

• CLINICAL RESEARCH •

Study on the function of pharynx & upper esophageal sphincter in globus hystericus

Jing Sun, Bin Xu, Yao-Zong Yuan, Jia-Yu Xu

Jing Sun, Bin Xu, Yao-Zong Yuan, Jia-Yu Xu, Department of Gastroenterology, Ruijin hospital, Shanghai Second Medical University, Shanghai 200025, China

Correspondence to: Yao-Zong Yuan, Department of Gastroenterology, Ruijin hospital, Shanghai Second Medical University, Shanghai 200025, China. yyz28@hotmail.com

Telephone: +86-21-64370045-665242 **Fax:** +86-21-64150773

Received 2001-12-20 **Accepted** 2002-02-19

Abstract

AIM: Globus pharyngeus is not an uncommon symptom. Presently, its unclear dated pathophysiology remains unclear and the disease can not be evaluated correctly with routine diagnostic methods. The objective of this study is to establish the normal values of pharyngeal and UES pressure, pharyngeal transit time in healthy volunteers and to compare the differences between healthy volunteers and patients with globus pharyngeus.

METHODS: Twenty-four healthy volunteers and thirty-two patients clinically diagnosed as globus pharyngeus entered the study. Pressures of pharynx and UES were measured. Pharyngeal transit time was measured by videofluoroscopic procedure.

RESULTS: Normal pressure of pharynx, and normal resting pressure of UES were 157.81 ± 63.86 mmHg and 68.33 ± 37.56 mmHg, respectively. The corresponding values in the patients were 175.50 ± 93.47 mmHg and 71.38 ± 41.42 mmHg. The pharyngeal transit time was 1.44 ± 0.30 s in normal control group, among them there were 4 cases with stasis of barium in the valleculae and one in the piriform sinus. No laryngeal penetration or aspiration was found. In the patient group, the pharyngeal transit time was 1.37 ± 0.41 s, among them there were 6 cases with stasis of barium in the valleculae and 5 in the piriform sinus. 9 cases had laryngeal penetration and 2 had aspiration. There were no statistical differences of pressures of pharynx, UES and the pharyngeal transit time between the two groups. But there was an association between laryngeal penetration and globus pharyngeus.

CONCLUSION: Radiographic examination of the pharynx show specific findings of pharyngeal dysfunction in patients with globus pharyngeus. UES pressure is normal in most patients. Hence, we find no role for UES hypertonicity as an etiologic factor in globus pharyngeus.

Sun J, Xu B, Yuan YZ, XU JY. Study on the function of pharynx & upper esophageal sphincter in globus hystericus. *World J Gastroenterol* 2002; 8(5):952-955

INTRODUCTION

Globus sensation (globus pharyngitis, globus pharyngeus) is best described as a constant sensation of something stuck or a lump or tightness in the throat. Typically, a lump, or crumb-like (foreign body) sensation, a constriction or choking^[1-3] is complained. Nearly half of the general population has had intermittent symptoms resembling globus^[4-6]. More severe and distressing symptoms comprise up to 4 % of referrals to otolaryngological specialists^[4]. In addition to emotional stress, mood, and personality disorders, it has been attributed to a high upper esophageal sphincter (UES) resting pressure, gastroesophageal reflux (GER)^[7,8], esophageal dysmotility, hiatal hernia, kinematic pharyngeal transit time and local anatomic abnormalities^[9-16]. Although the associations are diverse and broadly investigated, the etiology of globus still remains unclear^[4].

The aim of our study was to investigate the association of globus pharyngeus with UES resting pressure and kinematic pharyngeal transit time.

MATERIALS AND METHODS

Study subject

Two groups of persons were studied: globus pharyngeus patients and the control group. The globus pharyngeus group comprised thirty-two consecutive patients presenting themselves to the otolaryngology and gastroenterology departments with predominant symptom of globus pharyngeus with no abnormality on examination of neck, larynx, or pharynx between December 2000 and March 2001. The diagnostic criteria of the globus sensation is in accordance with Rome II criteria: At least 12 weeks, which need not be consecutive, in the preceding 12 months of: (1) The persistent or intermittent sensation of a lump or foreign body in the throat; (2) Occurrence of the sensation between meals; (3) Absence of pathologic gastroesophageal reflux, achalasia, or other motility disorder with a recognized pathologic basis as scleroderma of the esophagus. The control group consisted of twenty-four healthy volunteers. The male: female ratio in the globus pharyngeus group was 1:1.29, as compared with 1:1.4 in the control group. The mean age in the globus pharyngeus group was 47 ± 11 years (range: 28-73 years), as compared with 49 ± 17 years (range: 21-77 years). These differences were not significant. A single investigator examined all patients by videofluoroscopy and esophageal manometry.

Esophageal manometry

After an overnight fast, manometry was performed using a solid-state intraluminal transducer assembly (Konigsberg Instruments, Inc., Pasadena, USA). The catheter consists of a flexible tube containing four pressure microtransducers. The distal two are circumferential transducers that record the average pressure over 360°. The circumferential transducer consists of a 4.6-mm-diameter silastic annulus enclosing a small transducer within a castor oil-filled chamber. The two

proximal transducers with a single sensor oriented in one direction. The transducers, starting at the distal end, are separated by 3, 2 and 5 cm. Pressure data are collected on-line by means of a computerized motility system and analyzed using Polygram equipment and software [Synectics (Medtronics), Shoreview, Minnesoda].

Before the examination, the transducers were calibrated at 0 mmHg and 50 mmHg after balneum in 37 °C water 10 minutes. Manometry of the UES and pharynx was performed in the upright position. The catheter was passed through a nostril into the stomach. Then it was withdrawn in 1-cm increments every 20 seconds back into the esophagus. UES resting pressure was assessed using a station pull-through of the distal transducer with at least 15-sec intervals for stabilization between each 1-cm movement of the catheter, since the UES is somewhat reactive to the catheter movement. After identifying the high-pressure zone during this slow pull-through, at least 15-sec is allowed to elapse before measuring the resting UES pressure. Maximal stable pressure is recorded in millimeters of mercury using esophageal pressure just distal to the UES as zone baseline. Five 5-ml water (room temperature) swallows were used to assess UES relaxation, pharyngeal contraction, and UES/pharyngeal coordination. Swallows were 30 seconds apart. The swallows were performed with the circumferential transducer placed just proximal to the high-pressure zone of the UES to allow accurate recording of the pressure throughout the cycle of elevation of the sphincter during deglutition. Placement of the circumferential transducer proximal to the high-pressure zone of the sphincter compensates for orad movement during swallowing.

Mamometry helped clarify the specific timing of pressure events during pharyngeal contraction and UES relaxation^[17].

Videofluoroscopy

Detailed sequential analysis of videofluoroscopic images recorded at 25 frames/s clarifies timing of the events that occur during pharyngeal contraction and UES opening. It clearly defines the key role of muscle contraction occurring early in the swallowing sequences that produce the elevation of the hyoid and larynx, which is an essential element in the opening of the UES^[18-20].

Kinematic pharyngeal transit time is defined as the time from the first movement of the bolus, which results in a complete swallow, to the time the epiglottis returns to its initial position. The definition excludes oral preparation time and tongue movements that do not result in a complete swallow^[21].

Videofluoroscopy was completed in both anteroposterior and lateral projections with 5-ml thin barium at room temperature^[22-23]. To standardize the evaluations in our study, timing measurements were completed in the lateral projection.

The following data were collected by one physician evaluator: (1) quantitative kinematic pharyngeal transit times including the time of arrival of the head of the bolus reaching the level of the posterior inferior border of C₂ vertebral body (C₂L), the inferior level of the valleculae (BV), the posterior inferior border of C₄ vertebral body (C₄L), and the time at which the epiglottis returned to its original position (Em); These data points were selected to provide more easily identifiable radiologic landmarks for measurement^[21,24-26]. (2) The presence or absence of vallecular or piriform pooling, and (3) the presence or absence of penetration of part of the bolus to or through the true vocal cord^[27-29].

Statistical analysis

Fisher *P* test was used to compare patients and controls, with statistical significance set at the level of 0.05.

RESULTS

Kinematic pharyngeal transit time

The data of kinematic pharyngeal transit time from the control group and globus pharyngeus group were presented in Table 1.

Table 1 Kinematic pharyngeal transit time

	Control group(n=24)	Globus sensation group(n=32)	<i>P</i>
C ₂ L	0.50±0.27	0.45±0.33	>0.05
BV	0.57±0.26	0.51±0.34	>0.05
C ₄ L	0.67±0.27	0.63±0.36	>0.05
EM	1.44±0.30	1.37±0.41	>0.05

Note: Times are given in seconds.

There was no statistically significant difference between the control group and globus pharyngeus group, which showed ^a*P*>0.05. There were four cases of volunteers presenting stasis of barium in the valleculae and one in the piriform sinus. No laryngeal penetration and aspiration were found. Meanwhile, there were six and five of patients representing stasis of barium in the valleculae and piriform sinus respectively. Nine and two of patients had laryngeal penetration and aspiration. The results of valleculae and piriform sinus stasis and airway aspiration had no statistically significant differences between the two groups. But there was an association between laryngeal penetration and globus pharyngeus.

Esophageal manometry

The data of esophageal manometry from the control group and globus pharyngeus group were presented in Table 2.

Table 2 Data of esophageal mamometry

	Control group (n=24)	Globus pharyngeus group(n=32)
UES		
Resting pressure	68.33±37.56mmHg	71.38±41.42mmHg
Residual pressure	-7.30±6.48mmHg	-11.04±6.90mmHg
Relaxation time (from the beginning of relaxation to the nadir)	0.27±0.06s	0.28±0.15s
Duration (time from beginning of relaxation to the end)	0.54±0.08s	0.59±0.15s
Recovery (time from nadir of relaxation to the end)	0.27±0.08s	0.33±0.15s
Pharynx		
Peak pressure	157.81±63.86mmHg	175.50±93.47mmHg
contraction time (from the beginning of contraction to the nadir)	0.20±0.06s	0.22±0.08s
duration (time from beginning of contraction to the end)	0.42±0.08s	0.44±0.12s
Recovery (time from peak of contraction to the end)	0.22±0.05s	0.22±0.06s

There was no significant difference between the two groups ($P>0.05$). And also no difference in gender in the two groups (Table 3)

Table 3 Data of male and female in two groups

	Control group		Globus pharyngeus group	
	Male	Female	Male	Female
UES resting pressure(mmHg)	65.55±34.02	70.32±38.49	67.61±34.39	73.65±44.00
UES residual pressure (mmHg)	-9.33±6.80	-5.84±5.82	-8.80±6.98	-12.39±6.49
Pharyngeal peak pressure(mmHg)	165.72±69.19	151.45±57.36	163.19±105.47	182.89±81.99

DISCUSSION

Globus pharyngeus is a common disorder, accounting for 3-10 % of otolaryngologic outpatient referrals^[1,4]. The cause is unknown, and is likely to be of multifactorial origin. Abnormal function of the upper esophageal sphincter (UES) may produce the globus sensation symptom^[14,30]. Disorders of the UES include the hypertonic and hypotonic sphincter and various abnormalities of relaxation. Globus sensation has been associated with hypertonic upper esophageal sphincter and a persistent cricopharyngeal impression (i.e., bar), and Zenker diverticulum may be seen in patients with abnormal sphincter relaxation^[9-13,30-31].

Hypertonicity of the UES was suggested as an etiologic factor in the genesis of globus sensation by Watson and Sullivan^[32] in a study involving only nine patients suggested hypertonicity of the UES as an etiologic factor in the genesis of globus pharyngeus. This observation was in contradiction with a previous controlled study by Calderelli *et al*^[33], who found normal UES pressures in their patients with globus sensation. The techniques used for UES manometry in both studies might have questionable accuracy, as they did not count for the radial asymmetry of the UES pressure profile. In a more recent study, Cook *et al*^[34] failed to demonstrate any difference in resting UES pressure between normal controls and those with a history of globus sensation. Our study, using computerized solid-state manometry with a circumferentially recording transducer has not shown increased prevalence of UES hypertonicity in patients with globus sensation.

Through studies using multi-lumen catheters, radial asymmetry of the UES has been demonstrated over a number of years^[35,36]. Pressures recorded in the anterior and posterior directions were usually two or three times greater than pressures recorded laterally. This was believed to result from the anatomical disposition of the cricopharyngeus, but might be due in some extent to the compressive effect of the posterior lamina of the cricoid cartilage against the vertebral bodies of the cervical spine. So we believe that values for UES pressure are best obtained using a circumferential sensing solid-state transducer^[37]. In addition to radial asymmetry, oral movement of the sphincter during deglutition complicates the manometric assessment of the UES. With the transducer located in the sphincter high-pressure zone, a recording artifact will usually occur. As the swallow is initiated, the sphincter moves oral, leaving the transducer recording esophageal pressure. This fall in pressure may be erroneously interpreted as sphincter relaxation. If, however, the transducer is located proximal to the high pressure zone, when the subject swallows and the

larynx elevates, the UES (which has not yet relaxed) moves onto the transducer, which then records a rise in pressure followed by a fall in pressure as the sphincter relaxes. The pressure rises again as the sphincter regains tone and falls as the larynx returns to its original position, moving the sphincter distal to the transducer. The manometric recording in the UES that results from this sequence of events resembles the letter 'M' and this configuration can be used to ascertain correct transducer placement^[38-41].

The manometric findings in our study did not demonstrate any possible origin for the globus sensation. Detailed sequential analyses of videofluoroscopic images recorded at 25 frames/s have clarified timing of the events that occur during pharyngeal contraction and UES opening^[42,43]. These studies have clearly defined the key role of muscle contractions occurring early in the swallowing sequence that produce the elevation of the hyoid and larynx which is an essential element in the opening of the UES^[44,45]. Videofluoroscopy was completed in both anteroposterior and lateral projections with 5 ml 250 % barium sulfate liquid^[27].

The initiating event in our kinematic times is approximately at the beginning of the oropharynx. Consequently, BV in our study represents transit time through the oropharynx and mesopharynx. Pharyngeal dysfunction was defined as the presence of one or more of the following findings: (1) poor laryngeal elevation and epiglottic motion, (2) laryngeal penetration or aspiration, and (3) stasis of barium in the vallecula and piriform sinuses^[46,47].

Radiographic evidence of pharyngeal dysfunction such as stasis and aspiration was seen in patients, but these findings were not specific for upper esophageal sphincter dysfunction. Batch and Wilson *et al* also found that pharyngeal abnormalities were rarely seen at radiography in patients with globus pharyngeus^[48-50]. Thus, radiographic findings suggestive of upper esophageal sphincter dysfunction were rarely present in patients with globus sensation^[30].

In conclusion, findings by radiographic examination of the pharynx may show specific findings of pharyngeal dysfunction in patients with globus pharyngeus. Results of the pressures of the UES are normal in most patients with this symptom. So we find no role for UES hypertonicity as an etiologic factor for globus, but a strong association between laryngeal penetration and globus pharyngeus.

REFERENCES

- 1 **Clouse RE**. Functional esophageal disorders. *Gut* 1999; **45**: II 31- II 36
- 2 **Batch AJR**. Globus pharyngeus I . II. *J Laryngol Otol* 1988; **102**: 152-158, 227-230
- 3 **Wilson JA**, Heading RC, Maran AGD. Globus sensation is not due to gastro-esophageal reflux. *Clin Otolaryngol* 1987; **12**: 271-275
- 4 **Corso MJ**, Pursnani KG, Mohiuddin MA, Gideon RM, Castell JA, Katzka DA, Katz PO, Castell DO. Globus Sensation is associated with hypertensive upper esophageal sphincter but not with gastroesophageal reflux. *Dig Dis Sci* 1998; **43**: 1513-1517
- 5 **Thompson WG**, Heaton KW. Heartburn and globus is apparently in healthy people? *Can Med Assoc J* 1982; **126**: 46-48
- 6 **Moloy PJ**, Charter R. The globus symptom. *Arch Otolaryngol* 1982; **108**: 740-744
- 7 **Shaker R**, Milbrath M, Ren J, Toohill R, Hogan WJ, Li Q. Esophagopharyngeal distribution of refluxed gastric acid in patients with reflux laryngitis. *Gastroenterology* 1995; **109**: 1575-1582

- 8 **Smit CF**, Tan J, Devriese PP, Mathus LM, Brandsen M, Schouwenburg PF. Ambulatory pH monitoring at the upper esophageal sphincter. *Laryngoscope* 1998; **108**: 299-302
- 9 **Logemann JA**, Veis S, Colangelo L. A screening procedure for oropharyngeal dysphagia. *Dysphagia* 1999; **14**: 44-51
- 10 **Wilson JA**, White A, von Heacke NP, Marnn AGD, Heading RC, Pryde A, Dphil JR. Gastroesophageal reflux and posterior laryngitis. *Ann Otol Rhinol Laryngol* 1989; **98**: 405-410
- 11 **Jacob P**, Kahrilas PJ, Herzog G. Proximal esophageal pH-metry in patients with reflux laryngitis. *Gastroenterology* 1991; **100**: 305-310
- 12 **Koufman JA**. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-h pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. *Laryngoscope* 1991; **101**(Suppl 53): 1-78
- 13 **Dodds WJ**, Stewart E, Logeman J. Pathophysiology and radiology of the normal oral and pharyngeal phases of swallowing. *AJR* 1990; **154**: 953
- 14 **Hill J**, Stuart RC, Fung HK, Ng EK, Cheung FM, Chung SC, Hassett A. Gastroesophageal reflux, motility disorders and psychological profiles in the etiology of globus pharyngis. *Laryngoscope* 1997; **107**: 1373-1377
- 15 **Weisskopf A**. Reflux esophagitis: a cause of globus. *Otolaryngol Head Neck Surg* 1981; **89**: 780-782
- 16 **Wilson JA**, Pryde A, Piris J, Allan PL, Macintyre CCA, Maram AGD, Heading RC. Pharyngoesophageal dysmotility in globus sensation. *Arch Otolaryngol Head Neck Surg* 1987; **115**: 1086-1090
- 17 **Linsell JC**, Anggiansah A, Owen WJ. Manometric findings in patients with globus sensation [abstract]. *Gut* 1987; **28**: 1378
- 18 **Jones B**, Donner MW. Examination of the patient with dysphagia. *Radiology* 1988; **167**: 319-326
- 19 **Robbins J**, Hamilton JW, Lof GL, Kempster GB. Oropharyngeal swallowing in normal adults of different ages. *Gastroenterology* 1992; **103**: 823-829
- 20 **Jones B**, Kramer SS, Donner MW. Dynamic imaging of the pharynx. *Gastrointest Radiol* 1985; **10**: 213-224
- 21 **Johnson ER**, McKenzie SW, Rosenquist CJ, Lieberman JS, Sievers AE. Dysphagia following stroke: quantitative evaluation of pharyngeal transit times. *Arch Phys Med Rehabil* 1992; **73**: 419-422
- 22 **Mujica VR**, Conklin J. When it's hard to swallow, what to look for patients with dysphagia. *Postgrad Med* 1999; **105**: 131-134, 141-142, 145
- 23 **Dantas RO**, Dodds WJ, Massey BT, Kern MK. The effect of high-vs-low-density barium preparations on the quantitative features of swallowing. *AJR* 1989; **153**: 1191-1195
- 24 **Cook IJ**, Dodds WJ, Dantas RO, Kern MK, Massey BT, Shaker R. Timing of videofluoroscopic manometric events and bolus transit during the oral and pharyngeal phases of swallowing. *Dysphagia* 1989; **4**: 8-15
- 25 **Woo P**, Noordzij P, Ross J. Association of esophageal reflux and globus symptom: comparison of laryngoscopy and 24-hour manometry. *Otolaryngol, Head Neck Surg* 1996; **115**: 502-507
- 26 **McConnel FMS**, Cerenko D, Jackson RT, Guffin TN. Timing of major events of pharyngeal swallowing. *Arch Otolaryngol Head Neck Surg* 1988; **114**: 1413-1418
- 27 **Ekberg BO**, Nylander G. Cineradiography of the pharyngeal stage of deglutition in 150 individuals without dysphagia. *British J Radiol* 1982; **55**: 253-257
- 28 **Logemann JA**. Screening, diagnosis, and management of neurogenic dysphagia. *Seminars in Neurology* 1996; **16**: 319-327
- 29 **Levine MS**, Rubesin SE. Radiologic investigation of dysphagia. *AJR* 1990; **154**: 1157-1163
- 30 **Ott DJ**, Ledbetter MS, Koufman JA, Chen MY. Globus pharyngeus: Radiographic evaluation and 24-hour pH monitoring of the pharynx and esophagus in 22 patients. *Radiology* 1994; **191**: 95-97
- 31 **Mason RJ**, Bremner CG, Demeester TR, Crookes PF, Peters JH, Hagen JA, Demeester SR. Pharyngeal swallowing disorders. *Ann Surg* 1998; **228**: 598-608
- 32 **Aviv JE**. Clinical assessment of pharyngolaryngeal sensitivity. *Am J Med* 2000; **108**: 68s-72s
- 33 **Smit CF**, Leeuwen JA, Mathus LM, Devriese PP, Semin A, Tan J, Schouwenburg PF. Gastropharyngeal and gastroesophageal reflux in globus and hoarseness. *Arch Otolaryngol, Head Neck Surg* 2000; **126**: 827-830
- 34 **Cook IL**, Dent J, Collins SM. Upper esophageal sphincter tone and reactivity to stress in patients with a history of globus sensation. *Dig Dis Sci* 1989; **34**: 672-676
- 35 **Triadafilopoulos G**, Hallstone A, Nelson-abbott H, Bedinger K. Oropharyngeal and esophageal interrelationships in patients with nonobstructive dysphagia. *Dig Dis Sci* 1992; **37**: 551-557
- 36 **Sears VW**, Castell JA, Castell DO. Radial and longitudinal asymmetry of human pharyngeal pressures during swallowing. *Gastroenterology* 1991; **101**: 1559-1563
- 37 **Castell LA**, Castell DO. Recent developments in the manometric assessment of upper esophageal sphincter function and dysfunction. *Dig Dis* 1997; **15**(Suppl): 28-39
- 38 **Welch RW**, Luchmann K, Ricks PM, Drake ST, Gates GA. Manometry of the normal upper esophageal sphincter and its alteration in laryngectomy. *J Clin Invest* 1979; **63**: 1036-1041
- 39 **McConnel FMS**. Analysis of pressure generation and bolus transport during pharyngeal swallowing. *Laryngoscope* 1988; **98**: 71-78
- 40 **Knauer CM**, Castell JA, Dalton CB, Nowak L, Shaker R. Pharyngeal/upper esophageal sphincter pressure dynamics in humans-effects of pharmacologic agents and thermal stimulation. *Dig Dis Sci* 1990; **35**: 774-779
- 41 **Kahrilas PJ**, Dodds WJ, Dent J, Logemann JA, Shaker R. Upper esophageal sphincter function during deglutition. *Gastroenterology* 1988; **95**: 52-62
- 42 **Kahrilas PJ**. A method for continuous monitoring of upper esophageal sphincter pressure. *Dig Dis Sci* 1987; **32**: 121-128
- 43 **Curtis DJ**, Cruess DF, Berg T. The cricopharyngeal muscle: a video recording review. *AJR* 1984; **142**: 497-500
- 44 **Johnson ER**, McKenzie SW, Sievers A. Aspiration pneumonia in stroke. *Arch Phys Med Rehabil* 1993; **74**: 973-975
- 45 **Dodds WJ**, Logemann JA, Stewart ET. Radiologic assessment of abnormal oral and pharyngeal phases of swallowing. *AJR* 1990; **154**: 965-974
- 46 **Jones B**. The pharynx disorders of function. *Radiol Clin Nor Am* 1994; **32**: 1103-1115
- 47 **Ott DJ**, Pikna LA. Clinical and videofluoroscopic evaluation of swallowing disorders. *AJR* 1993; **161**: 507-513
- 48 **Ekberg O**, Olsson R. Dynamic radiology of swallowing disorders. *Endoscopy* 1997; **29**: 439-446
- 49 **Isberg A**, Nilsson ME, Schiratzki H. Movement of the upper esophageal sphincter and a manometric device during deglutition. *Acta Radiol Diag* 1985; **26**: 381-388
- 50 **Färkkilä MA**, Ertama L, Katila H. Globus pharyngis, commonly associated with esophageal motility disorders. *AJR* 1994; **89**: 503-507

Edited by Wu XN