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Objective Prediction of Pharyngeal Swallow Dysfunction in Dysphagia through Artificial Neural Network Modelling

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Short title: Swallow dysfunction modelled by Artificial Neural Networks

Abstract

BACKGROUND: Pharyngeal Pressure-Flow Analysis (PFA) of high resolution impedance-manometry (HRIM) with calculation of the Swallow Risk Index (SRI) can quantify swallow dysfunction predisposing to aspiration. We explored the potential use of Artificial Neural Networks (ANN) to model the relationship between PFA swallow metrics and aspiration and to predict swallow dysfunction.

METHODS: 200 consecutive dysphagia patients referred for videofluoroscopy and HRIM were assessed. Presence of aspiration was scored and PFA software derived 13 metrics and the SRI. An ANN was created and optimized over training cycles to achieve optimal classification accuracy for matching inputs (PFA metrics) to output (presence of aspiration on videofluoroscopy). Application of the ANN returned a value between 0.00-1.00 reflecting the degree of swallow dysfunction.

RESULTS: Twenty one patients were excluded due to insufficient number of swallows (<4). Of 179, 58 aspirated and 27 had aspiration pneumonia history. The SRI was higher in aspirators (aspiration 24 [9, 41] vs. no aspiration 7 [2, 18], $p<0.001$) and patients with pneumonia (pneumonia 27 [5, 42] vs. no pneumonia 8 [3, 24], $p<0.05$). The ANN Predicted Risk was higher in aspirators (aspiration 0.57 [0.38, 0.82] vs. no aspiration 0.13 [0.4, 0.25], $p<0.001$) and in patients with pneumonia (pneumonia 0.46 [0.18, 0.60] vs. no pneumonia 0.18 [0.6, 0.49], $p<0.01$). Prognostic value of the ANN was superior to the SRI.

CONCLUSIONS: In a heterogeneous cohort of dysphagia patients, PFA with ANN modelling offers enhanced detection of clinically significant swallowing dysfunction, probably more accurately reflecting the complex interplay of swallow characteristics that causes aspiration.

Study highlights

WHAT IS CURRENT KNOWLEDGE?

- Swallowing disorders are common and deglutitive aspiration often causes respiratory complications
- Understanding of underlying mechanisms is needed to guide therapy
- Automated Impedance Manometry describes the relation between pressure and bolus flow during swallowing
- The Swallow Risk Index combines 4 impedance-manometry parameters and is predictive of aspiration

WHAT IS NEW HERE?

- an artificial neural network model including 13 impedance-manometry parameters predicts aspiration more accurately
- aspiration risk predicted by this model is elevated in relation to aspiration pneumonia and hospitalization

List of Abbreviations

PFA	pressure flow analysis
HRIM	high resolution impedance manometry
SRI	swallow risk index
ANN	artificial neural networks
AIM	automated impedance manometry
UES	upper esophageal sphincter
ROI	region of interest
PP	peak pressure
NI	nadir impedance
TNIPP	time from nadir impedance to peak pressure
PNI	pressure at nadir impedance
PSIR	post swallow impedance ratio
UES IR	upper esophageal sphincter impedance ratio
UES RI	upper esophageal sphincter relaxation interval
UES MRP	upper esophageal sphincter minimal resting pressure
UES IBP	upper esophageal sphincter intrabolus pressure
UES resist	upper esophageal sphincter resistance
MS	multiple sclerosis
ALS	amyotrophic lateral sclerosis
ENT	ear nose throat
COPD	chronic obstructive pulmonary disease
NaCl	sodium chloride
VF	videofluoroscopy
ROC	Receiver Operator Curve

Introduction

Oropharyngeal dysphagia is common in many disease states including neurological conditions such as stroke and Parkinson's disease, head and neck cancers and progressive neuromuscular disease [1]. Also, the healthy elderly population may be predisposed to dysphagia due to loss of functional swallowing reserve [2]. Dysphagia is often associated with aspiration which in turn can lead to respiratory life-threatening complications such as pneumonia [3]. Isolated swallow characteristics such as breathing pattern during swallowing, reduced anterior hyoid movement, poor bolus propulsion and longer pharyngeal bolus dwell time have been associated with aspiration [4-7]. However, because the cause of aspiration can be multifactorial, these radiological features alone do not always predict aspiration risk [4-7].

The current gold standard to diagnose aspiration is videofluoroscopy [8], however routine clinical interpretation can be subjective. Pressure Flow Analysis (PFA), a novel technique based on pharyngeal high resolution impedance-manometry (HRIM) assessment of swallowing, has been previously described as a sensitive method to quantify swallow motor dysfunction in pediatric, adult and aged patients with dysphagia [9-16]. PFA may be an objective, non-radiological test of swallowing function, both as a stand-alone test or to complement videofluoroscopy. PFA can quantify the 'risk' of aspiration based on measures which characterize different aspects of the swallow mechanism such as contractile vigour, intrabolus pressure, bolus dwell time, bolus propulsion, luminal opening diameter and post-swallow residue [9-16]. Recognizing that the pathophysiology of aspiration is multifactorial, a global Swallow Risk Index (SRI) has been described based on four key PFA metrics which differ during swallows associated with an observed aspiration event [9]. Within the context of a busy clinical service, derivation of the SRI may be clinically very useful, because it can be rapidly calculated and defines the degree of swallow motor dysfunction on a continuous numerical scale. Reliable global predictors of swallow dysfunction can also be determined based upon pattern recognition techniques which use statistical models to identify associations between objective measures and relevant outcomes (e.g. aspiration). In a recent pilot study, we applied an artificial neural network (ANN)

modelling approach to HRIM derived PFA metrics with promising results, achieving 89% classification accuracy for distinguishing between individual swallows with and without aspiration [17].

The first aim of this study was to apply the ANN modelling approach to a large cohort of dysphagia patients who were referred to a tertiary care centre for combined videofluoroscopy and HRIM assessment of swallowing. We hypothesised that an ANN model would distinguish swallowing dysfunction predisposing to aspiration risk. Our second aim was to compare the prognostic value of ANN model based assessment compared to the established SRI. Our final aim was to compare and contrast SRI and ANN model-based predictions of swallowing dysfunction across different patient subgroups and in relation to other relevant clinical features such as aspiration pneumonia.

Methods

Subjects

In this cross-sectional study, 200 consecutive adult patients with dysphagia (116 males, mean age 66 years, age range 17-92 years) referred for concurrent videofluoroscopy and HRIM were assessed. The protocol was approved by the Research Ethics Committee, University Hospitals Leuven, Belgium (reference S58093). Based on a previous reliability study, we excluded 21 patients because less than four liquid swallows were captured during the test [14]. Of the remaining 179 patients (100 males, mean age 66 years, age range 17-92 years) analyses were based on at least five swallows (168, 94%).

Clinical Sequelae of Aspiration

Information on medical diagnosis, hospitalization, history suggestive of aspiration pneumonia and frequency of upper respiratory infections was retrieved from medical records. The clinical profile of the cohort is detailed in Table 1. Thirty seven percent of patients had a neurological disorder. Patients were defined as 'hospitalised' if they were inpatients at the time of testing or were referred for swallowing assessment following a recent admission to hospital (within 2 months). Patients were defined as having a clinical 'aspiration pneumonia history' if they had suffered a recent episode (within 6 months) of pneumonia and/or

with infiltrate in the right lower lobe and/or preceded by a choking incident witnessed by others, and/or associated with a history of frequent choking. Patients were defined as having 'frequent respiratory infections' if, based on their 1 year history, they had suffered two or more episodes within 6 months which were characterized by coloured secretions indicative of infection and required antibiotic treatment.

Measurement Protocol

Studies were performed in the Radiology Department, University Hospital Leuven. Continuous videofluoroscopy sequences (25 frames/s) of swallows were captured. HRIM data were acquired simultaneously at 20Hz (Solar GI acquisition system, MMS, The Netherlands) with a 3.2mm diameter solid state HRIM catheter (Unisensor USA Inc, Portsmouth, NH). Three separate catheter configurations were used, incorporating 32 or 36 1cm-spaced pressure sensors and 12 or 16 adjoining impedance segments, each of 2 cm length. Patients were intubated after topical anesthesia (lignocaine gel) and the catheter was positioned transnasally with sensors straddling the entire pharyngo-esophageal segment (velopharynx to proximal esophagus). Consistent with routine clinical protocol, subjects were evaluated sitting upright, with 5 boluses of liquid in the lateral (x2), left and right oblique (x2) and frontal (x1) views. The liquid contrast material was either barium (Micropaque® suspension) or alternatively, a low osmotic hydrosoluble iodine compound (UltravistH™), in case of clinical suspicion of aspiration. NaCl (1%) was added to bolus stock to enhance bolus conductivity [10].

Analysis of Videofluoroscopic images

Videofluoroscopic images were analysed by a geriatrician specialized in swallowing disorders (Author ED) who was present during acquisition, but was blinded to all pressure-flow metrics. Aspiration on videofluoroscopy was defined as the presence of contrast material below the level of the true vocal folds [18], which can be considered equivalent to a score ≥ 6 on the established Penetration-Aspiration Scale [19]. Patients were dichotomously classified as 'aspirators' when aspiration occurred in at least one of the liquid swallows captured.

Analysis of Pressure-Impedance Measurements

Pharyngeal Pressure-Flow Analysis (PFA) was performed as previously described [9-12]. Each swallow was exported in ascii-format (.csv file) and uploaded into a purpose designed software (AIMplot, Copyright Author TO, developed using MATLAB, The MathWorks Inc.). In brief, HRIM recordings are displayed as pressure topography plots with embedded impedance recordings which show bolus flow movements, the pharyngeal stripping wave, and relaxation and movement of the upper esophageal sphincter (UES). On selection of spatio-temporal landmarks on the pressure topography space-time plot (with embedded impedance recordings), specific regions of interest (ROI) are mapped. The landmarks identified are: 1. time of onset of pharyngeal swallow, 2. position of the UES proximal margin post-swallow, 3. position of the velopharynx and 4. position of the UES distal margin pre-swallow. There are three ROI encompassing the pharynx, distal pharynx and UES.

Pressure-Flow Metrics of Pharyngeal and UES Function

Within each ROI, the PFA metrics were derived. Peak pressure (PP) defines the maximum contraction whereas the nadir impedance (NI) defines the centre of the swallowed bolus. The NI is a correlate of diameter [13,20], with a high UES NI indicating a narrower UES diameter. The UES NI/NI ratio, defines the relative diameter of the UES to pharyngeal opening, with a ratio >1 indicating that the UES is narrower than the pharynx during swallow. The pressure at nadir impedance (PNI and UES PNI) defines pharyngeal and UES intrabolus pressures respectively. The time from nadir impedance to peak pressure (TNIPP) measures the latency from bolus passage to pharyngeal contraction. The flow interval represents pharyngeal bolus dwell time. The integrated ratio of NI during bolus passage to the impedance post-swallow, is known to be elevated in patients with post-swallow residue [12]. This metric was formerly called iZ_n/Z , but further referred to as the post swallow impedance ratio (PSIR).

Pressure Only Metrics of UES Function

The method of Ghosh et al. [21] was used to determine UES relaxation interval (UES RI), minimum relaxation pressure (UES MRP), UES intrabolus pressure (UES IBP) and deglutitive UES Resistance (UES Resist). The algorithms to perform this analysis were imbedded in AIMplot and therefore these data were generated simultaneously with all other metrics.

Swallow Risk Index

The swallow risk index (SRI) amplifies differences seen in key swallow metrics altered with swallow dysfunction and aspiration risk [9]. The SRI is a potential predictor of the overall level of swallowing dysfunction predisposing to aspiration risk. Validation studies using concurrent videofluoroscopy (VF) have previously shown that the average SRI from aspirating patients and those with post-swallow residue are significantly higher [9,10,14]. Amongst asymptomatic subjects, the SRI increases with age [15] and the upper limit of the normative range for liquid swallows (SRI 14.6 [15]) is closely aligned to the diagnostic cut off optimally predictive of aspiration risk (SRI 15.0 [9]).

Artificial Neural Network Model

Pressure-Flow Analysis derives a large amount of data from each individual swallow. The SRI provides a composite score of global swallow dysfunction. However, of the 13 individual metrics derived, defining different aspects of pharyngeal and UES function during swallow, only four metrics are used to calculate the SRI. We therefore explored the potential for pattern recognition techniques with the goal of modelling the relationship between all swallow metrics currently measured and the degree of swallow dysfunction defined by presence of aspiration.

Pattern recognition neural networks are feed-forward networks that can be trained to classify inputs according to target classes. The target data for pattern recognition networks consist of a vector of all zero values except for a 1 in elements where the target class is represented. In this case the inputs for the network were the objectively derived values for the 13 metrics (excluding the SRI) from the patients. The

outputs were aspiration risk on VF defined as zero, when no aspiration was observed for any liquid swallow, and 1, when aspiration was observed in at least one liquid swallow during the VF assessment.

An optimal ANN based on our data was created using the Neural Network Toolbox available with MATLAB software (version R2014a, The MathWorks Inc.). This program automatically creates and trains a network and then evaluates its performance using cross-entropy and confusion matrices. When the ANN is presented with the known data, the data are randomly assigned into three data samples:

- i. A 'training' sample, which presented to the network during training, enabling the network to be adjusted according to any error.
- ii. A 'validation' sample, to measure network generalisation, and to halt training when generalisation stops improving.
- iii. A 'testing' sample, to provide an independent measure of network performance during and after training.

The application goes through these sampling stages using a network training function that updates weight and bias values according to the scaled conjugate gradient back propagation method. For the current analysis, the data set was randomly partitioned for training (80% of samples), testing (10%) and validation (10%). To optimize performance, the network architecture, consisting of the number hidden neurons, was modified between 10-80 neurons over multiple training cycles. Optimization was undertaken as part of an iterative process (data not shown). The data presented are based on the ANN which achieved the best level of classification accuracy overall and which had a network architecture consisting of 40 neurons.

Statistical Analyses

Statistical analysis was performed using SigmaPlot v11.1 Statistics Package (Systat Software Inc, Chicago USA). Data from multiple liquid swallows were averaged for each patient. Data across the study cohort were not normally distributed and therefore medians [inter-quartile range] are presented. Mann-Whitney Rank Sum Test was used for dichotomous comparisons and Kruskal-Wallis ANOVA on ranks with pair-wise multiple

analysis procedures (Dunn's method) for multiple comparisons. Prognostic value was defined by calculation of sensitivity, specificity and the area under the Receiver Operator Curve (ROC).

Results

Metrics in relation to aspiration and aspiration pneumonia

Aspiration was observed in 58 patients, with 27 patients having a history suggestive of aspiration pneumonia. Aspirating patients had greater swallow dysfunction compared to patients without aspiration as indicated by PFA metrics. Moreover, amongst UES variables, the UES NI was shown to be increased in aspirating patients showed statistical significance (Table 2). The impedance ratio (IR) indicative of post-swallow residue, and the SRI, indicative of global swallow dysfunction, were also significantly higher in patients with aspiration (Table 2). Patients with an aspiration pneumonia history had a higher SRI and, amongst individual metrics, the TNIPP was shorter, indicating poor coordination between bolus flow and pharyngeal contraction, the Flow Interval longer thus, longer bolus dwell time and the UES NI was higher suggestive of a narrower UES diameter.

Artificial Neural Network Model

Application of the ANN to the database returned a number between 0.00-1.00 defining the risk of swallowing dysfunction for each patient. This is based on the 13 pressure-flow metrics (excluding SRI) used as the inputs and aspiration on VF used as the outputs. The ANN model predicted risk was higher in relation to aspiration (0.13 [0.4, 0.25] vs. 0.57 [0.38, 0.82], $p < 0.001$ for non-aspirators vs. aspirators) and aspiration pneumonia history (0.18 [0.6, 0.49] vs. 0.46 [0.18, 0.60], $p < 0.01$ for no pneumonia vs. pneumonia).

The ANN model had superior prognostic value for predicting clinically significant swallow dysfunction when compared to the SRI or IR (Figure 1). When patients were stratified based on neurological sequelae, the SRI did not discriminate presence of aspiration amongst neurological patients (Figure 2a). In contrast, the ANN model based risk was significantly different in relation to aspiration for both non-neurological and neurological patients (Figure 2b). Amongst the specific patient sub-groups, a range in severity of swallow

dysfunction was observed with the groups with greater model predicted risk also exhibiting a greater incidence of aspiration overall (Figure 3).

When considered in relation to neurological status, the SRI did not discriminate patients with a history of aspiration pneumonia (Figure 2c). In comparison, the ANN model did discriminate an aspiration pneumonia history, but only in the non-neurological patients (Figure 2d). Furthermore, the ANN model based aspiration risk was uniquely higher in those patients who were hospitalized (hospitalized 0.39 [0.14,0.57] vs. not hospitalized 0.17 [0.05,0.4], $p=0.015$) and a trend was found towards higher model predicted risk in patients with frequent upper respiratory infections (frequent 0.37 [0.28,0.56] vs. no frequent 0.2 [0.06,0.52], $p=0.051$).

Discussion

In this study, we report PFA findings in relation to aspiration on simultaneous videofluoroscopy. Overall, the pattern of differences in individual PFA metrics that related to observed aspiration was consistent with past validation studies. The SRI, a global measure of swallowing dysfunction, also predicted aspiration. However prediction of aspiration risk was superior when based upon a pattern recognition ANN model.

Amongst the key pharyngeal pressure-flow metrics, a higher PNI, a shorter TNIPP and a longer flow interval were observed in relation to aspiration, consistent with past reports [9,11]. Pharyngeal peak pressure has been less consistently linked with aspiration previously, and was not significantly different in the current study. As in previous studies, UES relaxation pressures and UES resistance were not significantly different between aspirating and non-aspirating patients [9]. This confirms that amongst dysphagia patients as a population there is no specific directionality of pharyngeal peak pressures and UES relaxation pressures in relation to aspiration risk. This might also reflect the importance of the coordination and interplay between several swallow motor components in the pathophysiology of dysphagia and aspiration. Our findings reaffirm that, when measured in isolation, the pressure generated by the pharynx and UES is not a very good global predictor of swallowing dysfunction. For example, weak pharyngeal swallow may lead to post-swallow

aspiration due to residue, however pharyngeal swallow can also be entirely normal in cases of pre-swallow aspiration due to poor oral bolus containment. And, as described by Williams et al., among patients with failed manometric UES relaxation, UES opening is potentially normal in circumstances when pharyngeal contraction is well preserved, resulting in only mild dysphagia [22]. Therefore, pressure needs to be interpreted in the context of other important features of swallowing such as bolus flow timing and UES opening. Such features can be elucidated using the PFA method.

As previously reported, the SRI was significantly higher in aspirating patients [9,11]. However, the results from the current study also show a diminished prognostic value of the SRI when applied to this substantially larger and more pathologically diverse patient cohort, more akin to the diverse range of patients seen in clinical practice. A main driver of the lost performance of the SRI appears to be the inability of the SRI to distinguish aspiration risk amongst the neurological subgroup of patients studied. Our data show superior performance of an ANN model versus the SRI overall and, moreover, unlike the SRI, the ANN model predicted risk was significantly elevated in relation to aspiration in both non-neurological and neurological subgroups. This is by virtue of the fact that the model was configured to include all 13 PFA metrics and was also optimized for maximum performance within our test dataset. However, it remains to be determined how well the optimized ANN model will perform when applied to other independent patient datasets.

The use of statistical models to recognize patterns of difference in functional measures that link to aspiration risk is a logical extension of the PFA method. Within a heterogeneous group of dysphagia patients, there is clearly a complex interplay of several swallow characteristics, with different patterns of swallow dysfunctions leading to aspiration in individual patients. In clinical practice, it is important to have a diagnostic tool that quantifies swallowing dysfunction that predispose to aspiration risk and, ideally, this should be applicable to all patients regardless of the underlying pathological mechanisms that lead to symptoms of dysphagia.

An objectively derived and bio-mechanically based global index of swallowing function, such as the SRI or a statistical model, may be very useful clinically. In the first instance, it allows quantification of the degree of

swallowing dysfunction present and whether or not this exceeds a level at which aspiration may be likely. Furthermore, it can be re-measured to objectively document longitudinal recovery or deterioration of swallowing function over time or after therapeutic interventions. Finally, a global assessment of swallowing dysfunction may prompt examination of the individual PFA metrics contributing to a high global index. These may provide insights into the specific subtype of motor dysfunction. Our ongoing research program is currently focused of discovering patterns of PFA metrics that can distinguish specific disorder subtypes which can be challenging even when videofluoroscopy is used. For example, distinguishing poor oral containment from delayed swallow trigger [29] and distinguishing reduced UES opening due to anatomical obstruction from weak bolus propulsion and/or reduced hyoid elevation.

This is the first study to report an association between a pressure-impedance based global assessment of swallowing dysfunction and a history suggestive of aspiration pneumonia. This observation is consistent with a recent study which correlated increased swallowing dysfunction on videofluoroscopy with the presence of community acquired pneumonia in the aged [23]. However, whilst there appears to be an association of pneumonia history and swallowing dysfunction, it is important to distinguish these observations from a causal link in terms of the prediction of risk for pneumonia prospectively. There are many other factors unrelated to dysphagia and aspiration, such as smoking and underlying chronic respiratory and cardiovascular disease, which are known risk factors potentially contributing to pneumonia in adults [24]. It is notable that the ANN model predicted swallow risk, whilst significantly higher in relation to pneumonia overall, was not different in relation to aspiration pneumonia history in the sub-group of neurological patients. The very severe levels of dysfunction seen amongst these patients may have made it more difficult to show differences. It could also well be due to the fact that other co-factors predominant in neurological patients, but unrelated to swallowing function, may be influencing the incidence of pneumonia. The literature shows that factors such as stroke-induced immunosuppression and immobility may predispose to pneumonia in this specific patient group [25,26].

Our study focused on the detection and prediction of aspiration risk and therefore we based our assessments on liquid bolus swallows which, apart from being most likely aspirated, were also the most frequently tested bolus consistency during videofluoroscopy allowing for a more reliable assessment based on a greater number of repeat measurements. In a swallowing evaluation, different bolus consistencies are routinely used, as swallowing potential might differ among consistencies and this can eventually be translated into management and therapy [18]. Moreover, it is suggested that mechanisms of aspiration might differ for different food consistencies [27], therefore it is crucial to incorporate semisolid and solid consistencies in future studies.

In this study, two different contrast media were used (Micropaque® suspension or Ultravist® hydrosoluble non-ionizing contrast medium) and 1% NaCl solution was added to enhance conductivity, important when measuring impedance. However the extent to which the use of different contrast boluses with differing conductive properties can influence the prognostic value of PFA is yet to be determined. We hope that in the future, PFA can also be performed independently of videofluoroscopy, and thus test boluses can be better standardized. Normal saline for example is commonly used in esophageal HRIM [28]. Therefore, further studies are needed to determine if the concurrent, but not simultaneous, capture of liquid saline swallows with HRIM, performed within a narrow time frame around the videofluoroscopy assessment can also predict aspiration risk.

In terms of the way the ANN model has been derived and validated, future studies are needed to test the prognostic value of the model in independently acquired databases and amongst large homogeneous patient cohorts with a single pathological entity. Whilst our study shows that a highly predictive ANN model can be created, we recognize that there are additional statistical operations that can be applied to the raw dataset that may further improve the ANN classification accuracy (normalization of data, principal component analysis, level reduction). The ANN approach to pattern recognition is also limited in that the algorithms defining the classification cannot be easily interrogated to determine which specific metrics drive accuracy and how weightings are applied. Whilst, other pattern recognition methods offer this capability, we

chose to use ANN model in the first instance because it is relatively easy to derive and apply using widely available software.

In conclusion, in a large heterogeneous cohort of dysphagia patients we report that objective pressure-flow analysis of pressure-impedance recordings, combined with pattern recognition modelling, has the potential to determine global predictors of clinically relevant levels of swallow dysfunction. Use of pattern recognition techniques has the potential to simplify the clinical assessment of multiple metrics which collectively define the complex interplay of the dysfunctional swallow characteristics that lead to aspiration. Our findings appear to correlate with relevant clinical sequelae, such as aspiration, aspiration pneumonia and hospitalization. However, future research is needed to replicate these results in independent and homogeneous cohorts and by way of prospective studies to address clinical applicability through correlation with clinical outcomes.

References

1. Roden DF, Altman KW. Causes of dysphagia among different age groups: a systematic review of the literature. *Otolaryngol Clin North Am* 2013; 46: 965-987
2. Holland G, Jayasekera V, Pendleton N et al. Prevalence and symptom profiling of oropharyngeal dysphagia in a community dwelling of an elderly population: a self-reporting questionnaire survey. *Dis Esophagus* 2011; 24: 476-480
3. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM et al. Meta-analysis of dysphagia and aspiration pneumonia in frail elders. *J Dent Res* 2011; 90: 1398-1404
4. Cvejic L, Harding R, Churchward T et al. Laryngeal penetration and aspiration in individuals with stable COPD. *Respirology* 2011; 16: 269-275
5. Steele CM, Bailey GL, Chau T et al. The relationship between hyoid and laryngeal displacement and swallowing impairment. *Clin Otolaryngol* 2011; 36: 30-36
6. Butler SG, Stuart A, Leng X et al. The relationship of aspiration status with tongue and handgrip strength in healthy older adults. *J Gerontol A Biol Sci Med Sci* 2011; 66: 452-458
7. Power ML, Hamdy S, Goulermas JY et al. Predicting aspiration after hemispheric stroke from timing measures of oropharyngeal bolus flow and laryngeal closure. *Dysphagia* 2009; 24: 257-264
8. Clavé P, Rofes L, Carrión S et al. Pathophysiology, relevance and natural history of oropharyngeal dysphagia among older people. *Nestle Nutr Inst Workshop Ser* 2012; 72: 57-66
9. Omari TI, Dejaeger E, van Beckevoort D et al. A method to objectively assess swallow function in adults with suspected aspiration. *Gastroenterology* 2011; 140: 1454-1463
10. Omari TI, Dejaeger E, Van Beckevoort D et al. A novel method for the nonradiological assessment of ineffective swallowing. *Am J Gastroenterol* 2011; 106: 1796-1802
11. Omari TI, Papathanasopoulos A, Dejaeger E et al. Reproducibility and agreement of pharyngeal automated impedance manometry with videofluoroscopy. *Clin Gastroenterol Hepatol* 2011; 9: 862-867
12. Omari TI, Dejaeger E, Tack J et al. An impedance-manometry based method for non-radiological detection of pharyngeal postswallow residue. *Neurogastroenterol Motil* 2012; 24: e277-284
13. Omari TI, Ferris L, Dejaeger E et al. Upper esophageal sphincter impedance as a marker of sphincter opening diameter. *Am J Physiol Gastrointest Liver Physiol* 2012; 302: G909-913
14. Omari TI, Dejaeger E, Tack J et al. Effect of bolus volume and viscosity on pharyngeal automated impedance manometry variables derived for broad Dysphagia patients. *Dysphagia* 2013; 28: 146-152
15. Omari TI, Kritas S, Cock C et al. Swallowing dysfunction in healthy older people using pharyngeal pressure-flow analysis. *Neurogastroenterol Motil* 2014; 26: 59-68
16. Rommel N, Sellselagh M, Hoffman I et al. Objective assessment of swallow function in children with suspected aspiration using pharyngeal automated impedance manometry. *J Pediatr Gastroenterol Nutr* 2014; 58: 789-794
17. Hoffman MR, Mielens JD, Omari TI et al. Artificial neural network classification of pharyngeal high-resolution manometry with impedance data. *Laryngoscope* 2013; 123: 713-720
18. Logemann J. Evaluation and treatment of swallowing disorders. Austin (Texas): Pro-ed; 1998
19. Rosenbek JC, Robbins JA, Roecker EB et al. A penetration-aspiration scale. *Dysphagia* 1996; 11: 93-98
20. Kim JH, Mittal RK, Patel N et al. Esophageal distension during bolus transport: can it be detected by intraluminal impedance recordings? *Neurogastroenterol Motil* 2014; 26: 1122-1130
21. Ghosh SK, Pandolfino JE, Zhang Q et al. Deglutitive upper esophageal sphincter relaxation: a study of 75 volunteer subjects using solid-state high-resolution manometry. *Am J Physiol Gastrointest Liver Physiol* 2006; 291: G525-531
22. Williams RB, Wallace KL, Ali GN et al. Biomechanics of failed deglutitive upper esophageal sphincter relaxation in neurogenic dysphagia. *Am J Physiol Gastrointest Liver Physiol* 2002; 283: G16-26
23. Almirall J, Rofes L, Serra-Prat M et al. Oropharyngeal dysphagia is a risk factor for community-acquired pneumonia in the elderly. *Eur Respir J* 2013; 41: 923-928

24. Torres A, Peetermans WE, Viegi G et al. Risk factors for community-acquired pneumonia in adults in Europe: a literature review. *Thorax* 2013; 68: 1057-1065
25. Brogan E, Langdon C, Brookes K et al. Respiratory infections in acute stroke: nasogastric tubes and immobility are stronger predictors than dysphagia. *Dysphagia* 2014; 29: 340-345
26. Westendorp WF, Nederkoorn PJ, Vermeij JD et al. Post-stroke infection: a systematic review and meta-analysis. *BMC Neurol* 2011; 11: 110
27. Choi KH, Ryu JS, Kim MY et al. Kinematic analysis of dysphagia: significant parameters of aspiration related to bolus viscosity. *Dysphagia* 2011; 26: 392-398
28. Gyawali CP, Bredenoord AJ, Conklin JL et al. Evaluation of esophageal motor function in clinical practice. *Neurogastroenterol Motil* 2013; 25: 99-133
29. Ferris L, Omari T, Selleslagh M et al. Pressure flow analysis in the assessment of preswallow pharyngeal bolus presence in Dysphagia. *Int J Otolaryngol.* 2015; 2015:764709.

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