Airway Closure Delay: The Predominant Pathophysiology in Reflux-Associated Dysphagia

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Abstract

Objective. Reflux disease is common in patients with oropharyngeal dysphagia, but the impact of reflux on oropharyngeal swallowing physiology is not known. This study uses objective measures of swallowing function from modified barium swallow studies to describe the pathophysiology of dysphagia in a group of patients whose only associated condition is reflux.

Study Design. Retrospective chart review.

Setting. Tertiary care voice and swallowing clinic.

Subjects and Methods. The Swallowing Database at the University of Utah was queried for patients with a diagnosis of reflux without additional conditions known to affect swallowing function. Pharyngeal transit time (TPT), distance of hyoid elevation (Hmax), maximum opening size of the upper esophageal sphincter (UESmax), area of pharynx at maximum constriction (PAmax), airway closure timing relative to the arrival of the bolus at the UES, and penetration/aspiration (Pen/Asp) score were assessed.

Results. Of the 122 patients who met inclusion criteria for the study, 42% had normal pharyngeal swallowing function, 57% had at least 1 abnormal swallowing measure, and 47.5% demonstrated a delay in airway closure relative to arrival of the bolus at the UES. The incidence of prolonged TPT, diminished Hmax, poor UESmax, and enlarged PAmax were 2.5%, 8%, 4%, and 11.5%, respectively. Sixty percent with a delay in airway closure had a normal Pen/Asp score.

Conclusion. A delay in airway closure relative to the arrival of the bolus at the UES is the most common abnormality of swallowing function found in patients with reflux-associated dysphagia but may not be identified using the Pen/Asp score.

Keywords
dysphagia, reflux, swallowing

A diagnosis of gastroesophageal reflux disease is common in the outpatient population presenting with swallowing difficulty or dysphagia. Tertiary outpatient swallowing centers have found a high prevalence of reflux disease associated with swallowing complaints. Cho et al determined the annual prevalence of dysphagia in the United States to be 19.5% and that symptoms of reflux disease such as frequent heartburn, acid regurgitation, and chest pain or discomfort are all significantly associated with frequent dysphagia. Inversely, dysphagia symptoms have been found to be common in patients with reflux disease. In a meta-analysis, including over 1 million subjects with reflux disease, Roden and Altman found dysphagia was present in up to 60%. Bollschweiler et al, studying reflux patients in Germany, found dysphagia significantly increased in patients with reflux (28%) compared to controls (3%).

Despite the prevalence of reflux in patients with dysphagia, the impact of reflux disease on oropharyngeal and esophageal swallowing physiology has not been defined. Studies of swallowing pathophysiology due to reflux disease are rare. Clinicians might assume that dysphagia symptoms in patients with reflux are caused by the impact of reflux on the esophagus rather than on oropharyngeal swallowing function. Indeed, the few studies of esophageal function in reflux patients suggest that, in the minority of patients, esophageal abnormalities may account for dysphagia symptoms. In addition to manometric abnormalities, altered esophageal visceral sensation and esophageal wall compliance abnormalities due to inflammation are possible contributors.

It is unknown, however, if reflux leads to changes in oropharyngeal swallowing physiology. Patients with dysphagia and reflux do not consistently complain of swallowing symptoms that are clearly due to esophageal dysfunction. Many reflux patients complain of oropharyngeal dysphagia symptoms. Oropharyngeal dysphagia symptom questionnaires, such as the Dysphagia Handicap Index (DHI), are

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Received September 26, 2018; revised November 20, 2018; accepted December 20, 2018.
scored higher in patients with documented reflux compared to patients without reflux.\textsuperscript{7-9}

This preliminary retrospective study sought to determine if specific patterns of pathophysiologic oropharyngeal swallowing function could be identified in patients with dysphagia and reflux. The study uses objective measures of swallowing function from Modified Barium Swallow Study (MBS) examinations to describe oropharyngeal swallowing function in this patient population. The identification of a prominent pathophysiology associated with reflux, if one exists, is an important first step toward understanding the links between reflux disease and oropharyngeal dysphagia complaints.

**Methods**

The Swallowing Database at the University of Utah was queried for patients with a diagnosis of reflux. Reflux is listed in the database as an associated diagnosis for a given patient if they have a documented medical history of reflux, are on reflux medications, or complain of symptoms consistent with reflux disease such as heartburn more than twice a week. No distinction between esophageal and laryngopharyngeal reflux is made, and a confirmation with pH monitoring was not required. Patients were asked to confirm reflux during the history-taking part of the dysphagia evaluation, and reflux disease was not recorded if the patient was felt to be under questionable empiric treatment for the condition.

Individual swallows for a given patient were not included in the study if they had another diagnosis with the potential to affect swallowing function. Patients were excluded if they had a preexisting diagnosis of a condition known to cause abnormal swallowing physiology such as central or peripheral neuro-motor disease, head and neck carcinoma, vocal fold paralysis, or a history of spine surgery. Patients were also excluded if they were found to have a Zenker’s diverticulum on the swallowing study. Esophageal abnormalities (by history or suspected due to an abnormal esophageal screen) were not considered exclusion criteria for the study.

Individual swallows for a given patient were not included in the study if they were not recorded or performed. Institutional review board approval for this study was provided by the University of Utah No. 45048. Patients underwent an Institutional review board approval for this study was provided by the University of Utah No. 45048. Patients underwent an MBS study based on complaints of dysphagia at time of assessment in the Voice and Swallowing Disorders Clinic.

**MBS Studies**

The radiographic studies were performed at the University of Utah Medical Center and analyzed by speech-language pathologists associated with the University of Utah Voice and Swallowing Disorders Clinic, in accordance with routine radiographic protocols approved by the institution. A radiopaque marker with a known circumference was taped at midline on the patient’s chin to calibrate pixels to centimeters prior to analysis of the digitized image. For the purposes of this study, videofluoroscopic recordings were made for liquid swallows of a 1-cc, 3-cc, and 20-cc bolus volume. Varibar thin barium sulfate (Bracco Diagnostics, Monroe Township, New Jersey) was reconstituted to the company’s standard consistency with water, measured via syringe, and then delivered to the patient via teaspoon and cup. Additional swallows of paste, graham cracker with paste, pill, and a 20-cc thin liquid swallow with an esophageal screen were performed in accordance with institutional protocol but were not quantitatively measured due to a lack of available normative data. Pulsed videofluoroscopy recorded the studies at 25 frames per second. All studies were available for frame-by-frame poststudy analysis through PACS (version 3.6; Philips Medical Systems, Andover, Massachusetts).

**MBS Study Analysis**

Quantitative measures were made from all 3 liquid bolus swallows. The studies were imported into Swallowtail (Beldev Medical, LLC, Arlington Heights, Illinois), a software application that allows for frame-by-frame analysis of videofluoroscopic swallow evaluations, image distance calibration, and quantitative measures of displacement with options for adjustment of contrast and brightness. Timing measures evaluated for this study included total pharyngeal transit time (TPT) and the timing of airway closure relative to the arrival of the bolus at the upper esophageal sphincter (UES). Airway closure completed more than 0.1 seconds after arrival of the bolus at the UES is considered abnormally delayed.\textsuperscript{10} All spatial measures were obtained from lateral views and included maximal hyoid displacement ($H_{\text{max}}$), upper esophageal sphincter opening size ($UES_{\text{max}}$), and pharyngeal area at maximum constriction ($PA_{\text{max}}$). A technical description with definition and normative data for these measures has been previously published.\textsuperscript{10-12}

The completion of airway closure occurs when the arytenoid cartilages elevate and approximate the down-folding epiglottis, effectively closing off the supraglottic airway. Supraglottic airway closure is considered the first line of defense for preventing material from entering the airway during swallowing.\textsuperscript{13} This event can be observed on the MBS filmed in a lateral view. Although not observed on an MBS, true vocal fold closure occurs in addition to supraglottic airway closure and is a secondary defense for airway protection.\textsuperscript{14} In a previous study of supraglottic airway closure timing in 60 young and 63 elderly control subjects without dysphagia, 93% of subjects closed the supraglottic airway prior to arrival of the bolus at the UES. In those subjects who completed airway closure after arrival of the bolus at the UES, the delay was never greater than 0.1 seconds and was not affected by subject age or bolus size.\textsuperscript{10} In the present study, a delay in airway closure was defined as airway closure occurring greater than 0.12 seconds after the arrival of the bolus at the UES. This conservative definition was adopted to ensure validity of the findings.

The penetration-aspiration (Pen/Asp) scale score was judged and recorded for each MBS study.\textsuperscript{15} This scale is
designed to judge airway protection by rating depth of bolus entry into the larynx or lower airway, as well as the patient’s response to laryngeal penetration or aspiration. The Pen/Asp scale uses a predetermined range, with a score of 1 indicating no bolus entrance into the laryngeal vestibule and a score of 8 indicating aspiration without spontaneous patient attempts to clear aspirated material. A score of 3 or greater is considered abnormal.

The esophageal screen was judged as either normal or abnormal based on the presence of bolus stasis, abnormal esophageal contour, or contractions.

**Statistical Analysis**

Patient quantitative measures were defined as abnormal if they fell outside of the range measured from a group of normal controls (n = 147). Data from patients younger than 65 years old were compared to data collected from 60 control subjects ranging from 18 to 65 years in age. Data collected from patients older than 65 years were compared to data from 87 control subjects ranging in age from 67 to 87 years. Pen/Asp score and an esophageal screen were also assessed. Type and number of abnormalities found in the patient cohort were calculated. Fisher’s exact test (2-tailed) was used to assess the relationship of age, sex, Pen/Asp score, and abnormal esophageal screen to the presence of swallowing abnormalities (GraphPad Software, San Diego, California).

**Results**

At the time of this study, the University of Utah Swallowing Database contained data collected from February 2013 to September 2017 and included 645 entries. In total, 151 patients presented with a primary diagnosis of reflux disease and an additional 183 patients had a secondary diagnosis of reflux disease, for an overall 52% incidence of reflux. Although 334 patients presented with reflux, 122 patients had no other condition potentially contributing to dysphagia (36.5%) and were included in the study. Only 5 patients were not already taking reflux medication. The study population included fewer males (n = 55, 45%) than females (n = 67, 55%) and was relatively evenly distributed between patients younger than 65 years old (n = 59, 48%) and older than 65 years old (n = 63, 52%). Figure 1 illustrates the age range of the study population.

**Quantitative Measures**

In total, 362 swallows were analyzed for the study (1 cc, n = 120; 3 cc, n = 122; 20 cc, n = 120). Fifty-two (42%) patients had no abnormality identified from quantitative measures of the swallow study. Seventy (57%) patients had at least 1 abnormal measure. Table 1 shows results for each bolus size. Neither age (P = .855) nor sex (P = .1959) were associated with the presence of abnormal swallowing measures. The overall incidence of prolonged TPT, diminished UESmax, and enlarged PAmax was 2.5%, 8%, 4%, and 11.5%, respectively (Table 2).

**Airway Closure Delay**

A delay in airway closure relative to the arrival of the bolus at the UES was the most common abnormality, identified in 58 (47.5%) patients. Of the patients with any abnormal quantitative measure on the swallow study, 83% (58/70) demonstrated a delay in airway closure, and in 41 patients (35% of 122), a delay in airway closure was the only abnormality identified. Fourteen (11%) patients with airway closure delay demonstrated a delay for all 3 bolus sizes, 18 (15%) demonstrated a delay for 2 bolus sizes, and 26 (21%) demonstrated a delay on 1 bolus size. Nineteen patients had a single airway closure delay as their only swallowing abnormality (16% of 122).

**Other Abnormal Measures**

Twenty-eight patients (23% of 122) had abnormal quantitative measures other than a delay in airway closure on the swallow study. Fifteen of those 28 (54%) had a delay in airway closure in addition to the other abnormalities. Only 13 (10.7% of 122) patients had abnormalities identified on the swallow study without a delay in airway closure (5 older females, 8 young females, 6 young males, and 9 older males).

**Multiple Abnormal Measures**

Forty-one patients (34% of 122) had more than 1 abnormal measure. Twenty-two (52% of those with abnormalities and 18% of the total patient population) of those only had multiple airway closure delays and no other physiologic abnormality. All but 3 of the other patients with multiple abnormal measures also had airway delays. Thus, 84% (16/19) of patients with more than 1 physiologic abnormality had airway closure delay on at least 1 swallow.

**Penetration/Aspiration Score**

Thirty-two (26%) patients had an abnormal rating of 3 or greater on Pen/Asp score. Abnormal quantitative measures were statistically associated with an abnormal Pen/Asp
score ($P = .003$). However, 45 patients (50%, 45/90) with a normal Pen/Asp score had abnormal quantitative measures. In addition, 60% (35/58) of patients with a delay in airway closure had a normal Pen/Asp score. The Pen/Asp score did not correlate with the presence of an airway closure delay ($P = .0789$).

**Esophageal Screen**

Thirty-one (25%) patients had an abnormal esophageal screen. Seventeen (55%) of those patients with an abnormal esophageal screen also had quantitative measurement abnormalities. Most of the patients with an abnormal esophageal screen and additional quantitative measurement abnormalities had a delay in airway closure ($n = 13, 76\%$). Only 1 patient in this group had a decrease in UES opening size. The presence of an abnormal esophageal screen was

<table>
<thead>
<tr>
<th>Measure</th>
<th>Swallow, No.</th>
<th>% Swallows</th>
<th>Young Female, No.</th>
<th>Young Male, No.</th>
<th>Older Female, No.</th>
<th>Older Male, No.</th>
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</thead>
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<tr>
<td>1 cc bolus, n = 120</td>
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<tr>
<td>Prolonged bolus pharyngeal transit time</td>
<td>2</td>
<td>1.6</td>
<td>2</td>
<td></td>
<td></td>
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<tr>
<td>Decreased UES opening size</td>
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<td>0.8</td>
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<td>5</td>
<td>4</td>
<td>2</td>
<td></td>
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<tr>
<td>Delay in airway closure</td>
<td>32</td>
<td>26.6</td>
<td>8</td>
<td>4</td>
<td>6</td>
<td>14</td>
</tr>
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<td>0.8</td>
<td></td>
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<td>1</td>
</tr>
<tr>
<td>Decreased UES opening size</td>
<td>3</td>
<td>2.5</td>
<td>2</td>
<td>1</td>
<td></td>
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<tr>
<td>Enlarged pharyngeal area max constriction</td>
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<td>10.6</td>
<td>3</td>
<td>3</td>
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<td>Diminished hyoid elevation</td>
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<td>5.7</td>
<td>1</td>
<td></td>
<td>2</td>
<td>4</td>
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<td>35</td>
<td>9</td>
<td>9</td>
<td>11</td>
<td>14</td>
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<tr>
<td>20 cc bolus, n = 120</td>
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<tr>
<td>Prolonged bolus pharyngeal transit time</td>
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<td>2.5</td>
<td>2</td>
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<td></td>
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<tr>
<td>Decreased UES opening size</td>
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<td>0.8</td>
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<tr>
<td>Enlarged pharyngeal area max constriction</td>
<td>7</td>
<td>5.8</td>
<td>1</td>
<td>2</td>
<td></td>
<td>4</td>
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<tr>
<td>Diminished hyoid elevation</td>
<td>3</td>
<td>2.5</td>
<td></td>
<td></td>
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<tr>
<td>Delay in airway closure</td>
<td>28</td>
<td>23</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td>10</td>
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<td>Total</td>
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<tr>
<td>Prolonged bolus pharyngeal transit time</td>
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<td>1.6</td>
<td>5</td>
<td>1</td>
<td></td>
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<tr>
<td>Decreased UES opening size</td>
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<td>1.4</td>
<td>2</td>
<td>1</td>
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<td>Enlarged pharyngeal area max constriction</td>
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<td>7</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td>13</td>
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<tr>
<td>Diminished hyoid elevation</td>
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<td>3.6</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Delay in airway closure</td>
<td>103</td>
<td>29</td>
<td>21</td>
<td>24</td>
<td>20</td>
<td>38</td>
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</tbody>
</table>

Abbreviation: UES, upper esophageal sphincter.

**Table 2. Number of Patients with Oropharyngeal Swallowing Abnormalities.**

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>No. of Patients</th>
<th>% of Patients</th>
<th>1 cc, No.</th>
<th>3 cc, No.</th>
<th>20 cc, No.</th>
<th>% of Swallows</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transit time delays</td>
<td>3</td>
<td>2.5</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>1.6</td>
</tr>
<tr>
<td>UES opening diminished</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Pharyngeal area at maximum constriction enlarged</td>
<td>14</td>
<td>11.5</td>
<td>5</td>
<td>13</td>
<td>7</td>
<td>7</td>
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<tr>
<td>Hyoid bone elevation weakness</td>
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<td>8</td>
<td>3</td>
<td>7</td>
<td>3</td>
<td>3.6</td>
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<td>Airway closure delay</td>
<td>58</td>
<td>47.5</td>
<td>32</td>
<td>42</td>
<td>28</td>
<td>29</td>
</tr>
</tbody>
</table>

Abbreviation: UES, upper esophageal sphincter.

**Table 3. Degree of Airway Closure Delay in Seconds for Each Bolus Size.**

<table>
<thead>
<tr>
<th></th>
<th>1 cc</th>
<th>3 cc</th>
<th>20 cc</th>
</tr>
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<tbody>
<tr>
<td>Average</td>
<td>0.34</td>
<td>0.35</td>
<td>0.32</td>
</tr>
<tr>
<td>Median</td>
<td>0.30</td>
<td>0.20</td>
<td>0.19</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.230436</td>
<td>0.47797</td>
<td>0.379636</td>
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</table>
not statistically associated with the presence of abnormal oropharyngeal quantitative measures ($P = .1418$). Only 14 patients (11.5% of 122) had normal quantitative measures and an abnormal esophageal screen.

Including the 14 patients whose only abnormal finding was on the esophageal screen, the total number of patients with an abnormal swallow was 84 (69%). Thirty-eight patients (31%) had a normal swallow study.

**Discussion**

This study is the first to use quantitative measures of swallowing function to analyze swallowing pathophysiology in a large cohort of patients with oropharyngeal swallowing complaints and reflux disease. One-third of the study group had no identifiable abnormality on the swallowing study. Almost half of the patients, however, demonstrated a delay in airway closure on the MBS for at least 1 swallow. In one-third of the patients, a delay in airway closure was the only abnormal finding. Airway closure delay was not influenced by bolus size. Abnormalities of oropharyngeal swallowing function, other than a delay in airway closure, were unusual, with poor pharyngeal constriction being the second most common, found in only 11% of patients.

Surprisingly, an abnormal esophageal screen was present in only a quarter of the patients but was accompanied by oropharyngeal swallowing abnormalities in over half of those patients. Forty-two percent of patients with an abnormal esophageal screen also had a delay in airway closure. This finding supports the work of others who have found that esophageal dysmotility, when present, may be contributing to dysphagia in these patients but is not present in most patients with reflux.5,6 The presence of an esophageal abnormality in one-fourth of the patients on the esophageal screen reaffirms our conviction that an esophageal screen is an essential component of the MBS, especially since 11% of the patients with esophageal abnormalities had no other abnormality on the swallowing study.

The results of this study identify an association of airway closure delay with a diagnosis of reflux but do not establish causation. Mechanisms by which reflux might cause a delay in airway closure are unclear. In general, a delay in airway closure is proposed to be the result of a problem with oropharyngeal sensation, leading to a lack of a timely response to the position of the bolus in the pharynx. Aviv et al.17 identified a decrease in laryngeal sensation in patients with laryngopharyngeal reflux disease and dysphagia. They noted postcricoid edema to be associated with the symptoms.18 The Aviv study supports the idea that reflux disease may cause sensory abnormalities that lead to dysphagia due to a lack of coordination of airway closure with bolus transit. The Aviv study did not offer an explanation as to how these sensory deficits occur, unless they are a part of the inflammatory response leading to postcricoid swelling. Further study of the impact of reflux on both sensory and neuromuscular aspects of oropharyngeal swallowing function is needed.

Timely airway closure is likely 1 element of a complex system with many factors contributing to airway protection from aspiration.13,14 The Pen/Asp score is a commonly used visual/perceptual judgment used to assess the effectiveness of airway protection from an MBS. It is an excellent way to document movement of bolus material into the airway. However, it does not assess physiologic mechanisms of penetration or aspiration. Aspiration may occur before, during, or after the swallow, as the result of different pathophysiologic problems. Quantitative measures of event coordination such as the timing of airway closure relative to arrival of the bolus at the UES are much more sensitive methods for specifically identifying problems with airway closure coordination.19 In this study, 60% of patients with airway closure delay had a normal Pen/Asp score. Based on these results, the Pen/Asp score should not be relied upon to identify airway closure delay. Interestingly, in the 6 study patients who had an abnormal Pen/Asp score and normal airway protection timing, the aspiration occurred before swallow with early spillage of the bolus into the pharynx, possibly the result of sensory abnormalities.

The retrospective design and clinical nature of this study precluded the ability to confirm the diagnosis of reflux disease in the study population by testing such as pH monitoring. As a result, patients may have been included who were erroneously diagnosed with reflux disease. The results of this study should be viewed as preliminary, and future studies with strict inclusion criteria are needed to confirm these findings. Nonetheless, the study highlights the importance of careful evaluation of airway closure timing in this patient population. When airway closure delay is identified, it can be effectively corrected with swallowing therapy.10

**Conclusion**

Although a third of patients with reflux-associated dysphagia had no identifiable abnormality of swallowing function on the MBS, a delay in airway closure was the most common measurable abnormality in the patient population. The Pen/Asp score cannot be relied upon to identify airway closure delays as a delay in airway closure was not associated with aspiration events. The etiology of airway closure delay is not known but may be related to sensory problems.

**Author Contributions**

Katherine A. Kendall, developed research question, designed study, completed data collection, performed statistical analysis, and wrote manuscript.

**Disclosures**

**Competing interests:** None.

**Sponsorships:** None.

**Funding source:** None.

**References**


