ASSOCIATION BETWEEN MAXIMUM TONGUE PRESSURE AND SWALLOWING SAFETY AND EFFICACY IN AMYOTROPHIC LATERAL SCLEROSIS

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ABSTRACT

Background Oropharyngeal dysphagia (OD) is common in ALS, leading to a reduction of swallowing safety and efficacy. The tongue has an important role in swallowing function for oral processing and bolus propulsion through the pharynx. The study aims to analyze the association between instrumental findings of OD and tongue pressure.

Methods Patients with ALS referred for FEES were recruited. FEES was conducted to test swallowing function with liquid (5ml, 10ml, and 20ml), semisolid (5ml, 10ml, and 20ml), and solid. FEES recordings were assessed for swallowing safety, using the Penetration Aspiration Scale (PAS), and for swallowing efficacy, using the Yale Pharyngeal Residue Severity Rating Scale (YPRSRS). PAS scores >2 were suggestive of penetration, PAS scores >5 of aspiration, and YPRSRS scores >2 of residue. Maximum tongue pressure (MTP) and tongue endurance were measured using the Iowa Oral Performance Instrument. Tongue pressure measurements were compared between patients with and without penetration, aspiration or residue.

Key Results Fifty-five patients with ALS were included. Mean MTP was 29.7 kPa and median tongue endurance was 10s. Patients with residue in the pyriform sinus had a significantly lower MTP than patients without residue in the pyriform sinus with semisolids 10ml (p=0.011) and 20 ml (p=0.032). Patients with a tongue endurance <10 seconds exhibited higher frequency of penetration with liquids 5ml (p=0.046), liquids 10ml (p=0.015), and solids (p=0.22).

Conclusion & Inferences In patients with ALS, MTP is significantly associated with an impairment of swallowing efficacy and tongue endurance was significantly associated with an impairment of swallowing safety.

Keywords: amyotrophic lateral sclerosis, tongue, deglutition, deglutition disorders, pharyngeal diseases

INTRODUCTION

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease characterized by progressive degeneration of upper and lower motor neurons [1]. Regardless of the site of onset, oropharyngeal dysphagia (OD) occurs at some point throughout ALS progression in 85% of the patients [2]. OD in ALS is the result of different pathological mechanisms: rigidity and/or weakness of muscles directly involved in pharyngeal swallowing (facial, tongue, pharyngeal, and laryngeal muscles), weakness of respiratory muscles, and sensory impairment [3-5]. Alteration of all phases of swallowing have been reported, although OD is usually characterized by initial impairment of the oral phase in the early stage and subsequent impairment of the pharyngeal phase [6]. Concerning the pharyngeal phase of swallowing, both safety and efficacy are impaired in this population. Swallowing safety is the ability to transfer the bolus from the mouth to the stomach without penetration or aspiration into the lower airways (i.e. penetration and aspiration) and is associated with respiratory complications [7]. Swallowing efficacy refers to the ability to transfer the bolus from the mouth to the stomach without post-swallow pharyngeal residue and is associated with nutritional complications [7]. Findings of impaired efficacy seem to be more frequent than findings of impaired safety in patients with ALS [8] and pharyngeal residue showed the strongest correlation with disease severity [9]. Nonetheless, literature in ALS shows a predominance of studies focusing on swallowing safety, while less than one third of the studies addressing the issue of swallowing efficacy [10]. Moreover, swallowing safety and efficacy are influenced by the bolus consistency and volume [11-13], but the majority of the studies tests only liquids and pureed boluses and small volumes (3-5 ml). Therefore, although dysphagia is a common and highly relevant symptom in ALS, swallowing function is still poorly characterized in this population.

The tongue plays an important role in swallowing function. During the oral phase, tongue contributes to bolus formation, placement, and transportation within the oral cavity. In the pharyngeal phase, the tongue generates a driving force for bolus propulsion through the pharynx and into the upper esophageal sphincter (UES) [14]. In the elderly and in patients with Parkinson's disease, reduced tongue pressure has been reported to be associated with OD, aspiration, and a lower amount of food and drink intake [15-17].

In ALS, literature has investigated the clinical value of measuring tongue pressure. Weikamp and colleagues found that maximum tongue pressure (MTP) was independently associated with time to death [18] in 54 patients with ALS. In 2013, Easterling et al reported that anterior MTP significantly decreased over a 6-month period both in bulbar and spinal onset patients and concluded that MTP can be used as an indicator of disease progression, together with other measures such as forced vital capacity [19]. More recently, Hiraoka and colleagues showed that MTP can be a marker for the early detection of bulbar symptoms' onset in patients with ASL and spinal onset [20].

Despite the growing attention on MTP in ALS, to date, the association between MTP and pharyngeal findings of OD is poorly studied in this population. Hiraoka et al reported a reduced MTP in patients with ALS with post-swallow pharyngeal residue compared to patients without post-swallow pharyngeal residue [20], but the investigation was limited to patients with the spinal onset and with 3ml semisolid bolus. To the best of our knowledge, no data is available on other consistencies and findings of impaired safety. Analogously, no data on the association between tongue endurance and OD are available in ALS. Tongue endurance, defined as the duration an individual can maintain submaximal force [21], has been suggested to be a measure of fatigue [22]. Fatigue is a common symptom in ALS [23]. Therefore, a reduced tongue endurance may increase the frequency of pharyngeal residue or lower airway invasion during the meal. Understanding the association between tongue pressure measurements and findings of OD may shed light on the role of the tongue in the development of pharyngeal OD in patients with ALS and provide information to guide OD management in this population.

The study aimed to investigate the association between tongue pressure measurements (MTP and tongue endurance) and instrumental findings of OD (penetration, aspiration, residue) in patients with ALS with a variety of consistencies and bolus volumes. The hypothesis was that MTP and tongue endurance would be decreased in patients with ALS exhibiting findings of OD, particularly with more viscous consistencies and larger volumes which requires higher pressure generation during swallowing. The secondary aim of the study was to characterize OD in patients with ALS using different bolus types.

MATERIAL AND METHODS

The study was carried out according to the Declaration of Helsinki and was previously approved by the Institutional Review Board of the Luigi Sacco Hospital (n.2016/ST/262) and from the Ethics Committee of Istituti Clinici Scientifici Maugeri IRCCS. All participants provided written informed consent.

Subjects

Patients were consecutively recruited among inpatients and outpatients referred for fiberoptic endoscopic evaluation of swallowing (FEES) at the ALS Center of the Istituti Clinici Scientifici Maugeri IRCCS, Milan, between March 2017 and December 2018. Inclusion criteria were a diagnosis of definite, possible, clinically probable, or clinically probable laboratory-supported ALS based on the Revised El Escorial criteria [24], full oral nutrition, age 18-90 years. Exclusion criteria were a history of head and neck cancer, known gastrointestinal diseases, or other concomitant neurological diseases.

Functional assessment

All patients were functionally rated by a neurologist using the ALS Functional Rating Scale-Revised (ALSFRS-R) [25] to describe the overall functional status of the patients' sample. The ALSFRS-R is a functional rating system of independence in activities of daily living for patients with ALS. The scale is made up of 12 items, divided into 4 domains (bulbar, upper limb, lower limb, and respiratory functions). The bulbar domain includes 3 items (speech, salivation, and swallowing). Each item is rated on a 5-points scale from 0 (total loss of function) to 4 (no loss of function). The total score ranges from 0 to 48, while the bulbar score from 0 to 12.

Tongue pressure measurement

MTP and tongue endurance was measured with the Iowa Oral Performance Instrument (IOPI) (model 2.3; IOPI Medical LLC, Carnation, WA) to provide an objective measure of tongue pressure and endurance [26]. The IOPI is a portable device manometer that measures the amount of tongue pressure being exerted on an air-filled pliable plastic bulb, connected with a plastic tube to the device. A display on an LCD panel of the device shows the pressures obtained in kPa. Previous studies indicate a high inter- and intra-rater reliability of the IOPI device for tongue measurements [14, 27]. Calibration of the device was checked and, if necessary, a new calibration using the syringe was performed before obtaining measures until a value of 0 or 1 kPa was achieved.

MTP was measured by asking the participants to obtain maximal tongue elevation pressure. The bulb was placed in the patient's oral cavity by the clinician. The standard placement of the bulb was along the central groove of the tongue blade just posterior to the upper alveolar ridge and patients were asked to rest their incisors on the tubing of the IOPI bulb, according to previous literature [26]. To ensure the same positioning among different trials, a mark was made on the tube of the bulb just anterior to the incisors. Then, patients were instructed to "push the bulb against the roof of your mouth as hard as you can." All trials were motivated by verbal encouragement from the examiner. The measurement was repeated 3 times, with a resting period of 30 seconds after each trial. The highest MTP measurement was recorded in kPa.

Tongue endurance was defined as the maximum time the patients were able to sustain 50% of their MTP. The 50% of the MTP was calculated and the examiner manually set the pressure using the arrows on the device until the desired pressure was indicated on the IOPI's display. The bulb was placed in the same position as the MTP trials. Patients were instructed to sustain the target pressure for as long as possible. A series of LED lights on the right side of the device automatically alerted the patients when they reached the target pressure. Time was measured using the stopwatch incorporated in the IOPI device. Timing starts when the pressure meets the target pressure and stops when the pressure drops steeply, the pressure is maintained between 40 and 50 % of MTP for 2 seconds or more, or the pressure stays below 40 % of MTP for at least 0.5 seconds [26]. The measurement was repeated 3 times, with a resting period of 2 minutes between the trials. The longest endurance performance was recorded in seconds.

All measures were acquired on the same day of the fiberoptic endoscopic examination of swallowing (FEES), at least 1 hour after meals and before FEES to avoid potential fatigue effects secondary to meal consumption or FEES trials.

Fiberoptic endoscopic evaluation of swallowing

FEES were performed using a PENTAX FNL-10RBS flexible endoscope with a diameter of 3.5 mm and a length of 300 mm (PENTAX Europe GmbH, Hamburg, Germany) mounted on a PENTAX EPK-1000 video processor (PENTAX Europe GmbH, Hamburg, Germany). All the examinations were stored in an anonymous form in.AVI format on the system's hard drive, and saved on external memories as backup copies. FEES were conducted with liquids (5-10-20 ml of blue-dyed milk x 3 trials for each volume; <50 mPa·s at 50s-1 and 300s-1), semisolids (5-

10-20 ml of apple sauce x 3 trials for each volume; 918.33±35.13 mPa·s at 50s-1 and 252.5±7.61 mPa·s at 300s-1), and solids (half cracker x 2 trials). The milk was selected to test the liquids because the literature suggests that it increases the ability to detect penetration and aspiration compared to water during FEES [28]. The apple sauce was chosen to test the semisolid because it was judged to be more similar to the semisolid food usually consumed during meals in Italy compared to other semisolids often tested in FEES. Finally, the GranPavesi® Cracker was selected to test solids being the standard cracker used to assess oral phase efficiency [29]. The order of bolus administration was the same for all the patients, starting with liquids (3x5ml, 3x10ml, 3x20 ml), then semisolids (3x5ml, 3x10ml, 3x20 ml), and finally solids. The protocol was reduced in case a consistency or a volume was not considered safe to be administered. In particular, a bolus type was not tested if: 1) the patient showed aspiration but was not able to eject the aspirated material (Penetration-aspiration scale score equal to 7 or 8) with the previous volumes of the same consistency; 2) if the patient was not able to hold the bolus in the mouth because of anterior leakage of the bolus from the lips; 3) if the patient was not able to prepare the bolus because of severe impairment of oral preparatory swallowing stage (for solids). Each FEES was video-recorded, de-identified, and assessed by 2 independent speech and language therapists (SLTs) using validated ordinal scales for swallowing safety and efficacy. In case a difference >1 level at each FEES rating scale occurred between the 2 raters, a 3rd SLT with >5-year experience on FEES assessed the videos and decide on the 2 ratings.

The Penetration-aspiration scale (PAS) was used to assess swallowing safety [30]. The ordinal scale scores from 1 to 8. In particular, scores 1 and 2 represent no or minimal penetration within functional limits, scores 3 to 5 represent laryngeal penetration, and scores 6 to 8 represent tracheal aspiration.

Pharyngeal residue, as a measure of swallowing efficacy, was rated according to the Yale Pharyngeal Residue Severity Rating Scale (YPRSRS) [31]. The scale provides two scores based on the amount of post-swallow residue in the valleculae and the pyriform sinuses. The score ranges from 1 (no residue) to 5 (severe residue). For the present study, a score >2 was suggestive of the presence of clinically relevant residue.

Before FEES examination, typical oral intake was recorded with the Italian version of the Functional Oral Intake Scale (FOIS) [32]. The FOIS is a 7-point ordinal scale describing the functional level of oral intake of food and liquid. Level 7 represents a full oral diet with no restrictions, levels 6-4 indicate a full oral diet with restrictions, levels 3-2 describe a mixed oral and tube intake, while level 1 represents a totally tube-dependent intake.

Statistical analysis

Data are reported as absolute (relative) frequency and mean ± sd or median (IQR), according to the variable's distribution. Statistical analysis was performed with the IBM SPSS Statistics 25.0® package for Windows (SPSS Inc, Chicago, IL). The Kolmogorov-Smirnov test was used to assess the normality assumption of the tongue pressure measurement, which was verified for the MTP but not for the tongue endurance. MTP was compared among patients with FEES findings of OD and patients without FEES findings of OD for each bolus type using the independent-samples t-test. The frequency of residue, penetration, and aspiration was compared in patients with tongue endurance <10 seconds and patients with tongue endurance ≥10 seconds using the chi-squared test. Significance was set at $p<0.05$.

RESULTS

Subjects

Overall, 55 patients with a diagnosis of ALS and referred for FEES assessment were recruited. The demographic and clinical characteristics of the sample are shown in Table 1.

Tongue function

Distribution of MTP and tongue endurance is shown in Figure 1. MTP was on average 29.7 ± 14 kPa (range 4-66 kPa). Median tongue endurance was 10 s with an IQR 4-16 s (range 1-189 s). The tongue endurance measurements were highly skewed, with 29/55 (53%) patients being <10 s. ~~Thus, a statistical comparison was not performed for this variable.~~

Association between tongue pressure and swallowing safety and efficacy

MTP was compared among patients with FEES findings of OD and patients without FEES findings of OD for each bolus type. The results of the comparisons are reported in Table 2. Patients with residue in the pyriform sinus had a significantly lower MTP than patients without residue in the pyriform sinus with semisolids 10 ml and 20 ml (p=0.011 and p=0.014, respectively). No statistically significant different MTP was found between patients with or without residue in the valleculae, penetration, and aspiration.

Table 3 reports the frequency of residue, penetration, and aspiration in patients with a tongue endurance <10 seconds and in patients with a tongue endurance ≥10 seconds. Patients with a tongue endurance <10 seconds exhibited a higher relative frequency of residue in the valleculae, penetration, and aspiration compared to patients with a tongue endurance ≥10 seconds with all the bolus type, except for aspiration with semisolids 20ml and solids that was 0% in both groups. A statistically different distribution of penetration was found between the two groups of tongue endurance with liquids 5ml (χ^2=3.965, p=0.046), liquids 10ml (χ^2=5.969, p=0.015), and solids (χ^2=5.280 p=0.022).

Swallowing safety and efficacy

The frequency of findings of OD detected on FEES is depicted in Figure 2. Liquids were not tested in 1, 12, and 21 patients for the 5ml, 10ml, and 20 ml, respectively. All patients were tested with semisolids 5 and 10ml, whereas 20ml semisolids were not administered in 2 patients, while solids were not offered in 11 patients.

Residue in the valleculae was the most common finding, occurring in >60% of the patients tested with all the bolus types. Residue in the pyriform sinus occurred in 43-63% of the patients tested with liquids, in 27-51% of the patients tested semisolids, and in 23% of the patients tested with solids. Penetration mainly occurred with liquids (59-64% of tested patients), while its frequency decreased with semisolid (24-34% of tested patients) and solids (10% of tested patients). Aspiration occurred in <20% of the patients and mostly with liquids.

Table 4 shows the combination of residue in the valleculae, residue in the pyriform sinus, and penetration/aspiration within the same patient for each bolus type. The majority of the patients tested with liquids (61-71%) exhibited a combination of 2 or more findings of impaired safety and efficacy. With semisolids and solids, the most observed pattern (25-41%) was the presence of residue in the valleculae without any other findings of OD.

DISCUSSION

The present study aimed to clarify the association between MTP and OD in patients with ALS. Tongue pressure and swallowing function were assessed in a sample of 55 consecutive patients with ALS. OD in ALS was characterized using a variety of consistencies and volumes during the instrumental assessment of swallowing. Swallowing efficacy was more impaired than swallowing safety. A reduced MTP was associated with residue in the pyriform sinus, but not with residue in the valleculae and penetration/aspiration.

In ALS, MTP is recognized to be a marker of disease progression [19] and of bulbar involvement [20], as well as a poor prognostic factor for survival [18]. In other populations, MTP was reported to be associated with OD, mealtime performance, and malnutrition [16]. The measurement of MTP is associated with the concept of functional reserve. The functional reserve is defined as the difference in pressures generated in maximum isometric tasks compared to swallowing tasks [33]. As MTP reduces and tongue-to-palate pressure required for swallowing remains constant, a reduction of the functional reserve may potentially result in a disruption to the swallowing process. In other populations, reduced MTP has been reported to be associated with the presence of OD [16-17, 34-37]. In the sample of patients recruited in the study, MTP was on average 29.7 ± 14 kPa. Normal values of tongue pressure are not available for the Italian population but are available for other European countries, such as Belgium. Compared to Belgian normative data, 44% (24/55) of the patients included in the study showed an MTP below the 10th percentile of normal values (ranging between 10 and 43 kPa depending on the age and the gender) [26]. Therefore, around half of the patients with ALS seems to exhibit a reduced functional reserve.

Tongue endurance was <10 seconds and below the 10th percentile of normal values (ranging between 5 and 17 seconds depending on the age and the gender) [26] in half of the patients with ALS tested in the study (53% <10 s, 49% <normal values). Reduced tongue endurance represents an important finding. Endurance is related to physical fatigue, which is a frequent symptom and is associated with poor quality of life in patients with ALS [23]. To date, the importance of tongue endurance for swallowing function is not fully understood. When considering single swallows, the ability to sustain tongue-to-palate pressure for several seconds is probably not clinically relevant. However, tongue endurance may be important to reduce

fatigability during meal consumption. Kays and colleagues analyzed the effect of dining on MTP and tongue endurance in healthy subjects and reported a significant reduction of both measures despite the age of the subject [22]. As patients with ALS were found to exhibit a reduced baseline functional reserve (MTP) and tongue endurance, meal consumption may further reduce tongue pressure measures and, consequently, exacerbate swallowing difficulties. Patients with values of tongue endurance <10 seconds exhibited a higher percentage of findings of impaired safety and efficacy than patients with a tongue endurance ≥10 seconds, which was statistically significant for penetration with liquids 5ml and 10 ml and solids (Table 3). A possible hypothesis of the association between reduced tongue endurance and penetration is that tongue endurance decreases with the progression of bulbar symptoms and disease severity. Other hypothesis should be explored with future studies.

Patients with residue in the pyriform sinus with 10ml and 20ml semisolids had significantly lower MTP. Although not significant, a trend for lower MTP in patients with residue in the pyriform sinus was also observed for solids. Therefore, the hypothesis of a stronger association between MTP and findings of OD with more viscous consistencies and large volumes, requiring stronger muscle contraction, was confirmed. Concerning the physiopathological mechanism explaining the association with residue in the pyriform sinus, one hypothesis may be related to the mylohyoid muscle involvement in MTP generation. Indeed, Palmer and colleagues [38] quantified the contribution of different muscles on tongue-to-pressure generation. Posterior fibers of the genioglossus and mylohyoid muscle accounted for the majority of the tongue pressure. Mylohyoid muscle is involved in laryngeal elevation during swallowing and, thus, influence UES opening. Therefore, reduced MTP may be secondary to weakness of the mylohyoid muscle, leading to reduced laryngeal elevation, reduced UES opening, and accumulation of post-swallow residue in the pyriform sinus. Another possible explanation may be that reduced MTP reflects a more generalized weakness of bulbar muscles leading to other pathophysiological mechanisms associated to residue in the pyriform sinus. This hypothesis would be in accordance with the study by Waito and colleagues that found a significant effect of reduced pharyngeal constriction on the presence of residue both in the valleculae and in the pyriform sinus [39]. Future studies should provide a better insight into this association.

Interestingly, no association was found between the MTP and the residue in the valleculae. This finding was unexpected due to the role of the tongue in bolus propulsion through the pharynx. A possible explanation is related to the fact that MTP was investigated in the anterior portion of the tongue, as it was previously reported as a marker of disease progression and OD. Indeed, a difference between the anterior and the posterior MTP is known [26], mainly secondary to the different composition in the fibers' type. Thus, different results may be found for posterior MTP in ALS. Another possibility is that the high prevalence of residue in the valleculae, reaching 83% of the patients with semisolids, did not allow to detect differences in MTP because of the reduced number of patients with no residue in the valleculae. Based on the present result, residue in the valleculae seems to be an early onset sign of OD in the disease progression of ALS. This finding is in accordance with the previous study by Waito et al, who interpret that as a sign of the rostrocaudal pattern of ALS bulbar disease progression [39].

Impairment of swallowing efficacy (pharyngeal residue) was found to be a prominent feature of OD in ALS, with a higher prevalence than impairment of swallowing safety (penetration/aspiration). Previous studies have mainly focused on findings of swallowing safety, but assessing both aspects is relevant to address both pulmonary and nutritional complications of dysphagia [10]. Not surprisingly, findings of swallowing unsafety mainly occurred with liquids, whereas findings of swallowing inefficiency with more viscous consistencies. Only another study investigated swallowing function in ALS using 3 types of consistencies (liquids, semisolids, and solids) [9]. The present study added the analysis on different volumes. Observing the relative frequency of findings of OD in patients tested during

FEES, the frequency of residue seems to increase from 5ml volumes to 10ml volumes, with no further increase between the 10ml and 20ml, while penetration seems to remain stable among different volumes within the same consistency. However, the number of not assessed patients due to perceived safety issues increased with larger volumes and these patients generally exhibited lower MTP than patients with no sign of dysphagia (Table 2). The not assessed patients were likely to be the most severe patients, exhibiting PAS scores of 7-8 with smaller volumes or not being able to hold the bolus in the oral cavity due to poor lips continence or to prepare the bolus due to impairment of the oral phase. In healthy subjects, larger volumes require higher tongue swallowing pressure [40]. Therefore, the frequency of findings of OD with larger volumes and their association with MTP may be underestimated.

Implications for clinical practice

The existence of an association between tongue function and findings of OD in patients with ALS have an impact on both the assessment and the management of OD in this population. Firstly, it suggests that, when possible, including MTP and tongue endurance measures during swallowing assessment provides additional information on swallowing function, being, for instance, a potential outcome measure of eating-related fatigue. Patients with ALS and reduced MTP or tongue endurance, and, therefore, reduced functional reserve, may experience higher degrees of fatigue during meals. Thus, if proved by future studies, MTP and tongue endurance may be used as a marker of fatigue during meals in patients with ALS. Secondly, the fact that the association was found with larger volumes and more viscous consistencies has implications for diet recommendation in patients with ALS. In case of a reduction of MTP, smaller volumes may be recommended. However, tongue function represents just one of the elements that can guide clinicians' decisions on diet recommendation. Therefore, measures of tongue function should always be integrated with other information from the clinical and the instrumental swallowing assessment. Moreover, if swallowing safety is preserved, less viscous consistencies may be preferable. Finally, the lingual resistance training program may represent a potential rehabilitation strategy to slow the progression of OD. Lingual resistance training was found to be effective in contrasting sarcopenia in patients with presbyphagia, improving tongue strength, hyoid elevation, UES opening, and reducing residue in the pyriform sinus [41]. Although the applicability of strengthening program in patients with ALS is controversial, a progressive shift of the paradigm on rehabilitation in ALS toward the possibility to use low-load exercise, also to improve bulbar functions, was observed over the last decade [42-43]. A preliminary study on the efficacy of lingual resistance training in 2 patients with ALS showed no improvement in swallowing safety and patient-reported outcome, but swallowing efficacy was not included in the outcomes of the study [44]. A recent systematic review on different populations highlighted that the effects of lingual resistance training on both swallowing safety and swallowing efficacy are still controversial [45]. Thus, the feasibility and efficacy of lingual resistance training in ALS need to be further tested in future studies.

Limitations

The study has some limitations. The sample size of 55 patients is relatively limited, with a potential reduction of the power of the study. However, ALS is a rare disease and the sample size is in line with or even greater than the majority of the studies instrumentally assessing dysphagia in this population. The total and bulbar score of the ALSFRS shows a homogeneous distribution among the different scores levels, suggesting that the present sample is representative of a wide range of disease severity. However, patients with enteral nutrition were excluded from the study. Nevertheless, it may have resulted in the exclusion of patients with more severe OD. In the present study, only anterior MTP and tongue endurance were investigated because it was the location used for tongue pressure measurements as a marker of disease progression and bulbar onset in literature [18-20]. It is important to notice that different results on the association between tongue pressure and FEES findings could be found if posterior tongue pressure measurements would have been acquired. Finally, FEES was used to assess swallowing because a high number of boluses can be tested during the exam and to analyze swallowing function with several consistencies and volumes. Moreover, FEES is more sensitive to residue than videofluoroscopy [46]. However, videofluoroscopy and high-resolution manometry allows studying physiopathological mechanisms that may explain the association between MTP and residue in the pyriform sinus found in the study. Thus, future studies may be designed to overcome these limitations.

CONCLUSION

In patients with ALS, MTP is significantly associated with an impairment of swallowing efficacy, while tongue endurance is significantly associated with an impairment of swallowing safety. The association was found with larger volumes and more viscous consistencies, providing indications for diet recommendation in this population, additionally to data from the clinical and instrumental swallowing assessment.

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Compliance with Ethical Standards

Funding: no funding was provided for the present study

Conflict of interest: the authors declare that they have no conflict of interest

Ethical approval: all procedures performed in the study were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board of the Luigi Sacco Hospital (n.2016/ST/262)

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Table 1. Demographic and clinical characteristics of the patients

Variable		Mean ± sd or n (%)
AGE *years*		67.8 ± 10
GENDER	*M*	30 (54.5%)
	F	25 (45.5)
SITE OF ONSET	*Spinal*	39 (70.9%)
	Bulbar	16 (29.1%)
AGE OF ONSET *years*		63.5 ± 10
DISEASE DURATION *years*		4.2 ± 4.8
ALSFRS-R	*Total*	27.4 ± 8.6
	Bulbar	8.4 ± 3
DIET TYPE	*FOIS 7*	16 (29.1%)
	FOIS 6	15 (27.3%)
	FOIS 5	11 (20%)
	FOIS 4	13 (23.6%)

LEGEND. FOIS = Functional oral intake scale. FOIS 7 = total oral intake with no restrictions; FOIS 6 = total oral intake with restriction to specific foods or liquid items; FOIS 5 = total oral intake of multiple consistencies requiring special preparation; FOIS 4 = total oral intake with homogeneous pureed diet

Table 2. Results of the t-test for the comparison of MTP between patients with and without FEES findings of OD

		NOT ASSESSED†		PRESENT		ABSENT		p
Bolus type	Sign of dysphagia	N	Mean ± sd	N	Mean ± sd	N	Mean ± sd	
LIQUID 5ml	*Residue valleculae*	1	10	37	30 ± 13.2	17	30.1 ± 15.7	.994
	Residue pyriform sinus	1	10	25	29.1 ± 12.5	29	30.8 ± 15.1	.657
	Penetration	1	10	32	27.1 ± 13.1	22	34.3 ± 14.1	.060
	Aspiration	1	10	11	27.5 ± 13.2	43	30.7 ± 14.1	.495
LIQUID 10ml	*Residue valleculae*	12	21.3 ± 12.1	33	32.9 ± 13.0	10	29.1 ± 16.4	.449
	Residue pyriform sinus	12	21.3 ± 12.1	27	29.2 ± 13.2	16	36.8 ± 13.7	.082
	Penetration	12	21.3 ± 12.1	26	30.8 ± 12.4	17	33.8 ± 15.7	.494
	Aspiration	12	21.3 ± 12.1	5	35.4 ± 11.3	38	31.6 ± 14.1	.565
LIQUID 20ml	*Residue valleculae*	21	23.6 ± 2.7	26	35.6 ± 12	8	26.3 ± 17.9	.096
	Residue pyriform sinus	21	23.6 ± 2.7	19	32.2 ± 13.1	15	34.9 ± 15.2	.579
	Penetration	21	23.6 ± 2.7	22	32.7 ± 14.1	12	34.6 ± 14.1	.723
	Aspiration	21	23.6 ± 2.7	5	33.4 ± 9.4	29	33.4 ± 14.7	.998
SEMISOLID 5ml	*Residue valleculae*	0	-	35	28.6 ± 12.6	20	31.6 ± 16.4	.458
	Residue pyriform sinus	0	-	15	25.3 ± 13.7	40	31.3 ± 13.9	.162
	Penetration	0	-	13	27 ± 13.4	42	30.5 ± 14.3	.437
	Aspiration	0	-	1	12	54	30 ± 13.9	.206
SEMISOLID 10ml	*Residue valleculae*	0	-	44	30.3 ± 13.6	11	27.3 ± 16.2	.531
	Residue pyriform sinus	0	-	24	**24.3 ± 12.4**	31	**33.8 ± 14**	**.011**
	Penetration	0	-	17	27.8 ± 13.7	38	30.5 ± 14.3	.518
	Aspiration	0	-	1	12	54	30 ± 13.9	.206
SEMISOLID 20ml	*Residue valleculae*	2	21 ± 15.6	44	30.2 ± 13.6	9	29.1 ± 16.6	.837
	Residue pyriform sinus	2	21 ± 15.6	27	**25.4 ± 12.5**	26	**34.8 ± 14.1**	**.014**
	Penetration	2	21 ± 15.6	18	29.3 ± 16	35	30.4 ± 13.1	.791
	Aspiration	2	21 ± 15.6	0	-	53	30 ± 14	-
SOLID	*Residue valleculae*	11	19.6 ± 15.4	27	31.1 ± 11.5	17	33.9 ± 14.5	.470
	Residue pyriform sinus	11	19.6 ± 15.4	10	27.5 ± 8	34	33.6 ± 13.5	.186
	Penetration	11	19.6 ± 15.4	4	25.5 ± 7	40	32.9 ± 12.9	.272
	Aspiration	11	19.6 ± 15.4	0	-	44	32.2 ± 12.6	-

Statistically significant p are reported in bold.
†MTP of patients not assessed for safety reasons for each bolus type are reported as descriptive results but are not included in the comparison

Table 3. Frequency of residue, penetration, and aspiration in patients with tongue and endurance <10 seconds (n=27) and patients with tongue endurance ≥ 10 seconds (n=28) and results of chi-squared comparison

		Tongue endurance <10s		Tongue endurance ≥10 s		
Bolus type	Sign of dysphagia	N Patients tested	n (%)	N Patients tested	n (%)	p
LIQUID 5ml	*Residue valleculae*	26	20 (77%)	28	17 (61%)	0.200
	Residue pyriform sinus	26	14 (54%)	28	11 (39%)	0.284
	Penetration	26	**19 (73%)**	28	**13 (46%)**	**0.046**
	Aspiration	26	6 (23%)	28	5 (18%)	0.634
LIQUID 10ml	*Residue valleculae*	20	17 (85%)	23	16 (70%)	0.232
	Residue pyriform sinus	20	14 (70%)	23	13 (57%)	0.362
	Penetration	20	**16 (80%)**	23	**10 (43%)**	**0.015**
	Aspiration	20	4 (20%)	23	1 (4%)	0.110
LIQUID 20ml	*Residue valleculae*	14	11 (79%)	20	15 (75%)	0.809
	Residue pyriform sinus	14	10 (71%)	20	9 (45%)	0.127
	Penetration	14	11 (79%)	20	11 (55%)	0.157
	Aspiration	14	4 (29%)	20	1 (5%)	0.056
SEMISOLID 5ml	*Residue valleculae*	27	20 (74%)	28	15 (54%)	0.114
	Residue pyriform sinus	27	9 (33%)	28	6 (21%)	0.322
	Penetration	27	8 (30%)	28	5 (18%)	0.304
	Aspiration	27	1 (4%)	28	0 (0%)	0.304
SEMISOLID 10ml	*Residue valleculae*	27	24 (89%)	28	20 (71%)	0.106
	Residue pyriform sinus	27	15 (56%)	28	9 (32%)	0.080
	Penetration	27	10 (37%)	28	7 (25%)	0.334
	Aspiration	27	1 (4%)	28	0 (0%)	0.304
SEMISOLID 20ml	*Residue valleculae*	27	23 (85%)	26	21 (81%)	0.669
	Residue pyriform sinus	27	16 (59%)	26	11 (42%)	0.217
	Penetration	27	11 (41%)	26	7 (27%)	0.288
	Aspiration	27	0 (0%)	26	0 (0%)	-
SOLID	*Residue valleculae*	20	14 (70%)	24	13 (54%)	0.283
	Residue pyriform sinus	20	5 (25%)	24	5 (21%)	0.743
	Penetration	20	**4 (20%)**	24	**0 (0%)**	**0.022**
	Aspiration	20	0 (0%)	24	0 (0%)	-

Data are reported as absolute frequency and relative frequency (n/n patients tested)
Statistically significant p are reported in bold

Table 4. Combination of FEES findings in patients with ALS

Bolus type	N Patients tested	No findings	Isolated residue valleculae	Isolated residue pyriform sinus	Isolated penetration /aspiration	Residue valleculae + pyriform sinus	Residue valleculae + enetration/aspiration	Residue pyriform sinus + penetration/aspiration	Residue valleculae + pyriform sinus + penetration/aspiration
Liquid 5ml	54	10 (19%)	6 (11%)	2 (4%)	3 (6%)	4 (7%)	10 (19%)	2 (4%)	17 (31%)
Liquid 10ml	43	5 (12%)	5 (12%)	2 (5%)	2 (5%)	5 (12%)	4 (9%)	1 (2%)	19 (44%)
Liquid 20ml	34	3 (9%)	4 (12%)	1 (3%)	2 (6%)	4 (12%)	6 (18%)	2 (6%)	12 (35%)
Semisolid 5ml	55	20 (36%)	16 (29%)	0 (0%)	0 (0%)	6 (11%)	4 (7%)	0 (0%)	9 (16%)
Semisolid 10ml	55	7 (13%)	17 (31%)	4 (7%)	0 (0%)	10 (18%)	7 (13%)	0 (0%)	10 (18%)
Semisolid 20ml	53	7 (13%)	13 (25%)	2 (4%)	0 (0%)	13 (25%)	6 (11%)	0 (0%)	12 (23%)
Solid	44	14 (32%)	18 (41%)	2 (5%)	1 (2%)	6 (14%)	1 (2%)	0 (0%)	2 (5%)

Data are reported as absolute frequency and relative frequency (n/n patients tested)

FIGURE LEGEND

Figure 1. Distribution of MTP and tongue endurance in 55 patients with ALS

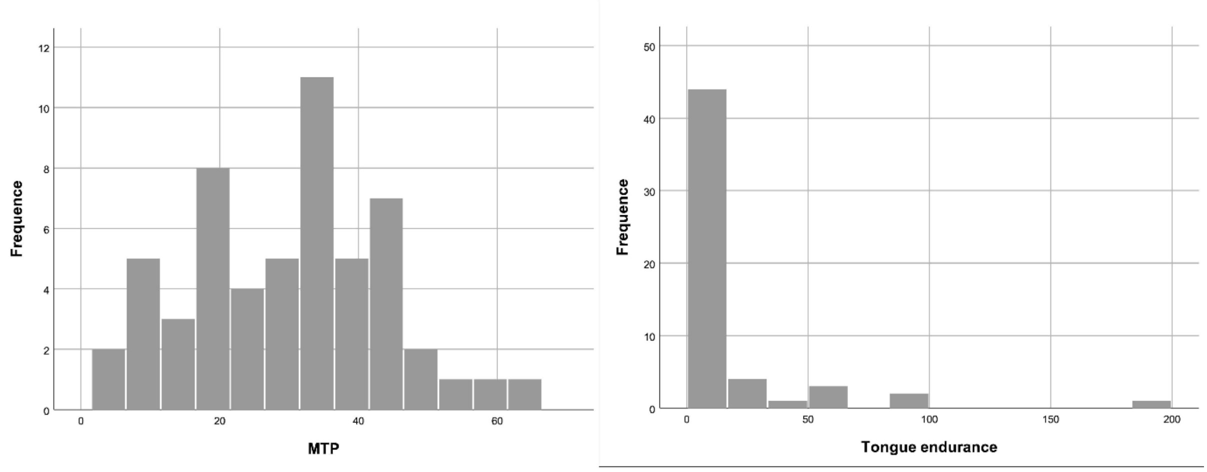
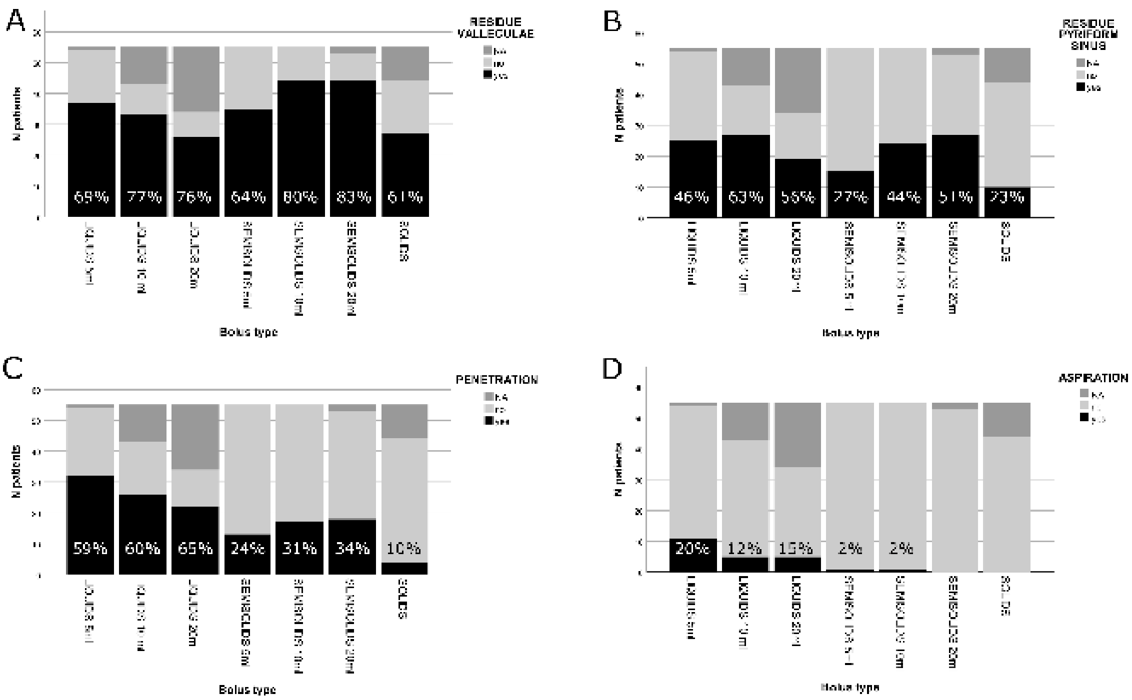


Figure 2. Frequency of findings of impaired safety (penetration/aspiration) and efficacy (residue) during FEES with different bolus consistencies and volumes



A. Residue in the valleculae; B. Residue in the pyriform sinus; C. Penetration; D. Aspiration. The relative frequency of residue, penetration, and aspiration reported in the figure was calculated as the number of patients exhibiting residue or penetration or aspiration divided by the number of patients tested with the bolus type.

LEGEND. NA = Bolus type not administered for safety reasons