BIOMECHANICS OF FAILED DEGLUTITIVE UPPER ESOPHAGEAL SPHINCTER (UES) RELAXATION IN PATIENTS WITH NEUROGENIC DYSPHAGIA

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Abbreviations: UES (upper esophageal sphincter), CP (cricopharyngeus)

Running Head: Failed UES relaxation

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ABSTRACT

**Background:** The biophysical properties and etiology of the non-relaxing upper esophageal sphincter (UES) are unknown. Our aims, in patients with manometrically confirmed failed UES relaxation, were to examine: 1) the etiology and biomechanical properties of the UES, 2) the relationship between UES opening and failed relaxation and determinants of sphincter opening. **Methods:** We examined the relationships among swallowed bolus volume, hypopharyngeal intrabolus pressure, sagittal UES diameter, the pharyngeal swallow response, and geniohyoid shortening in 18 patients with failed UES relaxation and compared them with 23 healthy aged controls and 15 patients with Zenker's diverticulum. **Results:** From 374 combined videoradiographic and manometric studies we identified 18 (4.8%) with failed UES relaxation which was attributed to: medullary disease (56%); Parkinson's or extrapyramidal disease (33%); and idiopathic (11%). The extent of UES opening ranged from absent to normal and correlated with the degree of preservation of the pharyngeal swallow response \( (P=0.012) \) and geniohyoid shortening \( (P=0.046) \). Intrabolus pressure was significantly greater when compared with aged controls \( (P<0.001) \) or Zenker's \( (P<0.001) \). A significant \( (P<0.0001) \) bolus volume-dependent increase in intrabolus pressure, evident in the two control groups, was not observed in failed UES relaxation. **Conclusions:** The non-relaxing UES, displays a constant increased resistance to bolus flow 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 UES with a fixed stenosis displays a fixed loss of compliance which is only operative once the limit of sphincter expansion has been reached.

Keywords: deglutition manometry pharynx sphincter cricopharyngeus physiopathology dysphagia
INTRODUCTION

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 (UES) relaxation. The term “cricopharyngeal achalasia” has long been used inappropriately (4; 6; 7; 17; 40) to describe the radiological abnormality which 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 trans-sphincteric 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 non-relaxing 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 an large number of cases referred to a tertiary referral centre, who were all studied systematically using techniques which not only permitted the manometric detection of failed UES relaxation but also enabled evaluation of the biomechanical properties of the non-relaxing UES by correlating pharyngo-sphincteric 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 trans-sphincteric bolus flow of the non-relaxing UES with that of the normal sphincter and with that 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 non-relaxing UES, 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 v2.0, Claris Corporation, 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 symptoms, 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 radiotherapy 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 of 68 ± 10 yrs) and from whom we have previously derived age-specific normal range data for all radiographic and manometric measures. All these healthy subjects had been carefully screened and had no swallowing difficulties nor medical illness which 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 yrs). This patient control group was chosen because UES opening in those with Zenker’s diverticulum is known to be restricted while 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 swallows required to clear the pharynx; deglutitive coughing and/or choking; or post-nasal regurgitation (3). A global assessment of dysphagia severity was made clinically by one author (IJC) and was classified on a 5-point scale as mild (amenable 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 non-oral 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); ESR, CPK, and ANA. Brain imaging (CT and MRI scanning) was done where 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 antero-posterior projections using a 9” Toshiba (Kawasaki, Japan) image intensifier. Fluoroscopic images were recorded on video tape at 25 frames per sec by a VHS video recorder (Panasonic, AG6500, Osaka, Japan) for later analysis. The correction factor for magnification was determined prior to each study by placing two metallic markers set 3cm apart in the field of the image intensifier, above the subject’s head but in the plane of the UES. Subjects swallowed, as tolerated, duplicate 2, 5, 10 and 20ml boluses of high density liquid barium suspension (250% (wt/vol.), E-Z-HD, E-Z EM Inc., 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 oesophagus inferiorly.

Pharyngeal pressures were measured using both perfusion and solid state manometric techniques. Initially we passed transnasally a 9 lumen (O.D. 6mm; I.D. each lumen 0.5mm) silastic/polyvinyl chloride manometric catheter, incorporating five perfused sideholes spaced at 1.5cm intervals and a 6cm sleeve assembly (Dentsleeve, Wayville, South Australia). The sleeve was positioned to straddle the UES to accommodate the axial mobility of the sphincter. The sleeve sensor had a 5x3mm 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 1.5cm, 3cm and 6 cm distal to the proximal sleeve margin, aided positioning the sleeve such that its midpoint was in the centre of the UES high pressure zone at rest. The sleeve assembly and sideholes were perfused by a low compliance pneumohydraulic
perfusion system at 0.6ml/min. The side holes 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 (GastroMac, Neomedix Systems, Sydney, Australia) on a Macintosh computer (Apple, Cupertino, CA, USA) using Gastromac software (Neomedix Systems). All pressures were referenced to basal hypopharyngeal pressure. A purpose-built, video digital timer unit (Practel Sales International, Holden Hill, South 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 60mmHg a separate catheter with 5 solid state transducers, spaced at 1.5 cm intervals, (Gaeltec, Dunvegan, Isle of Skye, 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 mid pharyngeal pressures, lay at the level of the valleculae.

**Data Analysis**

*Videoradiographic measures and definitions*

Radiographic indicators of oropharyngeal dysfunction in patients were analysed 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 post-swallow 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, proximal-distal, 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. Post-swallow pooling, defined as any posts-wallow 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 antero-superior excursion of the hyoid bone, was determined by measuring the interval between the antero-inferior corner of the hyoid bone and the postero-inferior margin of the symphysis menti. 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 sagittal plan 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 ± 2S.D for healthy controls; “partial” if opening was observed but maximal sagittal diameter fell below the lower limit of normal (<5.63 mm for 2ml barium bolus); and was defined “absent” if no contrast penetrated the sphincter zone during attempted deglutition. UES opening duration was similarly classified as normal, partial (< 0.31 sec) or absent.

Manometric measures and definitions
UES pressures were referenced to resting, pre-swallow, hypopharyngeal pressure. Basal UES pressure was determined by averaging end-expiratory UES pressure over a 1-minute period interval 10 minutes after catheter placement to permit subject adaptation. UES relaxation was assessed solely on manometric criteria while UES opening was defined on radiological criteria (see Videoradiographic measures and definitions). The adequacy of UES relaxation was determined from the nadir UES pressure measured
during dry swallows, prior to 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 55yrs of age or more, or exceeded 13 mmHg in individuals < 55yrs of age (1; 3; 37).

The recording site, from which "mid pharyngeal" pressure was measured lay 4.5 cm proximal to the mid point of the UES at the apogee of its upward deglutitive motion. Hypopharyngeal intrabolus pressure was measured at theperfused sidehole immediately proximal to the UES at the proximal margin of the sleeve in controls and in all patients in whom some trans-sphincteric 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 where there was a dwell time by the bolus head at the hypopharyngeal sidehole $\geq$ 100msec, mid intrabolus pressure was estimated from the time point midway between the onset and termination of that particular instance of trans-sphincteric 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 when the basal UES pressure began to fall abruptly. Maximum UES relaxation was defined as the point in time when 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 1.5cm distal to the proximal sleeve margin (seen fluoroscopically to lie within the UES at the time of sphincter closure) and 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 repeat-measure 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 2mL barium boluses as 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 greater than 2ml, usually due to inadequate airway protection. The association between degree of geniohyoid reduction and extant of UES opening was made using a factorial ANOVA. Comparisons of geniohyoid shortening among subsets of patients demonstrating normal, partial or absent UES opening and aged controls were made using a unpaired Student’s t-test, corrected using a Bonferroni-Dunn procedure; alpha (P-value) significant at <0.0083, correction for four multiple comparisons). A Chi-squared test were used to make inferences regarding proportions with and without various these types of pharyngeal dysfunction and for data relating to the association of the preservation of the pharyngeal swallow response. All values are represented as mean ± SEM unless otherwise stated. Statistical calculations were performed using StatVIEW 4.5 (Abacus Concepts Inc, Berkery, 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 yrs; range: 19 – 82 yrs).

With the exception of the two patients in whom the etiology was uncertain (S17 and S18), all cases had an underlying central nervous system disorder accounting for their dysphagia (Table 1). Two broad neuroanatomical categories accounted for all cases in
whom 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 with lateral medullary infarction and failed UES relaxation had severe dysphagia while none of the Parkinsonian patients had severe dysphagia. One patient had no dysphagia (S5) but had Parkinson’s diseases and was studied as part of a disease control group.

One patient (S3) had a normal videofluoroscopic examination. When compared to aged, healthy controls, the prevalence of the following abnormalities was significantly greater in patients ($P < 0.0001$): pharyngeal wall coating (59% vs 0%); post-swallow pooling in pyriform sinuses (88% vs 11%); 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 (mean $43 \pm 5$ mmHg) and aged controls ($44 \pm 5$ mmHg). Nadir UES pressure in patients, recorded during dry swallows, ranged from 15 – 100 mmHg and was significantly higher in patients than in aged controls ($34 \pm 5$ vs $2 \pm 4$ mmHg, $P < 0.05$) (Fig. 1).

**Biomechanical properties of the non-relaxing UES**

To assess the biomechanical properties of the UES in the context of failed relaxation, we examined the volume-dependency 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
UES opening related to bolus volume and intrabolus pressure to conceptualise 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 IBP 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 IBP generation could be compared in a valid manner with controls in this subset.

Hypopharyngeal intrabolus pressure was significantly greater over all bolus volumes in patients with failed UES relaxation when compared with aged controls \( (P<0.001) \) and patients with Zenker’s diverticulum \( (P<0.001) \) (Figure 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 which was not influenced significantly by increased swallowed bolus volume (Figure 2a). Maximal UES sagittal diameters were significantly lower when compared with aged controls \( (P<0.0001) \) but did not differ significantly when compared with Zenker’s controls \( (P= 0.12) \) (Fig 2b). The extent of UES opening in those with Zenker’s virtually peaks at 5ml 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 (Figure 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 non-relaxing 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 while 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 absent. The inter-relationships among failed UES relaxation, UES opening, and the degree of preservation of the pharyngeal swallow response are illustrated by three examples (Figures 3-5). When the pharyngeal swallow response is well preserved, extent of UES opening can be normal and dysphagia 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 whom 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 in order 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 in order to detect cases of failure of deglutitive UES relaxation. Our findings indicate that failure of manometric UES relaxation is uncommon in patients with oral-pharyngeal dysphagia. The prevalence in this tertiary referral population being just under 5% of
patients studied comprehensively. The two commonest causes of this disorder are various medullary lesions and Parkinson's disease. The resistance to trans-sphincteric flow is increased in both disease states. However, the biomechanical properties of the non-relaxing sphincter during trans-sphincteric bolus flow are distinctly different from those of the normal UES and from the sphincter associated with Zenker's diverticulum. The non-relaxing UES displays an increased resistance to flow which 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 (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 the dynamics of that compliance are quite different in the two conditions. The compliance of the non-relaxing 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 is normal at low distending volumes but, once the extent of opening approaches and the restricted maximal limit of opening, UES compliance is likely to be falling rapidly. Both the extent of UES opening of the non-relaxing 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 non-relaxing 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 non-relaxing 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 intra-mural EMG 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 intra-sphincteric pressure drop occurring during the swallow sequence.
Approximately 200msec prior to 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 intra-sphincteric pressure will result from anterior traction forces being applied to the cricoid cartilage from the larnygo-hyoid complex. This second effect can result in transient drops in intra-sphincteric pressure to sub-atmospheric 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 intra-sphincteric pressure to supra-atmospheric levels (onset of the so-called intrabolus pressure domain) (12; 23; 25). Thus, the residual or nadir intra-sphincteric pressure, at a given time in the swallow sequence, may be either sub-atmospheric, 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 hypothesised to have “failed UES relaxation”, demonstrated supra-normal residual (nadir) intra-UES pressures during dry swallows, with co-existent normal or near-normal anterior traction force (as indirectly quantified by geniohyoid shortening). We eliminated the confounding factor of trans-sphincteric bolus flow in generating supra-atmospheric, intra-UES pressure by testing only “dry” swallows, prior to the delivery of any test boluses. Thus, the finding of elevated intra-sphincteric 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 and 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 non-relaxing UES also shows increased resistance to trans-sphincteric 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 trans-sphincteric flow in the non-relaxing UES occurs under distinctly different mechanisms, presumably due to high residual active muscle tension within the opened sphincter zone. This is demonstrated by the observation that: a) the non-relaxing sphincter retains the normal, essentially linear, relationship between swallowed bolus volume and extent of opening; b) the potential for complete opening is preserved; c) intrabolus pressure, while markedly increased compared with healthy controls, does not vary as a function of swallowed bolus volume. In summary, the stenosed sphincter in Zenker's 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 tonicity within the non-relaxing sphincter applies a resistance to pharyngeal outflow which 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, while relaxation is defined manometrically. In the present study we have shown that the extent of UES opening of
the non-relaxing sphincter may range from normal to absent, while the stenotic sphincter with normal manometric relaxation has limited maximal opening. Upper esophageal sphincter relaxation and opening are not synonymous and while 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 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 one had the radiological appearance of a cricopharyngeal bar and the radiological contours in the remainder were unremarkable (Figs 3 and 4).

The etiology of oral-pharyngeal dysphagia is not always certain after thorough clinical, laboratory and radiological assessment including magnetic resonance imaging (10). The present study suggest that the finding of manometrically confirmed failed UES relaxation, in the context of an otherwise non-contributory neurological workup in the dysphagic patient, is likely to indicate a brainstem lesion in its etiology. Similarly, the evaluation of oral-pharyngeal dysphagia in an individual with a recognized brainstem lesion or Parkinson’s disease might be relative indications for pharyngeal manometry because the detection of failed UES relaxation is arguably an indication for cricopharyngeal dilatation, myotomy, or botox injection (6; 35; 36; 39). However, while 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 8 patients with an absent pharyngeal swallow response did not swallow at all and that the complete absence of a swallow accounts for an apparent failure of UES relaxation. There are several reasons why we believe this is a most unlikely explanation. 1) 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 swallow 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. 2) Three of the 8 with an absent pharyngeal response, did actually open the sphincter. Indicating preservation of ancillary deglutitive motor responses sufficient to effect UES opening. 3) 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: hyo-laryngeal 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 8 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, when compared to healthy controls, the resistance to trans-sphincteric 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.

REFERENCES


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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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FIGURE LEGENDS

Figure 1
Nadir UES pressure recorded during dry swallows in patients and healthy controls. The two dashed lines represent the upper (age-dependent) limit of normal for aged controls (10 mmHg) and young controls (13 mmHg).

Figure 2a
a) Intrabolus pressure (top) and b) maximal sagittal UES diameter (bottom) both expressed as a function of swallowed bolus volume in patients with failed UES relaxation. Shown also are data from a disease control group with a fixed, structural UES opening disorder (Zenker's) and healthy aged controls. a) Intrabolus pressure overall in the group with failed UES relaxation was significantly greater than that seen in Zenker's (P<0.001)* or in healthy aged controls (P<0.001)*. The significant volume-pressure gradient seen in both control groups, is not observed in the context of failed UES relaxation. b) Maximal sagittal diameters in the group with failed UES relaxation were significantly lower when compared with aged controls (P<0.001) but did not differ significantly from diameters in Zenker’s controls. Note that the normal, bolus volume-dependent increase in sagittal diameter is preserved in patients with failed UES relaxation and in healthy controls. The capacity for increased UES opening of a non-relaxing UES approaches normal for swallowed bolus volumes of 20ml. In contrast, the extent of UES opening in Zenker's rapidly peaks at 5ml but changes very little with
further increases in swallowed bolus volume. (Numbers in parentheses denotes subjects able to swallow bolus volume specified. *Two factor ANOVA, mixed design).

**Figure 3.**
Videoradiographs and corresponding manometric traces from a patient with mild dysphagia and failed UES relaxation due to syringobulbia (S15). The pharyngeal 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 post-deglutitive residual contrast in the hypopharynx (time T4) and, in particular, that the UES opens fully with good trans-sphincteric flow (T3). Note also that the intrabolus pressure (arrowed) is markedly increased. The horizontal bar represents the interval of trans-sphincteric bolus flow determined radiologically (T3). T1 –T4 represent the times corresponding to the 4 radiographs which are similarly labeled.

**Figure 4**
Videoradiographs and manometry trace from a patient with moderate dysphagia due to Parkinson’s disease (S4) in whom 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 post-swallow hypopharyngeal residual barium and laryngeal vestibular penetration (T3), resulting in moderately severe dysphagia.

**Figure 5**
Example of a swallow in which the pharyngeal swallow response is absent in a patient (S14) who had surgical removal of an ependymoma from the floor of the 4th ventricle. There is a complete absence of UES opening and no bolus clearance from the hypopharynx. The UES motor pattern is highly abnormal with a marked paradoxical augmentation of UES pressure in place of relaxation despite the presence of reasonable geniohyoid reduction (15%) on this swallow attempt (T1 vs T3). Note the severe pre- and post-swallow aspiration (T1 & T4). The minor elevation in pharyngeal pressure at most proximal recording site (+6cm above mid-sleeve level) results from posterior
tongue action but which does not result in a "common-cavity" pressure rise throughout the pharynx (contrast with example in figure 7).

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

**Figure 7**
Relationship between extent of UES opening and geniohyoid shortening used as a measure of the external traction force upon 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).*
Dry swallow related nadir UES pressure (mmHg)

Failed UES relaxation
Young healthy controls
Aged healthy controls

*
Hypopharyngeal intrabolus pressure (mmHg)

Maximal sagittal UES diameter (mm)

Bolus volume (mL)

Failed UES relaxation

Zenker's

Aged controls

Failed UES relaxation

Zenker's

Aged controls

Failed UES relaxation

Zenker's

Aged controls

Failed UES relaxation

Zenker's

Aged controls

Failed UES relaxation

Zenker's

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Zenker's

Aged controls

Failed UES relaxation

Zenker's

Aged controls

Failed UES relaxation

Zenker's

Aged controls

Failed UES relaxation

Zenker's

Aged controls

Failed UES relaxation

Zenker's

Aged controls
Maximum Geniohyoid Shortening (%)

Aged Controls

Patients

Normal UES opening

Partial UES opening

Absent UES opening