ORIGINAL ARTICLE

The deglutition of patients with amyotrophic lateral sclerosis

Émille Dalbem Paim[1], Munique Jarces[2], Patricia Zart[3], Daniel Lima Varela[4]

ABSTRACT

Objective: Evaluate the deglutition characteristics of patients with Lateral Amiotrophic Sclerosis by videofluoroscopy. **Methods:** 20 patients were included, aging 43 - 75 years, with no other concomitant disease, without the use of tracheostomy or other alternative feeding tubes. After an anamnesis, the patients received three servings of food, one liquid, one pasty and one solid, and underwent the deglutition videofluoroscopy. The exam was filmed for further analysis. **Results:** In the liquid consistency, the most significant alteration was the presence of residues on the vallecula of 11 patients. The pasty consistency caused reduction in the larynx elevation in 12 patients and residues in pharyngoesophageal transition of 12 patients. In the solid consistency, 10 patients had tongue mobility reduction and residues in the oral cavity was found in 10 patients. Out of the 20 included patients, 11 had discrete dysphagia. **Conclusion:** All patients had dysphagia, most of them at a discrete degree. The pharyngeal phase was the most compromised for the pasty and liquid phases, with residues in vallecula and pharyngoesophageal transition, followed by the oral phase, with increased oral transit time and reduced tongue mobility in the solid consistency.

Keywords: Deglutition Disorders, Amyotrophic Lateral Sclerosis, Speech, Language and Hearing Sciences, Rehabilitation

[1] Phonoaudiologist, Resident at Universidade Federal de Ciências da Saúde de Porto Alegre - UFCSPA - Brazil.
[2] Phonoaudiologist.
[3] Phonoaudiologist, Phonoaudiology Professor at Universidade de Passo Fundo - UPF - Brazil.
[4] Medical Doctor, Neurology and Neurocirurgy Department at Passo Fundo - RS - Brazil.

Mailing address:
Universidade Federal de Ciências da Saúde de Porto Alegre
Émille Dalbem Paim
Rua Tiradentes, 215
CEP 99074-170
Passo Fundo - RS
E-mail: fono.emille@yahoo.com.br

Received on August 7, 2016.
Accepted on September 20, 2016.

DOI: 10.5935/0104-7795.20160023

INTRODUCTION

The Amyotrophic Lateral Sclerosis (ALS), also known as Charcot or Lou Gehrig's disease, is a progressive degenerative neuromuscular disease which affects either the superior or inferior motor neuron, progressively degrading the motor neuron cells of spinal cord, brainstem, and corticospinal and corticobulbar pathways.[1] By losing the capacity of transmitting the nerve impulses, these neurons cause this disease which compromises motor functions, even with evidence of multisystemic engagement, especially cognitive, but occasionally sensitive or autonomic.[2]

The survival of patients with ALS is, approximately, 4 to 5 years.[1,2] As for the etiology, there are studies evidencing that genetical elements can be related to the establishment of ALS and that the family history, allied with environmental components, is also elicited as a risk factor, characterizing this disease as complex and multifactorial.[3,4]

Around the world, ALS represents a prevalence of 7/100,000 and an incidence of 2/100,000 inhabitants.[2] In Brazil, it is present more incident in the male population, whose first symptoms emerge around 52 years of age.[3,4]

The principal characteristics of this disease are muscle weakness, atrophy, fasciculation, hypertonia, and muscle cramp, all related to inferior motor neuron. Moreover, as related to superior motor neuron, the patient presents hyperactive tendon reflexes, Babinski reflex, clonus, and spasticity.[1,2]

Initially, the patient diagnosed with ALS reports a decrease in the limbs, trunk, and pharyngeal and respiratory muscle function, that occurs asymmetrically and progresses non-randomly, therefore suggesting a focal and anatomically contiguous pathological process.[4] Dysphagia, dysarthria and sialorrhea are also diagnosed, considering that, in approximately 30% of the patients, these are the initial symptoms.[5]

The dysphagia is one of the most relevant problems of ALS, being considered the main cause of death, due to respiratory complicatioins.[5] It occurs as a result of the inefficiency of the oral transit mediated by the reduction of the tongue mobility, the laryngeal elevation and anteriorization, and the pharyngeal contraction.[6]

The delay in the deglutition reflex trigger, and the ineffective closing of the larynges and nasopharynges cause food to deviate to the respiratory tract.[7] In the late stages of the disease, the indication of an alternative feeding pathway is required, once, due to the severe dysphagia, the muscle fatigue, and/or respiratory insufficiency the food ingestion solely by the oral pathway become unfeasible, what justifies the relevance of a precise evaluation of deglutition.[8]

To evaluate the degree of deglutition impairment, a clinical phonoaudiological evaluation is substantial, which can be complemented by objective imaging exams, such as deglutition videofluoroscopy, for the visualization of the food trajectory.[6-8]

Some studies elect the videofluoroscopy as the most useful exam for diagnostical investigation of patients with deglutition disorders and suggest that this method can identify the deglutition degree with high precision.[5,9-11]

OBJECTIVE

Analyze the deglutition of patients with Amyotrophic Lateral Sclerosis by videofluoroscopy and elicit the principal characteristics found in this function.

METHODS

This study was approved by the Institutional Ethics Review Board and received the approval number 447.792. It is a cross sectional descriptive study[12] which was executed from November 2013 to July 2014. The study was performed in a referral hospital of *Passo Fundo*, RS - Brazil. The sample of 20 subjects were diagnosed by a neurologist medical doctor as ALS patients, based on the electroneuromyography (ENMG) and the criteria of El Escorial.[4]

They were of both sexes, aging from 43 to 75. The inclusion criteria were: medical diagnosis of ALS; cognitive capacity to understand the instructions; exclusive oral pathway diet; and the patient or family informed consent to participate in the study. Patients who did not agree to participate, who underwent tracheostomy, and whose diet was administered through alternative pathways were excluded, once these aspects could bias the results of the deglutition exam.

The patients were contacted by phone after the referral of the neurologist medical doctor, as well as by social media of ALS patients communities. After that, a date and time for the exam was arranged. The procedures were divided in: establishment of a bond between the patient/family and the researchers with the application of an adapted anamnesis,[13] in which data on identification, early symptoms, diagnosis time, main complaints, previous pathologies and feeding characteristics were collected; and the videofluoroscopy itself.

The videofluoroscopy was executed by a radiology technician and a phonoaudiologist responsible for this service in the institution. The equipment used for the diagnosis was a Shimadzu® intensifier, full model. For analyzing the exam, an adapted videofluoroscopic evaluation protocol of deglutition was used,[13,14] and, for classifying the dysphagia degree, a specific scale was used.[15] The images of the exam were collected by a Samsung® digital camera, model WB350F 16.3MP, for further analysis.

Each exam time was approximately 15 not continuous minutes, when the patients ingested, in a metal teaspoon, liquid food (Clight® juice), pasty food (cream) and solid food (bread) in standardized volumes of three servings of 5ml and one bread serving of 5g. All the servings were mixed with the Bariogel® contrast. The deglutition dynamics images were analyzed by the responsible phonoaudiologist, who is experienced and collaborator of this study, along with the other researchers.

A statistical analysis was performed for evaluating a possible correlation among the variables of each domain of the anamnesis, as well as the exam results. The numeric variables were expressed as mean ± standard deviation or median (25^{th} percentile - 75^{th} percentile) per presence or absence of normality. The categorical variables were presented as absolute or relative frequency.

The comparison between the degree of dysphagia and the fonoaudiological follow up as well as between the diagnosis time of ALS and the degree of dysphagia were evaluated with the Mann-Whitney statistics. The correlation between the degree of dysphagia and the age of the patients was evaluated based on the Sperman correlation coefficient. The tests with p-value > 0.05 were considered statistically significant.

All patients, or their caregivers, received and signed the Informed Consent Form, agreeing with their participation in the research, per resolution 196/96 of the National Council of Health (Brazil) and the Helsinki Declaration (2000).

RESULTS

With the anamnesis, a total of 20 patients were analyzed, ranging from 43 to 75 years of age, and mean age of 57.3 ± 9.5 years. Most of the patients were male (n = 13) and the diagnosis mean time was 12 months (6.5 - 14.8).

The Table 1 shows the information obtained during the application of the anamnesis.

Out of the 20 patients included, 14 (70.0%) were dependent for feeding. No patients reported nasal reflux, food refusal, dehydration or malnutrition. Concerning the feeding posture, only 1 of the patients (5.0%) reported feeding in an inadequate position (lying), whereas the others fed in adequate position (sitting). Pneumonia episodes were reported by 3 patients (15.0%) and the phonoaudiology follow up was part of the treatment of 13 patients (65.0%).

The Table 2 presents the early symptoms of the disease, noticed by the patients before the diagnosis.

Difficulties to speak was reported by three patients (15.0%) as related to the first manifestation of the disease, whereas difficulties to feed and muscle weakness was reported by 3 (15.0%) and 14 (70.0%) respectively as the first manifestation.

The Table 3 presents the variables analyzed in the deglutition videofluoroscopy exam, as well the number of subjects who had changes in any of the variables studied.

Concerning the different deglutition phases for liquid, pasty and solid food, the prevailing characteristics featured in the liquid consistency were: premature posterior escape observed in 6 patients (30.0%); vallecula deglutition reaction observed in 14 patients (70.0%); and residues in pharyngeal region observed in 11 (55.0%) patients. Therefore, this phase was considered the most compromised.

Regarding the pasty consistence, the principal characteristics were: posterior escape observed in 8 patients (40.0%); reduced laryngeal elevation in 12 patients (60.0%); residues in pharyngeal region, predominantly in the tongue base in 11 patients (55.0%); pharynx esophagus transition in 12 patients (60.0%); multiple deglutition occurred in 7 patients (35.0%); and aspiration in one patient (5.0%). This phase was considered the most compromised in the pharyngeal phase.

The solid consistence, in its turn, evidenced increased the total oral transit time of 7 patients (35.0%); reduced tongue mobility of 10 patients (50.0%); residues in oral cavity of 10 patients (50.0%); deglutition reaction prevalently in the vallecula region observed in 11 patients (55.0%) and pharynx esophagus transition in 8 patients (40.0%); residues in pharyngeal region present in vallecula in 10 patients (50.0%) and in tongue base in 9 patients (45.0%); increased pharyngeal transit time in 16 patients (80.0%); and multiple deglutition in 7 patients (35.0%). In this consistency, the oral phase was the most compromised, what influenced the results of the laryngeal phase.

The Table 4 presents the data of dysphagia classification, according to the findings of the deglutition videofluoroscoy.

Concerning the functional aspects of deglutition, 2 patients (10.0%) presented deglutition characteristics within the normal limits, 11 patients (55.0%) had discrete dysphagia, 5 patients (25.0%) had discrete to moderate dysphagia, and 2 patients (10.0%) had moderate dysphagia.

No differences on the deglutition pattern were found when age and dysphagia degree were compared, therefore there is no statistically significant correlation, r = 0.06, p = 0.801.

No statistically significant correlation was observed between the diagnosis time and the dysphagia degree, r = - 0.09, p = 0.717. There was no statistically significant association between the phonoaudiological follow up and the degree of dysphagia. The patients who underwent the follow up presented degree 5.0 (4.0 - 5.0), as well as those without follow up, who presented degree 5.0 (4.5 - 5.0), p = 0.895.

Table 1. Clinical and demographic characteristics of the studied population (n = 20)

Variable	Statistics
Male patients	13 (65.0%)
Mean age (years)	57.3 ± 9.5
Diagnosis time (months)	12 (6.5 - 14.8)
Feeding dependence	14 (70.0%)
Cough during feeding	5 (25.0%)
Oral escape	12 (60.0%)
Nasal reflux	-
Feeding refusal	-
Dehydration	-
Malnutrition	-
Pneumonia	3 (15.0%)
Phonoaudiological follow up	13 (65.0%)

The values represent absolute and relative frequencies, mean ± standard deviation, median (25^{th} - 75^{th} percentiles).

Table 2. First manifestation of the disease

	First manifestation
Difficulties to speak	3 (15.0%)
Difficulties to feed	3 (15.0%)
Muscle weakness	14 (70.0%)

The values represent absolute and relative frequencies.

DISCUSSION

In this study, the objective was to verify the deglutition characteristics of patients with ALS. It was evident that most of the patients are male (n = 13), a data that repeats most part of the literature, which reports a larger prevalence of men in the ALS population when compared to women, at a proportion of 2:1, whereas after 70 years of age, this prevalence decreases and the disease are equally reported in both sexes.[2,16]

Regarding the mean age of the patients (57.3 years), there was agreement with the epidemiology of the disease, in which the mean age of the early symptoms is 57 years.[13] Another study, however, have reported a mean age of 65 years.[16]

Concerning help for feeding, it was observed that 14 patients (70.0%) required help, justifying this research, once ALS causes, in

Table 3. Videofluoroscopical findings of deglutition (n = 20)

	Food consistency		
	Liquid	Pasty	Solid*
Increased Oral Transit Time	4 (20.0%)	3 (15.0%)	7 (35.0%)
Reduced Tongue Mobility	5 (25.0%)	4 (20.0%)	10 (50.0%)
Residues in Oral Cavity	3 (15.0%)	9 (45.0%)	10 (50.0%)
Anterior Escape	3 (15.0%)	8 (40.0%)	-
Premature Posterior Escape	6 (30.0%)	5 (25.0%)	2 (10.0%)
Deglutition Reaction			
Pharynx Esophagus Transition	3 (15.0%)	7 (35.0%)	8 (40.0%)
Vallecula	14(70.0%)	13 (65.0%)	11 (55.0%)
Larynx Vestibule	3 (15.0%)	-	-
Tongue Base	-	-	1 (5.0%)
Reduced Laryngeal Elevation	10 (50.0%)	12 (60.0%)	5 (25.0%)
Residues in Pharyngeal Region			
Tongue Base	9 (45.0%)	11 (55.0%)	9 (45.0%)
Vallecula	11 (55.0%)	10 (50.0%)	10 (50.0%)
Larynx Vestibule	1 (5.0%)	4 (20.0%)	1(5.0%)
Pharyngoesophageal Transition	11 (55.0%)	12 (60.0%)	5 (25.0%)
Pharyngeal Transit Time Aumentado	5 (25.0%)	4 (20.0%)	16 (80.0%)
Multiple Deglutition	4 (20.0%)	7 (35.0%)	7 (35.0%)
Laryngeal Penetration	4 (20.0%)	3 (15.0%)	2 (20.0%)
Laryngeal Aspiration	-	1 (5.0%)	-

The values present absolute and relative frequency. * It was not possible to test the solid food with patient number 1, therefore it was rated as altered.

Table 4. Functional Results of Deglutition[15]

Variable	Statistics
Oral Pathway (normal diet)	
Level 6, within functional limits	2(10.0%)
Modified Oral Pathway	
Level 5 Discrete Dysphagia	11(55.0%)
Level 4 Discrete/Moderate Dysphagia	5(25.0%)
Level 3 Moderate Dysphagia	2(10.0%)

The values present absolute and relative frequencies.

the short term, the loss of functional dependence.[17] As the patient becomes severely disabled and dependent, the presence of a caregiver, who is generally the spouse or a close family member, becomes substantial.[18]

As for the first symptoms, 6 patients (30.0%) reported difficulty to speak and feed, whereas 14 patients (70.0%) reported muscle weakness. Out of these patients, it was observed that only 2 (10.0%) reported changes their communication abilities. These findings are consonant with the literature that reports muscle weakness as the initial sign of the disease in 60% of this population, due to the compromise of the motor neurons, followed by dysphagia, phonatory changes and dysarthria.[4,5,18,19]

The deglutition aspects, analyzed by the videofluoroscopy, allowed some observations: in the oral phase, for all the food consistencies, the oral transit was increased, the tongue mobility was reduced, there was residues in the oral cavity, and, except for the solid consistency, there was anterior escape. Moreover, the solid consistency led to higher difficulty. These findings are also equivalent to the literature, which reports that the principal characteristics of patients with ALS are: losses in the oral phase, decreased period of voluntary deglutition phase, and oral residues.[5,7,20]

In the pharyngeal phase, there was evidence of: premature posterior escape, deglutition reaction triggered in the pharyngoesophageal transition and vallecula, reduced larynx elevation, residues in pharyngeal region, tongue base, vallecula, laryngeal vestibule and pharyngoesophageal transition, multiple deglutitions, and laryngeal penetration. Opposed to the oral phase, in the pharyngeal phase the most relevant alterations were found in the pasty consistency, when an episode of aspiration was found. Similar results were found in studies that used flexible endoscopic evaluation of deglutition (FEES) of patients with dysphagia whose findings were: residues in vallecula and pyriform sinus, pharyngeal constriction weakness, premature escape, reduced larynx elevation, and events of aspiration.[21] Furthermore, other studies reported that pharyngeal residues are commonly observed in food of pasty and liquid consistencies.[7,18,22]

Based on the data, it was possible to observe that function inefficiency was present in the oral phase and the pharyngeal phases, the most compromised. Due to the motor loss and muscular weakness caused by the disease, the structures elicited for the preparation of the food bolus are also compromised, what may justify the reduced tongue mobility and, consequently, the increased oral transit time. The changes in the pharyngeal phase, as the increased amount of residues in the pharyngeal region and the pharyngoesophageal transition, are also related to the pharyngeal muscle inefficiency which is probably caused by the muscle weakness, a characteristic of the disease. The data are consonant with the study where 82.0% of the patients presented inefficiency in the muscles of the tongue, directly influencing the pharyngeal phase.[21]

Based on the classification of dysphagia degree, per O'Neil scale,[15] 2 patients (10.0%) had deglutition within the functional limits, 2 patients (10.0%) had moderate dysphagia, 11 patients (55.0%) had discrete dysphagia, and 5 patients (25.0%) had discrete/moderate dysphagia. In this research, no patient had normal deglutition or severe dysphagia. These findings were similar to the study that, using other evaluation and classification tools, found not only slight and moderate dysphagia, but also severe dysphagia and normal deglutition.[17]

Concerning the phonoaudiological follow up, 13 patients reported maintaining this assistance as part of the therapy. Even without receiving more detailed data on the therapy approach and the follow up time, it was possible to observe that these patients had the same degree of dysphagia as compared to

those who did not report being assisted by a phonoaudiologist. Given that the patients with phonoaudiology assistance had longer diagnosis time, this result may assure that the phonoaudiologist interference may extend a safe oral pathway feeding, postponing the need to use alternative pathways.

It is relevant to emphasize that, along the execution of this research, all patients were assisted by their families, who provided them with more safety during the exam, what may possibly have positively influenced their quality of life. Researches have evidenced that patients without the attention of family and friends lose their hope, causing the disease to progress faster.[18,22] The patients with ALS face many obstacles which directly influence their emotional status, due to the limitations caused by the disease.[19] The quality of the given care is considered substantial to the feeling of well-being of the patients.[23] Combined with the family, the multidisciplinary care is substantial once it provides comfort, quality of life and a better prognosis of the disease.[24]

CONCLUSION

This research made it possible to confirm that the deglutition videofluoroscopy is an efficient and fundamental method for evaluating the functional aspects of the deglutition of patients with ALS, once it allows the precise identification of changes and the follow up along the disease evolution. Regarding the deglutition characteristics, all patients had dysphagia and the pharyngeal phase was the most compromised for the deglutition of pasty and liquid food, with significant presence of residues in vallecula and pharyngoesophageal transition, followed by the oral phase, where the oral transit time was increased and the longue mobility was reduced as solid consistency food was given to the patients. It is important to emphasize that patients who received phonoaudiological follow up as part of their therapy had a slower progression of dysphagia degree, allowing the conclusion that the phonoaudiological treatment is efficient and may extend the feeding period by the oral pathway, therefore improving the quality of life of patients with ALS.

REFERENCES

1. Bandeira FM, Quadros NCL, Almeida KJQ, Caldeira RM. Avaliação da qualidade de vida de pacientes portadores de Esclerose Lateral Amiotrófica (ELA) em Brasília. Rev Neurocienc. 2010;18(2):133-8.
2. Lima SR, Gomes KB. Esclerose lateral amiotrófica e o tratamento com células-tronco. Rev Bras Clin Med. 2010;8(6):531-7.
3. Worms PM. The epidemiology of motor neuron diseases: a review of recent studies. J Neurol Sci. 2001;191(1-2):3-9. DOI: http://dx.doi.org/10.1016/S0022-510X(01)00630-X
4. Talbot K. Motor neuron disease: the bare essentials. Pract Neurol. 2009;9(5):303-9. DOI: http://dx.doi.org/10.1136/jnnp.2009.188151
5. Pontes RT, Orsini M, Freitas MRG, Antonioli RS, Nascimento OJM. Alterações da fonação e deglutição na esclerose lateral amiotrófica: revisão de literatura. Rev Neurocienc. 2010;18(1):69-73.
6. Chiappetta ALM, Oda AL. Doenças neuromusculares. In: Ferreira LP, Befi-Lopes DM, Limongi SCO. Tratado de fonoaudiologia. São Paulo: Roca; 2004. p. 330-41.
7. Luchesi KF, Kitamura S, Mourão LF. Management of dysphagia in Parkinson's disease and amyotrophic lateral sclerosis. CoDAS 2013;25(4):358-64. DOI: http://dx.doi.org/10.1590/S2317-17822013000400010
8. Morim L, Rocha J. Intervenção da terapêutica da fala na esclerose lateral amiotrófica (ELA). Cad Comun Ling. 2009;1(1):119-30.
9. Costa MM. Videofluoroscopy: the gold standard exam for studying swallowing and its dysfunction. Arq Gastroenterol. 2010;47(4):327-8. DOI: http://dx.doi.org/10.1590/S0004-28032010000400001
10. Lima NMF, Guerra CC, Teixeira LC, Silva LBC Sordi M, Mourão L, et al. Tradução e validação da versão brasileira da escala de gravidade na esclerose lateral amiotrófica (Egela). Fisioter Pesqui. 2009;16(4):316-22. DOI: http://dx.doi.org/10.1590/S1809-29502009000400006
11. Groher ME, Crary M. Dysphagia: Clinical management in adults and children. St. Louis: Mosby; 2009.
12. Pereira MG. Epidemiologia teoria e prática. 8 ed. Rio de Janeiro: Koogan; 2005.
13. Jotz GP, Angelis EC, Barros APB. Tratado da deglutição e disfagia: no adulto e na criança. Rio de Janeiro: Revinter; 2010.
14. Gonçalves MIR, Vidigal MLN. Avaliação videofluoroscópica das disfagias. In: Furkin AM, Santini CS. Disfagias orofaríngeas. 2 ed. São Paulo: Pró-Fono; 2004. p. 189-202.
15. O'Neil KH, Purdy M, Falk J, Gallo L. The Dysphagia Outcome and Severity Scale. Dysphagia. 1999;14(3):139-45. DOI: http://dx.doi.org/10.1007/PL00009595
16. Pupillo E, Messina P, Logroscino G, Beghi E; SLALOM Group. Long-term survival in amyotrophic lateral sclerosis: a population-based study. Ann Neurol. 2014;75(2):287-97. DOI: http://dx.doi.org/10.1002/ana.24096
17. Goldstein LH, Atkins L, Landau S, Brown R, Leigh PN. Predictors of psychological distress in carers of people with amyotrophic lateral sclerosis: a longitudinal study. Psychol Med. 2006;36(6):865-75. DOI: http://dx.doi.org/10.1017/S0033291706007124
18. Mello MP, Orsini M, Nascimento OJM, Pernes M, Lima JMB, Heitor C, et al. O paciente oculto: qualidade de Vida entre cuidadores e pacientes com diagnóstico de Esclerose Lateral Amiotrófica. Rev Bras Neurol. 2009;45(4):5-16.
19. Paris G, Martinaud O, Petit A, Cuvelier A, Hannequin D, Roppeneck P, et al. Oropharyngeal dysphagia in amyotrophic lateral sclerosis alters quality of life. J Oral Rehabil. 2013;40(3):199-204. DOI: http://dx.doi.org/10.1111/joor.12019
20. Teismann IK, Warnecke T, Suntrup S, Steinsträter O, Kronenberg L, Ringelstein EB, et al. Cortical processing of swallowing in ALS patients with progressive dysphagia: a magnetoencephalographic study. PLoS One. 2011;6(5):e19987. DOI: http://dx.doi.org/10.1371/journal.pone.0019987
21. Luchesi KF, Kitamura S, Mourão LF. Higher risk of complications in odynophagia-associated dysphagia in amyotrophic lateral sclerosis. Arq Neuropsiquiatr. 2014;72(3):203-7. DOI: http://dx.doi.org/10.1590/0004-282X20130244
22. Ruoppolo G, Schettino I, Frasca V, Giacomelli E, Prosperini L, Cambieri C, et al. Dysphagia in amyotrophic lateral sclerosis: prevalence and clinical findings. Acta Neurol Scand. 2013;128(6):397-401. DOI: http://dx.doi.org/10.1111/ane.12136
23. Körner S, Hendricks M, Kollewe K, Zapf A, Dengler R, Silani V, et al. Weight loss, dysphagia and supplement intake in patients with amyotrophic lateral sclerosis (ALS): impact on quality of life and therapeutic options. BMC Neurol. 2013;13:84. DOI: http://dx.doi.org/10.1186/1471-2377-13-84
24. Brooks BR. Managing amyotrophic lateral sclerosis: slowing disease progression and improving patient quality of life. Ann Neurol. 2009;65 Suppl 1:S17-23. DOI: http://dx.doi.org/10.1002/ana.21544