Parameters of FEES	Spearman's Rho ALSFRS	p	Spearman's Rho b-ALSFRS	p
Premature spillage-L	-0.304	**Liquid** p<0.0001	-0.428	**Liquid** p<0.0001
Residue-L	- 0.500		- 0.525	
Premature spillage-SS	- 0.338	**Semisolid** p<0.0001	- 0.421	**Semisolid** p<0.0001
Residue-SS	-0.509		-0.482	
Premature spillage-S	- 0.328	**Solid** p<0.0001	- 0.446	**Solid** p<0.0001
Residue-S	- 0.510		- 0.455	

Table 3: Spearman correlation test (Spearman's rho) ALSFRS and b-ALSFRS for premature spillage and post-swallowing residue with liquid (L), semisolid (SS) and solid (S) bolus.

Aspiration	Spearman's rho	p
ALSFRS (mean±SD)	- 0.335	p < 0.0001
b-ALSFRS (mean±SD)	- 0.405	p < 0.0001

Table 4: Spearman correlation test (Spearman's rho) ALSFRS and b-ALSFRS for aspiration.

Aspiration	NO	YES	Independent T-Test
ALSFRS (mean±SD)	32.27±10.3	23.86±9.6	p < 0.0001
b-ALSFRS (mean±SD)	10.02±1.9	5.98±5.2	p < 0.0001

Table 5: Statistically significant difference between mean ALSFRS and b-ALSFRS scores in the presence/absence of aspiration.

swallowing parameters, such as premature spillage and post-swallowing residue, with severity of the disease[21].

Among the 220 patients studied, the correlation between the value of the scores (ALSFRS and b-ALSFRS) and the parameters obtained through the FEES investigation (premature spillage,post-swallowing residue and aspiration), revealed a highly significant correlation for all the bolus textures administered (p <0.0001), showing a close relationship between severity of the disease (assessed by the ALSFRS and b-ALSFRS scores) and severity of dysphagia (assessed by the categorized premature spillage, post-swallowing residue and aspiration variables). The FEES parameters considered in our study (premature spillage, post-swallowing residue, aspiration) are hence strongly correlated with the severity of the disease, both in bulbar onset forms and in spinal onset types, regardless of the bolus consistency used (Tables 3, 4).

By performing an analysis of variance between the mean value of the score (ALSFRS and b-ALSFRS) and presence/absence of aspiration, we found a highly significant difference (p <0.0001) between the mean ALSFRS and b-ALSFRS score and the presence/absence of aspiration. In particular, patients with spinal onset had a higher mean ALSFRS score in the absence of aspiration (absence of aspiration: 32.27 ± 10.3 vs. presence of aspiration: 23.86 ± 9.6) with a statistically significant difference (p <0.0001). Similarly, the mean b-ALSFRS score in patients with bulbar onset was higher in the absence of aspiration (absence of aspiration: 10.02 ± 1.9 vs. presence of aspiration: 5.98 ± 5.2) with a highly significant difference (p <0.0001) (Table 5). These data indicate that patients with aspiration events have lower mean scores, therefore the disease is more serious in their case. Thus, even this statistical analysis confirms that aspiration assessed by FEES is closely related with the clinical stage of disease severity.

Among the FEES parameters, post-swallowing residue

FEES parameters	p ALSFRS	p b-ALSFRS
Aspiration	0.486	< 0.0001
Residue-Solid	0.025	< 0.0001
Premature spillage-Solid	0.148	< 0.0001
Residue-Semisolid	0.034	< 0.0001
Premature spillage-Semisolid	0.281	< 0.0001
Residue-Liquid	0.093	< 0.0001
Premature spillage-Liquid	0.246	< 0.0001

Table 6: Kruskal - Wallis Test.

resulted the most significant one for correlating the endoscopic investigation with the clinical stage of the disease. Moreover, in patients with bulbar onset, who have greater difficulty in managing the boluses, particularly since the oral-pharyngeal muscles are involved, the post-swallowing residue parameter detected with the liquid bolus correlates the severity of the disease better (compared to other consistencies) with the result of the FEES. In fact, patients with spinal onset had a more significant value for the post-swallowing residue parameter with all three consistencies (Spearman's Rho ≤ - 0.500), while in those with bulbar onset the most significant value was always for post-swallowing residue, but only in the case of the liquid bolus administration (Spearman's Rho = - 0.525).

The analysis of variance between variables and the FEES scores categorized into classes (Class I, II and III for the ALSFRS and b-ALSFRS scores) showed that the classes of severity in the bulbar forms (b-ALSFRS) are associated in a highly significant manner with all the FEES parameters studied, no matter what type of the bolus was administered (p <0.0001), whereas in the spinal forms (ALSFRS) it revealed a statistically significant correlation only for the post-swallowing residue parameter in the case of solid boluses (p= 0.025) and semisolid boluses (p= 0.034) (Table 6). Hence, in the bulbar form of ALS evaluated according

to the b-ALSFRS scale, which takes into account language, salivation and swallowing, the FEES investigation allows to follow the clinical course of the disease through all the parameters considered, regardless of the texture of the bolus. In fact, the severity of the disease and its evolution is mainly linked to deficit of the oro-pharyngeal-laryngeal structures involved, that is to say, swallowing. However, in patients with spinal onset form, evaluated into classes of gravity through the more general ALSFRS scale (which globally considers bulbar functions, gross motor tasks, fine motor tasks and respiratory function), the most sensitive FEES parameter for monitoring the severity of the disease in classes is post-swallowing residue of solid and semisolid boluses. The post-swallowing residue parameter with FEES and its division into subclasses (0 = Absent, 1 = Coating; 2 = Minimum, 3 = Maximum) demonstrate an overall remarkable precision, and in particular a considerable sensitivity for monitoring the progressive worsening of the symptoms even in the spinal forms.

The FEES parameters studied and the severity of the disease assessed through ALSFRS and b-ALSFRS revealed a highly significant relationship: in patients belonging to classes of greater severity, a greater deterioration of the FEES parameters is also observed. FEES is a good indicator of the severity of dysphagia and of its progression in patients with ALS, as well as of the clinical progression of the disease. It makes FEES a suitable, useful and reliable test for the follow-up of oro-pharyngeal dysphagia in patients with ALS, whether of spinal or bulbar onset.

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