Unrevealing the sequence of dysphagia progression in ALS: An event-based, FEES-driven staging approach

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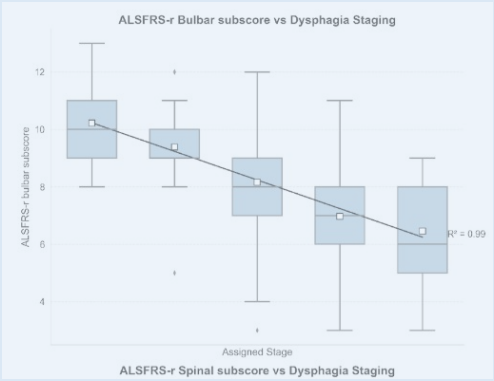
Objectives: Dysphagia is a major driver of morbidity and mortality in amyotrophic lateral sclerosis (ALS) yet remains poorly characterized by existing staging systems. There is a critical need for a dedicated, instrumentally derived dysphagia staging framework to improve monitoring and intervention.

Materials and Methods: In this prospective study, 78 ALS patients underwent serial fiberoptic endoscopic evaluation of swallowing (FEES), with 108 assessments analyzed using the Italian-Yale-Pharyngeal Residue-Severity-Rating-Scale (IT-YPRSRS) across four bolus consistencies. We applied an event-based model (EBM) to reconstruct the probabilistic sequence of swallowing impairment and developed a novel FEES-based dysphagia staging system. Construct, convergent, discriminant, and prognostic validity were evaluated against established ALS clinical measures. Sensitivity to change was assessed using longitudinal data.

Results and Discussion: EBM analysis revealed that the sequence of swallowing impairment is solids, semisolids, liquids, saliva. The resulting dysphagia staging system, ranging from "0" to "4" showed strong construct validity, distinguishing bulbar-onset from spinal-onset ALS ($p = 0.003$) and correlating with both ALSFRS-R bulbar subscore ($\rho = -0.50$, $p < 0.001$) and LMN bulbar score ($\rho = 0.39$, $p < 0.001$). Discriminant validity was confirmed by weak associations with spinal/respiratory measures. Prognostic value was demonstrated by the evidence that all King's stage IV patients were characterized by advanced dysphagia stage. Longitudinal analysis demonstrated the system's sensitivity to clinically meaningful progression ($p = 0.026$).

Conclusions: We present a novel, data-driven dysphagia staging system for ALS, capturing the sequential accumulation of swallowing dysfunction. This instrumentally anchored scale offers refined patient stratification, enhances clinical monitoring, and provides a new paradigm for bulbar disease tracking in ALS.



References: 1) Oxtoby NP, Leyland LA, Aksman LM, Thomas GEC, Bunting EL, Wijeratne PA, Young AL, Zarkali A, Tan MMX, Bremner FD, Keane PA, Morris HR, Schrag AE, Alexander DC, Weil RS. Sequence of clinical and neurodegeneration events in Parkinson's disease progression. Brain. 2021 Apr 12;144(3):975-988. doi: 10.1093/brain/awaa461. PMID: 33543247; PMCID: PMC8041043.
2) Pascuzzo R, Oxtoby NP, Young AL, Blevins J, Castelli G, Garbarino S, Cohen ML, Schonberger LB, Gambetti P, Appleby BS, Alexander DC, Bizzi A. Prion propagation estimated from brain diffusion MRI is subtype dependent in sporadic Creutzfeldt-Jakob disease. Acta Neuropathol. 2020 Aug;140(2):169-181. doi: 10.1007/s00401-020-02168-0. Epub 2020 Jun 13. PMID: 32535770; PMCID: PMC7360647. 3)Firth NC, Primativo S, Brotherhood E, Young AL, Yong KXX, Crutch SJ, Alexander DC, Oxtoby NP. Sequences of cognitive decline in typical Alzheimer's disease and posterior cortical atrophy estimated using a novel event-based model of disease progression.Alzheimers Dement. 2020 Jul;16(7):965-973. doi: 10.1002/alz.12083. Epub 2020 Jun 2. PMID: 32489019; PMCID: PMC8432168.