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Hyperdynamic Upper Esophageal Sphincter Pressure: A Manometric Observation in Patients Reporting Globus Sensation

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Abstract

OBJECTIVES—Although globus sensation is a common symptom, its pathogenesis is poorly defined. The aim of this study was to quantify the timing and magnitude of respiratory variation in upper esophageal sphincter (UES) pressure with high-resolution manometry (HRM) in patients with globus sensation, normal controls, and gastroesophageal reflux disease (GERD) patients without globus sensation.

METHODS—HRM recordings spanning from the hypopharynx to the stomach were analyzed in 131 consecutive globus patients with normal (64) and abnormal (67) distal esophageal motility. Resting UES pressure was analyzed up to 5 min before 10 5-ml water swallows. Change in UES pressure, its average magnitude between inspiration and expiration, and nadir UES relaxation pressure in globus patients were compared with those in 68 controls and 46 GERD patients without globus.

RESULTS—UES pressure typically increased during inspiration in both controls and patients. Respiration-related change in resting UES pressure was significantly amplified in globus patients (37.3 mm Hg) compared with controls (10.6 mm Hg) and GERD patients (13.0 mm Hg) ($P < 0.0001$). A respiratory change in UES pressure >27 mm Hg was found in $> 60\%$ of globus patients and $<15\%$ of controls and GERD patients without globus. This hyperdynamic UES was not associated with other abnormalities of esophageal motor function.

CONCLUSIONS—Hyperdynamic respiratory UES pressure changes were prevalent in patients reporting globus sensation irrespective of their deglutitive UES and distal esophageal motility. Although the etiology of this hyperdynamic UES is unclear, it does appear to be a frequent manometric observation in this patient group and may provide a new focus for further studies into pathogenesis and therapy.

INTRODUCTION

Globus has been defined as a non-painful, persistent, or intermittent sensation occurring between meals without accompanying dysphagia, odynophagia, or evidence of gastro-

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CONFLICT OF INTEREST

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esophageal reflux disease (GERD) as the cause, and without evidence of histologically based esophageal motility disorder (1). Globus sensation is reportedly experienced by up to 45% of the general population and may be associated with alterations in emotional state (2). Furthermore, 4% of 4,330 consecutive first-time patients in an otolaryngology clinic present with severe or persistent globus sensation (3). However, the etiology of globus sensation remains unknown, making it difficult to easily characterize or treat.

The search for underlying causes of globus has largely focused on psychosomatic origins. Co-morbid depression and hypochondriasis (4), obsessive-compulsive disorder (5), or anxiety (6,7) may be relevant to subsets of globus patients, but the etiological significance of these psychological and psychiatric characteristics is uncertain (8). However, it has also been reported that a number of patients with globus sensation have an underlying organic cause, such as GERD, esophageal dysfunction, or changes in the anatomy and/or functionality of the upper esophageal sphincter (UES). Thus, methods such as intraesophageal pH monitoring, manometry, endoscopy, and videofluoroscopy may be useful in establishing the association between globus sensation and GERD (9–11) or motility disorders (8,12,13). This approach also isolates patients who truly fulfill the Rome III criteria for globus (1), with the implication that treatment of esophageal dysfunction and/or GERD will remove the globus symptom, which may not always be the case. A continuing or worsening globus sensation was reported in 58 % of the patients a year after the treatment for esophageal dysmotility and GERD (14). Hence, detection of common abnormality across the patient groups may assist in treatment of globus.

Among potential etiologies, alteration in UES pressure detectable by manometry and sensed as globus is a provocative theory. Some studies have reported increased UES pressure in globus patients (9,15,16), a finding not confirmed by others (17–19). Pilot data in our laboratory utilizing high-resolution manometry (HRM) showed that patients reporting globus may exhibit an exaggerated increase in UES pressure during inspiration relative to expiration, or occasionally a reversal of this pattern with augmentation occurring during expiration. We hypothesized that these alterations in the respiratory variation of UES pressure may be more prevalent in patients with globus sensation. Hence, the aim of this study was to quantify the timing and magnitude of respiratory variation of UES pressure with HRM in globus patients, normal controls, and patient controls (GERD patients without the globus sensation).

METHODS

Patients

We conducted a retrospective analysis of prospectively acquired clinical data. Manometric studies of 131 globus patients (31 males and 100 females, aged 20–86 years), 68 normal controls (35 males and 33 females, aged 19–48), and 46 GERD patients without globus (28 males and 18 females, aged 14–85) were analyzed. The globus patient population was identified in a consecutive manner from a pool of 990 patients referred for HRM between April 2004 and August 2006. Manometry laboratory intake questionnaires were reviewed to identify patients with the self-reported symptom of globus, irrespective of concomitant symptoms. The questionnaires documented perceived presence of dysphagia, heartburn, or globus at the time of the patient's visit to the manometry laboratory. The sensation of globus was either verbalized by or described to the patient as “a lump/something stuck in the throat” unrelated to meal times. Out of the 131 globus patients, isolated globus sensation was reported by 24 patients, concurrent heartburn was reported by 5 patients, dysphagia by 15, and both heartburn and dysphagia by 85 patients. From the pool of 990 patients, an additional 46 consecutive patients reporting heartburn, but not globus or dysphagia, and diagnosed with GERD by endoscopy and/or pH-metry served as the control patient group.

Normal controls consisted of volunteers recruited by advertisement or word of mouth. Control subjects had no history of gastrointestinal symptoms or upper gastrointestinal surgery and all were without any significant medical condition.

Globus patients were further divided into two groups based on the normality of deglutitive esophagogastric junction (EGJ) relaxation and distal esophageal peristalsis. This division was intended to distinguish a group of patients who largely fulfill diagnostic criteria for functional globus and those who would be excluded using the Rome III classification (1). The study protocol was approved by the Northwestern University Institutional Review Board.

HRM protocol

Manometric data were obtained using a solid-state manometric assembly (4.2 mm outer diameter) with 36 circumferential sensors spaced at 1-cm intervals (Sierra Scientific Instruments; Los Angeles, CA). This device uses proprietary pressure transduction technology (TactArray), which allows each of the 36 pressure-sensing elements to detect pressure over a length of 2.5 mm in each of the 12 circumferentially dispersed sectors. The sector pressures are then averaged to obtain a mean pressure measurement, making each of the 36 sensors a circumferential pressure detector with the extended frequency response characteristic of solid-state manometric systems. Before recording, the transducers were calibrated at 0 and 100 mm Hg using externally applied pressure. The response characteristics of each sensing element were such that they could record pressure transients in excess of 6,000 mm Hg s⁻¹ and were accurate to within 1 mm Hg of atmospheric pressure for measurements obtained for at least the final 5 min of the study, immediately before thermal recalibration (see HRM data analysis). The data acquisition frequency was 35 Hz for each sensor.

Studies were performed in a supine position after at least a 6-h fast. The subjects underwent transnasal placement of the manometric assembly, and the assembly was positioned to record from the hypopharynx to the stomach using nearly five intragastric sensors. The catheter was fixed in place by taping it to the nose. The manometric protocol included a time period of at least 5 min to assess basal sphincter pressure and also included 10 5-ml water swallows.

HRM data analysis

Manometric data were analyzed using ManoView analysis software (Sierra Scientific Instruments). First, data were corrected for the thermal sensitivity of the pressure-sensing elements using the thermal compensation function of ManoView.

After thermal correction, the 5-min recording before the first test swallow was subdivided into consecutive 30-s intervals. The position of the UES was readily identified on the pressure topography plots as a high-pressure zone demarcated by an abrupt increase in pressure relative to atmospheric pressure at its proximal margin and intrathoracic pressure at its distal margin. Periods within 5 s before the initiation of a swallow or 20 s thereafter were excluded. The UES high-pressure zone was outlined with a rectangular portable eSleeve tool. The portable eSleeve is an analysis tool emulating a sleeve sensor on a perfused manometric assembly. Its user-defined limits select the region of analysis, while excluding adjacent regions. The eSleeve selects among the sensors within the rectangle and derives a sleeve-type tracing of maximal pressure (Figure 1) (20). In the current application, the height of the eSleeve was dependent on the width of the UES high-pressure zone and did not include intrapharyngeal and esophageal pressures. The magnitudes of the UES pressure during peak inspiration and mid-expiration were then measured at time points selected

according to the regular pattern of respiratory changes at the EGJ and/or within the thoracic and gastric cavity. UES pressure measurements were referenced to atmospheric pressure.

The difference in UES pressure between the respiratory phases was determined for each subject by subtracting the average pressure during expiration from the average pressure during inspiration as measured over analyzable 30-s intervals (Figure 2). The difference was expressed as an absolute value. Mean UES pressure was calculated as the average of the inspiratory and expiratory values (21).

Deglutitive UES relaxation was characterized by the nadir UES relaxation pressure after 5-ml water swallows quantified using the isobaric contour tool. The isobaric contour tool allows delineation of the anatomic/temporal boundaries of a pressure domain of user-designated magnitude. Nadir UES relaxation pressure was measured by scaling down the isobaric contour tool to the pressure at which it disappeared, thereby defining the relaxation minimum (Figure 3).

The EGJ was identified on the pressure topography plots as the high-pressure zone with intrathoracic pressure at its proximal margin and intragastric pressure at its distal margin. Inspiratory EGJ pressure was defined as the maximal pressure during the normal respiratory cycle representative of crural diaphragm contraction (22). Expiratory EGJ pressure was measured at the midpoint between adjacent inspiratory pressures. Inspiratory and expiratory EGJ pressures were assessed within the 30-s intervals included in the analysis of resting UES pressure parameters using the same methodology. EGJ relaxation pressure was assessed using an automated measurement of the lowest mean residual pressure over a 3-s interval within the post-deglutitive period during 10 5-ml water swallows (ManoView eSleeve) (23). EGJ relaxation pressures greater than the 95th percentile detected in normal controls were considered abnormal.

The isobaric contour tool was used to assess distal esophageal peristalsis after each 5-ml water swallow. Peristaltic amplitude ≥ 30 mmHg and peristaltic velocity $< 8 \text{ cm s}^{-1}$ were considered normal (24,25). Failed or hypotensive peristalsis in > 30 % of test swallows or peristaltic velocity $> 8 \text{ cm s}^{-1}$ in ≥ 20 % of swallows were considered abnormal (26).

Statistical analysis

Respiration-related change in UES pressure, average UES pressure, nadir UES relaxation pressure, and EGJ pressures were summarized using medians and 5–95th percentile range. The Kruskal–Wallis non-parametric test was used to compare patient groups and controls. Post hoc analyses were performed with Dunn’s multiple comparison test with corrected *P* values of 0.0167 for four groups and 0.0024 for seven groups considered significant. Spearman’s rank correlation coefficient (ρ) was used to assess the relationship between respiratory augmentation of UES and EGJ pressures, as well as the effect of age on UES function.

RESULTS

Patient groups

Patient demographics are shown in Table 1. Out of 131 globus patients, 64 (49 %) had normal distal esophageal motility and deglutitive EGJ relaxation (≤ 15.5 mm Hg), whereas abnormal distal esophageal motility was observed in 67 patients (51%). Out of these 67 patients, abnormal EGJ relaxation pressure was observed in 16 (24 %), abnormal peristalsis in 41 (61 %), and both in 10 patients (15 %).

Resting and deglutitive UES pressure parameters

Medians and 5–95th percentile ranges for UES morphology and pressure values are shown in Table 2. The mean respiratory augmentation of UES pressure was 10.6 mm Hg in the normal controls with the normal range extending to 27 mm Hg. In the majority of subjects, UES pressure increased during inspiration. However, in 9/68 (13%) normal controls, 6/46 (13%) patient controls, and 17/131 (13%) globus patients, the increase in respiratory pressure occurred during expiration (Figure 2c). Respiratory fluctuations in UES pressure were over three-fold greater in globus patients with ($P < 0.001$) or without ($P < 0.001$) abnormal distal esophageal motility than those in either normal or patient controls (Table 2). This hyperdynamic augmentation of UES pressure (>27 mm Hg) was present in 40/64 (63%) globus patients with normal distal esophageal motility and 40/67 (60%) globus patients exhibiting abnormal distal esophageal motility (Figure 4). Only 4/68 (6%) normal controls and 7/46 (15%) GERD patients without globus showed exaggerated respiratory fluctuation of UES pressure.

Age had no significant effect on the magnitude of respiratory augmentation of UES pressure in normal controls ($\rho = 0.05$, $P = 0.70$), GERD patients ($\rho = -0.02$, $P = 0.90$), globus patients with normal distal esophageal motility ($\rho = 0.13$, $P = 0.32$), or globus patients with abnormal distal esophageal motility ($\rho = 0.07$, $P = 0.55$). On the basis of the upper age limit of normal controls, GERD and globus patients were further subdivided into ≤ 48 - and > 48 -year-old groups (Table 3). The respiratory augmentation of UES pressure detected in GERD patients aged ≤ 48 or > 48 years was compared with that of normal controls ($P = 0.63$ and $P = 0.05$, respectively). However, the augmentation was consistently greater in globus patients regardless of age group or the presence of distal esophageal dysfunction ($P < 0.0001$).

Mean UES pressure was comparable in all groups with the upper limit of normal being 85 mm Hg. Mean UES pressure was > 85 mm Hg in 4/46 (9%) patient controls, 9/64 (14%) globus patients with normal distal esophageal motility, and 13/67 (19%) globus patients with abnormal distal esophageal motility. Although a trend toward an age-related decrease in average UES pressure was detected in patient controls ($\rho = -0.26$, $P = 0.13$), with significance detected in globus patients with normal distal esophageal motility ($\rho = -0.24$, $P = 0.05$), this trend was absent in normal controls ($\rho = -0.06$, $P = 0.61$) and in globus patients with abnormal distal esophageal motility ($\rho = -0.04$, $P = 0.75$).

An increase in nadir UES relaxation pressure (> 11.9 mm Hg) was observed in 5/46 (11%) patient controls, 8/64 (13%) globus patients with, and 16/67 (24%) globus patients without normal distal esophageal motility. The nadir deglutitive UES relaxation pressure increased with age in globus patients (with normal distal esophageal motility: $\rho = 0.37$, $P = 0.003$; with abnormal distal esophageal motility: $\rho = 0.26$, $P = 0.03$). A similar trend was observed in patient controls ($\rho = 0.30$, $P = 0.08$), but was absent in normal controls ($\rho = -0.08$, $P = 0.5$).

Resting EGJ pressure parameters

Table 2 shows the EGJ pressure parameters among groups. Inspiration increased EGJ pressure in all subject groups ($P < 0.0001$), but in normal controls and globus patients, the augmentation was not correlated with respiratory variation in UES pressure ($\rho \leq 0.15$). A moderate correlation was detected in patient controls ($\rho = 0.34$). Exclusion of controls and patients with expiratory UES augmentation did not reveal any increase in correlation between inspiratory UES pressure and EGJ pressure augmentations either in normal controls and globus patients ($\rho \leq 0.16$) or patient controls ($\rho = 0.34$). No differences were observed in the expiratory ($P = 0.53$) or inspiratory ($P = 0.07$) EGJ pressure profiles between the two

groups of globus patients and controls. Inspiratory augmentation of EGJ pressures was diminished in GERD patients ($P < 0.05$).

Classification of globus patients

Out of the 131 patients with globus sensation, only 56 had normal distal esophageal motility and normal nadir UES relaxation pressures (Figure 5). Out of these, only 13 (10 %) had globus sensation without symptoms of GERD or dysphagia. Thus, the diagnosis of functional globus using the Rome III criteria was uncommon and was found in only 1 % (13) of 990 consecutive patients referred for manometry. In addition, the respiratory augmentation of UES pressure of 16.0 (1.6–36.9) mm Hg seen in this subgroup of globus patients was compared with that of normal controls ($P = 0.35$). Most globus patients also had dysphagia, GERD symptoms, or an abnormal manometry (118/131). Globus with dysphagia was reported in 15/131 patients (11 %). Abnormal nadir UES relaxation was noted in 1/15 and 11/15 patients presented with abnormal distal esophageal motility.

On the basis of manometric findings alone, the prevalence of a hyperdynamic augmentation of UES pressure was similar in globus patients regardless of whether or not they had abnormal distal esophageal motility or abnormal UES relaxation. The prevalence of a hyperdynamic UES was noted in approximately 60% of globus patients, and this was not linked to any specific manometric abnormality of the UES, distal esophagus, or EGJ (Figure 5). Thus, it appears that a hyperdynamic augmentation of UES pressure is associated with globus sensation independent of esophageal motor abnormalities or associated symptoms.

DISCUSSION

This is one of the largest studies of manometric characteristics of patients with globus sensation and the first to use high-fidelity HRM. The major finding was that the normal respiratory variation of UES pressure (10.6–13.0 mm Hg) was amplified to more than 35 mm Hg among the globus patients. A hyperdynamic UES, defined as exhibiting more than 27 mm Hg respiratory variation, was seen in more than 60% of globus patients and fewer than 15% of controls. Despite this hyperdynamic characteristic, the mean UES pressure of globus patients was compared with that of the control groups. Furthermore, neither EGJ respiratory variation, distal esophageal motility, nor deglutitive UES relaxation normality correlated with the presence of globus sensation. Hence, compared with normal and patient controls, a hyperdynamic UES was the only distinguishing manometric finding in globus patients.

Globus sensation is most pronounced during the inter-swallow period, making this the logical time to examine for related changes in UES pressure. Phasic increases in UES pressure typically occur during inspiration; (27–30) a finding corroborated in this study with the caveat that we found 13 % of all patient groups to exhibit augmentation of UES pressure during expiration, which we believe to be a novel observation. The magnitude of respiratory augmentation observed in our normal controls, 10.6 mm Hg, was compared with that of the 14.8 mm Hg reported in a recent study using water-perfused manometry with a sleeve sensor to measure UES tone in healthy subjects (29). However, no comparable data on UES pressure changes with respiration in globus patients have been reported. Rather, manometric studies of the UES in globus patients have focused on UES pressure across respiratory cycle and nadir deglutitive UES relaxation pressure. The majority of these studies showed no abnormalities (8,13,17,18,31), although some investigators did observe UES hypertonicity (9,16). However, there are significant methodological limitations in these earlier studies. Unlike solid-state manometry, a water-perfused sleeve sensor is slow to respond to a pressure increase (32), diminishing its utility in measuring the respiratory changes in UES pressure. Also, prolonged observation of UES pressure (34) is limited in studies utilizing a

station pull-through technique to define resting UES pressure, because of the stimulatory effect of the pull through itself (33).

The cause of the hyperdynamic UES in patients with globus sensation is not clear from this study and requires further investigation. The observation that the finding was equally prevalent among individuals with and without distal esophageal motility disturbances or other specific symptoms argues against it being predicated on those abnormalities.

Alternatively, one could speculate that this is another manifestation of visceral hypersensitivity wherein hypersensitivity leads to hyperreactivity, analogous to the linkage between chest pain and hypertensive peristalsis (35). Another possible mechanism for the hyper-dynamic UES could be related to emotional state and level of excitability. Supportive of this hypothesis, inspiratory UES pressure augmentations of 20.8 mm Hg have been observed in normal subjects during rapid eye movement sleep, a condition characterized by generalized excitability of the nervous system (29). It has also been observed that up to 96% of globus patients report experiencing globus during periods of high emotional intensity (2).

Our inclusion of patients who reported heartburn and dysphagia in addition to globus sensation may be viewed as a limitation, as they did not fulfill stringent Rome III criteria for globus, which stipulate the absence of concomitant dysphagia or GERD (1). However, excluding these patients would have severely restricted our study population, as only 13/131 patients would have qualified. Furthermore, there is an inconsistency in the literature regarding the link between GERD and globus with various studies finding the association prevalent (10,36), poorly associated (9,11), specifically related to proximal reflux (37), or unrelated (38). There is a similar lack of clarity regarding the relationship between globus and esophageal motor disorders. A variety of esophageal motor dysfunctions have been reported in patients with globus. These include achalasia or hypertensive EGJ in 10–56%, and non-specific esophageal motor disorders in 29–34% (8,13,14). By considering the disparity in these data and that the present analysis searched for a common feature among patients with globus, we concluded that inclusion of these patients with analysis of relevant subgroups was appropriate. Further critique could be aimed at the age disparity between our globus patients (ages 20–86) and normal control group (ages 19–48). However, the analysis of our data, that assessed age correlation and subdivided subjects according to age, still highlighted the presence of a hyperdynamic UES in patients with globus sensation that was not linked to age or any esophageal motor disorder. Our findings may be limited, as we only report this phenomenon in the supine position. We assessed the UES function during typical clinical manometry, although usually in a research setting, UES function is measured when upright. Future studies may benefit from assessing this phenomenon in varying positions, as it is possible that hyperdynamic respiratory UES pressure could be positional phenomenon unmasked only in the supine position. Lastly, globus sensation is often intermittent (1). Hence, it can only be assumed that the questionnaires reflected the patient's symptomatology on the day of the manometry, even though the questionnaires were not explicit in that regard. A prospective approach that documents globus sensation and its intensity at the time of the manometric recording may provide additional insight to our current findings. Although our finding of hyperdynamic UES in >60 % of patients with globus sensation suggests that the two phenomena are associated, it does not establish the hyperdynamic sphincter as the cause. Thus, from a therapeutic viewpoint, treatment of associated GERD, distal esophageal motility, UES dysfunction, or anxiety neurosis should be the initial strategy. Advocating specific therapy aimed at the hyperdynamic sphincter itself would seem overly speculative at this point. However, it would be of great interest to compare the UES function in globus patients before and after treatment, and to compare the function of the responders to the non-responders.

In summary, we used high-fidelity HRM to describe respiratory changes in UES pressure and identified a hyperdynamic UES pressure, defined as respiratory augmentation in excess of 27 mm Hg, in more than 60 % of patients reporting globus sensation. This phenomenon was found in <15% of normal and patient controls (GERD patients without globus) and was independent of other abnormalities of esophageal motor function. Although the etiology of this pressure change is unclear, it may prove to be a manometric marker of globus sensation providing focus for further studies into pathogenesis and therapy.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- Globus is a non-painful sensation most pronounced during the inter-swallow periods.
- The etiology of globus is unclear, but in some patients this sensation may be associated with changes in the functionality of the upper esophageal sphincter (UES).
- Manometric studies focusing on UES pressure during swallowing and at baseline measured across the respiratory cycle have been largely inconclusive.

WHAT IS NEW HERE

- Over 60% of patients reporting globus sensation showed marked fluctuation (>27 mm Hg) in UES pressure between inspiration and expiration.
- This hyperdynamic respiratory UES pressure change was consistent across a heterogeneous group of patients, including those with concomitant symptoms of dysphagia and gastroesophageal reflux, and this change was unrelated to distal esophageal dysmotility or UES deglutitive relaxation.
- The analysis tools offered by the current high-resolution manometric technology provide a new functional descriptor for patients with globus sensation, which may prove valuable in monitoring patients' progress post therapy.

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Figure 1.

Analysis of respiration-related change in resting upper esophageal sphincter (UES) pressure using the eSleeve tool in ManoView analysis software. A screenshot of a ManoView analysis interface shows the rectangular portable eSleeve domain (top, emphasized with dashed white line) used to assess three-dimensional pressure topography (middle) within a 12-s section of the high-pressure band representing resting UES pressure. The derived eSleeve pressure tracing is displayed within white rectangle and is placed above the color isocontour plot (bottom). This pressure time plot allows the measurement of UES pressure during changes in esophagogastric junction (EGJ), intrathoracic, and intragastric pressures, which identify the presence of inspiration (I) and expiration (E).

Figure 2.

Pressure–time plots of resting upper esophageal sphincter (UES) pressure during respiration in (a) an asymptomatic control, (b) a globus patient with hyperdynamic respiratory UES augmentation (31.7 mm Hg), and (c) a globus patient with a phase-shifted respiratory augmentation (34.1 mm Hg) such that maximal augmentation occurred during expiration. White and black arrows mark the midpoints of inspiration (I) and expiration (E), respectively (the respiratory cycles are individual specific). The magnitude of UES pressure detected at these points allows quantifying the change in pressure with respiration within a given time interval. Note that despite the significantly larger oscillations of pressure in tracings panels b and c compared with our control (a), the maximal pressure recorded is similar between the three subject types.

Figure 3.

Measurement of nadir upper esophageal sphincter (UES) relaxation pressure with the isobaric contour tool. The figure focuses on the UES before and at deglutition of 5 ml of water. Isobaric contour tool is scaled down to the pressure level immediately below the visible minimal pressure domain during UES opening. In both panels, the isobaric contour pressure setting is set at 12 mm Hg to highlight the distinction between a patient with normal UES relaxation (**a**) and a patient with abnormal UES relaxation (**b**). Note that in panel b, there is no period of time during which the nadir pressure decreases below 12 mm Hg.

Figure 4. Distribution of respiration-related change in resting upper esophageal sphincter (UES) pressure in (a) control subjects and gastro-esophageal reflux disease (GERD) patients without globus sensation and (b) globus patients with normal or abnormal distal esophageal motility. The values left of the vertical dashed line indicate subjects whose respiratory UES augmentation was below the 95th percentile (< 27.0 mm Hg) measured in control subjects.

Figure 5.

Classification of globus patients. Patients were categorized based on the presence of normal and/or abnormal distal esophageal motility and nadir upper esophageal sphincter (UES) relaxation pressure. The percentage of patients with and without a hyperdynamic UES was consistent regardless of distal esophageal motility and UES relaxation pressure with the majority of patients having a hyperdynamic UES (56–63%). It can be noted that only a small portion of our patients fulfilled the Rome III criteria for functional globus, as only 13 of the 56 patients with normal distal esophageal motility and UES relaxation pressure did not report gastroesophageal reflux disease (GERD) or dysphagia symptoms.

Table 1

Subject demographics

	Normal controls	Patient controls (GERD without globus)	Globus patients	
			Normal distal esophageal motility	Abnormal distal esophageal motility
<i>N</i>	68	46	64	67
Age (years) ^a	26 (22–42)	42 (23–71)	49 (23–67)	54 (31–77)
Gender (F/M)	1.0:1.1	1.0:1.6	4.3:1.0	2.5:1.0
BMI ^a (kg/m ²)	22.3 (18.6–26.6)	28.1 (19.8–34.5)	26.3 (18.7–38.6)	24.3 (18.6–38.9)
EGD –/pH –	—	—	9	8
EGD+/pH+	—	46	22	10
EGD –/no pH	—	—	29	41
No EGD and pH	68	—	4	8

BMI, body mass index; EGD; GERD, gastroesophageal reflux disease.

^aMedian (5–95th percentile); EGD+/-, endoscopy positive/negative for esophagitis and/or Barrett's esophagus; pH+/-, positive/negative pH study off therapy.

Table 2

UES and EGJ pressure parameters among subject groups

	Normal controls	Patient controls (GERD without globus)	Globus patients	
			Normal distal esophageal motility	Abnormal distal esophageal motility
Length of the UES high-pressure zone (cm)	3.7 (2.8–4.5)	3.6 (2.4–4.5)	3.6 (2.8–4.5)	3.8 (2.8–5.0)
Average UES pressure (mm Hg)	55.7 (26.3–85.1)	47.1 (20.9–87.6)	47.5 (18.6–106.2)	53.4 (18.8–112.0)
Respiratory augmentation of UES pressure (mm Hg)	10.6 (1.6–27.0)	13.0 (1.4–45.7)	37.3 ^{*,†} (1.6–93.0)	38.5 ^{*,†} (4.4–89.4)
Nadir deglutitive UES relaxation pressure (mm Hg)	6.2 (0.1–11.9)	6.7 (–2.1 to 12.5)	6.9 (0.6–13.8)	7.2 (1.0–19.2)
Expiratory EGJ pressure (mm Hg)	13.5 (5.0–27.2)	9.5 (2.7–19.7)	14.5 (4.7–35.0)	14.6 (1.8–36.4)
Inspiratory EGJ augmentation (mm Hg)	13.6 (7.9–28.9)	8.5 [*] (2.2–24.9)	14.9 (1.7–33.4)	18.4 (3.2–36.1)

EGJ, esophagogastric junction; GERD, gastroesophageal reflux disease; UES, upper esophageal sphincter.

Median (5–95th percentile); Kruskal–Wallis non-parametric test,

* $P < 0.02$ vs. controls,† $P < 0.02$ vs. GERD patients.

Table 3

Effect of age on UES pressure parameters among subject groups

Parameter	Age (years)	Normal controls	Patient controls (GERD without globus)	Globus patients	
				Normal distal esophageal motility	Abnormal distal esophageal motility
Average UES pressure (mm Hg)					
	≤48	55.7 (26.3–85.1)	57.3 (30.9–85.1)	48.4 (22.4–105.6)	55.6 (30.3–109.5)
	>48		46.9 (17.4–98.3)	38.3 (17.6–106.9)	44.7 (17.4–99.3)
Respiratory augmentation of UES pressure (mm Hg)					
	≤48	10.6 (1.6–27.0)	15.9 (0.8–36.4)	32.6 [*] (1.7–88.0)	40.9 [*] (3.0–81.9)
	>48		13.8 (2.9–99.9)	49.0 [*] , [†] (2.1–93.2)	37.4 [*] , [†] (5.1–90.4)
Nadir deglutitive UES relaxation pressure (mm Hg)					
	≤48	6.2 (0.1–11.9)	3.1 [‡] (–3.8 to 10.2)	6.2 [‡] (0–11.7)	4.2 [‡] (1.3–14.5)
	>48		8.4 (–0.8 to 15.7)	7.4 (2.8–14.4)	8.4 [*] (1.1–20.4)

GERD, gastroesophageal reflux disease; UES, upper esophageal sphincter.

Subjects were subdivided according to the upper age limit of the normal control group (≤48 years).

The median (5–95th percentile); Kruskal–Wallis non-parametric test,

* $P < 0.002$ vs. controls ≤48 years old,

[†] $P < 0.002$ vs. GERD patients ≤48 years old,

[‡] $P < 0.002$ vs. globus patients with abnormal distal esophageal motility >48 years old.