Assessment of dysphagia after stroke – state of the art and future directions

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Abstract:

Dysphagia is a major complication following acute stroke that affects a majority of patients. Clinically, Dysphagia after stroke (DAS) is associated with increased risk of aspiration pneumonia, malnutrition, mortality, and other adverse functional outcomes. Pathophysiologically, DAS is caused by disruption of an extensive cortical and subcortical swallowing-network. Clinical management of DAS should be provided as soon as possible, starting with bedside screening with simple water-swallowing tests or more elaborate multi-consistency protocols. Subsequently, a more detailed examination, ideally with instrumental diagnostics such as Flexible Endoscopic Evaluation of Swallowing or videofluoroscopy is indicated in selected patients. Emerging diagnostic procedures, technical innovations in existing assessment tools, and digitalisation will decisively improve diagnostic validity in the future. Advances in DAS diagnostics will enable dysphagia management based on individual patterns of dysfunction and predisposing risk factors for complications. Corresponding progress in dysphagia rehabilitation is essential to reduce mortality and improve patients' quality of life.

Introduction:

Dysphagia refers to an impairment of swallowing, the transport of food or liquid from the oral cavity through the pharynx and oesophagus to the gastric entrance. Impaired swallowing efficiency may cause insufficient oral nutrition and hydration. Compromised swallowing safety with bolus entry into the airway poses a risk of aspiration pneumonia. According to a recent meta-analysis, the prevalence of dysphagia after stroke (DAS) in the acute phase of the disease is ~42%, although the included studies are substantially heterogeneous. In studies which used instrumental gold-standard diagnostics, the prevalence was 75% and thus markedly higher.[1] In a study in patients with severely impaired oral intake, the median time to recovery of oral intake was 12 days, however, in 30% of patients oral intake was still insufficient after 30 days.[3] This underscores that although DAS can improve or resolve during rehabilitation, dysphagia may persist in the chronic phase of the disease, making stroke one of the most common causes of swallowing difficulty. DAS is associated with different serious complications resulting in significant impact to health. Recent studies with large sample-sizes provide good evidence of the association with aspiration pneumonia, with odds ratios (OR) for pneumonia due to DAS ranging from 3.0 to 7.3.[4–6] Further, DAS constitutes an independent predictor of malnutrition in stroke patients[7] thus compromising the effectiveness of rehabilitation.[8] Due to these complications, DAS leads to increased mortality. In a prospective, multicentre study of 827,314 stroke patients, DAS had an OR of 7.3 for in-hospital mortality, making it the second most important risk factor (after stroke severity) among a total of 17 independent predictors identified.[9] In addition, DAS leads to adverse functional outcome such as long-term dependency 3 months after stroke.[10,11] Besides causing medical complications, DAS and its sequelae have a significant impact on quality of life. Thus, patients with DAS have a threefold increased risk of depressive symptoms 3 months after stroke.[12] Further, dysphagia may result in longer hospitalisation and higher hospital costs.[13–16] Recent studies have specifically linked higher health care expenses to increased risk of malnutrition and aspiration pneumonia[14] and severe DAS with impaired secretion management.[16]

Given the critical role of DAS in the development of complications, accurate and early detection of dysphagia is crucial to prevent complications and thereby improve patient outcomes. For decades, until fairly recently, stroke medicine neglected dysphagia management, partly due to a lack of high-quality evidence. However, this has changed with a rich body of new data on diagnostic strategies. In addition, mechanistic knowledge of the pathophysiology of deglutition is increasing. Therefore, this review presents the current state of research on pathophysiology, screening and diagnostics of DAS and highlights future developments in the field. Advances in this area are needed to improve stroke patients' outcomes and quality of life, and to reduce mortality.

Glossary of terms

- **Dysphagia:** The term “dysphagia” is derived from the ancient Greek ("dys" = disturbed, "phagein" = eating). In the medical context, dysphagia refers to a swallowing disorder, i.e., impaired bolus transport from the oral cavity to the gastric entrance. The predominantly voluntary oral phase and the mainly reflexive pharyngeal and oesophageal phases of swallowing are differentiated. Dysphagia resulting from stroke frequently affects the oral and pharyngeal phases in combination, which is referred to as oropharyngeal dysphagia.
- **Swallowing safety, penetration, and aspiration:** In the oropharyngeal phase of swallowing, the bolus must be safely transported past the airways into the oesophagus. During a safe and functional swallow, the airway is closed by the epiglottis, the vocal folds, the vestibular folds and the mucosae and thus protected from bolus and saliva intrusion. In oropharyngeal dysphagia, the airway may be insufficiently protected, and bolus material enters the trachea (referred to as impaired swallowing safety). Bolus material entering the airway below the vocal folds is defined as aspiration. Bolus material that enters the laryngeal vestibule but remains above the vocal folds is defined as penetration. Penetration and aspiration can trigger protective reflexes such as coughing or throat clearing which may partially remove the bolus from the airway. If such reflexes are not elicited, this is referred to as silent penetration or aspiration. Aspiration can lead to pneumonia, which is then called aspiration pneumonia.
- **Swallowing efficiency:** In addition to swallowing safety i.e., the protection of the airway during the swallow, swallowing efficiency is a further dimension of impairment in oropharyngeal dysphagia. It refers to the ability to swallow sufficient amounts of nutrition and liquid. If swallowing efficiency is impaired, residue in the pharyngeal and/or oral cavities may occur. Due to impaired swallowing efficiency, oral food and liquid intake may

be insufficient resulting in a risk of malnutrition, dehydration or, ultimately, the need for tube-nutrition.

Search Strategy and selection criteria:

We searched for articles published in English on PubMed between 12/2017 and 12/2022 with the search terms "Dysphagia" AND "Stroke". We selected articles if they reported on diagnostics, pathophysiology, or outcome of post-stroke dysphagia. We also considered publications cited in these articles that did not appear in the search algorithm. Further, we included articles published at an earlier date, if we considered them still relevant to the field, e.g., if the previously selected articles cited a respective article frequently. The final selection of cited articles reflects our subjective assessment of their relevance with respect to the reported results and the methodological quality of the reported work.

Pathophysiology

Swallowing is a complex neuromuscular process that requires precise temporal yet stereotypical coordination of different motor processes such as targeted tongue movement, contraction of the pharyngeal muscles, closure of the airway, and opening of the upper oesophageal sphincter. Contrary to the historical assumption that swallowing is purely a brainstem reflex, clinical and neuroimaging studies have demonstrated that both cortical and subcortical swallowing networks are essential for the central control of swallowing (Panel 1), and swallowing is now considered a patterned response rather than a reflex.

Panel 1: Anatomy of the central swallowing network and its impairment in dysphagia after stroke (DAS).

Brainstem swallowing centres: The nuclei of six different cranial nerves (trigeminal, facial, glossopharyngeal, vagus, hypoglossal and accessory) located in the brainstem are involved in the motor coordination of the swallowing muscles and sensory feedback perception. In addition, the central pattern generators which are located in the medulla-oblongata integrate supramedullary input and sensory perception, elicit the pharyngeal patterned swallowing response, and generate spontaneous swallowing.[20] Thus, brainstem structures are of key importance for central swallowing control and brainstem lesions are particularly associated with DAS.[21,22]

Cortical control of swallowing: In recent years, the importance of supramedullary structures has been carefully scrutinised.[23] Researchers have used voxel-based lesion symptom mapping to describe lesions typically associated with DAS, including lesions in the primary sensorimotor areas[24] and the parietal lobe.[25] The secondary somatosensory association areas such as the inferior parietal gyrus appear to be additionally engaged in concert with the primary regions.[26] Other cortical regions associated with DAS include the insula, frontal operculum or inferior frontal gyrus, supramarginal gyrus, angular gyrus and superior temporal gyrus.[24,27,28]

Subcortical structures: Different subcortical areas are also associated with DAS such as the thalamus, amygdala and basal ganglia.[24,25,27,28] The latter are involved in the motor coordination of swallowing via the extrapyramidal circuitry. Further, isolated lesions in the cerebellum can lead to DAS, which likewise underscores the importance of the cerebellum in the extrapyramidal motor coordination of swallowing.[29] Finally, DAS can occur as a result of white matter lesions in the corticofugal projections or association fibres , e.g., the corticobulbar tracts.[24,28,30–33] In addition to acute cerebral white matter lesions resulting from stroke, leukoaraiosis, i.e. chronic cerebral white matter damage, also plays a decisive role in the development of DAS and has been associated with penetrations and aspirations.[34]

Lateralization of swallow representation: The extent to which central control of swallowing is asymmetrically lateralised or uniformly bihemispheric is now increasingly recognised as being more associated with the former hypothesis:[23] DAS has been associated with left hemispheric lateralisation in some studies,[26,27] right hemispheric lateralisation in others,[24,35] or no lateralisation at all.[25] Possibly, high inter-individual differences[35] as well as lateralisation depending on the timing of the swallowing phases may be responsible for these conflicting results.

Sensory impairment

Along with the primary motor system, intact sensorimotor feedback is required for safe and functional swallowing. Thus, a study based on swallowing endoscopy reported that DAS severity and impaired secretion management were closely related to pharyngeal sensory hypoaesthesia.[36] Mechanistically, hypoaesthesia may result in delayed or absent triggering of the swallowing response,[36] a dysphagia mechanism that is particularly common in stroke patients.[37] In addition, a study in acute stroke patients associated DAS with decreased spontaneous swallowing frequency,[38] which may also be attributable to pharyngeal hypoaesthesia and impaired sensory input to the medullary swallowing centres. Further, peripheral sensory stimulation induces enhanced excitability of the motor cortex in DAS,[39] illustrating the close modulatory connectivity between the sensory and motor systems. In line with this, a study in chronic stroke patients reported an asymmetric pattern of reduced ipsilesional sensory evoked potentials upon pharyngeal electrical stimulation associated with DAS.[40] In a further study, a prolonged duration of pharyngeal swallowing was associated with a decreased amplitude of sensory evoked potentials in the contralesional hemisphere.[41] These results point to a disturbed integration of pharyngeal sensory input.

In addition to the central impairment of the sensory system, interactions with peripheral sensory mechanisms also appear to contribute to and modulate DAS. Pharyngeal hypoaesthesia is assumed to be related to degeneration of sensory nerve endings that release substance-P into saliva, resulting in decreased substance-P levels. A study in acute stroke patients detected a decreased swallowing frequency in patients with reduced substance-P-levels in saliva.[42] In addition, a randomised controlled trial (RCT) described an increase in serum substance-P-levels with the application of capsaicin (which can be considered a pharmacological sensory stimulus) with subsequent improvement in swallowing function.[43]

Taken together, these results suggest that both central and peripheral mechanisms of sensory system impairment are involved in the development of DAS.

Breakdown of the swallowing network and neuroplasticity as recovery mechanism

The cortical areas that control swallowing are functionally interconnected across hemispheres.[44] Therefore, apart from lesions in the loci important for swallowing, the disruption of functional connectivity within the swallowing network is a predisposing factor for DAS. In line with this, patients with DAS exhibit a breakdown of central network connections compared to healthy participants.[44] Following the swallowing network breakdown, neuroplasticity, the brain's ability to adapt to a changing environment through neuronal remodelling, is critical for symptom recovery. Compared to extremity motor function, swallowing features a bilateral representation, which holds a high potential for compensatory neuroplasticity in the contralesional brain region. Consistent with this hypothesis, pioneering studies 25 years ago employing transcranial magnetic stimulation to map the pharyngeal motor cortex showed that motor representation of swallowing in the contralesional hemisphere was reduced in patients with DAS, but increased over time during DAS recovery.[45,46] Accordingly, a recent RCT combined with neuroimaging suggested compensatory recruitment of the contralesional somatosensory area as neural correlate of recovery from DAS after transcranial direct current stimulation.[47] The sensory system further gave evidence of reduced capacity in contralesional neuroplasticity as a DAS-mechanism inferred by a correlation between prolonged swallowing duration and lower amplitude of contralesional sensory evoked pharyngeal potentials.[41] Similarly, white matter analyses revealed evidence of contralesional neuroplasticity, with higher volume of the contralesional corticobulbar tract associated with better swallowing function in patients with DAS.[30] Conversely, contralesional impairment of the corticobulbar tract due to leukoaraiosis was association with persistence of DAS.[48] Furthermore, bilateral lesions of the basal ganglia or corticobulbar tract are associated with long-term persistence of DAS.[32,49] Thus, there is broad and multimodal evidence from clinical, electrophysiological, and imaging studies to suggest that recovery from DAS at sensory, motor and white matter levels is driven by neuroplasticity in the contralesional hemisphere. The integration of these studies has culminated in a model of compensatory contralesional neuroplasticity as a mechanism for DAS recovery, which is illustrated in Figure 1.

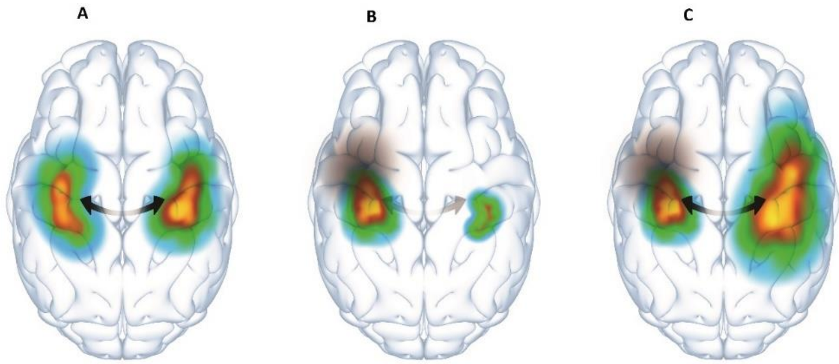

Figure 1: Model of compensatory contralesional neuroplasticity in dysphagia recovery: A: Physiological bihemispheric (partially lateralised) neural representation of swallowing (the coloured areas represent cortical activation during swallowing, with the color gradient from green to yellow to red illustrating particularly intensely involved cortical processing); B: Neural representation of swallowing in the acute phase of dysphagia after stroke (dark coloured area represents the stroke lesion): There is a disruption of the central swallowing network with diminished neural representation; C: Neural representation of swallowing in the chronic phase with recovery from dysphagia: Compensatory neuroplasticity in the healthy hemisphere with increased representation of swallowing in the contralesional hemisphere.

Diagnostics:

For appropriate management of oral nutrition, DAS must be identified at the earliest time possible. Different diagnostic procedures with varied objectives are proposed. Screening protocols aim to identify a high-risk population for further stepwise diagnostics. Detailed clinical swallowing evaluations allow conclusions about therapeutic options and dietary recommendations. The diagnostic gold-standard is instrumental dysphagia assessment, which more reliably and comprehensively evaluates swallowing function. Different international guidelines now include explicit recommendations for the diagnostic management of DAS (see Panel 2).

Panel 2: International guideline recommendations on diagnostic management of dysphagia after stroke published since 2017:

- European Stroke Organisation and European Society for Swallowing Disorders guideline for the diagnosis and treatment of post-stroke dysphagia.[17] The guideline recommends a formal dysphagia screening (water swallow test or multi-consistency test) in all acute stroke patients early after admission (quality of evidence: moderate ⨁⨁⨁, strength of recommendation: strong for intervention ↑↑). In addition, the guideline recommends dysphagia assessment complemented by instrumental diagnostics, preferentially FEES, in all patients with risk factors or patients failing the screening (quality of evidence: low ⊕⊕, weak for intervention ↑?).

- European Society for Clinical Nutrition and Metabolism guideline on clinical nutrition in neurology.[18] The guideline recommends a formalised screening for dysphagia for all patients before oral intake (grade of recommendation B – strong consensus with 95% agreement) and thereafter a more thorough assessment for failing patients (grade of recommendation B – strong consensus with 100% agreement) as early as possible.
- White paper of the European Society for Swallowing Disorders: Screening and Non-instrumental Assessment for Dysphagia in Adults.[19] The white-paper recommends the discontinuation of the use of non-validated dysphagia screening tools but the use of measures with optimal diagnostic performance and robust psychometric properties. It lists commonly used screens and assessments.

Screening protocols

The inter-professional team in stroke units and rehabilitation facilities has a special role to play in the implementation of screening procedures. Persons trained in DAS from different professional groups such as speech therapists, physicians, nurses, nutritionists, dietitians, and physiotherapists can and should be involved in the screening process. The most common procedures to screen for DAS are water-swallowing tests, where various protocols are available.[50] Here, depending on the protocol, different volumes of water are administered and clinical signs of aspiration are assessed during or after the swallow, such as coughing, throat clearing, drooling, stridor and a hoarse voice. In addition, there are more elaborate screening protocols that examine multiple bolus consistencies obtaining not only a binary result (in terms of high-risk vs. low-risk for DAS), but a result differentiated by consistencies combined with a diet recommendation. A common multi-consistency screening test for DAS is the Gugging-Swallowing-Screen (GUSS).[51] This is a step-by-step protocol that includes resting observation, saliva swallowing, and swallowing of semisolid, liquid, and solid consistencies. This test grades dysphagia in one of four categories (severe, moderate, mild or no dysphagia) and recommends a special diet and further strategies based on the severity code. Two recent meta-analyses found a high sensitivity of more than 95% but a rather low specificity of below 70% for the GUSS in detecting aspiration compared to the gold-standard of instrumental diagnostics.[52,53] Further, individual validation studies report associations with outcome parameters.[52] A recent Cochrane review concludes that the GUSS is the best performing multi-consistency test in stroke patients,[50] but points to limited evidence given the small sample size and risk of bias. Another multi-consistency test frequently used to evaluate DAS is the Volume Viscosity Swallowing Test (V-VST).[11,26,54–57] Here, 5ml, 10ml and 20ml of nectar-like, liquid and pudding-like consistency are administered. Apart from swallowing safety this test also evaluates clinical parameter of swallowing efficiency (labial seal, oral and pharyngeal residue, and piecemeal deglutition). Other proposed screening protocols include detection of decreased spontaneous swallowing frequency[58,59] or failed/delayed response to a sensory or swallowing stimulus.[60,61] Panel 3 provides an overview of different screening protocols and their diagnostic metrics compared to the instrumental diagnostic gold standard.

Panel 3: Listing of different screening protocols for dysphagia after stroke with their diagnostic metrics compared to the instrumental diagnostic gold standards Videofluoroscopic Swallowing Study (VFSS) or Flexible Endoscopic Evaluation of Swallowing (FEES). TOR-BSST: Toronto Bedside Swallowing Screening Test; GUSS: Gugging Swallowing Screen; V-VST: Volume Viscosity Swallowing Test. References are presented in supplementary material 1.

Screening test	Protocol	Study sample and timing	Diagnostic metrics
Water-swallowing tests			
30ml (Nishiwaki et al. 2005)	The test assesses two swallow trials with a teaspoon (5ml) of water followed by drinking 30ml of water from a cup. It assesses coughing or voice changes within 1 minute after swallowing.	61 stroke patients (n=28 within 1-month after stroke; n=11 within 3-month after stroke; n=22 with more than 3-month after stroke).	Sensitivity of 72% and specificity of 67% compared to aspiration on VFSS.
70ml (Daniels et al. 1998)	The test starts with a 5ml fluid bolus administered from a cup or straw and increases to 10ml and 20ml (each volume is administered twice, total volume 70ml). The test evaluates cough and voice change after swallowing.	59 acute stroke patients within 5 days of admission.	Sensitivity for cough after swallow of 62% and specificity of 79% and sensitivity for voice change after swallow of 31% and specificity of 88% compared to dysphagia on VFSS.
90ml (Suiter and Leder 2008)	The test assesses drinking 3oz of water (~90ml) from a cup without interruption. It evaluates coughing during or for 1 minute after drinking, the presence of a wet hoarse voice after swallowing, or the	Left-sided stroke (n=227), right sided stroke (n=203), brainstem stroke (n=38), no timing of stroke is provided.	Sensitivity of 98% and specificity of 45% for left sided stroke, Sensitivity of 93% and specificity of 45% for right sided stroke, sensitivity of 100%

	inability to drink the entire amount.		and specificity of 55% for brainstem stroke, each compared to liquid aspiration on FEES.
TOR-BSST (Martino et al. 2009)	This test assesses 4 items: (1) Baseline vocal quality, (2) tongue movement, (3) A total of 10 trials of swallowing teaspoons of water followed by drinking from a cup (total volume of 50 ml) with assessment of cough, voice change, or drooling during/after swallowing, and (4) final judgement of voice quality.	Acute patients (n=24, mean time from last seen healthy to screening: 6.1 day); chronic patients (n=35, mean time from last seen healthy to screening: 31.6 days).	Sensitivity of 91% and specificity of 67% compared to VFSS; interrater reliability: intraclass correlation coefficient=0.92.
Multi consistency tests			
GUSS (Trapl et al. 2007)	This test assesses vigilance and coughing, saliva swallowing, and swallowing of semisolid, liquid, and solid consistencies. It grades dysphagia in one of four categories (severe, moderate, mild or no dysphagia) and recommends a special diet based on the severity grading.	50 acute stroke patients within 24 hours of stroke onset.	Sensitivity (aspiration risk according to the GUSS) of 100% and specificity of 50% or 69% (depending on the cohort) compared to aspiration on FEES. Interrater reliability: The overall severity rating achieved excellent agreement (κ=0.835).
V-VST (Rofes et al. 2012)	This test assesses swallowing of 5ml, 10ml and 20ml of nectar-like, liquid and pudding-like consistencies. It evaluates swallowing safety (cough and/or fall in oxygen saturation ≥3%) as well as swallowing efficiency (labial seal, oral and pharyngeal	There is no validation in a cohort of stroke-only patients compared to gold-standard diagnostics available.	n.a.

	residue, and piecemeal deglutition).		

Several studies suggest health-benefits as a consequence of delivering dysphagia screening in patients with stroke. A retrospective registry study of 365,530 patients associated DAS screening (water swallow or multi-consistency tests) with decreased mortality, underscoring the importance of formalized dysphagia screening with appropriate dysphagia management and rehabilitation thereafter.[62] A further study in which 19 different stroke units were randomized into an intervention and a comparison group reported that patients had a higher probability of independence 90 day post-stroke if a screening including a water swallow test was performed in the first 24 hours.[10] A current meta-analysis pooling 24 observational studies and 6 RCTs concluded that dysphagia screening yields better outcomes with regards to pneumonia incidence, mortality, length of hospital stay, and dependency on care.[63] Similarly to patients with ischaemic stroke, administration of a water swallow test was associated with a decreased pneumonia rate in a cohort of 4,877 patients with subarachnoid hemorrhage.[4] However, evidence from RCTs comparing different dysphagia screening protocols is largely lacking.[64]

Clinical predictors

There are a number of clinical predictors associated with an increased prevalence of DAS and its persistence. These include facial palsy,[65] aphasia or impairment of speech,[2,27,65–69] and clinical stroke severity, i.e., increased National Institute of Health Stroke Scale (NIHSS).[2,11,21,22,25–27,70,71] The latter two can also be applied as predictors for DAS in patients with intracerebral hemorrhage.[28,72] A retrospective study validated optimal cut-off values for predicting DAS with the NIHSS when considering both sensitivity and specificity.[71] It established a cut-off ≥10 for patients with supratentorial and a lower cut-off ≥6 for patients with infratentorial stroke (both with moderate sensitivity and specificity). The lower cut-off value in infratentorial stroke reflects the reduced sensitivity of the NIHSS for posterior circulation stroke concomitant with a high prevalence of DAS in this patient group. In line with this, a combined retrospective-prospective study validated the POST-NIHSS score for posterior circulation stroke, which includes dysphagia besides conventional NIHSS and further clinical items.[73] In addition, a European prospective observational study developed the predictive swallowing score (PRESS), a prognostic model for DAS recovery in 279 ischemic stroke patients with severely impaired oral intake.[3] The PRESS considers age, NIHSS at admission, lesion involvement of the frontal operculum, initial aspiration risk according to screening tests, and initial oral intake, and estimates the risk for persistent impairment of oral intake after day 7 and after day 30. This score aims to guide decisions about enteral feeding strategies and is available as a smartphone app. However, clinicians using DAS predictors should be aware that in the mentioned studies, acute stroke therapy (and its influence on the predictor) was mostly not considered in the validation.

Clinical swallowing examination (CSE)

In addition to screening procedures, there are detailed and comprehensive clinical examination protocols for assessing swallowing function.[19] The CSE typically includes medical history, cognition and communication screening, physical examination of the oral cavity and cranial nerves, as well as an evaluation of oral motor function and a swallowing assessment of different consistencies. Similar to screening procedures, the CSE partly relies on clinical signs of aspiration and dysphagia such as coughing, throat clearing, coated voice and decreased laryngeal elevation during swallowing. Unlike the screening tests, assessment is performed by a dysphagia expert such as a speech-language therapist, and often serves as the basis for therapeutic management. Despite the widespread use of the CSI in clinical practice, there are very few recent studies demonstrating patient benefit or good agreement with gold-standard instrumental diagnostics.

Instrumental assessment

Some important shortcomings of the CSE are that relevant dysphagia pathologies, e.g., silent aspiration and pharyngeal residue, cannot be reliably detected. Further, there are a variety of different dysphagia mechanisms,[37] whereas these different patterns of swallowing pathology cannot be conclusively investigated with CSE. Therefore, a comprehensive detection of swallowing pathologies and characterisation of dysphagia mechanisms with incorporation into an individualised treatment plan requires detailed visualisation of swallowing. To accomplish this, instrumental procedures have been established as diagnostic modalities (illustration in Figure 2). Videofluoroscopic Swallowing Study (VFSS) evaluates swallowing of a contrast-enriched bolus during radiological recording. In Flexible Endoscopic Evaluation of Swallowing (FEES), the examiner inserts an endoscope transnasally into the pharynx, enabling direct visualization of pharyngeal and laryngeal structures and the swallowing outcome. The two instrumental procedures provide comparable findings with regards to relevant dysphagia pathologies such as penetrations, aspirations and pharyngeal residue and are thus both considered diagnostic gold-standards.[74] FEES and VFSS each have unique methodological advantages and disadvantages (for comparison, see Panel 4). The possibility of bedside examination even in non-cooperative patients with the added advantage of assessing secretion management and sensation supports the use of FEES. VFSS, on the other hand, allows assessment of the entire swallowing phases, including oesophageal transport of the bolus, as well as characterisation of biomechanical impairments and swallowing response metrics.

As a grading system for DAS, the Fiberoptic Endoscopic Dysphagia Severity Scale (FEDSS) was introduced[75] and has been widely adopted since then. This score divides DAS into 6 degrees of severity (from 1: no relevant dysphagia to 6: severe dysphagia with impaired secretion management). Protective dietary restrictions or rehabilitative measures for acute DAS management can be derived from the individual FEDSS-severity levels. The score not only demonstrates high inter-rater reliability,[75] but is also a valid predictor of complications such as pneumonia, the need for intubation, extubation failure, and worse functional outcome.[76,77] However, there is limited data on other psychometric dimensions such as structural validity. Further, the Rosenbek Penetration-Aspiration-Scale, originally developed for VFSS, is a widely used severity classification, which characterises the extent of bolus intrusion into the airway using an 8-point ordinal scale.[78] In addition, the Modified Barium Swallow Impairment Profile (MBSImP) for VFSS has been validated as a transdiagnostic score that assesses multi-dimensional impairments of swallowing such as oral and pharyngeal residue, reduced laryngeal elevation, and impaired pharyngoesophageal segmental opening.[79] Different research groups have proposed other visual perceptual measures, but there are few data for the stroke population, and data on psychometric properties are generally scarce, including the scores mentioned above.[80]

Various studies suggest superiority of instrumental diagnostics compared to clinical examination. The prevalence rates for DAS are significantly higher when instrumental diagnostics are used, indicating increased sensitivity.[1] Clinical evaluation with a multi-consistency test by nurses and detailed evaluation by a speech-and language therapist both demonstrated a low diagnostic agreement with instrumental DAS evaluation.[81] In line with this, a retrospective study showed that only about 31% of stroke patients had an appropriate diet recommendation before FEES was performed. A more restrictive diet would have been appropriate for approx. 32% of patients and a less restrictive diet for approx. 38%.[70] A multi-centre prospective FEES registry study with a total of 2401 patients (the majority of 61 % were stroke patients) obtained similar results. Again, FEES led to a change in oral intake in more than half of all patients, with a more liberal dietary regimen in the majority of cases.[82] Thus, besides increasing sensitivity for DAS, FEES may help to increase safely administered oral intake. In addition, the registry study suggests that FEES is a safe procedure that rarely results in complications, which then resolve self-limitingly.[82] Regarding outcome parameters, a retrospective observational study demonstrated that performance of FEES within the first 48 hours of admission followed by appropriate dysphagia management was an independent predictor of a shorter hospital stay.[83] Despite these convincing results, there is a lack of high-quality evidence from RCTs demonstrating the superiority of instrumental diagnostics in terms of relevant outcome parameters. Nevertheless, the use of instrumental diagnostics, especially FEES in acute stroke care is steadily increasing. In addition, various national and international societies have launched training initiatives to teach the handling and interpretation of instrumental swallowing diagnostics.

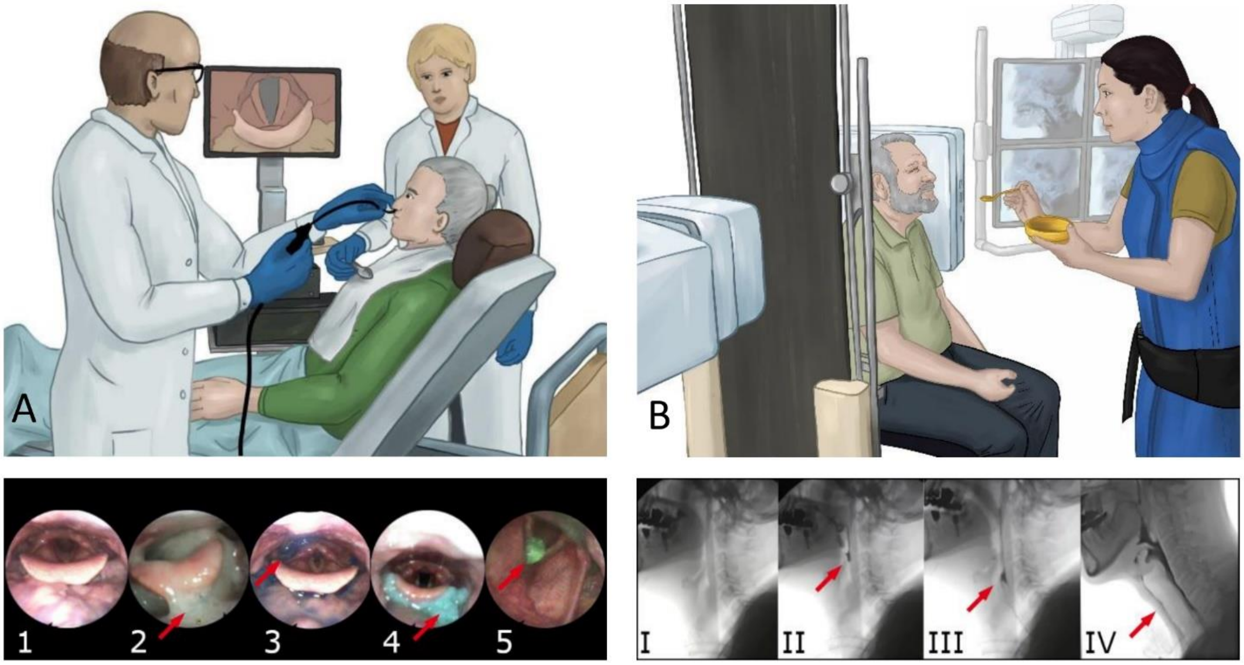

Figure 2: Schematic illustration of instrumental dysphagia diagnostics and typical dysphagia pathologies in stroke patients: A: Flexible Endoscopic Evaluation of Swallowing (FEES): an endoscope is inserted transnasally and the laryngeal structures are filmed; 1: visualisation of the laryngeal structures before swallowing; 2: pharyngeal saliva pooling; 3: premature bolus spillage of blue dyed water; 4: pharyngeal residue of solid consistency; 5: aspiration of green puree; B: Videofluoroscopic Swallowing Study (VFSS): a contrast-agent bolus is administered and swallowed during fluoroscopy; I: oropharyngooesophageal structures before swallowing, II: premature bolus spillage; III: pharyngeal residue; IV: aspiration.

Panel 4: Comparisons of methodological advantages and disadvantages of Flexible Endoscopic Evaluation of Swallowing (FEES) and Videofluoroscopic Swallowing Study (VFSS).

	FEES	VFSS
Advantage	• Bedside examination is possible • Examination of uncooperative patients is possible • Assessment of saliva management and sensory testing is possible • No radiation exposure with unrestricted examination times allowing for repetitions and follow-ups • Procedure is safe and feasible in acute stroke • Cost-effective, since only the expenses for the purchase of the endoscope, its sterilization and the personnel costs for an examiner and an assistant are incurred	• All swallowing phases can be assessed including the oral and the oesophageal phase • Particularly sensitive for detecting intra-deglutitive penetration and aspiration • Upper oesophageal sphincter opening can be assessed • Different phases of swallowing may be timed accurately
Disadvantage	• The oesophageal and oral phase of swallowing can only be assessed with indirect signs • There is a short intra-deglutitive period of white superimposition (white-out) during pharyngeal swallowing in which no direct assessment is possible	• Transportation to a radiological unit is necessary • Patients must cooperate and sit in an upright position • Patients are exposed to radiation, so concise examination protocols are necessary • Increased costs due to the use of radiological equipment and contrast agents as well as higher personnel effort (radiologist and speech-language therapist)

Dysphagia assessment is time critical

The vast majority of respiratory infections in dysphagic stroke patients occur in the early stages of the disease. Consequently, a nationwide, registry-based, prospective cohort study with 63,650 patients showed that a delay in both dysphagia screening and CSE was associated with an increased pneumonia rate (36% higher odds of pneumonia after approx. 6hr screening delay)[84]. On the same note, a prospective observational study on 3,309 acute stroke patients demonstrated that a delay in screening between 4-72 hours was associated with a greater risk of pneumonia (OR 1.4) and disability on discharge (OR 1.4). However, a screening delay beyond 3 days was associated with even more severe risk of pneumonia (OR 2.3), increased length of hospital stay (OR 2.1), disability on discharge (OR 2.5) and mortality (OR 3.8).[85] These findings suggest that dysphagia diagnostics at all levels are time-critical and should be conducted as early as possible.

Proposal for a two-step pragmatic diagnostic approach

With a variety of different examination protocols available, the question arises how to perform stepwise diagnostics. In this context, we propose a two-step pragmatic diagnostic algorithm based on the expert opinion of the authors and considering guideline recommendations and the available scientific evidence. This algorithm recommends screening as step 1 and detailed swallowing examination, preferentially with instrumental diagnostics, as step 2 (see Figure 3). We suggest differentiating whether or not a dysphagia expert is available within 24-48 hours. Although dysphagia experts are considered an integral part of the multi-disciplinary stroke team, they are not available everywhere at all times, so dysphagia may need to be managed based on screening alone. In this scenario a multi-consistency protocol seems pragmatic. Thus, unlike the binary result of a water-swallowing test (pass or fail) a differentiated recommendation for oral intake is possible based on this procedure. The results of a prospective observational study showing that trained nurses' recommendations for oral intake based on a multi-consistency protocol were highly consistent with detailed CSE by a speech therapist,[81] may support this suggestion. Further, a retrospective study compared a period of screening with a water swallow test with a period after introduction of the V-VST. The results hint at the probability that the introduction of the multi-consistency protocol reduced the rate of pneumonia and tube-feeding.[55] Thus, when instrumental diagnostics are not available, we recommend that a multi-consistency tests should be performed to further provide a dietary recommendation.

If detailed dysphagia assessment is available, a water-swallowing test and the above listed clinical predictors (i.e., sever aphasia or speech impairment, facial palsy or NIHSS ≥10 for supratentorial or ≥6 for infratentorial stroke) can be used to divide patients into those at high- and low-risk for DAS. Patients at high-risk should then undergo a detailed swallowing examination, preferably with instrumental diagnostics such as FEES.

Therapeutically, in addition to management of adequate oral intake, a recent guideline from the European Stroke Organisation and the European Society for Swallowing Disorders recommends a number of interventions, including nutritional interventions, oral hygiene, and behavioural interventions with a listing of the level of evidence.[17]

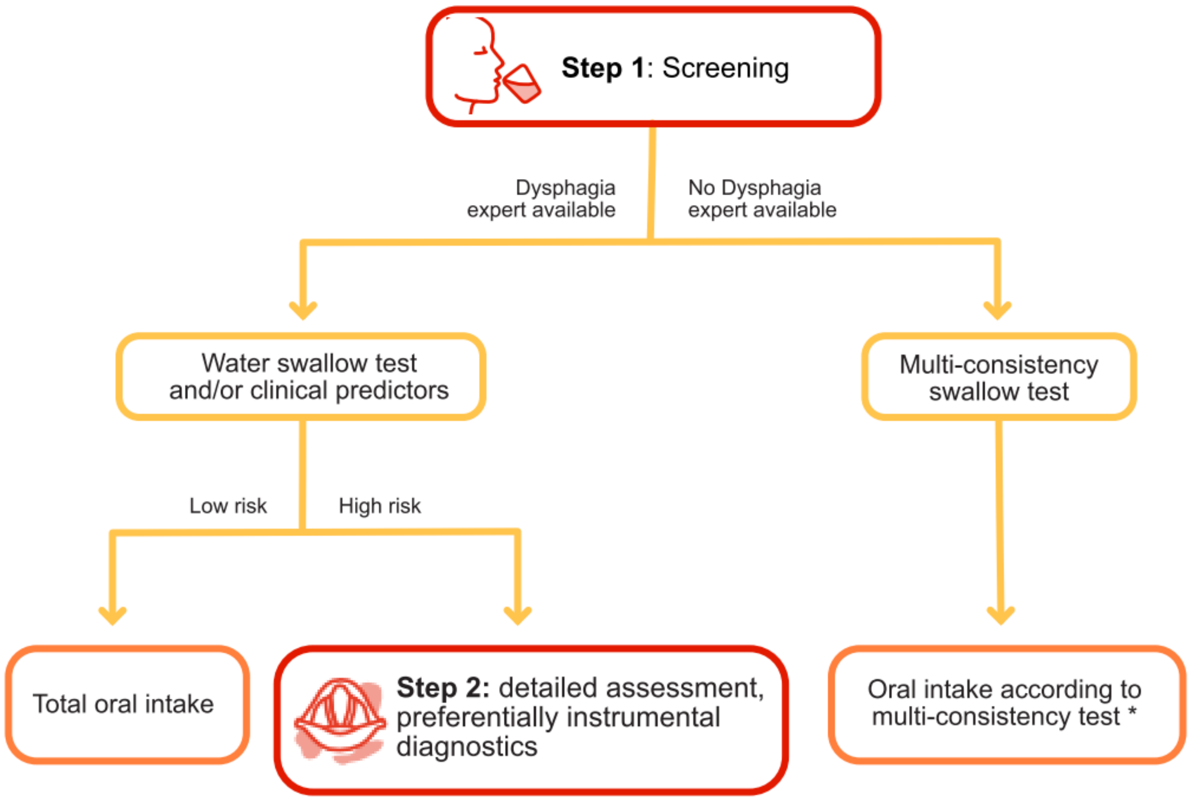

Figure 3: Two-step pragmatic diagnostic approach to detect dysphagia after stroke. This algorithm is based on the authors' expert opinion, taking into account current guideline recommendations and available scientific evidence. *: If sings of impaired swallowing safety or swallowing efficiency are present, we highly recommend further instrumental assessment by a dysphagia expert.

Conclusions and future directions:

DAS is a common complication of stroke. Therefore, it is critical that DAS becomes a diagnostic focus in stroke medicine. In this context, the multi-disciplinary team, which includes physicians, nurses, speech-language therapists, nutritional experts, physiotherapists, and other therapeutic groups is of particular importance. We recommend a stepwise diagnostic approach for the detection of DAS, with patients referred to gold-standard instrumental diagnostics as appropriate. The clock is not only ticking when it comes to acute recanalisation treatments for stroke itself, but also with regards to dysphagia management, as complications of DAS are particularly common in the early period after stroke. Pathophysiologically, a widespread cortical and subcortical swallowing network in the central control of swallowing has increasingly come into focus.

Peripheral mechanisms such as the secretion of the neuropeptide substance-P, also appear to play a role in sensorimotor control.

Figure 4 illustrates a pragmatic approach with the diagnostic focus in the disease course. Immediately after stroke onset, the diagnostic focus is on swallowing safety with the related key question of whether patients need to remain nil per mouth. Thereafter in the acute period, swallowing assessment aims to determine the appropriate nutritional strategy using specific scores such as the FEDSS. Behavioural manoeuvres to increase swallowing safety can be investigated. To this end, a simple and standardised procedure prevails due to the busy workload on the stroke-unit and the need for straightforward communication with the multi-professional team. In the follow-up period, when the clinical situation has stabilised, (repeated) dysphagia assessments should decipher the dysphagia mechanism of the individual patient. In this context, a retrospective study with more than 600 stroke patients has characterized different dysphagia mechanisms such as premature bolus spillage due to decreased oral containment, delayed or absent swallowing response, or bolus residue in different pharyngeal regions (valleculae or sinus piriformis) in the stroke population.[37] This mechanistic grouping will allow future studies to investigate targeted therapies based on the individual dysphagia pathology, promoting individualised treatments.

Diagnostic procedure	Dysphagia-Screen	(instrumental) assessment of dysphagia severity	(instrumental) assessment of the dysphagia phenotype and context
Clinical Questions	- Are there signs of aspiration? - Are there clinical predictors of dysphagia	- Is the swallow safe? - Is the swallow efficient? - Is tube feeding indicated? - What type of oral diet is appropriate? - Are there simple manoeuvres that improve swallowing performance?	- What is the impairment profile of the patient? - What is the prognosis of dysphagia (for example, may implantation of a PEG tube become necessary?) - What are the contextual factors? Are there protective factors or further risk factors?
	Immediate ≤ 2 h	Acute ≤ 48 h	Post-acute > 2 days

Figure 4: Time sequences of dysphagia diagnostic procedures and clinical questions in dysphagia assessment.

Contextualisation of dysphagia findings within a holistic diagnostic approach will become increasingly important in the future, to reliably estimate the risk for DAS complications. Thus, not only DAS, but a variety of other interacting factors in the development of aspiration pneumonia should be assessed (illustrated in Figure 5). An effective cough reflex may help clear the aspirated bolus from the airway, reducing the risk of pneumonia. A recent RCT resulted in a non-significant 2.2% reduction in pneumonia rate in the group of 192 patients with cough reflex testing compared with 190 patients with standard DAS assessment.[86] A further, prospective observational study with a pre-post comparison suggested that an assessment of the cough reflex embedded in instrumental DAS stage diagnostics may have contributed to a reduction in the pneumonia rate from 28% to 10%.[87] Further studies on cough-reflex testing are needed to investigate specific examination protocols, the diagnostic value, and the interaction with DAS. Another important factor that promotes aspiration pneumonia in DAS is poor oral hygiene. In line with this, a prospective observational study demonstrated that the oral cavity was colonised with Pseudomonas aeruginosa, Klebsiella pneumoniae and Escherichia coli in stroke patients and that bacterial colonisation had increased one-month post-stroke. Total bacterial levels were further associated with occurrence of pneumonia.[88] In addition to respiratory tract invasion by pathogenic bacteria, patients' immune status may also act as a predisposing factor and should be investigated in the future. Accordingly, a prospective multi-centre study with a total of 486 patients revealed that, besides DAS, stroke-induced immunodepression, i.e. decreased monocytic HLA-DR expression, was an independent predictor for the occurrence of pneumonia.[89] Two retrospective studies identified an elevated neutrophil-to-lymphocyte ratio as a risk factor for pneumonia after stroke, in addition to DAS.[90,91] Here, future studies are needed to identify and validate immunological predisposing biomarkers. Another contextual factor that should be considered in future research is the susceptibility to a hazardous outcome in case of existing pneumonia. Possible diagnostic instruments in this context may include geriatric assessment tools such as frailty. The outlined multidimensional and contextual DAS assessment will allow the risk of aspiration pneumonia to be individually assessed and appropriately addressed in the management of dysphagia.

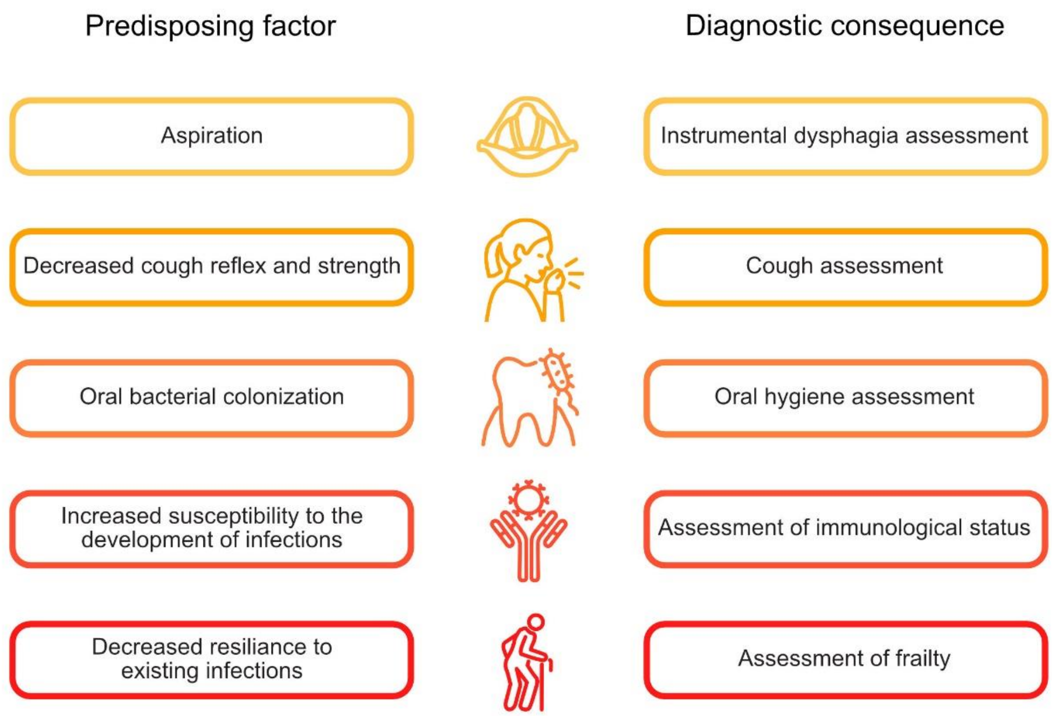

Figure 5: Contextual factors within which dysphagia contributes to the development of aspiration pneumonia: Predisposing factors and the corresponding diagnostic consequence within a holistic diagnostic approach are presented.

A further future direction in diagnostics is the improved validation and refinement of visuoperceptual measures and scores of instrumental DAS assessment. Future research should focus on scores that are sensitive to clinically relevant changes, so that therapeutic effects can be effectively assessed. In this context, surrogate parameters determined in VFSS such as delayed laryngeal vestibule closure and impaired tongue bolus propulsion, which have been associated with impaired swallowing safety[92] will have an important function. In the field of FEES, the so-called white-out could be characterized in more detail and investigated as a possible surrogate marker for pharyngeal contractility, similar to what has already been proposed in other diseases.[93] In addition, core outcome sets, i.e. consensus-based minimum requirements for the parameters to be reported in studies, will contribute to better comparability of study results and thus enable efficient pooling of patient data. Another source of progress in dysphagia diagnostics is the increasing establishment of novel, complementary instrumental modalities that have largely been used scientifically to date but may become clinically important in the future. High-resolution pharyngeal manometry can collect information about the pressure conditions in the pharynx and enable conclusions about disturbed swallowing patterns.[94] With increasing temporal resolution and decreasing costs, real-time MRI examination may also become relevant for swallowing assessment. Further, there are different neurophysiological techniques that can be used to study cortical activation related to swallowing and DAS. These include pharyngeal sensory or motor evoked potentials[39,41,95] and characterising the neural correlates of swallowing with magnetoencephalography.[96]

In addition to emerging diagnostic modalities, technical progress and innovation will contribute to the improvement of existing diagnostic procedures. Thus, as in the past, image quality is expected to steadily improve due to better spatial and temporal resolution in VFSS and FEES. In the latter procedure, special illumination sequences (such as narrow band imaging) may increase the diagnostic sensitivity for dysphagia pathologies.[74] Future three-dimensional image compilations may allow estimation of aspirate volume, which could contribute to more clinically relevant scores and associations with outcome parameters. Another major potential lies in advances in digitalisation. Machine learning could be established in FEES and VFSS image diagnostics or in the analysis of acoustic swallow and speech signals[97] and improve diagnostic validity. As in other areas, this would offer great potential to collect "real world" data beyond a brief and artificial examination protocol, e.g., acoustic signs of aspiration over the course of an entire day.

Besides developing and optimizing innovative diagnostics, it is equally important to increasingly implement evidence-based DAS management into clinical practice. To this end, structured education and training initiatives are needed to ensure that dysphagia experts are available in stroke facilities to provide standardized and state-of-the-art diagnosis and treatment. Corresponding advances in DAS rehabilitation have the potential to reduce mortality and improve the quality of life in stroke patients.

Contributors

BL: conceptualisation, literature search, visualisation, writing the original draft; EM: literature search, writing (review & editing); SH: literature search, writing (review & editing); MTG: literature search, writing (review & editing); SSK: writing (review & editing); PM: writing (review & editing); PB: literature search, writing (review & editing); RD: conceptualisation, literature search, visualisation, writing (review & editing).

Declaration of interests

BL: has received a research grant from the medical faculty of the University of Muenster for a clinician scientist rotational position;; SH: has received a research grant from MRC (UK) on cerebellar stimulation in dysphagic stroke paid to University of Manchester, a research grant from HTA/NIHR (UK) on pharyngeal stimulation in dysphagic stroke paid to University of Manchester, has received consulting fees from Phagenesis Ltd for acting as chief scientific officer, has received honoraria from the Chinese Dysphagia Research Forum 2021 for lecture/presentation on neuromodulation in dysphagic stroke, has received support for attending the ESSD 2022 conference, acted as chair for the TSC of a device for PPE; acts as chair of the medical technologies advisory committee April 2021-present, acts as board member and director of Phagenesis Ltd 2010-present, and holds foundation shares of Phagenesis Ltd and Anisys Ltd; MTG: has received payment for expert testimony from Phagenesis Ltd for involvement in a study as a reviewer of FEES-videos; SSK: was supported by an endowed professorship from the Else Kröner Fresenius Stiftung;; PMB: has received support from Phagenesis Ltd (provision of devices for NIHR HTA-funded PhEAST trial), and has received consulting fees from Phagenesis Ltd as member of the advisory board; RD: has received consulting fees from Daiichi Sankyo and Pfizer, has received honoraria for lectures from Daiichi Sankyo, Pfizer and Alexion, has received honoraria from Phagenesis Ltd paid to the University Hospital Münster for participating in the steering committees of different trials, and has received reimbursement of travel expenses as board member of the European Society for Swallowing Disorders and as board member of the German Dysphagia Society. The other authors declared no conflicts of interest.

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