

Research Article

Esophageal Dysmotility and the Utility of Barium Swallow: An Opaque Diagnosis

Aronova A^{1*}, Finnerty BM^{1*}, Moore M¹, Afaneh C¹, Turkmany K¹, Ciecierrega T², Crawford C³, Fahey TJ¹ and Zarnegar R¹

¹Department of Surgery, New York Presbyterian Hospital, Weill Cornell Medical College, New York, USA

²Division of Pediatric Gastroenterology, Department of Pediatrics, New York Presbyterian Hospital, Weill Cornell Medical College, New York, USA

³Division of Gastroenterology and Hepatology, Department of Medicine, New York Presbyterian Hospital, Weill Cornell Medical College, New York, USA

*Corresponding author: Anna Aronova, Department of Surgery, New York Presbyterian Hospital, Weill Cornell Medical College, New York, USA

Brendan M. Finnerty, Department of Surgery, New York Presbyterian Hospital, Weill Cornell Medical College, New York, USA

Received: January 18, 2017; Accepted: February 09, 2017; Published: February 10, 2017

Abstract

Background: The gold standard for diagnosis of esophageal dysmotility is high-resolution manometry (HRM); however, barium swallow studies are still routinely incorporated in the diagnostic algorithm by clinicians. We aim to assess the sensitivity of barium swallow to diagnose esophageal dysmotility using HRM for comparison.

Methods: We retrospectively reviewed 100 consecutive patients evaluated for esophageal dysmotility by both barium swallow and HRM. Dysmotility on barium swallow was graded as mild, moderate or severe. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated, including an achalasia subset analysis.

Results: Compared to HRM, barium swallow had an overall sensitivity, specificity, NPV, and PPV of 88%, 35%, 80%, and 51%, respectively, for detecting esophageal dysmotility. In achalasia patients (N=17), it detected dysmotility with 100% sensitivity and 30% specificity. Excluding achalasia patients, barium swallow had 81% sensitivity and 35% specificity; in other words, 65% of patients with normal HRM were misdiagnosed with dysmotility on barium swallow. For patients who exhibited normal, mild, moderate, and severe dysmotility as diagnosed on barium swallow, the concordance rates compared with HRM were 80%, 22%, 27%, and 89%, respectively.

Conclusion: Compared to the gold standard using high-resolution manometry, barium swallow accurately rules out patients with achalasia and is reliable in evaluating patients with severe dysmotility. However, it is a poor testing modality for diagnosis of esophageal dysmotility in patients without achalasia, especially in mild or moderate disease. As such, careful consideration of the diagnosis of esophageal dysmotility should be taken when using this technique.

Keywords: Barium swallow; Manometry; Esophageal dysmotility; Achalasia

Introduction

Esophageal motility disorders are a compilation of conditions resulting from inappropriate function of the lower esophageal sphincter (LES) and associated dysfunction of the peristaltic activity of the esophagus. Motor disorders of the esophagus may have ineffective or lost peristaltic function as in achalasia, or high or uncoordinated esophageal muscle contractions as in diffuse esophageal spasm and nutcracker esophagus, which may lead to failure of propagation of food into the stomach [1]. Given the variety of physiologic disturbances that occur in esophageal motility disorders, patients present with varied clinical complaints. Most commonly, patients complain of dysphagia and heartburn, although retrosternal chest pain, weight loss, regurgitation, and respiratory symptoms from aspiration may also occur [2–4].

In the diagnostic algorithm for dysphagia, upper endoscopy, barium esophagram (barium swallow), pH monitoring, and esophageal function tests (such as manometry) are indicated. While each testing modality offers unique contributions for the diagnosis of esophageal disorders, high resolution manometry (HRM) is typically considered the gold standard for diagnosing esophageal dysmotility [5–8]. In 2008, an international consortium created the Chicago

Classification scheme for primary esophageal motility disorders based on manometry metrics [9]. After several iterations, the most recent 2012 criteria now include four major diagnostic groups: achalasia, esophagogastric junction outflow obstruction, motility disorders not observed in normal subjects (distal esophageal spasm, hyper contractile esophagus, and absent peristalsis), and statistically defined peristaltic abnormalities (weak peristalsis, frequent failed peristalsis, rapid contractions with normal latency and hypertensive peristalsis) [10]. Despite its superiority for the diagnosis of esophageal motility disease, some centers do not have access to HRM. Therefore, many practitioners rely on barium swallow studies to assess for the presence of esophageal dysmotility particularly for screening studies as they are inexpensive and widely available. Radiologist interpretation typically includes a description of esophageal anatomy as well as the presence and degree of any dysmotility.

Given the variable use of barium swallow studies and HRM in the diagnosis of esophageal dysmotility disorders, we aimed to assess the reliability of barium swallow studies compared to the gold standard high resolution manometry in diagnosing esophageal dysmotility. By discerning the accuracy of these diagnostic techniques, we sought to better identify which patients are accurately diagnosed with a motility

disorder based on barium swallow findings, and those who require further diagnostic work-up. Based on radiographic characterization, we aim to prove only severe dysmotility is of clinical significance.

Materials and Methods

After Institutional Review Board approval, we retrospectively reviewed 198 patients who presented with symptoms suggestive of esophageal dysmotility and subsequently underwent HRM or barium swallow at the New York Presbyterian Hospital - Weill Cornell Medical College from January 2011 to July 2013. Included were patients who had both studies available for review. Exclusion criteria were patients who had undergone esophageal organo-gastric surgical procedures (e.g. Nissen fundoplication, Heller myotomy, bariatric surgery, etc), or who did not have adequate data for analysis. Demographic information was collected including age, sex, presenting symptoms including the Eckardt score [11], and proton-pump inhibitor (PPI) usage. Esophageal motility data were collected from HRM reports, as were barium swallow interpretations from radiologist reports. Barium swallow studies were performed according to standard protocol, [12] and dysmotility was graded as mild, moderate or severe by attending radiologists at our institution. At our institution, a radiologist may consider one tertiary contraction over the course of an exam in the supine position as mild versus multiple contractions in the upright position leading to delayed emptying from “to and fro” motion as moderate. In contrast, severe dysmotility would be unopposed contractile stimulation and aperistalsis.

High resolution manometry (HRM) was also performed following standard protocol [13]. It was completed and analyzed by a single physician at our institution (RZ). Results were reported as abnormal when there was evidence of esophageal dysmotility based on the reader's interpretation of the study results consistent with the Chicago Classification criteria, including diagnoses of achalasia, isolated hypertensive LES, esophageal spasm, and dysmotility not-otherwise-specified. Specific parameters of the manometry reports that were analyzed in this study included lower esophageal sphincter (LES) length (cm), presence of hiatal hernia, basal LES pressure (mmHg), residual LES pressure (mmHg), swallow characterization (peristaltic vs. simultaneous vs. failed), double- and triple- peaked waves (% of total number of swallows), wave amplitude (mmHg) at 3, 7, and 11 cm above the LES, intrabolus pressure (mmHg), and distal contractile integral (mmHg-cm-s).

Statistical analyses were performed using STATA, release 13 (StataCorp, College Station, TX). For comparison of categorical variables, Fisher's exact and Chi square tests were used for ≤ 5 and >5 observations, respectively. Student's t-test or Mann-Whitney U test was used to analyze continuous parametric and nonparametric variables, respectively. For all analyses, a two-tailed p-value of <0.05 was considered significant; independent predictors with p-value of <0.1 on univariate analysis were included in multivariate analysis (logistic regression with odds ratios).

Results

One-hundred patients met inclusion (criteria consisting of 56 females and 44 males with a mean age of 52 ± 16 years). Symptomatically, most patients presented with dysphagia (59%), followed by heartburn (57%), weight loss (48%), regurgitation

Table 1: Patient Demographics Classified by High-Resolution Manometry Findings.

	Overall (N = 100)	Degree of Dysmotility			P - value
		Achalasia (N = 17)	Other Dysmotility (N = 26)	Normal (N = 57)	
Age (years)*	52 ± 16	54 ± 18	56 ± 16	49 ± 14	0.15
Sex (Male)	44	9 (53%)	11 (42%)	24 (42%)	0.72
Symptoms					
Weight Loss	48	9 (53%)	4 (15%)	35 (61%)	$<0.001^a$
Dysphagia	59	14 (82%)	18 (69%)	27 (47%)	0.02 ^b
Chest pain	26	9 (53%)	8 (31%)	9 (16%)	0.007 ^b
Regurgitation	43	15 (88%)	9 (35%)	19 (33%)	$<0.001^c$
Heartburn	57	0 (0%)	14 (54%)	43 (75%)	$<0.001^c$
Eckardt Score†	2 (0 – 10)	6 (2 – 10)	2 (0 – 7)	1 (0 – 5)	$<0.001^d$
PPI Usage	81	13 (76%)	20 (77%)	48 (84%)	0.6

*mean ± standard deviation,

†Median (range),

a: Statistical significance between Dysmotility versus Achalasia/Normal groups,

b: Statistical significance between Achalasia versus Normal groups,

c: Statistical significance between Achalasia versus Dysmotility/Normal groups,

d: Statistical significance between all groups.

Table 2: Barium Swallow's Ability to Detect Dysmotility in Patients with and without Achalasia.

	Over all Cohort	Achalasia Patients	Non-Achalasia Patients
Sensitivity	88%	100%	81%
Specificity	35%	30%	35%
Negative Predictive Value	80%	100%	80%
Positive Predictive Value	51%	23%	36%

(43%), and retrosternal chest pain (26%). The median Eckardt score for the entire cohort was 2 (range, 0-10). Eighty-one percent of the cohort was taking proton-pump inhibitors upon initial presentation. Using HRM as the gold-standard for diagnosis, 57% of the cohort had normal motility findings. Of the 43 patients with dysmotility on HRM, the final diagnoses were achalasia (40%), dysmotility not-otherwise-specified (42%), esophageal spasm (16%), and isolated hypertensive LES (2%) Table 1. Summarizes patient characteristics between those with achalasia, other dysmotility, and normal motility as diagnosed on HRM.

Seventy-five percent of the cohort had some degree of dysmotility identified on barium swallow (denoted as mild, moderate, or severe); however, as noted above, only 43% of the cohort was diagnosed with esophageal dysmotility on HRM. Therefore, barium swallow results were concordant with HRM in only 58% of patients. The overall sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) for detecting dysmotility were 88%, 35%, 80%, and 51%, respectively. On subgroup analysis, barium swallow accurately identified dysmotility in achalasia patients with 100% sensitivity and 30% specificity. When noted in the radiology report, barium swallows diagnosed achalasia with 92% sensitivity and 99% specificity. Excluding achalasia patients from the analysis, barium swallow was able to detect dysmotility with sensitivity, specificity, NPV, and PPV of 81%, 35%, 80%, and 36%, respectively. In other words, 65% of patients with normal HRM were misdiagnosed as

Table 3: Patient Demographics & Manometry Parameters Classified by Barium Swallow Grade of Dysmotility.

		Normal (N = 25)	Mild Dysmotility (N = 27)	Moderate Dysmotility (N=11)	Severe Dysmotility (N = 19)	P-value
Demographics						
Age (years)*		44±14	49±14	58±14	56±18	0.09
Sex (Male)		11 (44%)	14 (52%)	3 (27%)	11 (58%)	0.41
PPI Usage		20 (80%)	22 (81%)	11 (100%)	16 (84%)	0.52
Eckardt Score†		1 (0 – 7)	1 (0 – 5)	1 (0 – 2)	5 (0 – 10)	<0.001 ^a
Manometric Parameters						
LES Length (cm)		3.0 (1.6 – 4.0)	3.0 (1.9 – 5.0)	2.2 (1.6 – 4.0)	3.0 (2.0 – 4.0)	0.12
Hiatal Hernia		1(4%)	2 (7%)	1(9%)	1(5%)	0.93
Basal LES Pressure (mmHg) †		19 (2 – 50)	17 (4 – 89)	15 (-1 – 41)	22 (-1 – 67)	0.79
Residual LES Pressure (mmHg)		3 (-6 – 21)	4 (-9 – 22)	5 (0 – 29)	13 (-4 – 49)	0.01 ^a
Swallow Motility† (% of swallows)	Peristaltic	100 (27–100)	100 (9 – 100)	100 (0 – 100)	0 (0 – 100)	<0.001 ^a
	Simultaneous	0 (0 – 10)	0 (0 – 91)	0 (0 – 10)	10 (0 – 100)	0.01 ^a
	Failed	0 (0 – 73)	0 (0 – 20)	0 (0 – 100)	20 (0 – 100)	0.02 ^a
Double-peaked Waves (% of swallows)		0 (0 – 80)	0 (0 – 89)	0 (0 – 30)	0 (0 – 60)	0.68
Triple-peaked Waves (% of swallows)		0 (0 – 0)	0 (0 – 44)	0 (0 – 0)	0 (0 – 40)	0.94
Wave Amplitude (mmHg)	11cm above LES	53 (24 – 146)	53 (10 – 121)	37 (0 – 142)	21 (0 – 104)	0.002 ^a
	7cm above LES	66 (21 – 144)	90 (21 – 229)	63 (0 – 190)	17 (0 – 123)	<0.001 ^{a,b}
	3cm above LES	55 (22 – 211)	111 (31 – 378)	67 (0 – 124)	20 (0 – 225)	<0.001 ^{a,b,c}
Intrabulbus Pressure (mmHg)		15 (6 – 59)	12 (0 – 96)	13 (0 – 80)	12 (0 – 31)	0.62
Distal Contractile Integral (mmHg-cms)		1152 (183 – 6732)	1628 (134 – 14074)	911 (0 – 3544)	617 (0 – 3789)	0.08
Diagnosis of Achalasia		0 (0%)	0 (0%)	0 (0%)	14 (74%)	<0.001 ^a

* mean ± standard deviation

† Median (range)

a: Statistical significance between “Severe” versus all other groups

b: Statistical significance between Mild versus Normal.

c: Statistical significance between Mild versus Moderate.

Table 4: Patient Characteristics of False Positive Barium Swallow Results.

	True Positive (N = 38)	False Positive (N = 37)	P-value
Age (years)*	56 ± 17	52 ± 14	0.21
Sex (Male)	17 (45%)	16 (43%)	0.90
Symptoms			
Weight Loss	11 (29%)	15 (41%)	0.29
Dysphagia	30 (79%)	14 (38%)	<0.001
Chest pain	17 (45%)	5 (14%)	0.005
Regurgitation	22 (58%)	12 (32%)	0.03
Heartburn	11 (29%)	29 (78%)	<0.001
Eckardt Score†	3 (0 – 10)	1 (0 – 5)	<0.001
PPI Usage	29 (76%)	32 (86%)	0.38
Tertiary Contractions (on Barium Swallow)	19 (50%)	21 (57%)	0.56

* mean ± standard deviation

† Median (range)

having dysmotility on barium swallow. These testing parameters are summarized in Table 2.

In order to clarify the utility of the typical radiologist-grading scheme (mild, moderate, severe) for barium swallow, we further compared selected manometric parameters between patients with

varying grades of dysmotility as reported on barium swallow (Table 3). Age, sex, and prior PPI usage did not differ between patients with normal motility and any degree of dysmotility. The median Eckardt score was higher in patients noted to have severe dysmotility on barium swallow. On manometry, there were no differences in LES length, hiatal hernia rates, basal LES pressures, double-peaked waves, triple-peaked waves, intrabulbus pressures, or distal contractile integrals between normal patients and those with any degree of dysmotility. However, patients with severe dysmotility on barium swallow were found to have a lower percentage of peristaltic swallows, a higher percentage of simultaneous and failed swallows, lower wave amplitudes at any length above the LES, and a diagnosis of achalasia on manometry compared to those with mild or moderate dysmotility or normal motility on barium swallow. Importantly, most parameters were not able to distinguish between normal versus mild and moderate dysmotility as graded on barium swallow.

Lastly, we evaluated the concordance rates between barium swallow and HRM dependent on the degree of dysmotility as reported by barium swallow. For barium swallow, findings of normal, mild dysmotility, moderate dysmotility, and severe dysmotility, the concordance rates when compared to HRM were 80%, 22%, 27%, and 89%. False positive results accounted for 88% of the discordance. Furthermore, false positives on barium swallow were associated with

heart burn symptoms on univariate analysis, while true positives were associated with dysphagia, chest pain, and regurgitation symptoms (Table 4). On multivariate analysis (excluding Eckardt score as a repetitive confounder), heart burn remained predictive of false positivity (OR 4.4, 95%CI: 1.3–14.7) while dysphagia (OR 4.3, 95%CI: 1.2–14.9) and chest pain (OR 5.8, 95%CI: 1.4–23.6) remained predictive of true positivity.

Discussion

Patients with esophageal motility disorders can present with fairly nonspecific symptoms such as weight loss and heartburn, or more specific symptoms such as retrosternal chest pain, regurgitation, and dysphagia. Workup of such patients typically entails esophagogastrosocopy, barium swallow, pH monitoring and manometry. However, results of these tests are not always congruent, especially in cases of esophageal dysmotility, and potentially lead to misdiagnosis and inappropriate management. In this study, we aimed to determine the accuracy of barium swallow studies in the diagnosis of esophageal dysmotility compared to the gold-standard, HRM.

We found that patients presented with a variety of initial complaints, but the most common were dysphagia and heartburn. Notably, 81% of patients were already on PPI therapy at presentation. Patients who underwent barium swallows were more likely to have abnormal exams (75%) in comparison to abnormal findings on manometry (43%) with only 57% of patients having concordant barium swallow and manometry results. In fact, examining the testing characteristics of barium swallow across the whole cohort, we found a specificity and positive predictive value of 35% and 51% for dysmotility, respectively, implying it has limitations in defining dysmotility. Furthermore, its sensitivity and NPV were 88% and 80%, respectively, indicating that it can potentially rule out dysmotility. In achalasia patients, barium swallow has a 100% sensitivity and NPV for detecting dysmotility, but has poor specificity (30%) and PPV (23%). Thus, barium swallow appears to be effective for ruling out achalasia-related dysmotility; however it may not correctly diagnose dysmotility if not associated with achalasia. Previously reported data on the accuracy of barium swallow for esophageal dysmotility shows similar findings in the case of achalasia. El-Takil et al. found low sensitivity of barium swallows in diagnosing achalasia when compared to manometry and concluded this was due to radiologists' oversight as well as the absence of characteristic radiologic features in many cases [14]. Fuller et al. similarly found poor predictive value of video esophagram in patients with suspected esophageal motility disorders. They found an overall sensitivity of 55% with a PPV of 53%, though sensitivity was highest in patients with achalasia and scleroderma (94% and 100%, respectively) [15]. Furthermore, excluding achalasia patients from their study of esophageal motility disorder patients, Shakespear et al. also found a 54.6% sensitivity and 72.2% specificity with a PPV of only 27.7% of video esophagram in correctly diagnosing these patients compared to manometry.8 Our study results mirror the findings noted in these previous reports as we also found a satisfactory sensitivity of barium swallow in the detection of achalasia, but not for overall accuracy of diagnosing dysmotility.

Upon evaluating the ability of barium swallow's dysmotility grading scheme (mild, moderate, or severe) to predict manometry findings, we found that only severe dysmotility on barium swallow

translates to true dysmotility on manometry, as evidenced by the significantly higher percentage of failed and simultaneous swallows, higher residual LES pressures, and lower wave amplitudes above the LES in the severe dysmotility group. In comparison, there were no significant differences between most other manometric parameters for normal, mild or moderate results on barium studies. These findings are further confirmed by the low concordance rates for mild and moderate dysmotility on barium swallow.

We further found on multivariate analysis that false positivity on barium swallows was predicted by a high rate of heartburn as a presenting symptom. Considering the distinction between primary and secondary esophageal motility disorders, with the latter being due to a secondary cause such as GERD, it is possible that the poor predictive ability of barium studies to diagnose primary motility disorders is confounded by the presence of reflux and associated changes in the GI tract. Herbella et al. found that two-thirds of patients with primary motility disorders of diffuse esophageal spasm and nutcracker esophagus presented with GERD [16]. Furthermore, assessing the relationship between esophageal motility and GERD in 1006 consecutive patients with 24-hour pH-monitoring-proven GERD, Diener et al. found that 21% of patients had severely impaired esophageal motility [17].

Nonetheless, while we found chest pain and dysphagia predictive of true positivity on barium swallow, the ambiguity of presenting symptoms in differentiating between motility disorders and other underlying causes highlights the need for a reliable test to diagnose esophageal diseases accurately. Vikal et al. studied 11,945 patients from 5 clinical trials with endoscopically-confirmed erosive esophagitis and found that 37% of them presented with dysphagia [18]. Furthermore, the American College of Gastroenterology states that such symptoms warrant further investigation for an underlying motility disorder, stricture, ring or malignancy [19].

Our study has a few limitations. It is retrospective in nature, introducing biases inherent in collecting data not initially intended for research purposes. For example, 18% of the cohort's barium swallow studies had an undefined grade. Furthermore, while one experienced physician interpreted all manometry reports, we were unable to have a single blinded radiologist review all the barium swallow studies, as would have been preferred.

Conclusion

In conclusion, barium swallow is a reliable test when compared to high resolution manometry for diagnosing achalasia and severe esophageal motility disorders; however, for mild or moderate dysmotility this test has limited value. Patients diagnosed with dysmotility on barium swallow who present with either dysphagia or regurgitation are more likely to have a true dysmotility disorder, while those with symptoms of heartburn are less likely. Therefore, high resolution manometry is recommended to accurately diagnose esophageal motility disorders.

References

1. Patti MG, Herbella FA. Achalasia and Other Esophageal Motility Disorders. *J Gastrointest Surg.* 2011; 15: 703–707.
2. Adler DG, Romero Y. Primary esophageal motility disorders. *Mayo Clin Proc.* 2001; 76: 195–200.

3. Parkman H, Maurer A, Caroline D, et al. Optimal evaluation of patients with nonobstructive esophageal dysphagia. Manometry, scintigraphy, or videoesophagography? *Dig Dis Sci*. 1996; 14: 1355–1368.
4. Fisichella PM, Carter SR, Robles LY. Presentation, diagnosis, and treatment of oesophageal motility disorders. *Dig Liver Dis*. 2012; 44: 1–7.
5. Imam H, Shay S, Ali A, et al. Bolus transit patterns in healthy subjects : a study using simultaneous impedance monitoring, videoesophagram, and esophageal manometry. *Am J Physiol Gastrointest Liver Physiol*. 2005; 288: 1000–1006.
6. Pandolfino JE, Kahrilas PJ. American Gastroenterological Association medical position statement: Clinical use of esophageal manometry. *Gastroenterology*. 2005; 128: 207–208.
7. Cho YK, Choi M-G, Park JM, et al. Evaluation of esophageal function in patients with esophageal motor abnormalities using multichannel intraluminal impedance esophageal manometry. *World J Gastroenterol*. 2006; 12: 6349–6354.
8. Shakespear JS, Blom D, Huprich JE, et al. Correlation of radiographic and manometric findings in patients with ineffective esophageal motility. *Surg Endosc*. 2004; 18: 459–462.
9. Kahrilas PJ, Ghosh SK, Pandolfino JE. Esophageal Motility Disorders in Terms of Pressure Topography: The Chicago Classification. *J Clin Gastroenterol*. 2008; 42: 627–635.
10. Bredenoord AJ, Fox M, Kahrilas PJ, et al. Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography. *Neurogastroenterol Motil*. 2012; 24: 57–65.
11. Eckardt AJ, Eckardt VF. Treatment and surveillance strategies in achalasia: an update. *Nat Rev Gastroenterol Hepatol*. 2011; 8: 311–319.
12. De Oliveira JM, Doinoff C, Einstein D, et al. Timed Barium Swallow: A Simple Technique for Evaluating Esophageal Emptying in Patients with Achalasia. *Am J Roentgenol*. 1997; 169: 473–479.
13. Lim CH, Choi MG, Baeg MK, et al. Novel disposable transnasal. endoscopy for assessment of esophageal motor function. *J Clin Gastroenterol*. 2014; 48: 402–406.
14. El-Takli I, Paterson W, O'Brien P. Clinical diagnosis of achalasia : How reliable is the barium x-ray? *Can J Gastroenterol*. 2006; 20: 335–337.
15. Fuller L, Huprich J, Theisen J, et al. Abnormal esophageal body function: radiographic-manometric correlation. *Am Surg*. 1999; 65: 911–914.
16. Herbella F, Raz DJ, Nipomnick I, et al. Primary versus secondary esophageal motility disorders: diagnosis and implications for treatment. *J Laparoendosc Adv Surg Tech A*. 2009; 19: 195–198.
17. Diener U, Patti MG, Molena D, et al. Esophageal Dysmotility and Gastroesophageal Reflux Disease. *J Gastrointest Surg*. 2001; 5: 260–265.
18. Vakil NB, Traxler B, Levine D. Dysphagia in patients with erosive esophagitis: Prevalence, severity, and response to proton pump inhibitor treatment. *Clin Gastroenterol Hepatol*. 2004; 2: 665–668.
19. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol*. 2013; 108: 308–328.