

## Review articles

# Fiberoptic endoscopic evaluation of swallowing in patients with amyotrophic lateral sclerosis: an integrative literature review

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**ABSTRACT**

**Purpose:** to provide an integrative review of the current evidence on the fiberoptic endoscopic evaluation of swallowing performing procedures and analysis parameters in patients with amyotrophic lateral sclerosis.

**Methods:** the study question followed the PECO strategy, and the search was performed in Medline, Cochrane, Scopus, Lilacs, Web of Science, and CINAHL databases, using keywords and specific free terms. Two authors screened eligible articles published from 2013 to October 2021 and extracted data on fiberoptic endoscopic evaluation of swallowing performing procedures and analysis parameters in patients with amyotrophic lateral sclerosis.

**Literature Review:** of the 1,570 articles initially identified, 14 were eligible. There was no consensus on the consistency, volume, and type of food, utensils, sequence, and number of repetitions of each task during the exam. The analysis parameters, when described, were distinct. Although with different classification criteria, the observation of pharyngeal residue, laryngeal penetration, and laryngotracheal aspiration was included in all studies.

**Conclusion:** fiberoptic endoscopic evaluation of swallowing performing procedures and analysis parameters are not standardized in studies with amyotrophic lateral sclerosis patients.

**Keywords:** Motor Neuron Disease; Amyotrophic Lateral Sclerosis; Deglutition; Deglutition Disorders; Endoscopy

## INTRODUCTION

Motor neuron diseases (MND) are characterized by weakness and generalized muscle atrophy<sup>1</sup>. MND consists of four clinical syndromes that are classified according to the initial symptoms and are considered different manifestations of the same disease: progressive muscular atrophy (PMA), progressive bulbar palsy (PBP), primary lateral sclerosis (PLS), and amyotrophic lateral sclerosis (ALS)<sup>2,3</sup>. The most common subtype of MND is ALS<sup>4</sup>.

In ALS, when the first motor neuron (or upper motor neuron) is affected, there are muscle weakness, tendon reflexes, and abnormal reflexes, such as the Babinski sign. If the second motor neuron (or lower motor neuron) is affected, there are fasciculations, muscle atrophy and atony, and muscle weakness<sup>3</sup>. The denervation of muscle fibers, caused by gliosis replacement in neuronal cells, gradually atrophies the musculature and decreases its function<sup>3</sup>. Muscle weakness and atrophy are related to oropharyngeal dysphagia (OD)<sup>5</sup>.

The prevalence of OD in patients with ALS is up to 85%<sup>6</sup>. This symptom causes dehydration, malnutrition, choking, aspiration pneumonia, and even death due to compromised airway integrity<sup>5</sup>. Thus, early screening, clinical and instrumental assessment, and monitoring of oropharyngeal swallowing during the disease progression are critical to reducing pulmonary and nutritional risks that negatively impact the quality of life and general clinical conditions of ALS patients<sup>7</sup>.

The fiberoptic endoscopic evaluation of swallowing (FEES) is one of the gold standards to investigate the pharyngeal findings of swallowing<sup>8</sup>. FEES uses a flexible fiberscope introduced through the nose to visualize in detail the anatomy and physiology of swallowing, especially in the pharyngeal phase<sup>8,9</sup>. It enables the analysis of the characteristics, site, amount, and management of pooling residue, aspiration of secretions, solid or liquid foods before or after swallowing, and potential structural impairments<sup>8,9</sup>. The FEES is easy to perform and is more frequently available in medical facilities; over time, it has become a refined tool to be used in both the complete diagnosis of OD and the therapeutic process<sup>8,9</sup>.

Studies that used FEES to evaluate OD in patients with ALS aimed to identify, among other findings, delayed pharyngeal response, posterior oral spillage, nasal regurgitation, impaired pharyngeal transit,

vallecular and pyriform sinus residue, laryngeal penetration, and laryngotracheal aspiration<sup>3,10-12</sup>. Although FEES has proved to be appropriate to evaluate the anatomy and physiology of swallowing in patients with ALS<sup>13</sup>, the performing procedures and analysis parameters of the exam for these patients do not seem to be standardized, which is a limitation for reproducibility, multicentric studies, and clinical decision-making.

Therefore, the purpose of this study was to provide a general and integrative review of the current evidence on the FEES performing procedures and analysis parameters in patients with ALS.

## METHODS

This study is an integrative literature review, with the following six steps<sup>14</sup>: (1) definition of the research question; (2) definition of search terms; (3) selection of articles according to the inclusion and exclusion criteria; (4) data collection, data extraction, reading, and critical analysis of the articles; (5) interpretation and discussion of the results; and (6) synthesis of knowledge and presentation of the review.

### Stage 1: Definition of the research question

The research question for this review was based on the PECO question (Patient, Exposure, Comparison, and Outcomes, respectively). The first element of the strategy (P) consisted of patients with ALS; the second element (E) corresponded to FEES; the third element (C), equivalent to “comparison group”, was not applied in this review; and the fourth element (O) was the procedures for performing as well as the parameters for analyzing FEES. Therefore, the research question was defined as follows: “What is the current evidence on FEES performing procedures and analysis parameters in patients with ALS?”

### Stage 2: Definition of the search terms

The search was carried out by two independent researchers in Medline, Lilacs, Cochrane, Scopus, Web of Science, and CINAHL based on the combination of MeSH keywords and free terms (Chart 1). The search was initially performed in May 2019 and updated in October 2021.

**Chart 1** - Search strategies used in databases.

Database	Descriptors
CINAHL	TX «Fiberoptic endoscopic evaluation of swallowing» OR TX «Fiberoptic endoscopy evaluation of swallowing» AND TX «amyotrophic lateral sclerosis» OR TX «motor neuron disease»
Cochrane	(«Fiberoptic endoscopy evaluation of swallowing») OR («Fiberoptic endoscopic evaluation of swallowing») AND («motor neuron disease») OR («amyotrophic lateral sclerosis»)
Lilacs	(«fiberoptic endoscopy evaluation of swallowing») OR («fiberoptic endoscopic evaluation of swallowing») AND («motor neuron disease») OR («amyotrophic lateral sclerosis») AND ( db:(«LILACS»))
Pubmed/ Medline	(((((«Fiberoptic endoscopy evaluation of swallowing») OR («Fiberoptic endoscopic evaluation of swallowing»)) OR (FEES[Title])) OR (videoendoscopy[Title/Abstract])) OR («fiberoptic endoscopic examination»)) OR («endoscopic examination») OR («fiber-optic endoscopic evaluation of swallowing»)) OR («endoscopic»)) AND (((«amyotrophic lateral sclerosis»[MeSH Major Topic]) OR («motor neuron disease»[MeSH Major Topic])) OR («amyotrophic lateral sclerosis»)) OR («motor neuron disease»))
Scopus	(ALL ( «Fiberoptic endoscopy evaluation of swallowing» ) OR ALL ( «Fiberoptic endoscopic evaluation of swallowing» ) OR TITLE ( fees ) OR TITLE-ABS-KEY ( videoendoscopy ) OR ALL ( «fiberoptic endoscopic examination» ) OR ALL ( «endoscopic examination» ) OR ALL ( «fiber-optic endoscopic evaluation of swallowing» ) OR TITLE-ABS-KEY ( «endoscopic» ) AND ALL ( «amyotrophic lateral sclerosis» ) OR TITLE-ABS-KEY ( «motor neuron disease» ) )
Web of Science	((ALL=(«Fiberoptic endoscopic evaluation of swallowing»)) OR ALL=(«Fiberoptic endoscopy evaluation of swallowing» )) AND ((ALL=(«motor neuron disease»)) OR ALL=(«amyotrophic lateral sclerosis»))

### Stage 3: Article selection

The inclusion criteria were scientific articles addressing the assessment of swallowing with FEES in individuals with ALS, regardless of clinical design, published in English, Portuguese, or Spanish between January 2013 and October 2021.

The studies were included from 2013 until present because in 2012 the European Federation of Neurological Societies (EFNS) guidelines were published and highlighted the dysphagia management in ALS<sup>15</sup>. The EFNS guidelines are constantly cited worldwide, including the most recent Clinical Protocol and Therapeutic Guidelines of Amyotrophic Lateral Sclerosis, published by the Brazilian Ministry of Health in 2021<sup>16</sup>.

Studies were excluded if they were review articles of any type, editorials, letters to the editor, and annals of congress. They were also excluded if other diseases were included along with the ALS patients or if the manuscript did not describe at least the FEES performing procedures or analysis parameters.

### Stage 4: Data collection, data extraction, reading, and critical analysis of the articles

After the initial data collection from the databases, duplicate articles were deleted. Subsequently, the articles were selected by two reviewers, independently, by reading the titles and abstracts. The full texts of the selected articles were read by the same reviewers. A third reviewer was consulted in cases of divergence. Eligible articles had the following data extracted to construct the analysis matrix: author, year of publication, the country where the study was carried out, study purpose, sample characteristics, FEES procedures (food consistency and volume; sequence and number of repetitions of each task; utensils; type of food), and analysis parameters.

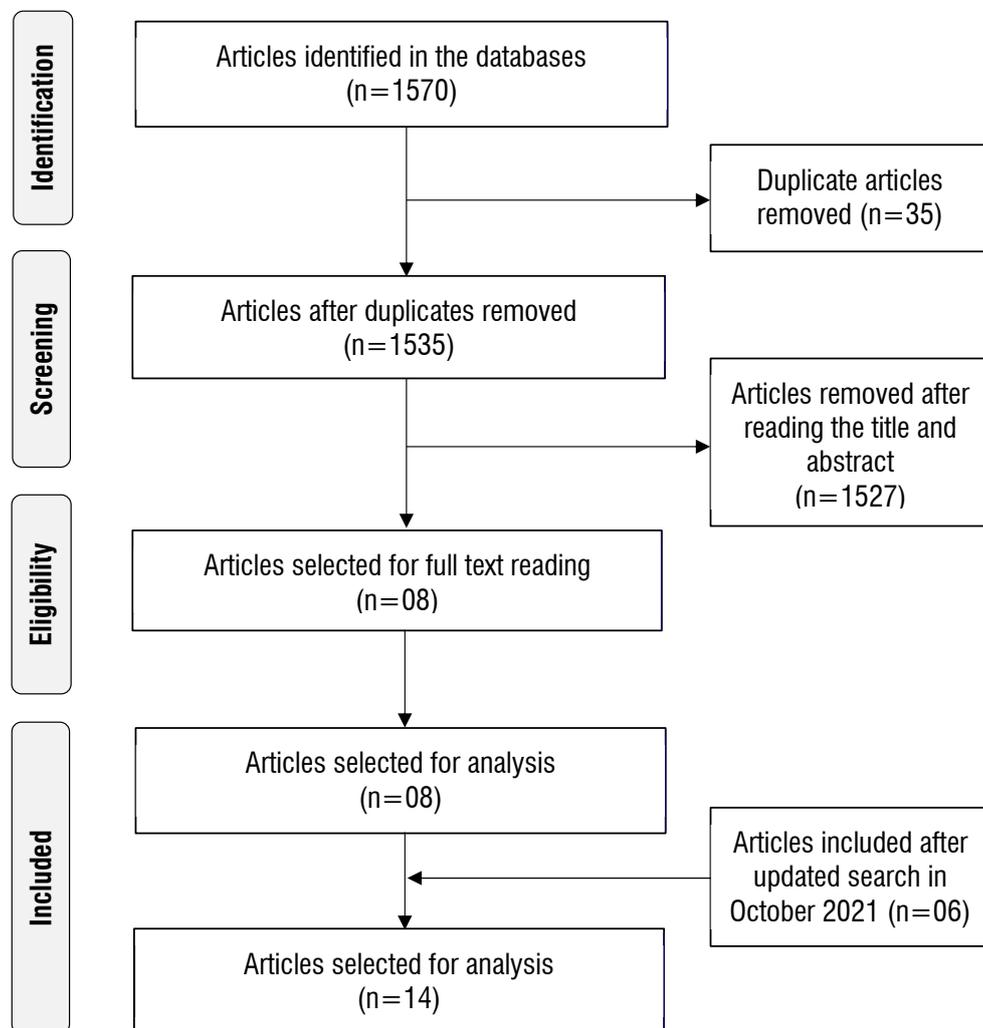
### Stages 5 and 6: Interpretation and discussion of the results/synthesis of knowledge and presentation of the review

The results were submitted to descriptive and integrative analyses, followed by a discussion to synthesize the knowledge produced by the studies and presentation of the review in this article.

## LITERATURE REVIEW

The search initially retrieved 1,570 articles, 14 of which<sup>17-30</sup> were selected for analysis after applying the eligibility criteria, as shown in Figure 1.

The publications selected were analyzed according to the variables of interest of this review, and the analysis matrix is shown in Charts 2 and 3.



**Figure 1.** Flowchart of the selection of studies on fiberoptic endoscopic evaluation of swallowing in patients with amyotrophic lateral sclerosis

**Chart 2.** Objective, sample characteristics, and main outcomes of the studies that used fiberoptic endoscopic evaluation of swallowing in patients with amyotrophic lateral sclerosis

Author, year, location	Objective	Sample characteristics	Main outcomes
D'Ottaviano, Filho, Andrade, Alves, Rocha, 2013, Brazil <sup>17</sup>	To evaluate the oral preparatory and oral and pharyngeal phases of swallowing in patients with ALS using FEES.	11 individuals: 5 women and 6 men.  Mean age: 61.7 ± 7.2 years  Initial symptoms: 9 bulbar and 2 spinal	- All patients undergoing FEES presented some disordered swallowing phase (63.6% in the oral preparatory phase and 100% in the oral and pharyngeal phases), regardless of the consistency of the food and the presence of a nasogastric tube. - Ten patients (90.9%) presented tracheal aspiration of food in liquid consistency during the pharyngeal phase of swallowing.
Ruopollo, Schettino, Frasca, Giacomelli, Prosperini, Cambieri, et al., 2013, Italy <sup>18</sup>	To characterize swallowing deficits in patients with ALS.	49 individuals: 15 women and 34 men  Mean age: 63.7 ± 10.9 years  Initial symptoms: 14 bulbar and 35 spinal	- There was a correlation between tongue muscle deficit and pharyngeal residue ( $r = 0.31$ ; $p = 0.03$ ) and between tongue muscle deficit and laryngeal penetration ( $r = 0.53$ ; $p < 0.001$ ); - The cough reflex was impaired in 10 patients (20.4%) but without a correlation with pharyngeal residue or laryngeal penetration; - Of the 26 longitudinally analyzed patients, nine (34.6%) presented with dysphagia.
Luchesi, Kitamura, Mourão, 2014a, Brazil <sup>19</sup>	To identify factors associated with the severity of dysphagia in patients with ALS.	49 individuals: 22 women and 27 men  Mean age: not reported  Initial symptoms: not reported	- Odynophagia was the only factor associated with moderate or severe dysphagia, classified according to the FEES result. - Based on FEES, the sample was divided according to the classification of the degree of dysphagia: 25 in group 1 (6.1% - normal swallowing and 44.9% - mild dysphagia); 24 in group 2 (40.8% - moderate dysphagia and 8.1% - severe dysphagia).
Luchesi, Kitamura, Mourão, 2014b, Brazil <sup>20</sup>	To analyze the clinical characteristics associated with worsened swallowing function and the need for an alternative feeding route in patients with ALS.  Patients followed up for 5 years and re-evaluated every 3 months.	33 individuals: 15 women and 18 men.  Mean age: not reported  Initial symptoms: 5 bulbar and 28 spinal	- The incidence of worsened swallowing function was 84.8% and of indication for an alternative feeding route was 36.4%. - At the 20th month of observation, there was a 60% probability of worsening of swallowing in cases of spinal onset and 40% in those with bulbar onset. - The swallowing worsened faster in older individuals and cases of bulbar onset. Indication of an alternative feeding route was associated with symptom onset in older patients and with a shorter disease duration.
Fattori, Siciliano, Mancini, Bastiani, Bongioanni, Caldarazzo Ienco E, et al, 2016, Italy <sup>21</sup>	To evaluate the possible relationship between the severity of ALS and premature oral spillage, pharyngeal residue after swallowing, and aspiration observed using FEES.	202 individuals: 95 women and 107 men.  Mean age: 64.68 ± 11.12  Initial symptoms: 66 bulbar and 136 spinal	- There was a significant correlation between the results of the functional scales and the FEES parameters for all the food consistencies. - There was a significant difference between the functional scale and the pharyngeal residue parameter, regardless of the bolus used in cases of spinal onset and the liquid consistency in cases of bulbar onset. - The score on the residue scale was worse in the presence of aspiration. - The score on the residue scale was worse in the presence of posterior oral spillage for all consistencies in individuals with bulbar onset.
Ruopollo, Onesti, Gori, 2016, Italy <sup>22</sup>	To investigate the correlation between laryngeal sensitivity and type of disease onset (bulbar or spinal).	114 individuals: 42 women and 72 men.  Mean age: 64 ± 10 years  Initial symptoms: 56 bulbar and 58 spinal	- The score for the pharyngeal residue, penetration, and aspiration scales was worse in cases of bulbar-onset ALS. - Co-occurrence of impairment in the oral and pharyngeal swallowing phases was more frequent in cases of bulbar-onset ALS and in cases in which there was a laryngeal sensory deficit. - Laryngeal sensory deficit was present in 33% of the sample, being more frequent in cases of bulbar-onset ALS. - All individuals with laryngeal sensory deficits were dysphagic and had worse scores in the pharyngeal residue, penetration, and aspiration scales than those without sensory deficits.
Onesti, Schettino, Gori, Schettino, Frasca, Biasiotta A, et al, 2017, Italy <sup>23</sup>	To describe the different clinical characteristics associated with dysphagia in patients with ALS, to investigate the impact of dysphagia on the diet and the use of riluzole; to analyze the risk of dysphagia in patients unable to recognize symptoms and to evaluate the effect of riluzole on survival when administered in an unusual way.	145 individuals: 55 women and 90 men.  Mean age: 62.2 ± 11.7 years.  Initial symptoms: 57 bulbar and 88 spinal. Patients were followed up for 9 to 110 months (mean of 20.0 ± 18.3 months).	- Oropharyngeal dysphagia was diagnosed in 58.6% of patients at baseline and 82.8% at the end of follow-up, being more frequent in those with bulbar-onset ALS. - Impairment in laryngeal adductor reflex was more frequent in those with bulbar-onset ALS. - Progressive worsening was observed in the penetration and aspiration scale during follow-up; and 8% of patients diagnosed with dysphagia by FEES did not perceive the disorder.
Gozzer, Cola, Onofri, Merola, Silva, 2019, Brazil <sup>24</sup>	To compare the FEES findings of oropharyngeal swallowing on distinct food consistencies in ALS.	20 individuals: 7 women and 13 men.  Mean age: 57 years.  Initial symptoms: not reported	- No impaired laryngeal sensitivity was found in this population. - There was no statistically significant difference in posterior oral spillage, penetration, and/or aspiration between food consistencies. - There was a statistically significant difference only related to pharyngeal residues of the thickened liquid and pureed consistency.

Author, year, location	Objective	Sample characteristics	Main outcomes
Pizzorni, Ginocchio, Bianchi, Feroldi, Vedrodyova, Mora, et al., 2020, Italy <sup>25</sup>	To investigate the association between tongue pressure measurements (maximum tongue pressure and tongue endurance) and instrumental findings of OD (penetration, aspiration, residue) in patients with ALS with a variety of consistencies and bolus volumes. The secondary aim of the study was to characterize OD in patients with ALS using different bolus types.	55 individuals: 25 women and 30 men.  Mean age: 67.8 years. Initial symptoms: 39 spinal onset and 16 bulbar onset.	- 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 with 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 semisolids (24%-34% of tested patients) and solids (10% of tested patients). - Aspiration occurred in < 20% of the patients, mostly with liquids.
Printza, Boziki, Triaridis, Kiouisi, Arnaoutoglou, Constantinidis, et al, 2020, Greece <sup>26</sup>	To evaluate tongue strength measurements, dysphagia questionnaire, the presence of pharyngeal secretions, and FEES findings in dysphagia management in ALS.	25 individuals: 13 women and 12 men.  Mean age: 63.92 years.  Initial symptoms: Not reported	- At enrollment, 60% of the patients had no secretions in the hypopharynx (Murray secretion scale 0). Half of the re-examined patients deteriorated from minimal secretions at enrollment to laryngeal vestibule secretions at follow-up. - In FEES, 28% of the patients were aspirators at enrollment, whereas most patients had no or minimal penetration (64% had a Penetration-Aspiration Score equal to one). - The presence of pharyngeal secretions and other endoscopic findings can guide the identification of patients with ALS at risk of inefficient and unsafe swallowing and support management decisions based on the principles of precision medicine for this population of patients who show characteristic phenotypic variability.
Mezzedimia, Vincib, Gianninic, Cocca. 2020, Italy <sup>27</sup>	To evaluate the possible correlation between dysphonia and dysphagia in ALS patients and whether deterioration of speech ability is isolated or associated with a worsening of dysphagia.	24 individuals: 6 women and 18 men.  Mean age: male - 69.9 years. Female - 68.5 years.  Initial symptoms: Not reported	- Preliminary findings indicate that the reduction in the maximum fundamental frequency is associated with dysphagia progression. Thus, monitoring the vocal parameters could help early rehabilitation.
Borges, Velasco, Ramos, Imamura, Roldão, Petrillo, et al, 2021, Brazil <sup>28</sup>	To compare the results of tongue strength and endurance measured by the Iowa oral performance instrument with the findings of the fiberoptic endoscopic evaluation of swallowing examination in patients affected by amyotrophic lateral sclerosis.	25 individuals: 10 women and 15 men.  Mean age: with dysphagia - 57.08 years. Without dysphagia - 52.00 years.  Initial symptoms: 20 spinal onset and 5 bulbar onset.	-There was also no statistically significant association between age, gender and time of diagnosis and the presence of dysphagia at the FEES, and also the type of disease, appendicular and bulbar. -Nineteen patients had impaired tongue strength test and seven had impaired endurance test. There was a statistically significant association between maximum tongue isometric pressure and dysphagia as well as endurance and dysphagia. - There was a strong negative correlation between the degree of dysphagia and the maximum pressure measured.
Adamske, Heyduck, Weidenmüller, Görlicke, Frank, Olthoff, 2021, Germany <sup>29</sup>	To evaluate bulbar motor dysfunction in patients suffering from ALS compared to a healthy reference group.	10 individuals: 7 women and 3 men.  Mean age: 69.3 years.  Initial symptoms: 4 spinal onset and 6 bulbar onset.  20 health individuals: 10 women and 10 men.  Mean age: 42.7 years.	-Sydney Swallow Questionnaire: in ALS patients a total mean ( $\pm$ SD) score of 399 ( $\pm$ 391) was consistent with impaired swallowing. The mean ( $\pm$ SD) score of healthy volunteers was 60 ( $\pm$ 41) and was significantly different from ALS patients ( $p < .001$ ). -FEES: Penetration and aspiration was evaluated with a mean ( $\pm$ SD) of 1.1 ( $\pm$ 0.3) for the patient group versus 1.0 ( $\pm$ 0.0) for healthy volunteers ( $p > .05$ ). Retention was scored with a mean of 1.0 ( $\pm$ 1.1), for the patient group versus 0.1 ( $\pm$ 0.2), for healthy volunteers. -Manometry: maximal pressure mean ( $\pm$ SD) was $-96.7 (\pm 86.0)$ mmHg in ALS patients and $-260.3 (\pm 120.7)$ mmHg in healthy group.
Mariani, Ruoppolo, Cilfone, Cocchi, Preziosi Standoli, Longo, et al, 2021, Italy, <sup>30</sup>	To investigate the progression of dysphagia in a cohort of ALS patients and to analyse whether there are variables linked to a faster progression of dysphagia and faster indication of PEG placement.	108 individuals: 58 women and 50 men  Mean age: 66.95 years  Initial symptoms: 40 spinal onset and 68 bulbar onset.	- At the first FEES examination, 27 patients had no penetration/aspiration, 77 had penetration, and only four patients had aspiration. - All patients in the sample experienced dysphagia onset, but only 87 achieved PEG indication, thereby 21 patients were not included in follow up due to death. - Patients with bulbar onset had higher monthly person-time incidence rates for PEG indication from symptom onset at 4.29% and 4.36%, respectively, compared to patients with spinal onset (2.64%).

ALS - amyotrophic lateral sclerosis; FEES - fiberoptic endoscopic evaluation of swallowing; OD – oropharyngeal dysphagia; PEG – percutaneous endoscopic gastrostomy; SD – standard deviation

**Chart 3.** Parameters and analysis procedures of fiberoptic endoscopic evaluation of swallowing in patients with amyotrophic lateral sclerosis

Author, year, location	Consistency and volume of food	Sequence and number of offers	Utensil	Type of food	Observed parameters	Analysis procedures
D'Ottaviano, Filho, Andrade, Alves, Rocha, 2013, Brazil <sup>17</sup>	Thickened - 5 and 10 ml (100 ml of water + 2 spoons of thickener); Liquid - 5 and 10 ml; Solid (½ cracker)	Not reported	Spoon	Water, food thickener, cracker; blue dye	- Posterior oral spillage; pharyngeal residue; laryngeal penetration; tracheal aspiration; the moment of tracheal aspiration; response to tracheal aspiration.  * The authors defined each parameter.	Impairment of the oral preparatory phase: observation of posterior oral spillage of food; impairment of the oral phase: the presence of residue in valleculae; and impairment of the pharyngeal phase of swallowing: the presence of pharyngeal residue in pyriform sinus.
Ruopollo, Schettino, Frasca, Giacomelli, Prosperini, Cambieri, et al., 2013, Italy <sup>18</sup>	Liquid - 3 ml; Thickened - 2 ml	Not reported	Not reported	Water, dye	- Premature pharyngeal spillage of the food bolus; pharyngeal residue; laryngeal penetration.  * The authors did not define each parameter.	Not reported
Luchesi, Kitamura, Mourão, 2014a, Brazil <sup>19</sup>	Liquid - 3 ml and 7 ml; Nectar - 3 ml and 7 ml Honey - 3 ml and 7 ml Pudding - 3 ml and 7 ml Solid - (½ cornstarch biscuit)	1 - Liquid and nectar in 4 offers: 3 ml, 3 ml, 7 ml, and 7 ml 2 - Honey in 4 offers: 3 ml, 3 ml, 7 ml, and 7 ml; 3 - Pudding in 2 tablespoons; 4 - Solid: ½ cornstarch biscuit.	20 ml in syringe and tablespoon	Lemonade, food thickener, cornstarch biscuit; green dye.	- Salivary stasis; - Pharyngeal residue; - Laryngeal sensitivity; - Food aspiration.  * The authors did not define each parameter.	The results were judged by two speech therapists and an otorhinolaryngologist, who classified dysphagia as level 0 to 3 according to the scale by Macedo Filho, Gomes, and Furkim (2000).  Individuals were divided into two groups according to dysphagia severity.
Luchesi, Kitamura, Mourão, 2014b, Brazil <sup>20</sup>	Liquid - 3 ml and 7 ml; Nectar - 3 ml and 7 ml Honey - 3 ml and 7 ml Pudding - 3 ml and 7 ml Solid - (½ cornstarch biscuit)	1 - Liquid and nectar in 4 offers: 3 ml, 3 ml, 7 ml, and 7 ml 2 - Honey in 4 offers: 3 ml, 3 ml, 7 ml, and 7 ml; 3 - Pudding in 2 tablespoons; 4 - Solid: ½ biscuit.	20 ml syringe and tablespoon	Lemon juice, food thickener, cornstarch biscuit; green food dye	Penetration and/or food aspiration.  * The authors defined each parameter.	The FEES results were classified as the presence or absence of penetration and/or aspiration. The authors used FEES results to classify individuals according to the Functional Oral Intake Scale.
Fattori, Siciliano, Mancini, Bastiani, Bongioanni, Caldarazzo Ienco E, et al, 2016, Italy <sup>21</sup>	Liquid - 5 ml Semisolid - 5 ml Solid - ¼ cup	Not reported	Not reported	Water, gelatin, cream cracker, and methylene blue.	The pharyngeal residue after swallowing; premature oral spillage; penetration and/or aspiration.  * The authors did not define each parameter.	The Pharyngeal Residue Severity Scale was used for the analysis of pharyngeal residue after swallowing; premature oral spillage and penetration or aspiration were classified as present or absent.
Ruopollo, Onesti, Gori, 2016, Italy <sup>22</sup>	Not reported	Not reported	Not reported	Not reported	Laryngeal sensitivity; Food residue.  * The authors did not define each parameter.	The PAS scale and the Pharyngeal Residue Severity Scale.
Onesti, Schettino, Gori, Schettino, Frasca, Biasiotta A, et al, 2017, Italy <sup>23</sup>	Puree – 5 ml, 10 ml, and 20 ml Liquid – 5 ml, 10 ml, and 20 ml.	Not reported	Not reported	Not reported	Laryngeal adductor reflex; post-swallowing pharyngeal residue; penetration/ aspiration.  * The authors did not define each parameter.	The PAS scale and the Pharyngeal Residue Severity Scale.

Author, year, location	Consistency and volume of food	Sequence and number of offers	Utensil	Type of food	Observed parameters	Analysis procedures
Gozzer, Cola, Onofri, Merola, Silva, 2019, Brazil <sup>24</sup>	Puree – 5ml Thickened liquid – 5ml Thin liquid – 5ml	Not reported	Not reported	Not reported	Posterior oral spillage, pharyngeal residue; penetration/ aspiration. and laryngeal sensitivity.	Posterior oral spillage was defined as the occurrence of anticipated oral spillage of the food bolus towards the hypopharynx beyond the area where the pharyngeal response should occur. Pharyngeal residues were defined as the permanence of contrasting material in the valleculae and pyriform sinus after the second deglutition. Laryngeal penetration was defined as the entire material being located above the vocal fold and laryngotracheal aspiration was defined as the passage of the material below the level of the vocal fold.
Pizzorni, Ginocchio, Bianchi, Feroldi, Vedrodyova, Mora, et al., 2020, Italy <sup>25</sup>	Liquid – 5ml, 10ml, and 20ml Semisolid – 5ml, 10ml, and 20ml Solid – half cracker.	liquids (3 × 5 ml, 3 × 10 ml, 3 × 20 ml), then semisolids (3 × 5 ml, 3 × 10 ml, 3 × 20 ml), and solids.	Not reported	Milk, apple sauce, and cracker.	Pharyngeal residue, penetration, and aspiration.	The PAS scale and the Yale Pharyngeal Residue Severity Rating Scale (>2 score = suggestive of the presence of clinically relevant residue)
Printza, Boziki, Triaridis, Kiouisi, Arnaoutoglou, Constantinidis, et al, 2020, Greece <sup>26</sup>	Liquids, semisolids, and solid Food. Volume was not reported.	Not reported	Not reported	Not reported	Velopharyngeal sufficiency, pharyngeal squeeze, vocal cord movement/ glottal closure, and pharyngeal-laryngeal secretions	The PAS scale and the Yale Pharyngeal Residue Severity Rating Scale. Velopharyngeal sufficiency, pharyngeal squeeze, and vocal cord movement were rated as full, weak, or absent, and secretions were rated according to the Murray secretion scale from 0 to 3.
Mezzedimia, Vincib, Gianninic, Cocca. 2020, Italy <sup>27</sup>	Thin Liquid - 5 ml. Semisolid - 5 ml Solid.	Not reported	Thin Liquid – spoon and cup. Semisolid – spoon.	Not reported	Pharyngeal residue in valleculae and pyriform recesses.	The Pooling-score.
Borges, Velasco, Ramos, Imamura, Roldão, Petrillo, et al, 2021, Brazil <sup>28</sup>	Liquid - 3, 5 and 10 mL Thickened liquid - 3, 5 and 10 mL Semi-solid - 3, 5 and 10 mL Solid - ¼ of a cracker.	Not reported.	Not reported.	Not reported for liquids and semi-solid. Cracker for solid.	Pharyngeal residue, penetration and aspiration.  * the authors did not provide a definition for each parameter.	-The degree of dysphagia was divided into mild, moderate and severe, according to the classification by Macedo Filho, Gomes, and Furkim (2000). The result was categorized as normal (absence of dysphagia) and altered (presence of mild, moderate or severe dysphagia).
Adamske, Heyduck, Weidenmüller, Göricke, Frank, Olthoff, 2021, Germany <sup>29</sup>	Honey thickness – 5ml.	An oral bolus of a teaspoon of green colored thickened water was applied to ensure a clear contrast to the tissues of the oropharyngeal tract.	Teaspoon	Water and green dye.	Retention, Penetration and aspiration.  * the authors did not provide a definition for each parameter	In addition to the Penetration-aspiration scale (score 1 to 8), the parameters leaking and retention (scores 0 to 3) were determined.
Mariani, Ruoppolo, Cifone, Cocchi, Preziosi Standoli, Longo, et al, 2021, Italy, <sup>30</sup>	Thin Liquid - <5ml, 5ml and 10ml. Soft Liquid – 10ml.	1. Two bolus of 5 ml soft liquid (yoghurt) 2. Bolus of <5 ml, 5 ml and 10 ml of thin liquid (milk) Ask the patient to hold the bolus in their oral cavity and then each time to swallow upon the command of the operator according to the Langmore procedure.	. Not reported.	Yoghurt, Milk.	Penetration and aspiration	The PAS scale (absence of penetration/ aspiration, score 1; presence of penetration, score 2–5; and presence of aspiration, score 6–8). The cut-off point for the diagnosis of dysphagia was PAS ≥ 3. The cut-off point for PEG indication was PAS ≥ 6. Indeed, the indication for PEG placement was undertaken when the risk of aspiration was evident and urgent measures for alternative feeding had to be initiated to prevent the patient from developing further complications.

ALS - amyotrophic lateral sclerosis; FEES - fiberoptic endoscopic evaluation of swallowing; PAS - Penetration-Aspiration Scale; PEG – percutaneous endoscopic gastrostomy.

Chart 2 shows that seven of the 14 studies were conducted in Italy<sup>18;21;22;23;25;27;29</sup> and five, in Brazil<sup>20;22;23;27</sup>. The studies included in the review aimed to understand the pathophysiology of OD in patients with ALS using FEES; however, only five<sup>21;22;25-27</sup> correlated the FEES outcomes with characteristics of the disease. The study of FEES protocol properties was not the focus of any of the 14 studies.

The sample size ranged from 11 to 202 patients, always with individuals of both sexes. The mean age, when reported, was between 61.7 and 69.9 years. Only four studies<sup>16;21;23;24</sup> did not mention the number of patients with bulbar or spinal onset symptoms (Chart 2).

Chart 2 shows that the main FEES-related conclusions of the studies indicated that patients with ALS have swallowing disorders, with the presence of pharyngeal residue, laryngeal penetration, or laryngo-tracheal aspiration, and sensory impairment. In addition, advanced age, onset symptoms (bulbar or spinal), and functional scales<sup>31;32</sup> were associated with FEES parameters.

The FEES procedures for performance and analysis parameters are shown in Chart 3. There was a wide variation in food consistency and volume offered during the exam. The sequence and number of trials were mentioned in only five studies<sup>19;20;25; 29; 30</sup>, and the utensils used for offering food were reported in five studies (20-ml syringe and spoon<sup>19;20</sup>, only spoon<sup>17,29</sup>, and spoon and cup<sup>27</sup>). Six studies<sup>22-24;26;27;28</sup> neither reported the type of food nor made it clear whether they used any type of dye. In the remaining eight studies<sup>17-21;25;29;30</sup>, this information was provided but it was not standardized.

Regarding the FEES parameters analyzed during the exam, penetration and aspiration appeared in all protocols, except for one study that considered only pharyngeal residue<sup>27</sup>. The pharyngeal residue is also a common parameter for FEES analysis and was not found in only three studies<sup>20;29;30</sup>. Four studies<sup>17;18;21;24</sup> mentioned premature oral spillage of the food bolus to the pharynx, and another four studies observed laryngeal sensitivity<sup>19;21-24</sup>.

Lastly, there was no consensus on how to analyze FEES parameters. One study<sup>18</sup> did not describe how FEES was analyzed. Three studies<sup>17;24;27</sup> considered the pathophysiological criteria visualized in FEES to define impairment in each swallowing phase. Two studies<sup>19;28</sup> used FEES data to classify the severity of OD according to a Brazilian scale<sup>33</sup>. Three studies<sup>20;25;26</sup>

classified patients in the Functional Oral Intake Scale (FOIS)<sup>34</sup> by the presence or absence of penetration and/or aspiration in the FEES. Four studies<sup>21-23;27</sup> used the Pooling-Score<sup>28</sup> for pharyngeal residue, and others<sup>22;23;25;26;28;29;30</sup> used the Penetration-Aspiration Scale<sup>26</sup>.

The performance of instrumental evaluation of swallowing during the investigation of OD is a fundamental step to diagnose dysphagia and plan these patients' rehabilitation, regardless of the etiology of the underlying disease. However, the absence of validated FEES protocols for such investigations precludes the performance of multicenter studies or studies with stronger scientific evidence<sup>35</sup>.

A recent systematic review identified the absence of standardized FEES protocols for the adult population with neurological diseases<sup>36</sup>. However, it is essential to understand that ALS patients have specific swallowing characteristics compared to other neurological diseases, such as Parkinson's disease or myasthenia gravis due to the different pathophysiology<sup>5</sup>.

Only two studies<sup>21;22</sup> used FEES protocols to establish relationships between swallowing and other variables in ALS. The other studies<sup>17-20;23-30</sup> only described the swallowing phases in ALS using FEES. Considering that ALS is a disease in which the oral phase of swallowing is impaired, there were expected to be few studies developed with this population using FEES. This may also explain why few research groups were interested in using FEES to investigate swallowing in ALS, considering that the studies were mostly concentrated in only two countries: Italy and Brazil. It is important to highlight that FEES is considered more sensitive in the investigation of the pharyngeal phase, including the detection of pharyngeal residue because it allows better visualization of the pharyngeal and laryngeal sites<sup>37</sup>. Also, it does not expose patients to radiation, and it is easier for health services to have access to than videofluoroscopy<sup>38,39</sup>.

Regarding the sample profile, most were males in eleven studies<sup>17-25;27;28</sup>. ALS is more frequent in males, although some studies suggest an increase in the number of cases of ALS in females<sup>40,41</sup>. The mean age of the patients in the studies ranges between 61.7 and 69.9 years; however, two studies did not report this variable<sup>19,20</sup>. Although the mean age at onset of ALS in Brazil is 57 years, it is between 40 and 70 years in Europe and North America<sup>40,41</sup>. Moreover, the mean age reported in the studies is related to the individual

in the evaluation period, which may or may not have coincided with the disease onset.

OD is a symptom that can manifest at disease onset, especially in individuals with bulbar-onset ALS<sup>42</sup>, and can be diagnosed using FEES. The findings of this review revealed that OD can be subclinical, as described by two studies<sup>17,23</sup>. Thus, it is important to investigate OD in this population via FEES as a routine procedure in the monitoring of patients with ALS, beginning with symptom onset, as early detection can significantly help control the risks associated with OD<sup>30</sup>.

Finally, OD was more frequent in individuals with bulbar onset in six studies<sup>20-23,25,26</sup>. One study<sup>27</sup> investigated only patients with bulbar onset. In the bulbar-onset type, OD and dysarthria are the main signs and symptoms initially presented by patients. This occurs because the motor nuclei of cranial nerves IX, X, XI, and XII and the corticobulbar tract undergo progressive degeneration<sup>43</sup>. Thus, individuals with bulbar-onset ALS have a higher frequency of OD, in whom it may also progress more rapidly.

The findings showed that there was not a standardized protocol on FEES-related aspects in ALS<sup>17-30</sup>. There was a wide variation both in terminology and standardization of food volume and consistency. In the study that created the FEES method, the authors recommended using 5 and 10 ml of liquid and 5 ml of puree<sup>8</sup>; however, there is no description of the formula for this standardization. Only one article<sup>17</sup> described the formula and only one article referred to the use of the International Dysphagia Diet Standardization Initiative (IDDSI)<sup>24</sup>. In addition, the foods used in FEES varied significantly, including thickened liquid, gelatin, lemon juice, milk, apple sauce, cornstarch biscuit, or cracker<sup>17,19-21,25,29,30</sup>.

The standardization of the consistency and type of food used to evaluate oropharyngeal swallowing should consider that the oral cavity is a sensory organ. In the oral cavity, some pairs of cranial nerves identify food textures, flavors, and temperatures<sup>44</sup> – and the identification of these characteristics provides specific reactions, such as chewing solids or maintaining muscle control for drinking liquids. Thus, the food types and flavors modify the swallowing dynamics<sup>44</sup>. In addition to these foods, others can be observed in several studies, demonstrating the lack of standardization of the offered type of food, not only regarding FEES in ALS<sup>12,13,45,46</sup>.

Only five studies<sup>17,19,20,27,29</sup> reported the type of utensil used to provide different food consistencies and

volumes during FEES. Two of these used a syringe<sup>19,20</sup> and three<sup>17,27,29</sup> used a spoon. Although supplying food using a syringe allows accurate volume control, this method impairs the neuromotor adjustments of the swallowing center control because, in the daily and natural process of eating, the individual uses a spoon or a cup. Conversely, serving food on a spoon or in a cup, although ordinary, can change the exact volume to be offered. In any case, few studies defined and reported the type of utensil used.

Only five studies<sup>19;20;25;29;30</sup> reported the sequence and number of trials, all coming from the same research group. Patients with ALS may have different oropharyngeal swallowing characteristics resulting in different trials due to muscle weakness and consequent adaptations in movement patterns<sup>47</sup>. Both the sequence and the number of trials may influence the vallecular or pyriform sinus residue accumulation, and the residue observed in a second or third offer may be originated from the first food offer. Thus, all dysphagic populations with severe muscle weakness, which includes patients with ALS, should undergo swallowing tests using food consistencies with lower risks of residue formation. Also, the number of swallows and sub-swallows should be counted as a predictive risk factor for aspiration. Thus, minimizing the accumulation of residue early in the exam would allow a more accurate investigation of swallowing biomechanics.

The use of blue or green dye for liquids is a technique derived from FEES exams, intended to help visualize the pharyngeal findings; notably, there is a consensus regarding this aspect of FEES<sup>48-51</sup>. Nevertheless, eight studies<sup>22-27;28;30</sup> did not mention or discuss this procedure. Five studies<sup>17-20; 29</sup> reported the use of blue or green dye during trials, and one study<sup>21</sup> used methylene blue, showing that there is no standardization even for this parameter.

One of the aspects of FEES protocols for any underlying disease with OD is the selection of the parameters to be investigated, which are usually posterior oral spillage, pharyngeal residue, laryngeal penetration, and laryngotracheal aspiration<sup>12</sup>. However, this review showed that in FEES protocols for ALS, there was no consensus regarding the observed parameters. Laryngeal penetration and laryngotracheal aspiration were the only parameters in almost all protocols<sup>17-26</sup>, and only one study<sup>20</sup> did not mention pharyngeal residue. It seems natural to find these parameters in almost all studies protocols because FEES is an exam to investigate the pharyngeal phase of swallowing.

Moreover, the studies on OD in ALS are more evidently concerned with the safety than the efficiency of oropharyngeal swallowing. Although FEES has limitations in investigating biomechanical events prior to the pharyngeal phase of swallowing, three studies selected in this review<sup>17,18,21</sup> analyzed the posterior oral spillage; however, the parameter definition and how it was evaluated were not consensual.

Regarding the analysis procedures, there was no consensus on scales or criteria for the analysis of exam results. Nine<sup>19,21-23,25,26;28;29;30</sup> of the 13 studies<sup>17,19-24,27;28;29;30</sup> that described FEES analysis procedures included at least one previously published scale. There were also those using present/absent criteria for different FEES analysis parameters<sup>17,20,21</sup>. This variability greatly impairs the interpretation of FEES results and the reproducibility of the protocols, minimizing the chances of good-quality multicenter studies.

The FEES performance and analysis protocols for individuals with ALS are heterogeneous. The only aspects common to all the protocols are the search for pharyngeal residue, laryngeal penetration, and laryngotracheal aspiration. Notably, the absence of FEES standardization is not restricted to ALS patients; several other studies in populations with myasthenia gravis<sup>51</sup>, Parkinson's disease<sup>52</sup>, stroke<sup>38;53;54</sup>, and so forth<sup>55</sup> are also performed with different protocols<sup>37,48</sup>.

This study has some limitations. There are no available specific MeSH terms for FEES. Therefore, it was necessary to include free terms into the search strategy. In addition, the results did not include the gray literature and the analysis of the methodological quality of the articles was not performed – although it is not a requirement for integrative literature reviews.

The findings of this review could contribute to a broad reflection on the relevance of standardizing FEES assessments. A consensus would be relevant to improve the reproducibility of FEES protocols and improve multicenter studies. Standardization could encourage safe performance and appropriate management of OD progression in ALS patients. Accurate and specific diagnoses of OD are a goal for clinical decision-making.

## CONCLUSIONS

The available FEES protocols for ALS patients are specific for ALS. There is no standardization of the FEES criteria for performing and analyzing the exam. However, there is a regular search for penetration, aspiration, and pharyngeal residue.

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