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Functional limitation of the masticatory system in patients with bulbar involvement in amyotrophic lateral sclerosis

N. Riera-Punet[1] | J. Martinez-Gomis[1,2] | E. Willaert[1,2] | M. Povedano[3] | M. Peraire[1,2]

[1]Department of Prosthodontics, School of Dentistry, Faculty of Medicine and Health Sciences, University of Barcelona, L'Hospitalet de llobregat, Barcelona, Spain

[2]Oral Health and Masticatory System Group (Bellvitge Biomedical Research Institute), IDIBELL, L'Hospitalet de llobregat, Barcelona, Spain

[3]ALS Unit, Department of Neurology, Bellvitge University Hospital, L'Hospitalet de llobregat, Barcelona, Spain

Correspondence
Jordi Martinez-Gomis, Campus de Bellvitge, Universitat de Barcelona, L'Hospitalet de Llobregat, Spain.
Email: jmartinezgomis@ub.edu

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Summary

Amyotrophic lateral sclerosis (ALS) with bulbar dysfunction affects the motor neurons responsible for controlling the muscles in the jaw, face, soft palate, pharynx, larynx and tongue. This cross-sectional study aimed to determine the functional limitation of the jaw in patients with ALS and bulbar dysfunction who had upper motor neuron (UMN), lower motor neuron (LMN) or balanced involvement. One hundred and fifty-three patients with ALS and 23 controls were included. All participants answered using the 8-item Jaw Functional Limitation Scale (JFLS-8). Patients with ALS were grouped by neurologic examination as follows: non-bulbar ALS, bulbar UMN-predominant ALS; bulbar LMN-predominant ALS; and bulbar balanced (UMN + LMN) ALS. Jaw limitation between the different groups was compared using the Kruskal-Wallis test. Patients with non-bulbar ALS had similar mandibular limitations to healthy participants. Only patients with balanced UMN and LMN bulbar manifestations reported greater difficulties in chewing soft food or in jaw mobility compared to the non-bulbar ALS group. Patients with bulbar involvement also had greater difficulties in chewing tough food or chicken and in swallowing and talking compared to the non-bulbar group, regardless of whether UMN or LMN predominant. No significant differences were found between the groups in smiling and yawning difficulties. Bulbar involvement in patients with ALS is associated with functional limitation of the masticatory system. However, balanced bulbar UMN and LMN involvement is associated with the worst impairments in chewing soft food and in opening the jaw widely.

KEYWORDS
amyotrophic lateral sclerosis, bulbar involvement, jaw functional limitation, JFLS-8

1 | INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a motor neuron disease characterised by progressive degeneration of motor neurons in the brain, brainstem and spinal cord. Affected individuals show significant variation in the locus of disease onset, presentation at diagnosis and rate of progression.[1] Incidence rates for ALS are approximately 1.4 and 2.1 per 100 000 person/year in Catalonia and Europe, respectively.[2,3] Sufferers develop progressive wasting and weakness of limb, bulbar and respiratory muscles and die on average within 3 years from symptom onset, usually from respiratory failure; however, roughly 10% of patients with ALS survive for ten or more years.[4] The mean age of onset for sporadic ALS ranges from 55 to 65 years, with a median age of onset of 64 years.[5] The diagnosis of ALS is based on the El Escorial and Airlie House Diagnostic Criteria.[6]

Approximately two-thirds of patients with a typical ALS disease pattern develop initial symptoms in the upper or lower extremities (limb or spinal onset), most commonly in distal muscles. The other third of patients have bulbar onset, usually starting with dysarthria,

but almost all demonstrate bulbar involvement at later stages. About 5% of patients present with respiratory weakness without significant limb or bulbar symptoms.[7,8] In patients with bulbar dysfunction, upper motor neuron (UMN) involvement causes supranuclear symptoms that are also commonly referred to as pseudobulbar palsy. The clinical characteristics of pseudobulbar palsy are spasticity and hyperreflexia of the bulbar muscles (ie jaw, face, soft palate, pharynx, larynx and tongue), emotional lability (pathological laughing and crying) and a brisk jaw jerk. Degeneration of lower motor neuron (LMN), with involvement of the cranial nerve nuclei in the medulla oblongata and pons that innervate the bulbar muscles, results in a bulbar palsy with flaccid paresis, muscular atrophy and fasciculations and/or tongue fibrillations.[7,9]

Oro-facial function is an important contributor to an individual's general health and quality of life. The masticatory system is responsible for complex biopsychosocial functions, where basic functions such as chewing, swallowing, eating and yawning manifest simultaneously with emotional functions such as smiling, laughing, screaming and kissing. Functional limitation and disability can be measured with generic, disease-specific or organ-specific instruments. The 20-item Jaw Functional Limitation Scale (JFLS-20) is a reliable and valid organ-specific instrument for measuring limitations in mastication, jaw mobility and verbal and emotional expressions, together with a global functional limitation score. Global limitation can also be determined with a short version, the JFLS-8. These scales have three subscales that cover mastication, vertical jaw mobility and emotional and verbal expressions. The properties of the JFLS-8 scales are ideal for both research and patient evaluation when assessing global functional limitation of the jaw.[10]

Masticatory function includes phenomena such as bite force, mandibular mobility and masticatory performance[11-13] and has been studied by assessing these phenomena in other neurological diseases.[14-19] However, to the authors' knowledge, functional limitation of the masticatory system has not been assessed in a large sample of patients with ALS. The main objective of this study was to determine the effect of bulbar involvement on functional limitation of the masticatory system in patients with ALS. This study also aimed to compare the functional limitation of the masticatory system between patients with ALS and a pseudobulbar palsy (UMN involvement) and patients with ALS and a bulbar palsy (LMN involvement). The working hypothesis was that bulbar involvement would cause functional limitation of the masticatory system in patients with ALS.

2 | MATERIALS AND METHODS

2.1 | Participants

In this cross-sectional study, 153 patients diagnosed with ALS according to the revised El Escorial and Airlie House Diagnostic Criteria at the Motor Neuron Disease Unit of the Bellvitge University Hospital were selected. A control group was included that comprised 23 participants recruited from the families or caregivers of patients with ALS and other age- and gender-matched people. All subjects participated in a previous investigation.[20] Patients were excluded if they could not be evaluated because of their clinical condition or sensory deficits. All participants were fully informed and signed an informed consent form approved by Bellvitge University Hospital Ethics Committee (Code PR260/15), and all experiments were carried out in accordance with the principles of the Helsinki Declaration.

2.2 | ALS-related characteristics

Bulbar dysfunction involvement was determined as UMN, LMN or balanced (UMN + LMN) based on neurologic examination by a neurologist, using upper motor signs (ie brisk jaw jerk, tongue spasticity and spastic dysarthria) and lower motor signs (ie tongue wasting, tongue fasciculations and flaccid dysarthria).[21]

2.3 | Functional jaw limitations scale

Functional limitation of the masticatory system was assessed using the JFLS-8.[10] This scale evaluates 8 items: (1) chew tough food, (2) chew chicken (eg prepared in oven), (3) eat soft food requiring no chewing (eg mashed potatoes, apple sauce, pudding, pureed food), (4) open wide enough to drink from a cup, (5) swallow, (6) yawn, (7) talk and (8) smile. The participants rated the level of limitation for each item during last month using a 0-10 numerical rating scale, with 0 corresponding to "no limitation" and 10 corresponding to "maximal limitation." The examiner interviewed each participant orally asking all JFLS items. The patient's caregiver helped answering in case the patient had some difficulties. Questionnaires were filled when the patients were attended by the ALS unit multidisciplinary team for a check-up. The median time elapsed between the first symptom onset and the questionnaire was 31 months, and the median time elapsed between the diagnostic and the questionnaire was 16 months (Table 1).

2.4 | Data analysis

Participants were distributed into 1 of the 5 groups. The control group included 23 healthy participants, and the 153 patients with ALS were grouped as those with non-bulbar ALS, bulbar UMN-predominant ALS, bulbar LMN-predominant ALS and bulbar balanced ALS (with both UMN and LMN) groups. Items from the same subscale of the JFLS-8 with similar results were averaged, such as the chew tough food and chew chicken items, the swallow and talk items, or the yawn and smile items. The degree of jaw limitation for each subscale and for the eight items was compared between the different groups using the Kruskal-Wallis test with adjustment for pairwise comparisons. All analyses were performed in IBM SPSS Statistics, version 24.0 (IBM Corp., Armonk, NY, USA), and *P*-values ≤.05 were considered statistically significant.

3 | RESULTS

3.1 | Participants

This study included 153 patients with ALS (mean age 62 years, SD 12 years; 46% women) and 23 controls (mean age 51 years, SD 12 years; 56% women). Patients with ALS were assigned to one of the four groups according to bulbar involvement, and their characteristics are summarised in Table 1. In total, 10% of patients with ALS received parotid botulin toxin injections, 32% required non-invasive ventilation, and although 76% had normal eating habits, 11% required supplemental tube feeding and 12% required either probe or oral feeding.

3.2 | Comparison of the bulbar and non-bulbar groups

Two of the three mastication subscale items of the JFLS-8, chew tough food and chew chicken, were averaged because the results were similar. Although patients in the non-bulbar ALS group were similar to controls on the chewing measures, patients in the bulbar ALS groups had greater difficulties in chewing tough food or chicken compared to those in the non-bulbar group, regardless of the motor neuron affected (Figure 1). However, only patients in the balanced bulbar ALS group reported greater difficulties in chewing soft food compared with the non-bulbar ALS group (Figure 2). Patients in the balanced bulbar ALS group reported greater difficulties in opening their mouths wide enough to drink from a cup compared to those in the non-bulbar group (Figure 3).

Although patients in the non-bulbar ALS group had no significant differences in swallow and talk difficulties compared with the control group, patients in the ALS groups with bulbar involvement had greater swallow and talk difficulties compared with the non-bulbar group regardless of the motor neuron affected (Figure 4). However, there were no significant differences in smiling and yawning difficulties between any of the groups (Figure 5).

Considering all items of the three subscales, patients without bulbar involvement in ALS had similarly low functional jaw difficulties

TABLE 1 Characteristics of healthy and patients with amyotrophic lateral sclerosis

Characteristics	Healthy (n = 23)	ALS Patients (n = 157)				
		No Bulbar affectation (n = 47)	Bulbar UMN-predominant (n = 28)	Bulbar LMN-predominant (n = 18)	Balanced bulbar UMN and LMN (n = 60)	*P*-value between each subgroup[a]
Sex (% of Male)	44	64	36	56	53	NS
Mean age (years)	51	62	62	69	60	<.0005
Median time elapsed since symptom onset (months)		35.4	35.0	33.2	24.4	.015
Median time elapsed since ALS diagnosis (months)		18.8	19	12.5	13.3	.554
Botulinum toxin (%)		2.1	3.6	16.7	16.9	.034
Non-invasive ventilation (%)		36.2	25	55.6	25	.074
Oral feeding (%)		100	92.9	83.3	81.7	.015
Use of tube feeding (%)		6.4	14.3	50	31.7	<.0005

[a]Chi-squared test or Kruskal-Wallis test.

POOR QUALITY FIG

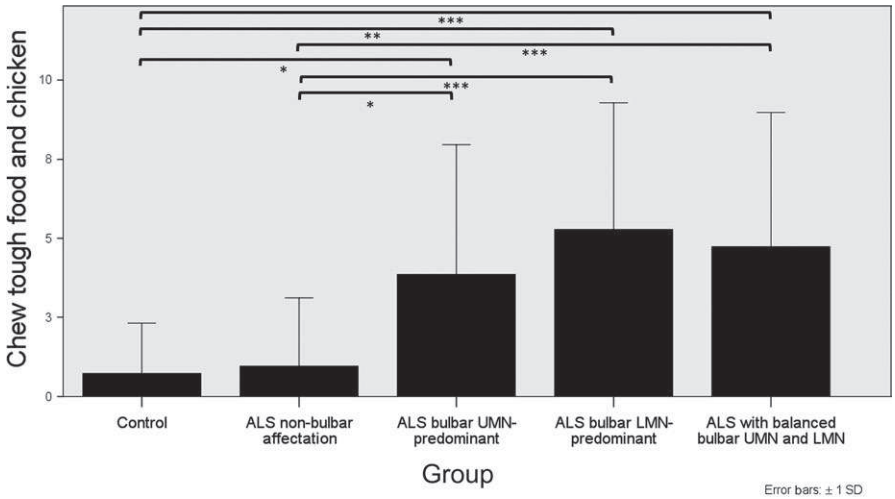

FIGURE 1 Means and standard deviation of limitation score of chewing tough food and chicken. *$P \leq .05$; **$P \leq .01$; ***$P \leq .001$ Kruskal-Wallis test and pairwise comparisons of different groups

POOR QUALITY FIG

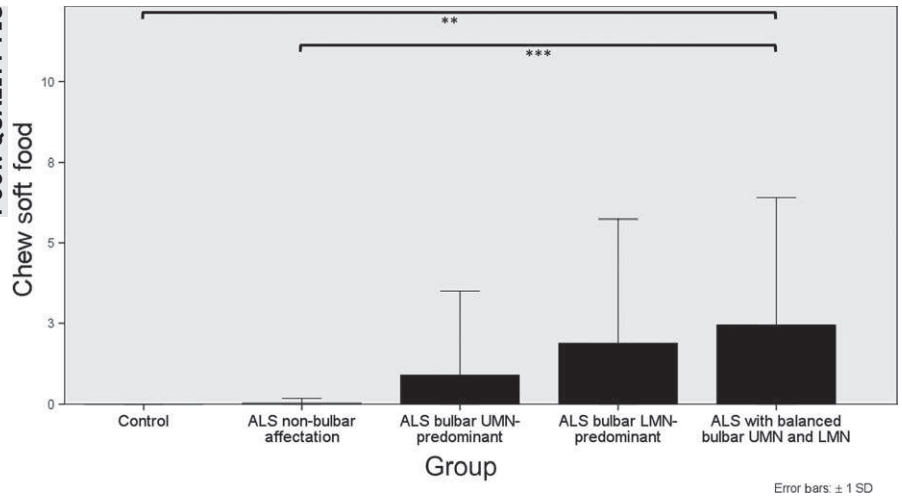

FIGURE 2 Means and standard deviation of limitation score of chewing soft food. $^{**}P \leq .01$; $^{***}P \leq .001$ Kruskal-Wallis test and pairwise comparisons of different groups

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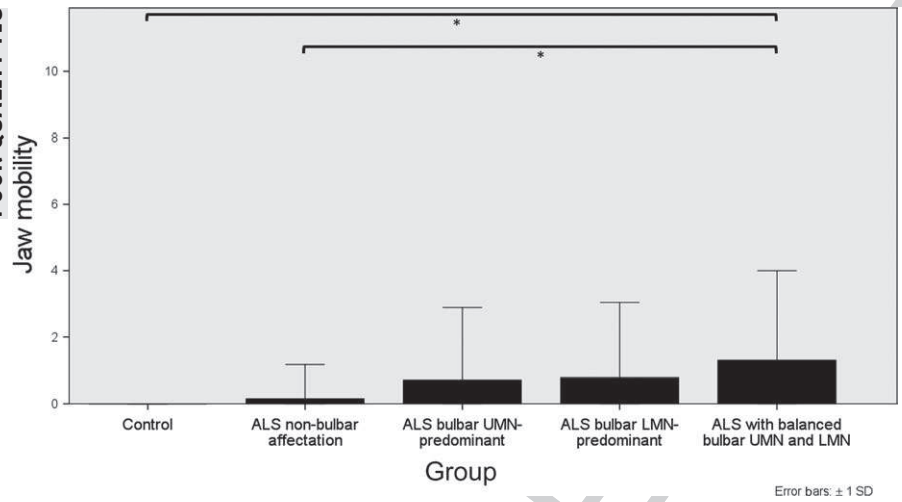

FIGURE 3 Means and standard deviation of limitation score of jaw mobility. $^{*}P \leq .05$ Kruskal-Wallis test and pairwise comparisons of different groups

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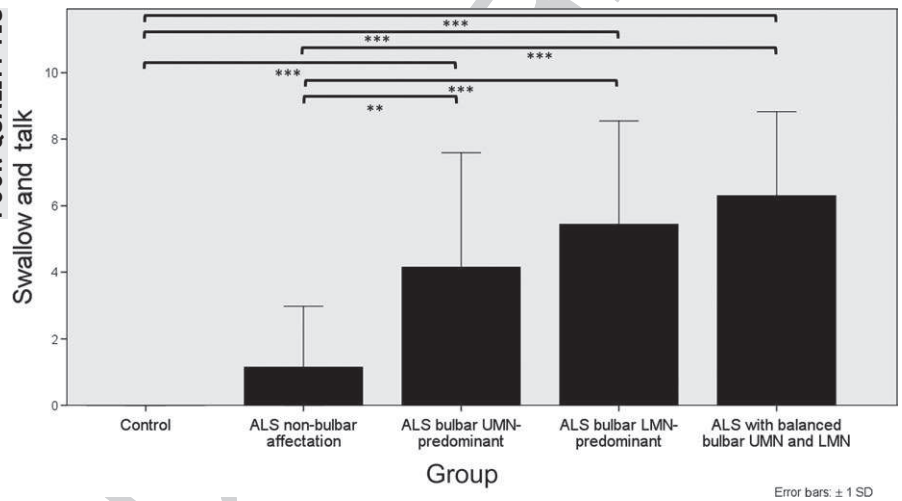

FIGURE 4 Means and standard deviation of limitation score of swallowing and talking. $^{**}P \leq .01$; $^{***}P \leq .001$ Kruskal-Wallis test and pairwise comparisons of different groups

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compared to healthy participants. By contrast, patients with bulbar involvement in ALS had greater functional jaw difficulties compared to those without bulbar involvement, regardless of the motor neuron affected (Figure 6).

4 | DISCUSSION

The results of this study indicate that bulbar involvement was significantly associated with perceived functional limitation of the

LOW RESOLUTION FIG

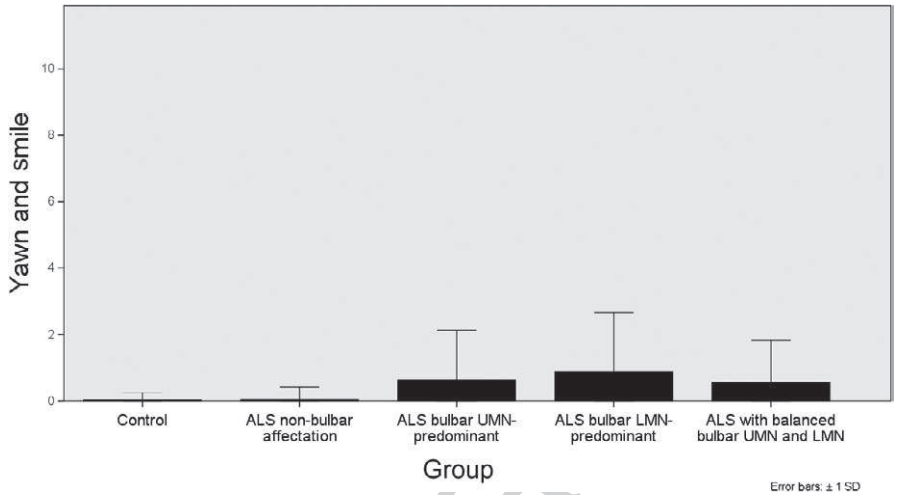

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FIGURE 5 Means and standard deviation of limitation score of yawning and smiling. $P > .05$ Kruskal-Wallis test and pairwise comparisons of different groups

POOR QUALITY FIG

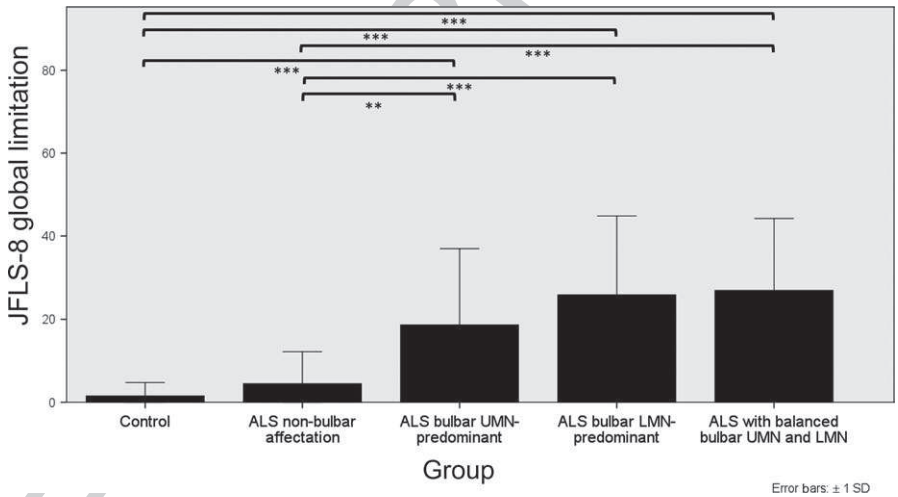

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FIGURE 6 Means and standard deviation of JFLS-8 global limitation score. $^{**}P \leq .01$; $^{***}P \leq .001$ Kruskal-Wallis test and pairwise comparisons of different groups

masticatory system in patients with ALS. In the bulbar group, the greatest impairment was seen in those with balanced UMN and LMN diseases, as evidenced primarily by difficulties in chewing soft food and opening the jaw widely, as well as difficulties in chewing tough food and chicken, swallowing and talking.

4

When patients have been grouped by symptom type at onset, aspects of masticatory function, like bite force and range of jaw mobility, were objectively shown to be reduced in bulbar-onset groups compared with spinal or respiratory onset groups.[20] Moreover, the bulbar-onset group showed more severe oro-facial impairment than the spinal-onset group assessed with the Nordic Oro-facial Test-Screening.[21] Results of the present study suggest that masticatory function is also affected when the involvement of the bulbar region occurs during the evolution of the disease. This is consistent with the fact that the bulbar target damages neurons responsible for controlling facial, masticatory, pharyngeal and laryngeal muscles. There are differences in neurological symptoms between UMN and LMN involvement.[8] Emotional lability, nasal speech, nasal regurgitation, excessive saliva, slow tongue and brisk jaw jerk and facial reflexes are characteristics of UMN. Slurred speech, difficulty in swallowing, excessive saliva, small and fasciculating tongue are characteristics for LMN.[8] The difficulties in masticatory function are related to upper motor neuron signs as tongue spasticity or to lower motor neuron signs as tongue atrophy. Despite the neurological differences between patients with upper or lower motor neuron involvement, no differences in mastication, jaw mobility or verbal and emotional expression were observed. However, when both motor neurons were affected, there was a greater degree of functional limitation in these measures.

Although the jaw mobility is reduced in balanced bulbar UMN and LMN ALS, yawning was not affected in this study. It is known that excessive yawning occurs in a substantial number of patients with ALS specially in those with a bulbar onset.[8,22] Probably this could be related to the inhibition of normal control mechanisms of emotions, which would mean that neurological paths controlling voluntary mandibular opening and yawning are different. However, to date, no physiological significance has been associated with yawning, and the neural pathways underlying it are not known.[23] Moreover, even though patients with bulbar symptoms experience facial weakness affecting the lower half of the face, no patient in this study reported difficulty smiling.

Amyotrophic lateral sclerosis (ALS) is a low-prevalent disease, and therefore, it should not be considered as a first-line differential diagnosis in patients with temporomandibular disorders. Nevertheless,

as most of the bulbar-onset patients reported the first symptoms in the oro-facial region, dentists should keep in mind this possibility in those situations in which, in a patient with apparent symptoms of temporomandibular disorders, there are incongruous signs or symptoms.[24] These signs and symptoms may include difficulty in mastication, speech or swallowing due to an impairment in tongue control or a weakness in masticatory muscles, and difficulty in mandibular mobility not attributable to muscular or articular pain or disc displacement.[7,8]

Mandibular mobility and/or bite force are also reduced in patients with other neuromuscular diseases, including spinal muscular atrophy,[14-16] bulbar myasthenia gravis[17,18] and Duchenne muscular dystrophy.[19] A reduced ability to open the mouth may hinder oral hygiene and perhaps even the efficacy of non-invasive ventilation. To minimise these complications, especially in patients with bulbar onset, an effective physiotherapy programme of active exercises is needed to slow the rate of reduction in mouth opening.[19] The physiotherapy programme could consist of moderate-load and moderate-intensity resistance and stretching exercise programme to improve mandibular mobility.[25] Moreover, the dentist could also manage ALS patients to avoid traumatic lesions in the lips, cheeks or tongue due to self-biting.[20] Recommendations for dental care in patients with ALS also include a regular oral maintenance care to maintain oral health and avoid dental disease, as well as counselling for dietary modifications.[26] Symptoms of dysphagia may occur at any time in the act of swallowing. Patients may report failure to chew or intolerance to texture in the oral preparatory phase and pocketing of food in the oral phase.[27] Recommendations to improve or mitigate swallowing function include compensatory manoeuvres, behavioural strategies, sensory tricks and dietary modifications such as mechanically altered food, thickened liquids, soft diet or liquidise food.[26] Consequently, dentists should also be included in the multidisciplinary team to improve the quality of life of patients with ALS.

The sample of this study was representative to the population of Catalonia, corresponding to 30% of the approximate 451 patients with ALS diagnosed among the 7 500 000 inhabitants.[2] However, the small sample size and recruitment method for the control group are potential limitations. Nevertheless, the prevalence of TMD and the range of mandibular motion in the control group were comparable to those reported in other studies.[28,29]

In conclusion, bulbar involvement in patients with ALS is associated with functional limitation of the masticatory system. However, balanced bulbar UMN and LMN involvement is associated with the worst impairments, affecting soft food chewing and opening the jaw widely.

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COMPETING INTERESTS

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

AUTHORS' CONTRIBUTIONS

Nina Riera-Punet contributed to the conception and design of the study, to the acquisition of data and analysis and interpretation of data. J Martinez-Gomis, E Willaert and M Peraire contributed to the conception and design of the study and analysis and interpretation of data. M Povedano contributed to the conception and design of the study, to the acquisition of data and analysis and interpretation of data. All co-authors participated in drafting the article and approved the version to be published.

ORCID

J. Martinez-Gomis http://orcid.org/0000-0003-3497-093X

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