.855
3. Globus sensation	0.798
4. Food sticking	0.734
5. Coughing after ingestion of solid food	0.845
6. Coughing after ingestion of liquids	0.815
7. Needs several swallowing actions to swallow solids	0.858
8. Cuts food into small pieces in order to swallow it	0.882
9. Takes many sips in order to drink	0.903
10. Weight loss	0.650

*Eigenvalue = 6.85 with 68.5% of total variance explained

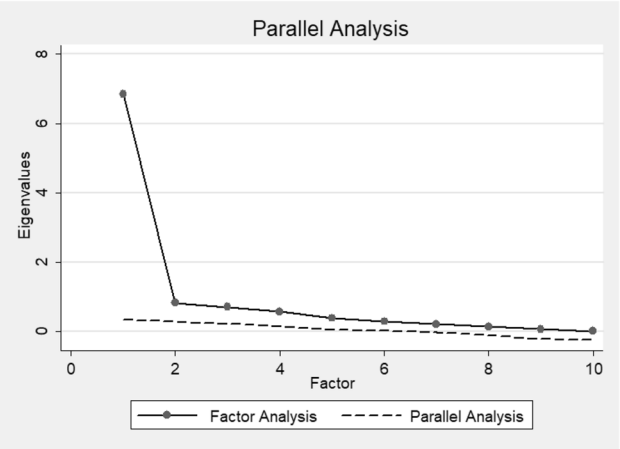

Fig. 1 Parallel analysis for the 10-items questionnaire DYMUS

(IQR 56–72.5), and the median diagnostic delay (time from symptoms onset to diagnosis) was 1 year (IQR 0–2). Patients characterized by bulbar onset were $n = 40$ (20%), and by spinal onset $n = 157$ (80%). The median ALSFRS-R total score of patients was 35 (IQR 28–39), and the bulbar subscore was 11 (IQR 9–12). The DYMUS questionnaire was administered to all ALS patients.

Study of dimensionality and reliability of DYALS questionnaire

The analysis of construct validity by means of EFA with Promax rotated matrix suggested the presence of a single dimension. We found one eigenvalue greater than 1 (eigenvalue = 6.85) explaining 68.5% of the total variance (Table 1). The graphic representation of the eigenvalues and the parallel analysis confirmed this result (Fig. 1).

In addition, the DYMUS questionnaire showed a high internal consistency in ALS cohort, given that the Cronbach's alpha was 0.88. The percentages of positive responses to the single questions, corresponding corrected item-total correlations, and Cronbach's alpha if item is deleted are reported in Table 2. There are no items with a low frequency of positive responses and inter-item correlation matrix range was 0.444–0.716. Cronbach's alpha would increase if item 3, 4, or 10 was deleted. These items were left in the questionnaire because of their clinical value.

Validity of DYALS questionnaire and relationships with detected variables

The median score for DYALS was 2 (IQR 0–6). The external validation of DYALS score was conducted through a Spearman's rank correlation analysis between DYALS and EAT-10. The result of the analysis showed a strong correlation between the two scales (rho = 0.90, $p < 0.0001$). We also investigated possible relationships between the

Table 2 DYMUS questionnaire submitted to 197 ALS patients: percentages of positive responses to the single questions, corresponding corrected item-total correlations and Cronbach alpha if item is deleted

	Frequency of positive responses	Corrected item-total correlation	Cronbach's alpha if item is deleted
1. Difficulty swallowing solid food	30.0%	,695	,866
2. Difficulty swallowing liquids	37.2%	,669	,867
3. Globus sensation	18.0%	,531	,877
4. Food sticking	25.5%	,502	,879
5. Coughing after ingestion of solid food	29.6%	,630	,870
6. Coughing after ingestion of liquids	39.5%	,617	,871
7. Needs several swallowing actions to swallow solids	32.0%	,645	,869
8. Cuts food into small pieces in order to swallow it	46.2%	,680	,866
9. Takes many sips in order to drink	45.5%	,716	,864
10. Weight loss	37.0%	,444	,884

DYALS score and other clinical scales and found statistically significant correlations between DYALS and ALSAQ5 (rho = 0.52, $p < 0.0001$), and between DYALS and ALSFRS-R (rho = −0.3652, $p < 0.0001$).

DYALS score was statistically higher in bulbar ALS than in spinal ALS (median = 6, IQR 4.5–9 vs median = 1, IQR 0–5, z = 6.253, $p < 0.0001$).

In addition, by dividing the distribution of DYALS score into quartiles, it was possible to identify 3 levels of severity of dysphagia (< 2 = low, 2–5 = intermediate, ≥ 5 = high). Given this classification, we found that about 59% ($n = 116$) of patients report an intermediate and high score value. Statistical differences were observed between bulbar and spinal patients ($\chi 2 = 32.35$, df = 2, $p < 0.0001$). Specifically, patients with bulbar onset result to have a more severe dysphagia level than patients with spinal onset: low level 5 vs 50.32%, intermediate level 40 vs 37.57%, and high level 55 vs 19.11%, respectively. A statistical significance association was also observed between severity of dysphagia and El Escorial criteria for the diagnosis of ALS ($\chi 2 = 16.26$, df = 6, $p = 0.012$). There were no statistically significant differences for sex and age (Table 3).

Discussion

Although early identification of dysphagia is pivotal in order to minimize the related complications (i.e. malnutrition, risk of aspiration, drugs manipulation) (1), a specific tool for the screening of dysphagia in ALS patients is lacking, with consequent heterogeneous approaches across different Italian ALS Centres.

With this study, we aim at validating the DYMUS questionnaire, that in MS patients resulted to have high internal consistency and reliability [13, 14], in an ALS cohort (DYALS) to uniform the evaluation of dysphagia in ALS Italian Centres. Even though the pathogenesis and the mechanisms of swallowing disturbances in MS and ALS patients are divergent [19–22], the clinical manifestations of neurogenic dysphagia can be early intercepted by the same questionnaire. Indeed, our results show that DYALS has very high internal consistency, and reliability in ALS patients with Cronbach's alpha = 0.88 but, unlike the DYMUS that could be divided into two subscales (dysphagia for solids and liquids), DYALS presented a single dimension.

In our cohort, more than half of the patients presented intermediate or high grade of DYALS score (≥ 2) confirming that dysphagia is a common symptom in ALS and it can be diagnosed in every phase of the disease. As awaited, bulbar patients demonstrated higher DYALS score (6 vs 1, $p < 0.0001$) and more frequently score ≥ 2 (95% vs 49.68%) than spinal ones, but 95% of them was unexpected if compared to the median ALSFRS-R bulbar score ($n = 11$). Even though we considered the bulbar items of ALSFRS-R (i.e. 1 + 2 + 3) instead of the isolated item 3 [10], this data support the higher sensibility of DYALS than the bulbar items of ALSFRSr for the screening of dysphagia, and a DYALS score of 2 could represent a cut-off for further diagnostic exams. A major weakness of this study is the lack of recruitment of patients with severe dysphagia, thus limiting the diagnostic yield of this scale in the clinical and research setting for this subgroup of patients.

We conducted the external validation through a Spearman's rank correlation analysis between DYALS and EAT-10 that has been validated as screening questionnaire for patients with ALS [11] although not specifically for neurogenic dysphagia. There were statistically significant correlations between DYMUS, ALSAQ5, and ALSFRS-R

Table 3 Associations between levels of severity of dysphagia and characteristics (N = 197)

	Low N = 81 (41.1%)	Intermediate N = 64 (32.5%)	High N = 52 (26.4%)	p.value
Sex, n (%)				
Female	32 (38.1%)	25 (29.8%)	27 (32.1%)	0.288**
Male	49 (43.4%)	39 (34.5%)	25 (22.1%)	
Age in years (median, IQR)	64.0 (54.0–71.0)	62.0 (55.5–73.0)	64.5 (59.0–72.5)	0.480*
Onset ALS, n(%)				
Bulbar	2 (5%)	16 (40.0%)	22 (55.0%)	< 0.0001***
Spinal	79 (50.3%)	48 (30.6%)	30 (19.1%)	
El Escorial criteria, n(%)				
Definite ALS	17 (24.7%)	27 (39.1%)	25 (36.2%)	0.012***
Possible ALS	17 (50.0%)	9 (26.5%)	8 (23.5%)	
Probable ALS	29 (46.7%)	21 (33.8%)	12 (19.3%)	
Probable ALS-Laboratory supported	18 (62.1%)	7 (24.1%)	4 (13.8%)	

N (%) or median (IQR) are shown when appropriate; *Kruskal–Wallis test; **Pearson's chi-square test or ***Fisher's exact test

confirming that the more serious dysphagia is the higher disability and the lower quality of life are. These results confirmed data of literature [23].

Although neuromuscular Disease Swallowing Status Scale (NdSSS) has been already proposed as a generic scale for dysphagia in patients with neuromuscular diseases [12], it is not indicated for the screening of symptoms referred by patients and does not take into account heterogeneity across neuromuscular disorders.

In conclusion, we confirm that DYALS scale is reliable, manageable, and easy to use in an outpatient setting. Further step will be the validation of DYALS with the instrumental evaluation (i.e. FEES). In the meantime, DYALS employment may help harmonization among Italian ALS centres on evaluation and management of dysphagia and allow to collect solid data for other studies and clinical trials.

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Declarations

Conflict of interest The authors declare no competing interests.

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Authors and Affiliations

Luca Diamanti[1] · Paola Borrelli[2] · Raffaele Dubbioso[3] · Margherita Capasso[4] · Claudia Morelli[5] · Christian Lunetta[6,7] · Antonio Petrucci[8] · Gabriele Mora[9] · Paolo Volanti[10] · Maurizio Inghilleri[11] · Lucio Tremolizzo[12] · Jessica Mandrioli[13,14] · Letizia Mazzini[15] · Marcella Vedovello[16] · Gabriele Siciliano[17] · Massimiliano Filosto[18] · Sabrina Matà[19] · Cristina Montomoli[20] · DYALS Study Group

1 IRCCS Mondino Foundation, Via Mondino 2, 27100 Pavia, Italy

2 Laboratory of Biostatistics, Department of Medical, Oral, and Biotechnological Sciences, University G. d'Annunzio Chieti-Pescara, Chieti, Italy

3 Department of Neurosciences, Reproductive Sciences and Odontostomatology, University of Naples Federico II, Naples, Italy

4 Neurologic Clinic, SS. Annunziata Hospital, Chieti, Italy

5 Department of Neurology and Laboratory of Neuroscience, Istituto Auxologico Italiano, IRCCS, Milan, Italy

6 NEMO Clinical Center, Serena Onlus Foundation, Milano, Italy

7 NEMO Lab, Milano, Italy

8 Center for Neuromuscular and Neurological Rare Diseases, Neurology and Neurophysiology Unit, San Camillo Forlanini Hospital, Rome, Italy

9 ICS Maugeri IRCCS, Milano, Italy

10 Department of Neurorehabilitation, Istituti Clinici Scientifici Maugeri IRCCS, Institute of Mistretta, Messina, Italy

11 Neuromuscular Rare Disease Centre, Department Human Neurosciences, University of Rome La Sapienza, Rome, Italy

12 Neurology, San Gerardo Hospital and University of Milano-Bicocca, Monza, Italy

13 Department of Biomedical, Metabolic and Neural Science, Center for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy

14 Neurology Unit, Azienda Ospedaliero Universitaria Di Modena, Modena, Italy

15 Department of Neurology and ALS Centre, University of Piemonte Orientale, Maggiore Della Carità Hospital, Novara, Italy

16 Neurology Unit, ASST Papa Giovanni XXIII, Bergamo, Italy

17 Center for Neuromuscular and Neurological Rare Diseases Neurological Clinic, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

18 Department of Clinical and Experimental Sciences, University of Brescia, NeMO-Brescia Clinical Center for Neuromuscular Diseases, Brescia, Italy

19 SOD Neurologia 1, Dipartimento Neuromuscolo-Scheletrico E Degli Organi Di Senso, Azienda Ospedaliero Universitaria Careggi, Florence, Italy

20 Department of Public Health, Experimental and Forensic Medicine, Unit of Biostatistics and Clinical Epidemiology, University of Pavia, Pavia, Italy