Biomechanics of failed deglutitive upper esophageal sphincter relaxation in neurogenic dysphagia

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Williams, Rohan B. H., Karen L. Wallace, Galib N. Ali, and Ian J. Cook. Biomechanics of failed deglutitive upper esophageal sphincter relaxation in neurogenic dysphagia. Am J Physiol Gastrointest Liver Physiol 283: G16–G26, 2002.—Our aims were to examine the etiology and biomechanical properties of the nonrelaxing upper esophageal sphincter (UES) and the relationship between UES opening and failed relaxation. We examined the relationships among swallowed bolus volume, intrabolus pressure, sagittal UES diameter, the pharyngeal swallow response, and geniohyoid shortening in 18 patients with failed UES relaxation, 23 healthy aged controls, and 15 with Zenker’s diverticulum. Etiology of failed UES relaxation was 56% medullary disease, 33% Parkinson’s or extrapyramidal disease; and 11% idiopathic. Extent of UES opening ranged from absent to normal and correlated with preservation of the pharyngeal swallow response (P = 0.012) and geniohyoid shortening (P = 0.046). Intrabolus pressure was significantly greater compared with aged controls (P < 0.001) or Zenker’s diverticulum (P < 0.001). The bolus volume-dependent increase in intrabolus pressure evident in controls was not observed in failed UES relaxation. The nonrelaxing UES therefore displays a constant loss of sphincter compliance throughout the full, and potentially normal, range of expansion during opening. Adequacy of UES opening is influenced by the degree of preservation of the pharyngeal swallow response and hyolaryngeal traction. In contrast, the stenotic UES displays a static loss of compliance, only apparent once the limit of sphincter expansion is reached.

deglutition; manometry; pharynx; sphincter; cricopharyngeus

IN CONTRAST TO THE WEALTH of information available from studies of esophageal achalasia, little is known of the etiology or biomechanics of failed upper esophageal sphincter (UES) relaxation. The term “cricopharyngeal achalasia” has long been used inappropriately (4, 6, 7, 17, 40) to describe the radiological abnormality that is best described morphologically as a cricopharyngeal bar (16, 18). However, incomplete opening of the UES need not necessarily equate with manometrically defined incomplete relaxation of the sphincter. It is logical that either intrinsic sphincter muscle fibrosis or persistent, active, neurogenically driven muscle tone might result in diminished sphincter opening. Furthermore, the biomechanical properties, during periods of transsphincteric bolus flow, of the poorly opening fibrotic sphincter are likely to differ from those of the sphincter displaying constant residual muscle tone but structurally normal muscle.

The literature on this topic is extremely confusing, because few studies have used manometry to confirm failure of UES relaxation and none have systematically examined the biomechanical properties of the nonrelaxing UES (2, 3, 19, 22, 24, 33, 35, 36, 38). In particular, the relationships among failure of sphincter relaxation, disordered UES opening, pharyngeal dysfunction, and severity of dysphagia have not been examined. This study drew on a large number of patients referred to a tertiary referral center, who were all studied systematically by using techniques that not only permitted the manometric detection of failed UES relaxation but also enabled evaluation of the biomechanical properties of the nonrelaxing UES by correlating pharyngosphincteric wall motion with intraluminal pressure. In a group of patients with manometrically confirmed failed UES relaxation, the study aims were to: 1) examine the relationship between UES opening and failed relaxation, 2) compare indirect measures of resistance to transsphincteric bolus flow of the nonrelaxing UES with that of the normal sphincter and with that of the UES known to have restricted opening but normal manometric relaxation (Zenker’s diverticulum), 3) determine which mechanical forces, if any, might facilitate opening of the nonrelaxing UES, and 4) categorize the etiology of failed UES relaxation.

METHODS

Patients and Controls

Patients with manometrically confirmed failed UES relaxation (see Manometric measures and definitions) were retrieved for this study from a customized, prospectively collected database (FileMaker Pro v. 2.0; Claris, Santa Clara, CA). The database comprised a total of 396 patients who, between 1989 and 1997, had undergone combined pharyngeal videoradiographic and manometric evaluation for the evaluation of oropharyngeal dysphagia or pharyngeal symp-
toms or who were studied as part of disease control groups. Patients were excluded from consideration if they had laryngeal or pharyngeal malignancy or prior laryngeal or pharyngeal surgery or radiation for malignant disease.

We compared these patients with two control groups. Group 1 comprised 23 healthy, aged subjects, recruited from the community by public advertisement (mean age 68 ± 10 yr) and from whom we had previously derived age-specific normal range data for all radiographic and manometric measures. All of these healthy subjects had been carefully screened and had no swallowing difficulties nor medical illness that might affect neuromuscular function. None were taking medication known to affect neuromuscular or salivary function. Group 2 consisted of 15 patients with unoperated Zenker’s diverticulum, causing dysphagia (mean age of 67 ± 3 yr). This patient control group was chosen because the UES opening in those with Zenker’s diverticulum is known to be restricted, whereas sphincter relaxation, measured manometrically, is normal (11, 13).

Clinical Assessment

Oropharyngeal dysphagia was defined as difficulty with the act of swallowing together with one or more of the following deglutitive symptoms: bolus holdup, multiple swallowings required to clear the pharynx, deglutitive coughing and/or choking, or postnasal regurgitation (3). A global assessment of dysphagia severity was made clinically by one author (I. J. Cook) and was classified on a five-point scale as mild (anteriorly to slight dietary modification), mild-moderate (dysphagia requiring dietary modification and with an increased time to complete a meal), moderate (dietary modification and minor symptoms of aspiration), moderate-severe (marked dietary modification required together with moderate aspiration symptoms), and severe (severe dysfunction with aspiration sufficient to necessitate introduction of nonoral feeding) (3). All patients had been assessed by a neurologist and routinely had the following laboratory investigations during the workup of their dysphagia: thyroid function tests (T4, T3, and TSH), erythrocyte sedimentation rate, creatine phosphokinase, and anti-nuclear antibody. Brain imaging (computed tomography and magnetic resonance imaging scanning) was done when considered appropriate to clinical circumstances.

Combined Videoradiography and Pharyngeal Manometry

Swallowing function was studied by simultaneous videoradiography and manometry as previously described (3, 12). Briefly, images of barium swallows were recorded in the lateral and anteroposterior projections using a 9-in. Toshiba (Kawasaki, Japan) image intensifier. Fluoroscopic images were recorded on videotape at 25 frames/s by a VHS video recorder (AG6500; Panasonic, Osaka, Japan) for later analysis. The correction factor for magnification was determined before each study by placing two metallic markers set 3 cm apart in the field of the image intensifier on the subject’s head but in the plane of the UES. Subjects swallowed, as tolerated, duplicate 2-, 5-, 10-, and 20-ml boluses of high-density liquid barium suspension [250% (wt/vol), E-Z-HD; E-Z EM, Westbury, NY]. Included in the field of view in lateral projection were the incisor teeth anteriorly, hard palate superiorly, cervical spine posteriorly, and proximal cervical esophagus inferiorly. Pharyngeal pressures were measured by using both perfusion and solid-state manometric techniques. Initially, we passed transnasally a nine-lumen (O.D. 6 mm, I.D. of each lumen 0.5 mm) Silastic/polyvinyl chloride manometric catheter, incorporating five perfused sideholes spaced at 1.5-cm intervals and a 6-cm sleeve assembly (Dentsleeve, Wayville, SA, Australia). The sleeve was positioned to straddle the UES to accommodate the axial mobility of the sphincter. The sleeve sensor had a 5 × 3-mm oval cross section to maintain its anteroposterior orientation within the UES. Five perfused sideholes proximal to the sleeve, with the most distal sidehole in the pharynx at the level of the proximal sleeve margin, recorded pharyngeal pressures. Additional sideholes, located 1.5, 3, and 6 cm distal to the proximal sleeve margin, aided positioning of the sleeve such that its midpoint was in the center of the UES high-pressure zone at rest. The sleeve assembly and sideholes were perfused by a low-compliance pneumohydraulic perfusion system at 0.6 ml/min. The sideholes were only perfused while swallows were being recorded to avoid fluid accumulation in the pharynx. Pharyngeal and UES pressures detected by the perfused catheter were registered by external transducers (Spectramed Medical Products, Singapore), and all signals were amplified and acquired at 200 Hz per channel on a Macintosh computer (Apple, Cupertino, CA) using GastroMac software (Neomedix Systems, Sydney, NSW, Australia). All pressures were referenced to basal hypopharyngeal pressure. A purpose-built, video digital timer unit (Praetel Sales International, Holden Hill, SA, Australia) imprinted simultaneously the elapsed time on the video images in hundredths of seconds and a signal on the pressure tracing each whole second, to permit precise correlation of video images with pharyngeal pressures.

If peak pharyngeal pressures exceeded 60 mmHg, a separate catheter with five solid-state transducers, spaced at 1.5-cm intervals, (Gaeltoc, Dunvegan, Scotland) was used to make repeat measures of peak pharyngeal pressures following removal of the perfused catheter (12). This catheter was passed transnasally, and the posterior orientation of the transducers was readily verified radiographically. The catheter was positioned such that the distal transducer lay just proximal to the UES to capture the UES pressure profile during maximal deglutitive ascent of the sphincter. In this position, the middle transducer, recording midpharyngeal pressures, lay at the level of the valleculae.

Data Analysis

Videoradiographic measures and definitions. Radiographic indicators of oropharyngeal dysfunction in patients were analyzed from videoradiographic recordings as previously described (3). The categories of dysfunction examined included abnormal pharyngeal wall motion, absent pharyngeal swallow response, aspiration, abnormal pharyngeal wall motion, coating of pharyngeal walls, and postswallow pooling or retention of barium in the valleculae and/or pyriform sinuses. Abnormal pharyngeal wall motion was defined as either a lack of contact between anterior and posterior pharyngeal walls at any point along the pharynx or a lack of sequential, peristaltic progression of the point of pharyngeal wall closure. A pharyngeal swallow response was deemed to be absent if no active motion of the posterior pharyngeal wall was apparent following attempted swallows. Aspiration was defined as penetration of any contrast beyond the vocal cords. Coating of the pharyngeal walls was defined as any residual barium adherent to the pharyngeal wall following the swallow, excluding any residual visible in the valleculae or pyriform sinuses. Postswallow pooling was defined as any postswallow retention of barium in the valleculae and/or pyriform sinuses. Because videofluoroscopy is only a semi-quantitative method of estimating pharyngeal clearance, we
only attempted to define contrast retention as either present or absent.

Minimum geniohyoid length during the swallow, a measure of maximum anterosuperior excursion of the hyoid bone, was determined by measuring the interval between the anteroinferior corner of the hyoid bone and the posteroinferior margin of the symphysis mentis. Minimum geniohyoid length was then expressed as a percentage of its resting length to normalize differences in hyoid excursion as a function of differences in neck dimensions among subjects (37).

Maximal UES dimensions during sphincter opening were measured fluoroscopically, for a range of bolus volumes, in the sagittal plane in all patients and in the transverse plane in those patients in whom sufficient swallows were tolerated before significant aspiration precluded further swallows. Extent of UES opening was classified as normal if maximal sagittal diameter lay within the laboratory normal range (mean ± 2 SD for healthy controls), partial if opening was observed but maximal sagittal diameter fell below the lower limit of normal (<5.63 mm for 2-ml barium bolus), or absent if no contrast penetrated the sphincter zone during attempted deglutition. UES opening duration was similarly classified as normal, partial (<0.31 s), or absent.

Manometric measures and definitions. UES pressures were referenced to resting, preswallow, hypopharyngeal pressure. Basal UES pressure was determined by averaging end-expiratory UES pressure over a 1-min period interval 10 min after catheter placement to permit subject adaptation. UES relaxation was assessed solely by manometric criteria, whereas UES opening was defined by radiological criteria (see Videoradiographic measures and definitions). The adequacy of UES relaxation was determined from the nadir UES pressure measured during dry swallows, before administration of any test boluses. Deglutitive UES relaxation was classified as failed if nadir UES pressure during 100% of dry swallows exceeded 10 mmHg in individuals 55 yr of age or more or exceeded 13 mmHg in individuals <55 yr of age (1, 3, 37).

The recording site from which midpharyngeal pressure was measured lay 4.5 cm proximal to the midpoint of the UES at the apogee of its upward deglutitive motion. Hypopharyngeal intrabolus pressure was measured at the perfused sidehole immediately proximal to the UES at the proximal margin of the sleeve in controls and in all patients in whom some transphincteric bolus flow was observed radiologically. Hypopharyngeal intrabolus pressure was defined, on the basis of correlation of manometry and fluoroscopy, as the pressure registered at the time point midway between the arrival of the bolus head and the departure of the bolus tail at that site (12, 13). In instances in which there was a dwell time by the bolus head at the hypopharyngeal sidehole ≥100 ms, midinintrabolus pressure was estimated from the time point midway between the onset and termination of that particular instance of transphincteric bolus flow. Temporal measures. The timings of five measures of UES relaxation and opening were referenced to swallow onset, defined as the initial movement of the tongue tip against the posterior surface of the maxillary incisors, as previously defined (12, 13). The time of UES opening and closure and the duration of UES flow were identified videofluoroscopically. UES relaxation onset was defined as the time point at which the basal UES pressure began to fall abruptly. Maximum UES relaxation was defined as the point in time at which the UES relaxation profile ceased to fall rapidly and leveled off. Because the proximal sleeve margin projects into the hypopharynx, the sleeve registers prematurely the apparent termination of UES relaxation (27). Accordingly, UES relaxation termination was measured from the tracing recorded by the sidehole 1.5 cm distal to the proximal sleeve margin (seen fluoroscopically to lie within the UES at the time of sphincter closure) and was defined as the onset of the pressure upstroke at completion of relaxation.

Statistical Analysis

Duplicate values for each subject were averaged before calculation of group mean data for each bolus volume swallowed. Group mean data were compared among patients and controls using a two-factor ANOVA. Data were first confirmed to be normally distributed by the Shapiro-Wilk statistic. Although appropriate and with greater statistical power, a repeated-measures ANOVA design was not adopted because not all patients could swallow the entire range of bolus volumes (9). For the classification of maximal opening diameter and geniohyoid shortening, we used data recorded for 2-ml barium boluses, because this was the only common volume available in all patients with failed UES relaxation. Patients with severe dysphagia are rarely able to handle a bolus volume >2 ml, usually because of inadequate airway protection. The association between degree of geniohyoid reduction and extent of UES opening was made by using a factorial ANOVA. Comparisons of geniohyoid shortening among subsets of patients demonstrating normal, partial, or absent UES opening and aged controls were made by using an unpaired Student’s t-test, corrected by using a Bonferroni-Dunn procedure [alpha (P-value) significant at <0.0083, correction for 4 multiple comparisons]. A χ² test was used to make inferences regarding proportions with and without various types of pharyngeal dysfunction and for data relating to the association of the preservation of the pharyngeal swallow response and degree of UES opening. All values are means ± SE unless otherwise stated. Statistical calculations were performed using StatVIEW 4.5 (Abacus Concepts, Berkeley, CA).

RESULTS

Prevalence, Etiology, and Clinical Features

Of a total of 396 patients in the database, 27 were excluded because of laryngeal or pharyngeal malignancy (5 cases), prior laryngeal or pharyngeal surgery, or radiotherapy for malignant disease (22 cases). Of the remaining 374 patients, 18 (4.8%) had manometrically confirmed failure of UES relaxation (12 male, 6 female; median age = 61 yr; range, 19–82 yr).

With the exception of the two patients in whom the etiology was uncertain (S17 and S18), all patients had an underlying central nervous system disorder accounting for their dysphagia (Table 1). Two broad neuroanatomic categories accounted for all cases in which a causative lesion could be identified: brain stem lesions (56%) and extrapyramidal (Parkinson’s and other) movement disorders (33%). One patient (S11) had previously undergone cricopharyngeal myotomy and laryngeal suspension but had persisting dysphagia with failed UES relaxation. Only one patient (S17) had a cricopharyngeal bar, and none had a Zenker’s diverticulum.

Dysphagia severity was highly variable, with 7 of 18 (39%) having none or mild dysphagia and 8 of 18 (44%) having severe dysphagia (Table 1). However, as a group, all patients with lateral medullary infarction

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and failed UES relaxation had severe dysphagia, whereas none of the Parkinsonian patients had severe dysphagia. One patient had no dysphagia (S5) but had Parkinson’s disease and was studied as part of a disease control group.

One patient (S3) had a normal videofluoroscopic examination. Compared with aged, healthy controls, the prevalence of the following abnormalities was significantly greater in patients ($P < 0.0001$): pharyngeal wall coating (59 vs. 0%), postswallow pooling in pyriform sinuses (88 vs. 11%), and abnormal pharyngeal wall motion (88 vs. 0%). Aspiration was very prevalent, being observed radiologically in 14 of 18 (78 vs. 0%) patients (Table 1). The pharyngeal swallow response was absent in 8 of 18 patients (44 vs. 0%), all of whom had severe dysphagia.

**Basal and Nadir UES Pressures**

Basal UES pressure did not differ significantly between patients with failed UES relaxation (43 ± 5 mmHg) and aged controls (44 ± 5 mmHg). Nadir UES pressure in patients, recorded during dry swallows, ranged from 15 to 100 mmHg and was significantly higher in patients than in aged controls (34 ± 5 vs. 2 ± 4 mmHg; $P < 0.05$; Fig. 1).

**Biomechanical Properties of the Nonrelaxing UES**

To assess the biomechanical properties of the UES in the context of failed relaxation, we examined the volume dependence of both hypopharyngeal intrabolus pressure and maximal UES sagittal diameter. In other words, we examined the manner in which intrabolus pressure varied as a function of swallowed bolus volume and how extent of the UES opening related to bolus volume and intrabolus pressure to conceptualize the "compliance" properties of the sphincter affected by different pathological processes. Patients with failed UES relaxation who had an absent pharyngeal swallow response were excluded from this analysis. This was done because the magnitude of hypopharyngeal intrabolus pressure is determined by a balance of UES-resistive forces acting against the propulsive forces of the pharyngeal stripping wave (12, 13), given that intrinsic bolus properties such as viscosity and specific gravity are constant under our experimental conditions (8, 29). Hence, unless some form of pharyngeal swallow response was evident, we could not be certain that the fundamental ingredients of intrabolus pressure generation could be compared in a valid manner with controls in this subset.

Table 1. Patient demographics and clinical data

<table>
<thead>
<tr>
<th>ID</th>
<th>Sex</th>
<th>Age</th>
<th>Indication for Videomanometry</th>
<th>Etiology</th>
<th>Other Clinical Information</th>
<th>Dysphagia Severity</th>
<th>Nonoral Feeding, dependance</th>
<th>Aspiration*</th>
<th>Pharyngeal Swallow Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>F</td>
<td>73</td>
<td>Dysphagia</td>
<td>Parkinsons disease</td>
<td></td>
<td>Mild</td>
<td></td>
<td></td>
<td>Present</td>
</tr>
<tr>
<td>S2</td>
<td>F</td>
<td>79</td>
<td>Dysphagia</td>
<td>Parkinsons disease</td>
<td></td>
<td>Mild</td>
<td></td>
<td></td>
<td>Present</td>
</tr>
<tr>
<td>S3</td>
<td>M</td>
<td>70</td>
<td>Dysphagia</td>
<td>Parkinsons disease</td>
<td></td>
<td>Mild</td>
<td></td>
<td></td>
<td>Present</td>
</tr>
<tr>
<td>S4</td>
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<td>82</td>
<td>Dysphagia</td>
<td>Parkinsons disease</td>
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<td>Present</td>
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<td>S5</td>
<td>F</td>
<td>73</td>
<td>Disease study group</td>
<td>Parkinsons disease</td>
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<td>None</td>
<td></td>
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<td>72</td>
<td>Dysphagia</td>
<td>Extrapyramidal movement disorder</td>
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<td>Severe</td>
<td>Pre/post</td>
<td>Absent</td>
<td></td>
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<tr>
<td>S7</td>
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<td>57</td>
<td>Dysphagia</td>
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<td>Severe</td>
<td>PEG, total</td>
<td>Post</td>
<td>Absent</td>
</tr>
<tr>
<td>S8</td>
<td>M</td>
<td>19</td>
<td>Dysphagia</td>
<td>Brain stem compression from cerebral hemorrhage</td>
<td>Tracheostomy, preexisting muscular dystrophy</td>
<td>Severe</td>
<td></td>
<td>Intra</td>
<td>Absent</td>
</tr>
<tr>
<td>S9</td>
<td>M</td>
<td>67</td>
<td>Dysphagia</td>
<td>Lateral medullary infarction</td>
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<td>Mild</td>
<td></td>
<td></td>
<td>Present</td>
</tr>
<tr>
<td>S10</td>
<td>M</td>
<td>76</td>
<td>Dysphagia</td>
<td>Lateral medullary infarction</td>
<td></td>
<td>Severe</td>
<td>Pre/post</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>S11</td>
<td>M</td>
<td>74</td>
<td>Dysphagia</td>
<td>Lateral medullary infarction</td>
<td>Previous CP myotomy &amp; laryngeal suspension</td>
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<td>PEG, partial</td>
<td>Intra/post</td>
<td>Absent</td>
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<tr>
<td>S12</td>
<td>M</td>
<td>68</td>
<td>Dysphagia</td>
<td>Lateral medullary infarction</td>
<td></td>
<td>Severe</td>
<td>NG, total</td>
<td>Post</td>
<td>Absent</td>
</tr>
<tr>
<td>S13</td>
<td>M</td>
<td>74</td>
<td>Dysphagia</td>
<td>Lateral medullary infarction</td>
<td></td>
<td>Severe</td>
<td>PEG, partial</td>
<td>Intra/post</td>
<td>Present</td>
</tr>
<tr>
<td>S14</td>
<td>F</td>
<td>33</td>
<td>Dysphagia</td>
<td>Surgical removal epipharyngeal floor 4th ventricle</td>
<td>Tracheostomy</td>
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<td>NG, total</td>
<td>Pre/post</td>
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<td>40</td>
<td>Dysphagia</td>
<td>Syringobulbia</td>
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<td>Mild</td>
<td>Post</td>
<td>Present</td>
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<tr>
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<td>F</td>
<td>64</td>
<td>Dysphagia</td>
<td>ALS</td>
<td></td>
<td>Mod-Sev</td>
<td>Intra/post</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>S17</td>
<td>M</td>
<td>32</td>
<td>Dysphagia</td>
<td>Idiopathic</td>
<td></td>
<td>Mild</td>
<td></td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>S18</td>
<td>M</td>
<td>49</td>
<td>Dysphagia</td>
<td>Idiopathic</td>
<td>Globus, prior head injury</td>
<td>Mild</td>
<td></td>
<td>Present</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Patient demographics and clinical data

*Level of dependence on nonoral feeding at time of initial study is given; NG, nasogastric feeding; PEG, gastrostomy feeding tube; CP, cricopharyngeal. *Aspiration was determined radiologically. Timing in relation to swallow was defined as pre-, intra-, or postswallow.
Hypopharyngeal intrabolus pressure was significantly greater over all bolus volumes in patients with failed UES relaxation compared with aged controls ($P < 0.001$) and patients with Zenker’s diverticulum ($P < 0.001$) (Fig. 2A). A statistically significant ($P < 0.001$) bolus volume-dependent increase in intrabolus pressure was evident in the two control groups. In contrast, in the patient group with failed UES relaxation, the intrabolus pressure assumed a relatively constant mean value that was not influenced significantly by increased swallowed bolus volume (Fig. 2A). Maximal UES sagittal diameters were significantly lower compared with aged controls ($P < 0.0001$) but did not differ significantly compared with Zenker’s controls ($P = 0.12$) (Fig. 2B). The extent of UES opening in those with Zenker’s diverticulum virtually peaks at 5 ml and changes very little with further increases in swallowed bolus volume. In contrast, the sagittal diameter in healthy controls and in those with failed UES relaxation steadily increased throughout the full range of swallowed bolus volumes, such that the maximal extent of UES opening achievable with failed UES relaxation was normal in some cases (Fig. 2B).

Mechanisms of UES Opening in the Context of Failed Sphincter Relaxation

The extent of maximal UES opening varied from normal (6 of 18) to partial (7 of 18) to absent (5 of 18) (Table 2). The extent of opening of the nonrelaxing UES was strongly associated with the degree of preservation of the pharyngeal swallow response. All patients who had an intact pharyngeal swallow response had some demonstrable UES opening, whereas 5 of the 8 patients with an absent pharyngeal swallow response had absent UES opening ($P = 0.006$). For example, 50% with an intact pharyngeal swallow response had maximal sagittal UES diameters within the normal range, compared with only 1 of 8 patients (13%) in whom the pharyngeal swallow response was impaired. As a result, the extent of UES opening in Zenker’s diverticulum rapidly peaks at 5 ml but changes very little with further increases in swallowed bolus volume. Numbers in parentheses denote subjects able to swallow bolus volume specified.

Table 2. Degree of UES opening determined from sagittal diameter: dependence on the degree of preservation of the pharyngeal swallow response

<table>
<thead>
<tr>
<th>Pharyngeal Swallow Response</th>
<th>Degree of Impairment of UES Opening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Intact</td>
<td>10</td>
</tr>
<tr>
<td>Absent</td>
<td>8</td>
</tr>
</tbody>
</table>

Data from 2-ml barium bolus swallows were used, because this was the only bolus volume able to be swallowed by all patients. A classification of normal indicates that the value lay within 2 SD of the mean. $P = 0.012$ ($\chi^2$ test).
absent. The interrelationships among failed UES relaxation, UES opening, and degree of preservation of the pharyngeal swallow response are illustrated by three examples (Figs. 3–5). When the pharyngeal swallow response is well preserved, extent of UES opening can be normal and dysphagia can be mild (Fig. 3). In cases in which the pharyngeal response is intact but dysfunctional, further derangement of pressure-flow patterning is evident, resulting in at least some reduction in UES opening, less effective bolus clearance, and more marked dysphagia (Fig. 4). Figure 5 shows a case in which the pharyngeal swallow response is absent and UES opening is completely absent. Notwithstanding the strong correlation between an absent pharyngeal swallow response and impaired or absent UES opening, an absent pharyngeal response did not invariably result in failed sphincter opening. In these circumstances, UES opening was possible if sufficient intrapharyngeal pressure was generated in response to compensatory tongue base motion (Fig. 6). The duration of UES opening was invariably within the normal range, irrespective of whether the pharyngeal swallow response was intact or absent, as long as some degree of UES opening was observed.

We examined the extent of hyoid excursion in the subgroups of patients with failed UES relaxation having normal, partial, or absent UES opening to determine the effect, if any, of external cricoid traction on extent of UES opening in this population. The degree of preservation of UES opening was significantly associated with the degree of preservation of geniohyoid shortening ($P = 0.046$, ANOVA). The relationship was most apparent in those with absent UES opening (Fig. 7). The extent of geniohyoid shortening in subsets with normal, partial, and absent UES opening was 21 ± 2, 19 ± 3, and 12 ± 4%, respectively.

DISCUSSION

In this study, we employed intraluminal manometric measurements of UES pressure to detect cases of failure of deglutitive UES relaxation. Our findings indicate that failure of manometric UES relaxation is uncommon in patients with oropharyngeal dysphagia, the prevalence in this tertiary referral population being just <5% of patients studied comprehensively. The two most common causes of this disorder are various medullary lesions and Parkinson’s disease. The resistance to transsphincteric flow is increased in both disease states. However, the biomechanical properties of the nonrelaxing sphincter during transsphincteric bolus flow are distinctly different from those of the normal UES and from the sphincter associated with Zenker’s diverticulum. The nonrelaxing UES displays an increased resistance to flow that remains constant throughout the range of swallowed bolus volumes irrespective of the extent of resultant sphincter opening. In contrast, the fibrotic stenosis of the UES associated with Zenker’s diverticulum results in a more marked resistance to flow that decreases with increasing bolus volume.

Fig. 3. Videoradiographs (left) and corresponding manometric traces (right) from a patient (S15) with mild dysphagia and failed UES relaxation due to syringobulbia. The pharyngeal (Phar) swallow response is preserved, and the pharyngeal pressure wave is of normal amplitude and propagates normally. The only radiological abnormality is a minor increase in postdeglutitive residual contrast in the hypopharynx (T4) and, in particular, that the UES opens fully with good transsphincteric flow (T3). Note also that the intrabolus pressure (arrow) is markedly increased. The horizontal bar represents the interval of transsphincteric bolus flow determined radiologically (T3). T1–T4 represent the times corresponding to the 4 radiographs, which are similarly labeled.
with Zenker’s diverticulum (11) demonstrates minimal resistance to flow with low swallowed bolus volume. However, once the extent of opening of that fixed stenosis is reached, the inability of the sphincter to open any further results in a rapidly progressive increase in resistance to flow and a steep rise in intrabolus pressure. These findings suggest that the compliance of the UES is impaired in these two conditions but that the dynamics of that compliance are quite different in the two conditions. The compliance of the nonrelaxing UES is likely to be reduced to the same extent throughout the full extent of sphincter opening. The compliance of the UES in Zenker’s diverticulum is normal at low distending volumes, but once the extent of opening approaches the restricted maximal limit of opening, UES compliance is likely to fall rapidly. Both the extent of UES opening of the nonrelaxing sphincter and the severity of symptoms vary widely, from complete absence of opening to normal opening and from none to severe dysphagia, respectively. The degree of opening achievable by the nonrelaxing sphincter correlates with the degree of preservation of the pharyngeal swallow response and of the external traction force operative on the UES as determined by geniohyoid shortening. Nonetheless, the nonrelaxing UES is capable of opening in the complete absence of a pharyngeal swallow response, as long as sufficient pharyngeal pressure can be generated by tongue base motion to achieve this.

The logical “gold standard” for detecting failure of neuromuscular UES relaxation would be intramural electromyogram recordings from the muscular components of the UES, including the cricopharyngeus (28, 30, 42). However, such recordings are not readily applicable in a clinical setting (34). The conceptual basis for our approach can be understood by examining the physiological and biomechanical elements that contribute to the intrasphincteric pressure drop occurring during the swallow sequence. Approximately 200 ms before the onset of UES opening, transient inhibition of vagal input to the muscular components of the UES lead to a loss of active tension in the sphincter region, leading to a drop in resting UES pressure to near-atmospheric levels (5, 28, 32) A further contribution to reduction in intrasphincteric pressure will result from anterior traction forces being applied to the cricoid cartilage from the laryngohyoid complex. This second effect can result in transient drops in intrasphincteric pressure to subatmospheric levels, resulting in actual sphincter opening (luminal wall separation) (23). The subsequent passage of a fluid bolus into the relaxed and opened sphincter zone will restore intrasphincteric pressure to supra-atmospheric levels (onset of the so-called intrabolus pressure domain) (12, 23, 25). Thus the residual or nadir intrasphincteric pressure, at a given time in the swallow sequence, may be either subatmospheric, atmospheric, or supra-atmospheric, depending on the balance of forces generated by UES muscle tension (active and passive), intrabolus pressure, and external traction forces on the cricoid (23). In the present study, patients hypothesized to have

Fig. 4. Videoradiographs and manometry trace from a patient (S4) with moderate dysphagia due to Parkinson’s disease in whom the UES opening is present but subnormal. Although radiologically the pharyngeal swallow response is present, the pharyngeal pressure waves are synchronous in onset due to the lack of pharyngeal wall closure. The radiological correlate of this phenomenon is an absence of a well defined bolus tail (T2–T4). Functionally, this swallow is less effective with reduced UES opening and a moderate increase in postswallow hypopharyngeal residual barium and laryngeal vestibular penetration (T3), resulting in moderately severe dysphagia.
“failed UES relaxation” demonstrated supranormal residual (nadir) intra-UES pressures during dry swallows, with coexistent normal or near-normal anterior traction force (as indirectly quantified by geniohyoid shortening). We eliminated the confounding factor of transsphincteric bolus flow in generating supra-atmospheric, intra-UES pressure by testing only dry swallows before the delivery of any test boluses. Thus the finding of elevated intrasphincteric pressure under these conditions implies that there is active tension being generated in the UES segment, the source of which can only result from a failure of deglutitive, vagally-mediated inhibition.

The degree of UES opening is also determined by a balance among three forces: UES muscle tension (active and passive), intrabolus pressure, and external traction forces on the cricoid (12, 23). During the normal swallow, once active muscle tone within the UES is abolished, the residual passive tension is counteracted by external traction forces on the cricoid to cause UES opening (30). In contrast, the persistence of high residual active sphincter muscle tension in the group with failed UES relaxation, combined in some cases with reduced traction from geniohyoid shortening, has the mechanical consequence that UES opening occurs in the presence of increased hypopharyngeal intrabolus pressure. Consequently, in this context, the relative integrity and the preservation of the pharyngeal constrictor muscle response is of paramount importance in determining the severity of deglutitive dysfunction.

It has been well established, on the basis of combined videoradiographic, manometric, and histopathological studies, that a structural muscular disorder exists in the cricopharyngeus muscle in Zenker’s diverticulum and that this limits muscle elasticity and sphincter opening capacity, causing a resistance to bolus flow across the UES (11, 13, 31, 41). Notably, manometric relaxation of the UES is normal in this structural disorder, which exhibits a strong correlation between swallowed bolus volume and hypopharyngeal intrabolus pressure (13).

The nonrelaxing UES also shows increased resistance to transsphincteric bolus flow, as evidenced by the elevated hypopharyngeal intrabolus pressure. But in contrast to the case of Zenker’s diverticulum, the present study shows that the mediation of the resistance to transsphincteric flow in the nonrelaxing UES occurs under distinctly different mechanisms, presumably due to high residual active muscle tension within the opened sphincter zone. This is demonstrated by the observations that: 1) the nonrelaxing sphincter retains the normal, essentially linear, relationship between swallowed bolus volume and extent of opening; 2) the potential for complete opening is preserved; and 3) intrabolus pressure, although markedly increased compared with healthy controls, does not vary as a function of swallowed bolus volume. In summary, the stenosed sphincter in Zenker’s diverticulum relaxes completely during deglutition. The sphincter then rapidly reaches the limit of its opening capacity, and the
intrabolus pressure thereafter continues to rise steeply as a function of bolus volume because flow rates across the stenosed sphincter are the same as those across the normal sphincter (13). In contrast, the persistent tonic-ity within the nonrelaxing sphincter applies a resistance to pharyngeal out-flow that remains roughly constant irrespective of the sphincter diameter achieved. These data clearly show that the conceptual thinking and the terminology used in this area must make a distinction between UES opening and UES relaxation. The onsets of the two phenomena have been shown previously to be separated in time (5, 25, 27–29). Furthermore, opening is defined radiologically, whereas relaxation is defined manometrically. In the present study, we have shown that the extent of UES opening of the nonrelaxing sphincter may range from normal to absent, whereas the stenotic sphincter with normal manometric relaxation has limited maximal opening. UES relaxation and opening are not synonymous, and although incomplete UES relaxation might be suspected radiologically, manometry is mandatory for its confirmation. The long-standing and common practice of describing the radiological appearance of the cricopharyngeal bar as cricopharyngeal achalasia (4, 6, 7, 17, 40) has no foundation and should be avoided. The

Fig. 6. Example of failed UES relaxation and an absent pharyngeal swallow response, but with some degree of UES opening, albeit reduced, and transsphincteric flow. The patient (S11) had severe dysphagia due to lateral medullary infarction. Despite the absence of a radiologically detectable pharyngeal swallow response (T1–T4), there is a low-amplitude, isobaric pressure waveform that is synchronous throughout the pharynx. Comparison of video images with manometry confirms that this waveform is a consequence of posterior motion of the tongue base (T1–T2), which reaches its maximal posterior excursion at T3. Some transsphincteric flow is evident (mainly T2–T3), but the patient has markedly impaired pharyngeal clearance and both intraswallow tracheal aspiration (T2 and T3).

Fig. 7. Relationship between extent of UES opening and geniohyoid shortening used as a measure of the external traction force on the UES. The degree of preservation of UES opening was significantly associated with the degree of preservation of geniohyoid shortening ($P = 0.046$). Geniohyoid shortening in those with absent UES opening was present but significantly reduced when compared with that of healthy controls ($^{*}P = 0.006$).
prevalence of the cricopharyngeal bar in our study cohort is no greater than an unselected radiological case series (15, 20, 21, 26). Indeed, of the 12 patients in whom UES opening was subnormal, only 1 had the radiological appearance of a cricopharyngeal bar, and the radiological contours in the remainder were unremarkable (Figs. 3 and 4).

The etiology of oropharyngeal dysphagia is not always certain after thorough clinical, laboratory, and radiological assessment, including magnetic resonance imaging (10). The present study suggests that the finding of manometrically confirmed failed UES relaxation, in the context of an otherwise noncontributory neurological workup in the dysphagic patient, is likely to indicate brain stem lesion in its etiology. Similarly, the evaluation of oropharyngeal dysphagia in an individual with a recognized brain stem lesion or Parkinson’s disease might be relative indications for pharyngeal manometry because the detection of failed UES relaxation is an indication for cricopharyngeal dilatation, myotomy, or botox injection (6, 35, 36, 39). However, although logical, there is no proof at present that such an approach is efficacious nor that it influences clinical outcome (14).

It might be argued that all eight patients with an absent pharyngeal swallow response did not swallow at all and that the complete absence of a swallow accounts for an apparently successful failure of UES relaxation. There are several reasons why we believe this is a most unlikely explanation. First, the remaining 10 of 18 cases had a preserved pharyngeal swallow response, indicating that failure of sphincter relaxation can certainly occur in the absence of a pharyngeal swallow response. The converse is also true. Of the 378 cases studied over the same time frame, all with normally relaxing sphincters, numerous instances of an absent pharyngeal swallowing response were observed. Hence there is unequivocal evidence that loss of individual components of the total pharyngeal swallow can occur in isolation and an absent pharyngeal swallow response per se is not a predictor of failure of UES relaxation or swallowing in general. Second, three of the eight patients with an absent pharyngeal response did actually open the sphincter, indicating preservation of accessory deglutitive motor responses sufficient to effect UES opening. Third, a number of motor events, outside of the pharyngeal constrictor actions themselves, contribute to the swallow or are evidence for its triggering. These events include hyolaryngeal motion, a stripping wave (contraction) traversing the sphincter zone itself, and a cervical esophageal peristalsis, which can be seen in cases of a failed pharyngeal swallow response. Indeed, in all but one of the eight cases with an absent pharyngeal swallow response, some hyolaryngeal motion was seen to occur coincident with the swallow. However, in the remaining case we cannot be certain that we were not seeing a totally absent swallow due to extensive medullary damage.

In conclusion, compared with healthy controls, the resistance to transspincteric bolus flow is increased in both disease states studied, but the UES in each case displays distinctly different biomechanical properties. Furthermore, manometrically-determined UES relaxation does not equate directly with the extent of sphincter opening during flow.

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Four of the patients included in this study formed part of a larger cohort of patients, all with Parkinson’s disease and dysphagia, the data from which has been previously published (3).

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REFERENCES