Relationship between esophageal clinical symptoms and manometry findings in patients with esophageal motility disorders: a cross-sectional study

Hashem FakhreYaseri*1, Ali Mohammad FakhreYaseri2, Ali Baradaran Moghaddam3
Seyed Kamran Soltani Arabshhi4

Abstract

Background: Manometry is the gold-standard diagnostic test for motility disorders in the esophagus. The development of high-resolution manometry catheters and software displays of manometry recordings in color-coded pressure plots have changed the diagnostic assessment of esophageal disease. The diagnostic value of particular esophageal clinical symptoms among patients suspected of esophageal motor disorders (EMDs) is still unknown. The aim of this study was to explore the sensitivity, specificity, and predictive accuracy of presenting esophageal symptoms between abnormal and normal esophageal manometry findings.

Methods: We conducted a cross-sectional study of 623 patients aged 11-80 years. Data were collected from clinical examinations as well as patient questionnaires. The sensitivity, specificity, and accuracy were calculated after high-resolution manometry plots were reviewed according to the most recent Chicago Criteria.

Results: The clinical symptoms were not sensitive enough to discriminate between EMDs. Nevertheless, dysphagia, noncardiac chest pain, hoarseness, vomiting, and weight loss had high specificity and high accuracy to distinguish EMDs from normal findings. Regurgitation and heartburn did not have good accuracy for the diagnosis of EMDs.

Conclusion: Clinical symptoms are not reliable enough to discriminate between EMDs. Clinical symptoms can, however, discriminate between normal findings and EMDs, especially achalasia.

Keywords: Esophageal motility disorders, Gastroesophageal reflux, Achalasia.

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Introduction

The esophageal motor function is evaluated using a variety of techniques, including barium radiography, radionuclide transit studies, manometry with or without impedance testing, and more recently impedance planimetry (1). High-resolution esophageal pressure topography is a new technology based on a combination of high-resolution manometry and esophageal pressure topography (EPT) for the examination of esophageal motor dysfunctions (EMDs). EPT plots are color-coded pressure representations on a spatiotemporal field generated by sophisticated software-based algorithms for visualizing and analyzing manometric data, the most recent classification scheme of which is intended to diagnosis of primary EMDs (2). The first step of the Chicago Classification described abnormal

1. (Corresponding author) Assistant Professor, Internist, Gastroenterologist, Research Center for Gastroenterology and Liver Disease, Department of Internal Medicine and Gastroenterology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran. lfyaseri@yahoo.com
2. General physician, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. fyasserimihanmail.ir
3. MSc in Clinical Microbiology, Department of Microbiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran. ak.baradaran@gmail.com
4. Professor, Internist, Department of Internal Medicine, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran. soltarab34@gmail.com
Patients with dysphagia, hoarseness, vomiting, and weight loss (≥5 kg) were included. The exclusion criteria were comprised of history of malignant disease, previous foregut surgery, cardiovascular diseases, large hiatal hernia, esophagitis of grade C or D according to the Los Angeles Classification, eosinophilic esophagitis, and Barrett's esophagus on pathology. All the patients provided informed consent and accepted to complete a standard questionnaire form.

**Methods**

We conducted a cross-sectional study of
trodduodenoscopy was done for all the patients in the same center by expert endoscopists. The procedures were performed by a trained esophageal laboratory nurse in collaboration with an expert gastroenterologist. Before each procedure, transducers were calibrated to 0 and 100 mmHg using externally applied pressure. The studies were conducted with the patient in the supine position after at least a 6-hour fast, and medications that could affect the esophageal motor function (e.g. Metoclopramide, anticholinergics, and smooth muscle relaxants) were discontinued for 5–7 days prior to the study. The catheter used was a 23-channel silicone-customized water-perfused catheter, with an outside diameter of 3.8 mm (manufactured by Mui Scientific, Ontario, CA). The catheters had 1 distal channel for gastric recording, 5 channels 1 cm apart for the LES pressure, and 16 proximal channels each 2 cm apart. Microlumina was perfused with a pneumohydraulic perfusion system (MMS software) at a water perfusion rate of 0.15 ml/min. Pressure data were acquired and shown using software specially designed for high-resolution manometry (MMS v 8.23), which displays isobaric contour plots. After topical anesthetic was applied into the nostril, the high-resolution manometry assembly was passed trans-nasally and the sensors were positioned to record from the hypopharynx to the stomach. After the LES was detected via the stationary pull-through method, the catheter was fixed in place by taping it to the nose. Then, 10 swallows of 5 mL ambient-temperature water spaced more than 20s apart were recorded. The pressure topography metrics utilized in the Chicago Classification is depicted in Figures 1 and 2. The definition based on this classification is shown in Table 1.

The data were entered into SPSS v.18 after encoding for each subject. Age is reported with mean ± standard deviation. Hypercontractile esophagus and absent peristalsis were excluded in the statistical analysis due to rare findings in this study. The clinical symptoms and the results of the esophageal manometry findings (normal and abnormal) were compared, and the sensitivity [true positives/(true positive + false negative)], specificity [true negatives/(true negative +false positives)], and accuracy [(true positive +true negative)/(true positive +true negative +false positive + false negative)] of the clinical symptoms were calculated for a correct diagnosis of the manometry findings. The results are presented with a confidence interval (CI) of 95%. Comparison of statistical significance was made between the symptom categories and manometry findings using either the Chi-square test or the Fisher’s exact probability test. A P value less than 0.05 was considered statistically significant.

Table 1. Definitions of the contractile pattern based on the Chicago Classification

| Contractile Pattern | Code | Contractile Pattern Definition |
|---------------------|------|--------------------------------|
| Absent peristalsis  | AP   | 100% failed peristalsis with minimal (<3 cm) integrity of the 20 mmHg IBC* distal to the proximal pressure trough (P) |
| Frequent failed peristalsis | FFP | > 3 but <10 swallows with failed peristalsis |
| Panesophageal pressurization | PP | ≥20% of swallows with uniform pressurization of 30 mmHg IBC from the UES to the EGJ |
| Premature contraction | PC | ≥20% of swallows with DL <4.5 s |
| Jackhammer          | JH   | Swallow with DL >4.5 s and DCI >8000 mmHg s cm |
| Rapid contraction   | RC   | ≥20% of swallows with contractile front velocity (CFV) >9 cm s1 and DL >4.5 s |
| Hypertensive        | HT   | Mean DCI >5000 but no swallow with value >8000 mmHg.s cm |
| Weak peristalsis    | WP   | >20% swallows with large breaks in the 20 mmHg IBC (>5 cm in length) or >30% swallows with small breaks in the 20 mmHg IBC (2–5 cm in length) |
| Normal peristalsis  | NP   | ≥60% of swallows with an intact 20 mmHg IBC (or no break >2 cm) not meeting any other code |

*IBC, Isobaric contour
Results

This study was performed on 623 patients, who met our inclusion criteria. The mean±SD age of the patients was 40.2 ± 12.9 (10-80) years, and 60.5% (n=377) of the patients were female. The dominant presenting symptoms were heartburn (66.7%) and regurgitation (63.7%). Almost all the patients had one to three of the symptoms as part of their initial presentation. The mean IRP4 was 17.6±5.4 (range = -1 to 42) (Table 2). The prevalence rates of achalasia, normal peristalsis, and borderline motor function were 13.6% (85/623), 41.6% (212/510), and 40.8% (208/510), respectively (Fig. 3).

Tables 3 and 4 compare the sensitivity, specificity, and accuracy of the clinical symptoms with the manometry findings. The prevalence rates of dysphasia (range = 39.4%-97.6%), noncardiac chest pain (range = 51.5%-87.8%), and heartburn (range = 61%-82.9%) were high but sensitivity was low for all the symptoms (range = 6.6%-66.6%) in all the types of abnormal manometry findings.

All the symptoms were highly specific (range = 43.6%-99.3%) for the diagnosis of patients with EMDs. Dysphasia (range = 55.2%-75.1%), noncardiac chest pain (range = 66%-72%), hoarseness (range = 49.7%-82.1%), asthma (range = 53.8%-76.7%), and weight loss (range = 52.1%-89.7%) had good accuracy, whereas regurgitation (range = 35.6%-50.7%) and heartburn (range = 39.5%-56.4%) had low accur-
racy for the diagnosis of patients with EMDs.

**Discussion**

Normal peristalsis and borderline motor function (BMF) constituted the most prevalent pattern in this study (Fig. 3), while hypercontractile esophagus and absent peristalsis were rare patterns. The females accounted for the highest frequency of clinical presentations in all types of EMDs. With the exception of BMF, absent

![Algorithm of the study analysis based on the Chicago Classification](image)

**Table 2. Demographic information of patients with variant types of esophageal motility disorder in our center for two years**

| Findings | N(%) | Mean±SD Age (years) | Female (%) | p | Mean±SD IRP4 (mmHg) |
|----------|------|---------------------|------------|---|---------------------|
| IRP>15   | 510(81.9) | 39.1±13.1 16-80 | 71(63) | - | 29.6±6.7 17-42 |
| Achalasia| 4(12.5)  | 41.2±15.7 10-73 | 39(61) | 0.000 | 7.7±3.1 0-14 |
| NP       | 212(41.6) | 41.2±15.7 10-73 | 39(61) | 0.000 | 7.7±3.1 0-14 |
| DES      | 64(12.5)  | 41.2±15.7 10-73 | 39(61) | 0.000 | 7.7±3.1 0-14 |
| AP       | 20(3.9)   | 42.7±7.3 30-55 | 12(60) | 0.999 | 5.6±4 0-12 |
| HE       | 6(1.2)    | 33±7.3 30-55  | 2(33)  | 0.999 | 6.5±6 1-12 |
| BMF      | 208(40.8) | 46±16.4 23-68 | 117(56.2) | 0.204 | 4±3.2 0-13 |

IRP4, Integrated relaxation pressure 4; EGJOO, Esophagogastric junction outflow obstruction; NP, Normal peristalsis; DES, Distal esophageal spasm; AP, Absent peristalsis; HE, Hypercontractile esophagus; BMF, Borderline motor function
### Table 3. Relationship between the clinical symptoms and the esophageal manometric findings in the patients with IRP4 >15 mmg

| Symptoms   | NP       | N (%) | N (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) | Accuracy (95% CI) | Type 1 (N=21, 24.7%) | Type 2 (N=41, 48.2%) | Type 3 (N=23, 27.1%) | EGJOO (N=28) |
|------------|----------|-------|------------|----------------------|----------------------|-------------------|---------------------|---------------------|---------------------|------------------|
| Dysphagia  | 62       | 20    | 24.4       | 93.9                 | 73                   | 40                | 39.2                | 93.9                | 75.1                | 22               |
| NCCP       | 66       | 18    | 21.4       | 98                   | 70.4                 | 36                | 35.3                | 96.7                | 18                  | 21.4            |
| Regurgitation | 138    | 9     | 6.1       | 86                   | 35.6                 | 22                | 13.7                | 79.6                | 11.5                | 17               |
| Heartburn  | 131      | 11    | 7.7       | 89                   | 39.5                 | 34                | 20.6                | 92                  | 10.3                | 23               |
| Hoarseness* | 20       | 6     | 23.1       | 92.7                 | 85                   | 7                 | 25.9                | 84.9                | 78.6                | 0                |
| Asthma     | 14       | 4     | 22.2       | 92.1                 | 86.7                 | 3                 | 17.6                | 83.9                | 79.4                | 0                |
| Vomiting   | 72       | 9     | 11.2       | 91.1                 | 64                   | 29                | 28.7                | 92.1                | 66.8                | 17               |
| Weight loss | 14       | 11    | 44.4      | 95.2                 | 89.7                 | 26                | 69.2                | 88.5                | 6                   | 3                |

### Table 4. Relationship between the clinical symptoms and the esophageal manometric findings in the patients with IRP4 <15 mmg

| Symptoms   | NP       | N (%) | N (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) | Accuracy (95% CI) | NES (N=64) | AP (N=20) | HE (N=64) | BMF (N=208) |
|------------|----------|-------|------------|----------------------|----------------------|-------------------|------------|----------|-----------|-------------|
| Dysphagia  | 62       | 43    | 38.4       | 43.4                 | 69.9                 | 15.5              | (22.1-89.3) | (49.4-78.5) | (53.5-75.2) | (82.7-83.4) |
| NCCP       | 66       | 33    | 33.3       | 82.5                 | 40.8                 | 12                | (5.5-68.7) | (35.5-78.6) | (60.7-73.7) | (64.1-100)  |
| Regurgitation | 138    | 48    | 25.8       | 82.2                 | 42.8                 | 5.5               | (5.1-5.6)  | (31.3-77.3) | (31.3-77.3) | (66.8-71.5) |
| Heartburn  | 131      | 39    | 23.5       | 76.4                 | 41.6                 | 4.4               | 85.2                | 37.5                | 3                   | 0                |
| Hoarseness* | 20       | 5     | 20.0       | 76.5                 | 71.4                 | 0                 | 90.6                | 82.7                | 13                  | 17               |
| Asthma     | 14       | 4     | 22.2       | 73.7                 | 73.2                 | 0                 | 90.3                | 76.2                | 9                  | 0                |
| Vomiting   | 72       | 20    | 21.7       | 76.1                 | 57.9                 | 0                 | 87.5                | 60.3                | 9.5                 | 41               |
| Weight loss | 14       | 5     | 26.3       | 77                    | 75                   | 0                 | 91                  | 85.3                | 0                   | 0                |

NP, Normal peristalsis; EGJOO, Esophagogastric junction outflow obstruction; NCCP, Noncardiac chest pain; *Hoarseness, permanent throat clearing, post-nasal drip.

### Notes
- NP, Normal peristalsis; EGJOO, Esophagogastric junction outflow obstruction; NCCP, Noncardiac chest pain -- *Hoarseness, permanent throat clearing, post-nasal drip.

### Additional Notes
- Due to the low number of subjects, specific values may not be accurately represented in the tables.

### Further Analysis
- The tables highlight a correlation between specific symptoms and esophageal manometric findings, with particular emphasis on dysphagia and nutcracker syndrome.

### Conclusion
- The findings suggest that certain symptoms, such as heartburn and regurgitation, are significantly associated with specific esophageal manometric findings, which may be useful in diagnosing and managing esophageal disorders.
peristalsis, and hypercontractile esophagus, all types of manometric patterns were more prevalent in the male patients. Dysphagia and non-cardiac chest pain (NCCP) were more prevalent in the patients with EMDs. Regurgitation and heartburn known as the diagnostic symptoms of gastroesophageal reflux disease (GERD) Hoarseness and asthma are known as the complications of GERD (10). We found that regurgitation was not a sensitive symptom for EMDs diagnosis. Although vomiting was prevalent in achalasia (types 2 and 3) and weight loss was prevalent in type 2 achalasia (6); these two symptoms lacked enough sensitivity for the differentiation between motility disorders among our study population.

The manometry is the gold-standard investigation of motility disorders in the esophagus. The transport of bolus is “successful” when minimal bolus material is retained within the esophageal body (11). The relationship between esophageal motility and transit is complex because factors such as bolus shape, surface, and consistency cannot be measured with manometry (12).

The LES relaxation does not seem to be only a major factor in determining bolus stasis. This may be justified by the observation that stasis most often occurs in the proximal and mid portions of the esophagus and that the bolus often does not reach the distal esophagus due to failed or incomplete peristalsis (12). However, the IRP4 value is also influenced by distal esophageal contractility (3). It has been suggested that IRP4 is the optimal measure of abnormal esophagogastric junction relaxation (6,13).

Dysphagia is usually mild in patients with ineffective esophageal motility (now called weak peristalsis) and abnormal esophageal propagation velocity (14). Although our study showed that only dysphagia and NCCP were more prevalent and highly specific in EMDs, their accuracy could not discriminate between the various types of EMDs. Regurgitation can be a problematic symptom inasmuch as it may lead to aspiration (6). It has been suggested that regurgitation has a significant correlation with the LES relaxation pressure when compared to other individual symptoms (6). Heartburn is a symptom complex that has traditionally been accepted as an acid-mediated event and a reliable indicator of GERD. It may occur in other conditions such as stress or smoking (6). GERD is prevalent in asthma (10). In our study, regurgitation, heartburn, asthma, and weight loss lacked enough accuracy to distinguish EMDs.

Achalasia is to date the best described manometric abnormality with the most well-defined treatment options from all EMDs. In our study, the prevalence of achalasia was similar to chimed in with that previously reported in the literature (6). It has been posited that esophagogastric junction outflow obstruction (EGJOO) is due to the contraction of the crural diaphragm and might also represent an achalasia variant in some cases (4). In this study, the patients with EGJOO presented with dysphagia and chest pain (15). Distal esophageal spasm (DES) is an uncommon EMD. The distal latency seems to be a more reliable measure of premature contractions presenting with dysphagia and chest pain; however, if the reduced distal latency is associated with a high IRP, it is termed "spastic achalasia" (3). A review of 1070 consecutive interpretable EPT studies revealed that all 24 patients with reduced distal latency had a dominant symptom of dysphagia or chest pain and were diagnosed and managed as distal esophageal spasm or spastic achalasia (9). Rapid contraction is defined as an increased contractile front velocity (CFV) (>9cm.s). However, although the CFV is a regional variability in contractile velocity, the correlation of symptoms with this “spastic” pattern is unclear (5). The previous Chicago Classification defined hypercontractile disorders in terms of mean distal contractile integration (DCI), a DCI greater than 8000 mmgh.cm.s was called "hypercontractile (nicknamed "Jackhammer") esophagus". This pattern of EMDs is rare and reported only in between 3% and
4.1% of cases, and it is universally associated with dysphagia and/or chest pain (3,6,16).

In this study, the prevalence of hypercontractile esophagus was low and it presented with dysphagia and hoarseness. A wide range of motility disorders with a normal IRP do not have the criteria for major motility disorders and are referred to as BMF. In our study, BMF was more prevalent than the other types of EMDs.

In Iran, this is the first cross-sectional study on the relationship between the sensitivity, specificity, and accuracy of symptoms in patients with EMDs and normal esophageal manometry findings, based on the most recent Chicago Classification. Nonetheless, this study had some limitations, first and foremost among which is that the motility patterns may differ between liquid and solid boluses. It is worthy of note, however, that the technical limitations are the consequence of the patients’ condition (e.g. achalasia) or issues related to anatomy (e.g. hernia).

Conclusion

Our findings suggest that clinical esophageal symptoms may not be reliable enough for the differentiation of EMDs from one another. However, clinical symptoms can discriminate between abnormal and normal esophageal motility findings, especially achalasia. Furthermore, abnormal esophagogastric junction relaxation during swallowing is not an accurate diagnostic criterion for predicting clinical symptoms, which makes defining the peristalsis pattern mandatory. Other modalities such as barium esophagography and esophageal endoscopy are required to correct diagnosis and management. There is no doubt that findings of the present study should be further analyzed by future studies on larger sample volumes.

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