

Volitional Control of the Upper Esophageal Sphincter With High-Resolution Manometry Driven Biofeedback

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Introduction: Dysfunction of the upper esophageal sphincter (UES) is associated with swallow dysfunction and globus pharyngeus. Although volitional augmentation of the UES has been previously documented, the ability of individuals to control UES pressure with high-resolution manometry (HRM) driven biofeedback has not been assessed.

Purpose: To evaluate the ability of patient driven HRM biofeedback to control UES basal pressure.

Methods: HRM data was collected from 10 patients undergoing esophageal manometry. Participants were trained on real-time HRM-driven biofeedback to both elevate and reduce UES pressure. Measures of baseline UES minimum, mean and maximum pressures (mmHg) were compared to biofeedback-driven volitional increases and decreases in UES pressures. Pre- and post-biofeedback data were compared with paired sample T-tests.

Results: The mean age (\pm standard deviation) of the cohort was 68 (± 12.7) years. Sixty percent (6/10) were female. The mean UES baseline pressure increased from 30.1 (± 15.3) mmHg to 44.8 (± 25.03) mmHg ($P = .02$) with biofeedback-driven UES augmentation ($P < .05$). Maximum UES pressures were also increased from 63.84 (± 24.1) mmHg to 152.4 (± 123.7) ($P = .04$). Although some individuals were able to successfully decrease basal UES tone with the HRM biofeedback, no statistically significant group differences were observed ($P > .05$).

Conclusion: Volitional control of UES pressure is possible with HRM-driven biofeedback. Patients vary in their ability to intentionally control UES pressure and some may require further training aimed at lowering UES pressure with HRM-guided biofeedback. These data may have significant implications for the future treatment of UES disorders and warrant further investigation.

Key Words: Upper esophageal sphincter, high-resolution manometry, globus, biofeedback, cricopharyngeal dysfunction, dysphagia.

Level of Evidence: 4

INTRODUCTION

The upper esophageal sphincter (UES) is a 2.5 to 4.5 cm high-pressure zone located between the pharynx and esophagus. It can be identified on high-resolution manometry (HRM) as a high pressure band corresponding to the area of the pharyngo-esophageal segment (Fig. 1). Resting pressure of the UES is highly variable and ranges from 35 to 200 mmHg.^{1,2} Baseline pressure drops to near atmospheric during swallow, when it allows bolus to pass into the esophagus. Resting pressure has been shown to decrease during sleep^{3,4} and increase during acute stress, when supine,^{5,6} and following esophageal acid exposure.^{7,8}

Abnormal UES resting pressure has been associated with symptoms of globus pharyngeus.^{6,9-11} Globus

pharyngeus is a functional esophageal disorder characterized by a sensation of a lump, retained food bolus, or tightness in the throat. Globus symptoms are common, experienced by nearly one-half of healthy adults in the United States during some point in their lifetime.¹² The clinical impact of this pervasive symptom is significant and globus complaints account for nearly 4% of general otolaryngology office visits annually.¹³ The etiology of globus sensation is unclear but may be multifactorial. It has been associated with visceral hypersensitivity,¹⁴ psychologic abnormalities,¹⁵ and reflux.¹⁶ Several studies have indicated hypertonicity of the UES as a possible cause of globus pharyngeus.^{6,9-11}

Considering the potential association of globus with abnormal UES pressure, some persons with globus symptoms may benefit from modulation of UES resting pressures. Modifying UES pressures volitionally can be challenging, since UES tone is generally not under voluntary control. Previous research studies have aimed to modulate UES tone and opening using swallowing strategies, such as the Mendelsohn maneuver or the tongue hold, yet these studies have focused on modifying the relaxation or opening of the sphincter specifically during swallowing.¹⁷⁻¹⁹ We proposed to use HRM as a biofeedback tool for influencing the resting pressure of the upper esophageal sphincter. The advantage of HRM is that the upper esophageal sphincter can easily be identified on pressure topography and changes in pressure are readily apparent on the screen as changes in color. Thus, HRM can provide visual cues to the patient to afford

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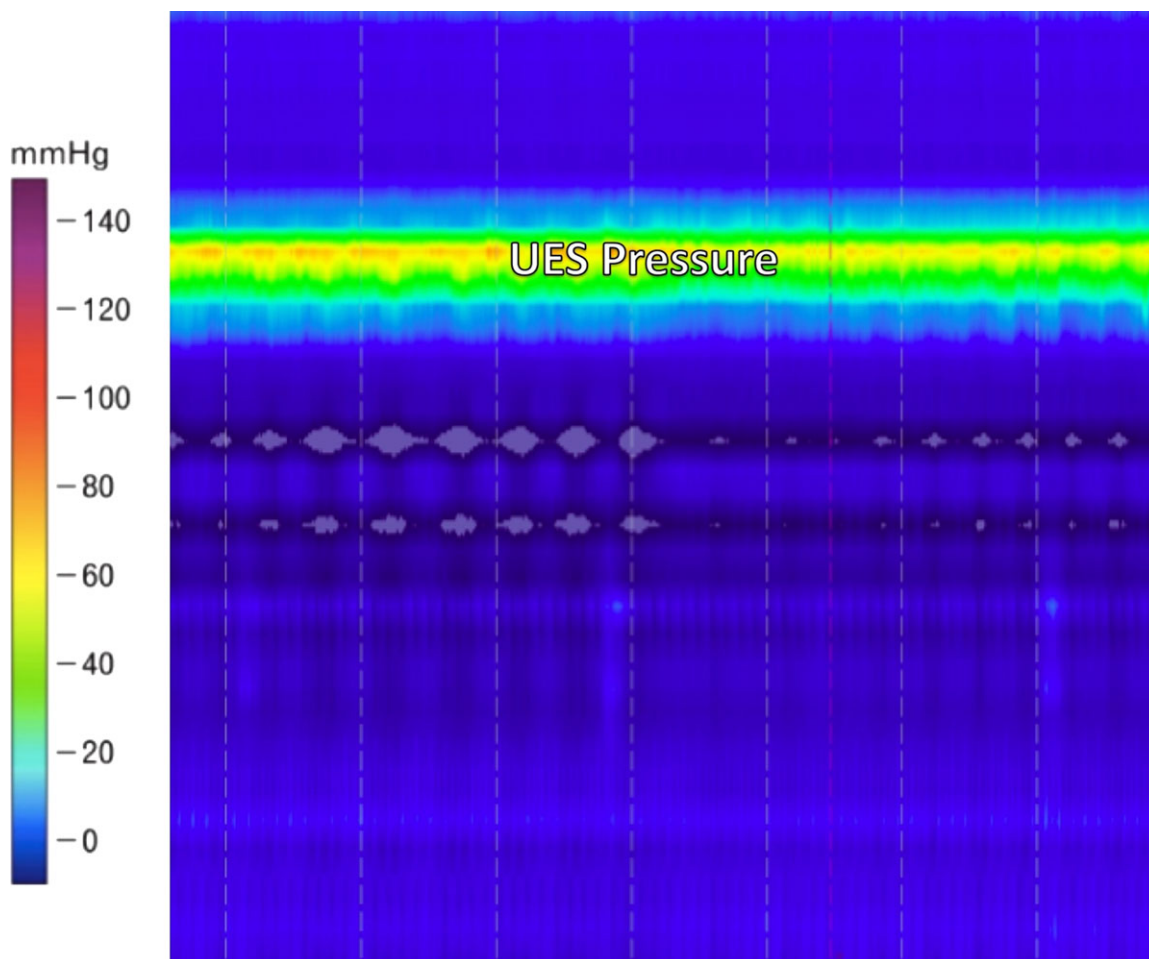


Fig. 1. Upper esophageal sphincter (UES) resting pressure displayed on high-resolution manometry (HRM) pressure topography. Pressure changes which are represented as color changes in the UES high pressure band can provide real-time visual feedback.

real time biofeedback (Fig. 1). Although HRM has shown promise as a biofeedback tool for improving pharyngeal contractility,²⁰ no study has evaluated the ability of HRM biofeedback to modify UES pressure. The purpose of this investigation was to evaluate the ability of patient driven HRM biofeedback to control UES basal pressure. Such control may hold therapeutic potential for patients with UES pressure abnormalities, such as patients with globus pharyngeus, cricopharyngeal spasm, or dysphagia.

METHODOLOGY

This study was approved by the Institutional Review Board at the University of California, Davis. Patients undergoing HRM for evaluation of dysphagia, globus, chronic cough, and gastroesophageal reflux were included in the study. Patients with a history of a severely obstructing cricopharyngeal bar, head and neck cancer, or lidocaine allergy were excluded.

A 4.2-mm outer diameter solid-state manometric assembly with 36 circumferential sensors spaced at 10-mm intervals was utilized for all trials (ManoScan, Given Imaging, Atlanta, GA). Before recording, the transducers were calibrated at 0 and 300 mmHg using externally applied

pressure. The data acquisition frequency was 50 Hz for each sensor. The catheter was lubricated with 2% viscous lidocaine and topical nasal decongestant and anesthetic spray (phenylephrine HCl 1% with lidocaine HCl 4%) was administered. The manometry catheter was placed through the patient's more patent nasal cavity. The catheter's position was determined and verified manometrically. Following a brief period to allow patient acclimation, 30 seconds of baseline UES pressure was recorded at rest. The clinical evaluation consisted of 12 5-ml saline bolus swallows. Following the clinical evaluation, participants were trained on utilizing pressure topography as biofeedback for elevating and lowering UES pressure. During the training session, participants were shown the UES high pressure topography band and the color coding of pressure intensity was reviewed. They were then instructed to practice turning the colors of the UES pressure band to the warmer colors during elevation biofeedback and to the cooler colors during relaxation biofeedback (Fig. 2). During this practice session, subjects were encouraged to modify their UES pressures in any way they could as long as it did not cause changes in their breathing pattern. Participants were then asked to sustain 30 seconds of UES tightening and 30 seconds of UES relaxation, separated by a 1-minute resting period.

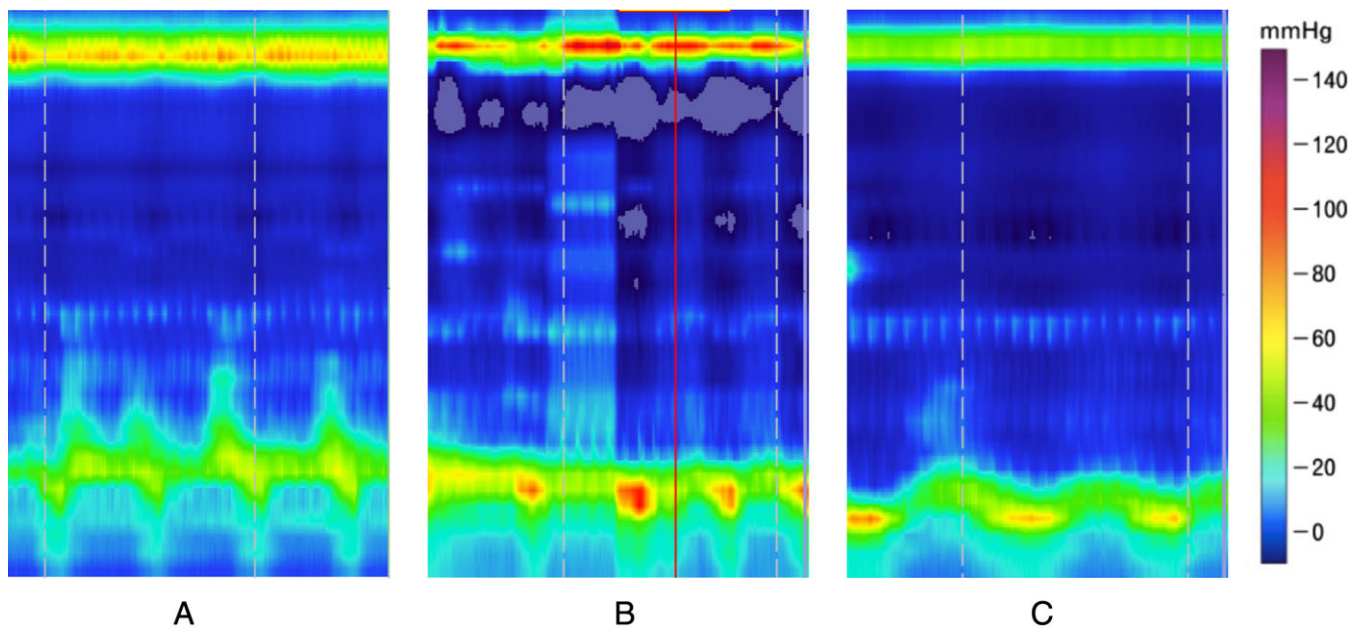


Fig. 2. High-resolution manometry (HRM) pressure topography displaying upper esophageal sphincter (UES) resting baseline pressures (A) tightening biofeedback (B) and relaxation biofeedback (C) in the same subject.

The manometric data was analyzed using Manoview ESO 3.0 (Given Imaging, Atlanta, GA). The median 10 seconds from the 30-second recordings of tightening biofeedback and relaxation biofeedback of the UES and 10 seconds of resting pressure prior to these recordings (baseline) were demarcated by investigators. Minimum (mmHg), mean (mmHg), and maximum (mmHg) pressures within this region were calculated automatically by the software. Manometric data was analyzed by two blinded investigators. A random sample of 30% of trials was analyzed by both investigators for the purpose of examining inter-rater reliability.

Statistical Analysis

All data was recorded and coded into SPSS 19.0 for Macintosh (SPSS Inc., Chicago, IL). Interrater reliability

was calculated for each rater using intra-class correlation coefficients (ICC). Baseline minimum (mmHg), mean (mmHg), and maximum (mmHg) UES pressures were compared to UES pressures during tightening and relaxation biofeedback by paired sample T-tests.

RESULTS

Twelve subjects enrolled in the study. The HRM procedure was well-tolerated in all but one patient who chose to terminate the study prior to completion. Data from one additional subject was not used in the analysis due to extremely low baseline UES pressures which precluded measurement. Data from 10 subjects were included in the analysis.

The mean age (\pm SD) of the cohort ($N = 10$) was 68 (± 13.3) years. Sixty percent (6/10) were female (see individual study patient demographic and clinical details in Table I). A statistical summary of baseline and biofeedback pressures is detailed in Table II. The mean UES pre-tightening baseline pressure was 30.1 (± 15.3) mmHg. This increased to a mean pressure of 44.8 (± 25.03) mmHg ($P < .05$) with biofeedback-driven UES tightening ($P = .02$). Maximum UES pressures were also increased from 63.84 (± 24.1) mmHg to 152.4 (± 123.7) mmHg ($P = .04$). Minimum UES pressures were similar between baseline and during tightening biofeedback (5.4 [± 4.3] vs. 4.7 [± 5.2]) ($P = .4$). The average group minimum and mean pressures were lower during relaxation biofeedback compared to baseline, however, no statistically significant differences were observed for any of the relaxation measures (see Table II). Inter-rater reliability for manometric analysis was high (ICC = 0.94). Fifty percent (5/10) of patients were able to volitionally reduce UES basal pressure.

TABLE I.

Subject Demographics and Clinical Characteristics.

Gender	Age	Relevant Medical History
1	M	75 GERD, dysphagia
2	F	60 Ineffective esophageal motility, chronic cough, dysphagia, globus sensation
3	F	74 Barrett's metaplasia, GERD
4	M	65 COPD, nutcracker esophagus, GERD, dysphagia, globus sensation
5	F	44 GERD
6	F	87 Esophageal dysmotility, Hiatal Hernia, solid food dysphagia, globus sensation, odynophagia, GERD
7	F	59 Chronic cough, GERD, globus sensation
8	M	75 Barrett's esophagus, Chronic cough, GERD
9	F	65 Solid food dysphagia, globus sensation
10	M	83 Chronic cough, globus sensation

GERD = gastroesophageal reflux disease, COPD = chronic obstructive pulmonary disease.

TABLE II.
Statistical Summary of Baseline and Biofeedback Pressures.

	Baseline prior to tightening Biofeedback	Tightening biofeedback	Baseline prior to relaxation Biofeedback	Relaxation biofeedback
Minimum pressure (mmHg)	5.4 (\pm 4.3) <i>P</i> = .4	4.7 (\pm 5.2) <i>P</i> = .4	4.9 (\pm 3.9) <i>P</i> = 1	4.9 (\pm 2.9) <i>P</i> = 1
Mean pressure (mmHg)	30.1 (\pm 15.3) <i>P</i> = .02	44.8 (\pm 25.3) <i>P</i> = .02	34.4 (\pm 21.9) <i>P</i> = .3	28.7 (\pm 12.9) <i>P</i> = .3
Maximum pressure (mmHg)	63.8 (\pm 24.1) <i>P</i> = .04	152.4 (\pm 123.7) <i>P</i> = .04	79.4 (\pm 41.8) <i>P</i> = .4	63.8 (\pm 38.9) <i>P</i> = .4

Values are mean \pm SD.

DISCUSSION

Globus pharyngeus and other symptoms such as throat tightness and dysphagia frequently localize to the region of the cricopharyngeus muscle and UES. Some studies have reported manometrically confirmed UES dysfunction in individuals with such complaints. In a small study, Watson and Sullivan reported an abnormally elevated mean UES resting pressure (176 mmHg) in patients with globus pharyngeus and a normal average resting pressure in their asymptomatic counterparts (96 mmHg).⁹ Corso et al., in a review of over 700 esophageal manometric studies, found that complaints of globus were present in 28% of individual with abnormally elevated UES resting pressure and in only 3% of those with normal UES resting pressure.²¹ In a recent study, Kwaitek et al.¹¹ found respiration-related change in UES resting pressure in more than 60% of globus patients and less than 15% of controls and GERD patients without globus.¹¹ A number of studies, however, have not found differences between resting pressures in globus patients and controls and the precise relationship between elevated UES pressure and globus remains uncertain.^{22,23}

Globus is often categorized as a functional esophageal disorder because the symptom typifies an esophageal disease without a readily identifiable structural or metabolic abnormality.²² Other conditions in this group include functional heartburn, chest pain, and dysphagia. The etiology of such conditions remains poorly understood and therefore treatment is challenging and frequently relies on multimodal therapy including neuromodulators, psychotherapy, cognitive-behavioral strategies, and relaxation techniques.

The goal of biofeedback is to train individuals to self-regulate a physiologic process that is normally not considered to be under voluntary control.²⁴ During education and training, patients are presented with biologic information (biofeedback) that is normally not accessible. Using this feedback, patients make conscious, voluntary efforts to alter a physiologic process in a specific way.¹⁹ Such actions or behaviors are practiced and repeated until they may be performed to achieve similar results with less or no biofeedback. Several investigators have reported success in targeting functional gastrointestinal disorders including constipation, fecal incontinence, dyssynergic defecation, anorectal pain and irritable bowel syndrome with biofeedback

methods.²⁵ Biofeedback has also shown promise in the treatment of functional chest pain.²⁶

In the present study, we sought to teach individuals biofeedback techniques in order to volitionally control UES pressure. Our preliminary findings suggest that HRM-driven biofeedback is feasible and can volitionally alter UES pressures in patients with complaints of dysphagia, heartburn, and globus. At pressure extremes, we observed an elevation of UES pressures of over 590% above baseline with tightening biofeedback and a 62% decrease in pressures following relaxation biofeedback. This preliminary investigation included a small sample size and only one brief session of biofeedback training. Although several of our patients had complaints of globus sensation, our objectives with this pilot study did not include assessment of symptom improvement and were focused on evaluating the feasibility of UES modulation by use of HRM biofeedback. A large degree of variability was observed in the ability of patients to decrease pressure with relaxation biofeedback, suggesting that some individuals may require more training to acquire this skill.

CONCLUSION

Volitional control of UES pressure is possible with HRM-driven biofeedback. Patients vary in their ability to volitionally control UES pressure and some may require further training to improve the ability to lower UES pressure with HRM-driven biofeedback. These data may have significant implications for the future treatment of UES disorders and warrant further investigation.

BIBLIOGRAPHY

- Castell JA, Dalton CB, Castell DO. Pharyngeal and upper esophageal sphincter manometry in humans. *Am J Physiol* 1990;258:G173-178.
- Wilson JA, Pryde A, Cecilia A, Macintyre CC, Heading RC. Normal pharyngeoesophageal motility. A study of 50 healthy subjects. *Dig Dis Sci* 1989; 34:1590-1599.
- Kahrilas PJ, Dodds WJ, Dent J, Haerberle B, Hogan WJ, Arndorfer RC. Effect of sleep, spontaneous gastroesophageal reflux, and a meal on upper esophageal sphincter pressure in normal human volunteers. *Gastroenterology* 1987;92:466-471.
- Jacob P, Kahrilas PJ, Herzon G, McLaughlin B. Determinants of upper esophageal sphincter pressure in dogs. *Am J Physiol* 1990;259:G245-251.
- Cook IJ, Dent J, Shannon S, Collins SM. Measurement of upper esophageal sphincter pressure. Effect of acute emotional stress. *Gastroenterology* 1987;93:526-532.
- Cook IJ, 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.
- Wallin L, Boesby S, Madsen T. The effect of HCl infusion in the lower part of the oesophagus on the pharyngo-oesophageal sphincter pressure in normal subjects. *Scand J Gastroenterol* 1978;13:821-826.
- Freiman JM, El-Sharkawy TY, Diamant NE. Effect of bilateral vagosympathetic nerve blockade on response of the dog upper esophageal sphincter (UES) to intraesophageal distention and acid. *Gastroenterology* 1981;81: 78-84.
- Watson WC, Sullivan SN. Hypertonicity of the cricopharyngeal sphincter: a cause of globus sensation. *Lancet* 1974;2:1417-1419.
- Linsell JC, Owen WJ. The globus sensation. *Clin Otolaryngol Allied Sci* 1986;11:303-305.
- Kwaitek MA, Mirza F, Kahrilas PJ, Pandolfino JE. Hyperdynamic upper esophageal sphincter pressure: a manometric observation in patients reporting globus sensation. *Am J Gastroenterol* 2009;104:289-298.
- Batch AJ. Globus pharyngeus (Part I). *J Laryngol Otol* 1988;102:152-158.
- Moloy PJ, Charter R. The globus symptom. Incidence, therapeutic response, and age and sex relationships. *Arch Otolaryngol* 1982;108:740-744.
- Chen CL, Szczesniak MM, Cook IJ. Evidence for oesophageal visceral hypersensitivity and aberrant symptom referral in patients with globus. *Neurogastroenterol Motil* 2009;21:1142-e1196.

15. Deary IJ, Smart A, Wilson JA. Depression and 'hassles' in globus pharyngis. *Br J Psychiatry* 1992;161:115-117.
16. Hill J, Stuart RC, Fung HK, et al. Gastroesophageal reflux, motility disorders, and psychological profiles in the etiology of globus pharyngis. *Laryngoscope* 1997;107:1373-1377.
17. Kahrilas PJ, Logemann JA, Krugler C, Flanagan E. Volitional augmentation of upper esophageal sphincter opening during swallowing. *Am J Physiol* 1991;260:G450-456.
18. Doeltgen SH, Witte U, Gumbley F, Huckabee ML. Evaluation of manometric measures during tongue-hold swallows. *Am J Speech Lang Pathol* 2009;18:65-73.
19. McCullough GH, Kim Y. Effects of the Mendelsohn maneuver on extent of hyoid movement and UES opening post-stroke. *Dysphagia* 2013;28:511-519.
20. O'Rourke A, Humphries K. The use of high-resolution pharyngeal manometry as biofeedback in dysphagia therapy. *Ear Nose Throat J* 2017;96:56-58.
21. Corso MJ, Pursnani KG, Mohiuddin MA, et al. Globus sensation is associated with hypertensive upper esophageal sphincter but not with gastroesophageal reflux. *Dig Dis Sci* 1998;43:1513-1517.
22. Galmiche JP, Clouse RE, Balint A, et al. Functional esophageal disorders. *Gastroenterology* 2006;130:1459-1465.
23. Sun J, Xu B, Yuan YZ, Xu JY. Study on the function of pharynx upper esophageal sphincter in globus hystericus. *World J Gastroenterol* 2002;8:952-955.
24. Gartha IV. What is Biofeedback? *Can Fam Physician* 1976;22:105-106.
25. Chiarioni G, Whitehead WE. The role of biofeedback in the treatment of gastrointestinal disorders. *Nat Clin Pract Gastroenterol Hepatol* 2008;5:371-382.
26. Shapiro M, Shanani R, Taback H, Abramowich D, Scapa E, Broide E. Functional chest pain responds to biofeedback treatment but functional heartburn does not: what is the difference? *Eur J Gastroenterol Hepatol* 2012;24:708-714.