Research Article

Identification of Phenotypic Patterns of Dysphagia: A Proof of Concept Study

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Purpose: The purpose of the current project was to explore the feasibility for subtyping dysphagia traits or patterns of scores in a subset of data from the Modified Barium Swallow Impairment Profile global registry in patients referred to videofluoroscopic swallowing studies across 5 common medical categories: (a) cardiothoracic, (b) gastroenterology, (c) head and neck cancer, (d) neurology, and (e) pulmonary. **Method:** Videofluoroscopic swallowing study imaging and Modified Barium Swallow Impairment Profile metrics were used to evaluate 235 patients with dysphagia grouped into 1 of the 5 categories. Two summative domain scores (oral total [OT] and pharyngeal total [PT]) and 17 component scores were tested for differences among the categories.

Results: When compared with the gastroenterology category, significantly higher OT/PT scores were observed in neurology and pulmonary categories (all p values < .05). Four oral and 6 pharyngeal domain components significantly differed across medical categories: tongue control during bolus hold (all p values < .04).

Conclusions: The results of this feasibility study demonstrate that summative scores of swallowing physiology alone are not sufficiently robust to distinguish subtypes of dysphagia in broad, heterogeneous medical categories. Using OT/PT as subtypes only separated gastroenterology from the other categories, suggesting overlap in OT/PT scores between the latter categories.

Classification or subtyping of complex diseases, facilitated by emergence of electronic medical records (Blumenthal, 2009; Shea & Hripcsak, 2010), identifies groups of patients who present with similar traits for refinement of the definition of multiorgan diseases. Subtyping reduces uncertainty in expected patient outcomes by guiding treatment (Schulam, Wigley, & Saria, 2015), assists in formulating prognosis and predicting costs (Chang, Clark, & Weiner, 2011), and improves effectiveness of clinical trials (Gundlapalli et al., 2008).

Dysphagia (swallowing impairment) is not a disease itself but, rather, a highly complex condition, involving multiple organs and systems and occurring with varying levels of severity and morbidity across diverse patient populations

(Martin-Harris, 2008; Martin-Harris & McFarland, 2012; Martin-Harris, Michel, & Castell, 2005). The complexity of dysphagia is further reflected when attempting to estimate the incidence and prevalence of the condition because dysphagia is not a reportable disease, is likely underreported, and is reliant upon population estimates obtained from small samples. Similar to problems faced by researchers investigating other complex health conditions, attempts to subtype dysphagia by pattern and severity of impairment characteristic of classes of disease or disorders is challenged by “nuisance variability,” including variations in the measurements used to assess dysphagia (e.g., nonstandardized approaches) that may result in biased estimates for group-level trajectories (Schulam et al., 2015). Because subtyping research involves distinguishing groups of patients by traits, one common trait in the context of dysphagia—albeit derived from varied assessment approaches—includes the individual physiologic components that contribute to the overall dysphagia impairment. To date, no central clinical registry has been available to record or query these physiologic dysphagic traits in like groups of patients.

Standardization in the identification and quantification of the most commonly used instrumental swallowing assessment, the videofluoroscopic swallowing study (VFSS), has resulted in the development and implementation of a global clinical registry of dysphagia traits—the online

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Editor-in-Chief: Krista Wilkinson

Editor: Julie Barkmeier-Kraemer

Received October 19, 2017

Revision received January 2, 2018

Accepted February 12, 2018

https://doi.org/10.1044/2018_AJSLP-17-0173

Disclosure: The authors have declared that no competing interests existed at the time of publication.

database of the Modified Barium Swallow Impairment Profile (MBSImP; Northern Speech Services, 2017). This international clinical registry is compliant with the Health Insurance Portability and Accountability Act, composed of over 23,000 patient entries, and used by over 2,000 clinicians across 20 countries worldwide. The MBSImP database includes demographic data combined with standardized, validated, and reliable metric scores of physiologic dysphagia impairment across both broad diagnostic medical categories and detailed medical diagnoses (Northern Speech Services, 2017). This feasibility study explored the former, subtyping dysphagia at the macrodiagnostic category level.

The MBSImP approach to perform VFSSs includes selective and validated swallowing tasks of varied volumes and viscosities using standardized contrast (barium) materials (Varibar, E-Z-EM, Inc.). The MBSImP metric includes 17 components of swallowing physiology across three functional domains: oral (Components 1–6), pharyngeal (Components 7–16), and esophageal (Component 17). Each component is scored using an ordinal scale from 0 to 2, 3, or 4, with higher scores indicating increasingly worse impairment (Martin-Harris et al., 2008; Northern Speech Services, 2017). Clinicians using the registry are further able to determine the effectiveness of their dysphagia intervention(s) by comparing swallowing physiology scores and patient-reported outcomes from initial (baseline) to postintervention VFSS.

The purpose of the current project was to explore the feasibility for subtyping dysphagia traits or patterns of scores in a subset of data from the MBSImP global registry in patients referred to VFSS across five common medical categories—(a) cardiothoracic, (b) gastroenterology, (c) head and neck cancer [H&N], (d) neurology, and (e) pulmonary—using summary (composite) scores and individual component scores derived from a well-tested, standardized interpretation approach—the MBSImP (Martin-Harris et al., 2008). If subtyping is feasible at this macrodata level, further studies will include subtyping within group patient diagnoses (microdata level; e.g., right hemisphere stroke, left hemisphere stroke, oropharyngeal cancer, etc.) included within these broad diagnostic categories.

Method

Three hundred twenty consecutive patient records were reviewed from the MBSImP global, clinical registry. For each of the 17 MBSImP components, we constructed an overall impression (OI) score equal to the maximum nonmissing score across all tasks presented during the VFSS (Martin-Harris et al., 2008; Northern Speech Services, 2017). OI scores were summed across Components 1 through 6 to represent oral total (OT), whereas OI scores across Components 7–16 represented pharyngeal total (PT). Scores of 1 were not included in the calculation of OT/PT scores for Components 1, 5, 15, and 16 because a score of 1 is considered normal on the basis of years of previous field testing. Therefore, only scores of 2 or greater for these four components were included in the calculation of OT/PT scores. The range of permissible scores for OT and PT are 0 to 22 and 0 to 29, respectively.

Statistical Considerations and Analysis

Patients were grouped into one of five categories (cardiothoracic, gastroenterology, H&N, neurology, and pulmonary) according to their primary medical diagnosis. OT and PT scores were derived from the individual component OI scores. If patients were missing one or more component OI scores, the lower and upper bounds for the respective component OI scores were used in the summation resulting in interval-censored OT and/or PT summary scores. Interval censoring occurs when a measurement is not known exactly but is known to be within a specific range. An example of an interval-censored OT score would be as follows: when five of six OT component OI scores are known and their sum is 10 and the scoring range of the missing score is 0–4, the interval-censored OT score is the range 10 to 14. Median scores and correlations were determined using the midpoints of the interval-censored results. Pairwise comparisons between each diagnostic category of the interval-censored OT and PT scores were completed using asymptotic two-sample Log-rank tests ($\alpha = .05$; Fay & Shaw, 2010). Impairment rates by diagnostic category were calculated for each physiologic component OI score. Fisher's exact test was used to test for associations between physiologic impairment and diagnostic category for each MBSImP component. A separate logistic regression with impairment (yes/no) as the outcome and medical category as an independent variable was then fit for each MBSImP component. Linear combinations of the resulting model coefficients were constructed to test equality of the odds of being impaired between pairs of diagnostic categories (Wald test, $\alpha = .05$). Statistical analyses were performed using SAS Version 9.3 and R Version 3.2.3 (R Core Team, 2013).

Results

Complete data were available for a total of 235 patients distributed across the five medical diagnostic categories. Sixty-nine records of the original 304 records were excluded because the primary medical category did not belong to one of the five medical categories selected for this project, with an additional 16 records excluded for missing all OI scores. The majority of the patient sample was Caucasian male, with a mean ($\pm SD$) age of 65 (± 16) years (see Table 1). The most frequent medical diagnostic categories were pulmonary (29%), followed by H&N (25%) and neurology (19%). Twenty-seven of the 235 patients had interval-censored OT scores, and 28 had interval-censored PT scores. The respective interval censoring rates by diagnostic category for cardiothoracic, gastroenterology, H&N, neurology, and pulmonary were 23%, 5%, 10%, 13%, and 10% for OT, respectively, and 8%, 0%, 10%, 24%, and 13% for PT, respectively.

Boxplots for OT and PT for each category are provided in Figures 1 and 2, respectively. The diagnostic categories ranked from the highest (worse) median score to lowest OT were neurology (12), pulmonary (11), cardiothoracic (10), H&N (8), and gastroenterology (8; see Table 2).

Table 1. Patient demographics and distribution across medical diagnostic categories.

Variable	Total (N = 235)
Age (years)	
<i>M</i> ± <i>SD</i>	65 ± 16
Range	18–98
Gender, <i>n</i> (%)	
Male	149 (63)
Female	86 (37)
Race/Ethnicity, <i>n</i> (%)	
White, non-Hispanic	188 (80)
Black, non-Hispanic	44 (19)
Unknown	3 (1)
Medical diagnostic category, <i>n</i> (%)	
Cardiothoracic	26 (11)
Gastroenterology	37 (16)
Head and neck cancer	58 (25)
Neurology	46 (19)
Pulmonary	68 (29)

Comparably, from highest to lowest PT were cardiothoracic (11), neurology (10), pulmonary (10), H&N (9) and, lastly, gastroenterology (6; see Table 2). OT and PT scores were highly correlated, with a Spearman rank correlation of .73, ranging from .59 to .78 for individual diagnostic categories.

OT Pairwise Comparisons Across Medical Diagnostic Categories

Pairwise comparisons of OT scores across each of the five medical diagnostic categories are provided in Figure 1. When compared to the gastroenterology category, significantly higher OT scores were observed in the H&N ($p = .04$), neurology ($p = .006$), and pulmonary categories ($p = .002$). No further significant differences were observed

for the remaining comparisons between medical diagnostic categories.

PT Pairwise Comparisons Across Medical Diagnostic Categories

Pairwise comparisons of PT scores across each of the five medical diagnostic categories are provided in Figure 2. When compared with the gastroenterology group, significantly higher PT scores were observed in the cardiothoracic ($p = .01$), H&N ($p = .01$), neurology ($p = .004$), and pulmonary categories ($p = .01$). No further significant differences were observed for remaining comparisons between medical diagnostic categories.

MBSImP Component Impairment Rates Across Medical Diagnostic Categories

To further attempt to delineate subtypes between the diagnostic categories, we explored individual MBSImP component impairment rates across the five medical diagnostic categories (Figure 3). Four (of six) oral domain components significantly differed across medical categories: tongue control during bolus hold ($p < .001$), bolus preparation/mastication ($p = .005$), bolus transport/lingual motion ($p < .001$), and oral residue ($p < .001$). Six (of 10) pharyngeal domain components were also found to significantly differ across medical categories: laryngeal elevation ($p = .048$), anterior hyoid excursion ($p = .02$), laryngeal vestibular closure ($p = .007$), pharyngeal stripping wave ($p = .03$), tongue base retraction ($p < .001$), and pharyngeal residue ($p < .001$). Differences in impairment rates observed across diagnostic categories approached but did not reach statistical significance for epiglottic movement and esophageal clearance components (both $p = .06$, respectively).

Figure 1. Boxplots for oral total scores for each medical diagnostic category. Midpoints are plotted for interval-censored observations.

Figure 2. Boxplots for pharyngeal total scores for each medical diagnostic category. Midpoints are plotted for interval-censored observations.

MBSImP Component Impairment Rates Between Medical Diagnostic Categories

Oral Domain

Four oral domain components had at least one significant difference observed between two medical categories. Impairment rates of lip closure (Component 1) were significantly different between gastroenterology and three categories: cardiothoracic ($p = .03$), H&N ($p = .03$), and pulmonary ($p = .03$). Further, impairment rates of tongue control during bolus hold (Component 2) were significantly different between gastroenterology and neurology ($p = .01$), gastroenterology and pulmonary ($p = .02$), and H&N and neurology ($p = .01$) and between H&N and pulmonary ($p = .01$). Bolus preparation/mastication (Component 3) significantly differed between gastroenterology and all remaining categories: cardiothoracic ($p = .04$), H&N ($p = .02$), neurology ($p < .01$), and pulmonary ($p < .01$) categories. Bolus preparation/mastication was also significantly different between H&N and pulmonary ($p = .04$). Lastly, bolus transport/lingual motion (Component 4) was significantly different between gastroenterology and cardiothoracic ($p = .02$) and gastroenterology and neurology ($p = .02$) medical categories. No significant differences were observed between any categories for oral residue (Component 5) or initiation of pharyngeal swallow (Component 6).

Pharyngeal Domain

The majority of components (8/10; 80%) in the pharyngeal domain had at least one significant difference observed between two medical categories (see Table 3). Soft palate elevation (Component 7) was significantly different only between gastroenterology and H&N ($p = .04$). Significant differences in impairment rates were also observed for laryngeal elevation (Component 8), anterior hyoid excursion (Component 9), epiglottic movement (Component 10), and tongue base retraction (Component 15) between gastroenterology and each of the remaining four categories (see Table 3). Although not reaching statistical significance, a trend was observed in impairment rates between gastroenterology and neurology for lip closure (Component 1; $p = .052$) and between gastroenterology and pulmonary for bolus transport/lingual motion (Component 4; $p = .052$). No further significant differences were observed between remaining medical category comparisons for Components 8, 9, 10, and 15 (see Table 3).

Significant differences in impairment rates for pharyngeal stripping wave (Component 12) were observed between H&N and pulmonary ($p = .048$), as well as neurology and pulmonary ($p = .03$) categories. Pharyngeal contraction (Component 13) and pharyngeal residue (Component 16) impairment rates significantly differed in gastroenterology compared with neurology and pulmonary categories (see

Table 2. Median oral total (OT) and pharyngeal total (PT) for each medical diagnostic category.

Diagnostic category	Cardiothoracic	Gastroenterology	H&N	Neurology	Pulmonary
<i>n</i>	26	37	58	46	68
Median OT	10	8	8	12	11
Median PT	11	6	9	10	10

Note. H&N = head and neck cancer.

Figure 3. Percent of impairment across Modified Barium Swallow Impairment Profile component for each medical diagnostic category. PESO = pharyngoesophageal segment opening; Cardio = cardiothoracic; Neuro = neurology; Gastro = gastroenterology; H&N = head and neck cancer.

Table 3). Although not reaching statistical significance, a trend was observed in impairment rates between cardiothoracic and pulmonary for pharyngeal stripping wave (Component 12; $p = .06$). No further significant differences were observed between any categories for laryngeal vestibular closure (Component 11) or pharyngoesophageal segment opening (Component 14; see Table 3).

Discussion

The purpose of the current project was to explore the feasibility for subtyping dysphagia traits or patterns of physiologic swallowing impairment in a subset of data from the MBSImP global clinical registry in patients referred to VFSS across five common medical diagnostic categories: (a) cardiothoracic, (b) gastroenterology, (c) H&N, (d) neurology, and (e) pulmonary. Our findings demonstrated that summative domain scores (OT/PT) did not differentiate well between diagnostic medical categories with the exception

of the gastroenterology category. Patients in the gastroenterology group were mostly observed to have less swallowing impairment as measured by MBSImP summative (OT/PT) and component scores when compared with the other four medical diagnostic categories (cardiothoracic, H&N, neurology, and pulmonary). This finding is not surprising as patients referred to VFSS for a primary gastrointestinal disorder are likely to present with oropharyngeal manifestations of incomplete esophageal clearance (Gullung, Hill, Castell, & Martin-Harris, 2012). However, the severity of impairment in the gastroenterology group was expected to be less severe when compared with the other medical categories. Patients with gastrointestinal disorders are more likely to be ambulatory and may have been more appropriate to undergo an esophagram rather than a VFSS. Outside of the gastroenterology category against the remaining categories, summative scores were not able to delineate between groups in this relatively small and heterogeneous sample.

Table 3. Pairwise comparison of impairment rates between medical diagnostic categories.

Medical categories compared		Oral components						Pharyngeal components									EC	
		1-LC	2-BH	3-BP/M	4-BT	5-OR	6-IPS	7-SPE	8-LE	9-AHE	10-EM	11-LVC	12-PSW	13-PC	14-PESO	15-TBR	16-PR	17-EC
GI	CT	.03	.49	.04	.02	.50	.99	.09	.03	.01	.01	.13	.13	.18	.21	.01	.11	.99
	H&N	.03	.95	.02	.23	.57	.99	.04	.04	.03	.01	.36	.14	.05	.67	.01	.15	.32
	Neuro	.05	.01	< .01	.02	.99	1.00	.11	.03	.01	.01	.07	.10	.01	.64	< .01	.05	.15
	Pulm	.03	.02	< .01	.05	.25	.99	.08	.01	.01	.04	.13	.80	.03	.53	< .01	.01	.87
CT	H&N	.69	.49	.70	.13	.79	.32	.82	.64	.27	.60	.40	.70	.72	.32	.51	.44	.99
	Neuro	.64	.09	.63	.65	.99	.99	.76	.79	.61	.55	.98	.90	.21	.36	.33	.92	.99
	Pulm	.71	.18	.23	.32	.82	.22	.78	.95	.32	.26	.71	.06	.58	.39	.99	.82	.99
H&N	Neuro	.90	.01	.27	.18	.99	.99	.61	.82	.48	.92	.30	.76	.25	.93	.06	.40	.50
	Pulm	.97	.01	.04	.42	.53	.82	.61	.59	.86	.45	.52	.05	.81	.82	.37	.18	.21
Neuro	Pulm	.87	.55	.41	.52	.99	.99	.96	.79	.56	.54	.63	.03	.34	.91	.24	.69	.09

Note. p values are reported, with significant values ($p < .05$) in bold. EC = esophageal clearance (upright position); LC = lip closure; BH = tongue control during bolus hold; BP/M = bolus preparation/mastication; BT = bolus transport/lingual motion; OR = oral residue; IPS = initiation of pharyngeal swallow; SPE = soft palate elevation; LE = laryngeal elevation; AHE = anterior hyoid excursion; EM = epiglottic movement; LVC = laryngeal vestibular closure; PSW = pharyngeal stripping wave; PC = pharyngeal contraction; PESO = pharyngoesophageal segment opening; TBR = tongue base retraction; PR = pharyngeal residue; GI = gastroenterology; CT = cardiothoracic; H&N = head and neck cancer; Neuro = neurology; Pulm = pulmonary.

In contrast to summative OT/PT scores, however, the individual physiologic swallow impairment traits (scores) did show the potential to distinguish patterns of impairment types between medical categories. Our findings, similar to the summative scores, revealed significant differences across the majority of components (11/17; 65%) when comparing the gastroenterology category with the remaining four other medical categories. Five components did not contribute at all to differences in impairment rates between categories: oral residue (Component 5), initiation of pharyngeal swallow (Component 6), laryngeal vestibular closure (Component 11), pharyngoesophageal segment opening (Component 14), and esophageal clearance in the upright position (Component 17). As a proof of concept study, we were able to demonstrate that the use of a standardized measurement system to detail oropharyngeal swallowing function has the potential to phenotype swallowing impairment across a variety of patient populations—both across and within categories.

Limitations

The medical diagnostic categories in this study are broad, and thus, a more informative approach would include less heterogeneous patient medical diagnostic categories, such as acute or refractory dysphagia, or subcategories within the broader groupings, such as stroke versus traumatic brain injury versus progressive motor neuron disease within the neurology category. An additional limitation is the small sample size and unequal distribution across the five medical diagnostic categories, with pulmonary and cardiothoracic categories comprising the highest and lowest patient numbers, respectively. We also had not accounted for the contribution of how other biological traits may contribute to swallowing outcomes, including age and sex.

Particularly in the older population, a patient can present with multiple comorbidities, with one or more that could potentially impact swallowing function. For purposes of this analysis, the medical diagnostic category chosen for classification among patients was the primary medical diagnosis at the time of the VFSS referral. Misclassification of the patients into the wrong medical category may have occurred, although this is unlikely because the specific primary medical diagnosis (e.g., stroke) was also entered into the global registry. Lastly, our study is a cohort study (i.e., measured swallowing impairment in patients at one moment in time), and therefore, longitudinal studies, particularly documenting recovery patterns, are also needed.

Lastly, OI scores were dichotomized as impaired versus not impaired, which may have attenuated subtle differences between medical categories.

Conclusion

The results of this feasibility study demonstrate that summative scores of swallowing physiology alone are not sufficiently robust to distinguish subtypes or patterns of dysphagia in broad, heterogeneous and relatively small diagnostic medical categories. Significant differences using

OT and PT as subtypes only separated the gastroenterology group from the other four categories, suggesting overlap in OT and PT scores between the latter groups. However, it is plausible that summative scores may be able to distinguish better defined patient samples that consist of like and detailed etiologies underlying dysphagia referrals (acute neurological events vs. progressive neurological diseases; head and neck tumor sites and stages; obstructive vs. restrictive lung disease, etc.). The data at the physiologic component level, however, do show promise for distinguishing subtypes of swallowing impairment patterns not only in narrow and well-defined diagnoses but also between broad diagnostic categories. Our future work will include similar methods using the entire clinical data base (> 23,000 swallowing examinations) to identify subtypes of physiologic swallowing impairment that characterize multiple diagnoses, estimates of impairment severity between these groups, and track changes in these subtypes over the course of recovery or disease processes. These data could serve to better inform patients, caregivers, providers, and payers regarding the resources needed for treatment planning and optimization of recovery.

Acknowledgments

The contents of this publication were developed under grants from the National Institutes of Health under Grant K23DC005764 (PI: Martin-Harris) and Grant 1K24DC12801 (PI: Martin-Harris).

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