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Diagnostic approach to patients with suspected motility disorders: one size does not fit all

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Abstract

Background Dysphagia and retrosternal chest pain are considered typical manifestations of major esophageal motility disorders (mEMD). High-resolution manometry (HRM) is the gold standard for mEMD diagnosis, while endoscopy and barium swallow are ancillary tools. We aimed to investigate the frequency of mEMD among patients referred for HRM with typical compared to non-typical symptoms. We also evaluated endoscopic and barium swallow data from patients with mEMD who underwent HRM.

Methods We retrospectively collected epidemiological, endoscopic, barium swallow, and HRM data from 302 patients. Atypical symptoms were considered to be heartburn, regurgitation, globus, oropharyngeal dysphagia, and epigastric pain.

Results The main referral symptoms were: esophageal dysphagia, 58.3%; chest pain, 13.7%; heartburn, 8.9%; regurgitation, 8.3%; and globus/oropharyngeal dysphagia/epigastric pain, 10.8%. A diagnosis of mEMD was more common when typical symptoms existed (69.9% vs. 15.4%, P<0.001). The majority of patients with mEMD in HRM, independently of their symptoms, had an abnormal barium study (typical: 94.8% vs. non-typical: 100%, P=0.633), while compatible endoscopic data tended to be observed more frequently among patients with typical symptoms (69.1% vs. 40%, P=0.057). An HRM diagnosis of mEMD among patients with compatible findings from either barium swallow or endoscopic examination was statistically more frequent among patients with typical symptoms (92.4% vs. 52.6%, P<0.001).

Conclusions More than half of patients referred for HRM will be diagnosed with mEMD, at a higher rate when typical symptoms are reported. A lack of compatible endoscopic and barium swallow findings, in the absence of typical symptoms, makes the diagnosis of mEMD almost impossible.

Keywords Major esophageal motility disorders, typical symptoms, high-resolution manometry, upper gastrointestinal endoscopy, time-barium esophagogram

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Introduction

According to the Chicago IV classification, major esophageal motility disorders (mEMD) include achalasia, distal esophageal spasm (DES), hypercontractile esophagus (HE), esophago-gastric junction outflow obstruction (EGJOO), and absent contractility. High-resolution manometry (HRM) is the gold standard for the diagnosis of mEMD [1], while esophageal dysphagia and retrosternal chest pain are considered the typical symptoms. However, in real clinical practice patients are referred for HRM because of several non-typical esophageal symptoms, such as globus, symptoms of gastroesophageal reflux disease (GERD), such as heartburn and regurgitation, oropharyngeal dysphagia or even epigastric pain, and the rate of EMD among those patients is largely unknown.

Approximately 20% of the general population will report symptoms of dysphagia at some point, especially women and

the elderly [2]. At the same time the prevalence of non-cardiac chest pain is 14-33%, with the most common causative factor being GERD in 30-60%, followed by mEMD in 15-30% [3]. Interestingly, even though chest pain is commonly attributed by clinicians to esophageal spasm, only 1-2% of patients will be finally diagnosed with an EMD [4].

Achalasia is the most common EMD [5]. Recent data from the USA revealed a rise in prevalence, especially among patients older than 65 years (162.1/100.000) [6]. Concerning DES, the rate of its diagnosis among symptomatic patients who undergo HRM is 2-9%, while the HE diagnosis rate is 1.5-3% [7,8]. Finally, EGJOO is diagnosed in 5-24% of patients who undergo HRM, though it is not always clinically meaningful, since different entities such as eosinophilic esophagitis or opioid use can present with similar findings in HRM [9]. As far as DES, HE and EGJOO are concerned, epidemiological data, especially since the new Chicago IV classification introduced stricter diagnostic criteria for these disorders, are lacking. For all 3 abovementioned entities compatible symptoms are needed, i.e., dysphagia and/or chest pain, whereas in order for EGJOO to be diagnosed positive complementary manometry maneuvers and additional testing with barium swallow and/or planimetry are needed [10-12].

Most importantly, most of the epidemiological studies in the field include only patients with typical esophageal symptoms (dysphagia and/or chest pain), even though, according to guidelines, HRM is needed for the diagnosis of different entities such as globus, or among patients with symptoms of GERD who do not respond to treatment [13,14]. However, data about the epidemiology of mEMD among patients with non-typical symptoms are lacking.

As previously stated, HRM is the gold standard for mEMD diagnosis, although the initial diagnostic approach in a patient with either typical or atypical symptoms includes upper gastrointestinal endoscopy. According to studies, the existence of compatible endoscopic findings among patients finally diagnosed with mEMD varies [15,16]. Additionally, a valuable weapon in the armory of diagnostic modalities used in patients with EMD is the barium swallow esophagogram [17]. Especially since the introduction of timed-barium swallow (TBE), its diagnostic accuracy has increased, particularly in the setting of achalasia. Since TBE is easier to perform than HRM, and not as expensive, its use will not be abandoned any time soon. Once again, there are insufficient data about the findings from endoscopic and barium studies among patients with non-typical esophageal symptoms who are referred for HRM.

The aim of our study was to evaluate the frequency of mEMD among patients with typical vs. non-typical symptoms referred for HRM in the era of the Chicago IV classification. A secondary aim of our study was to identify possible differences among findings in endoscopy and TBE between patients with typical or atypical symptoms who were referred for HRM.

Patients and methods

We retrospectively collected epidemiological, endoscopic (available in 263/302), time barium swallow (available in 176/302) and manometric data from consecutive patients referred for HRM in our center from January 2020 to December 2023. Typical symptoms of mEMD were considered to be dysphagia and chest pain. Atypical symptoms for which patients were referred for HRM included heartburn, regurgitation, globus, oropharyngeal dysphagia and epigastric pain. Patients with a previous diagnosis of mEMD, scleroderma or eosinophilic esophagitis, as well as those who were referred for presurgical evaluation for GERD, or had previously undergone gastroesophageal surgery, were excluded.

HRM protocol

After an overnight fast, patients underwent HRM (Medtronic, Minneapolis MN, USA). Studies were performed in the primary position (supine). Ten wet swallows were evaluated, and if necessary another 5 in the secondary position (upright) were added to the protocol. Except in the case of a positive study for achalasia diagnosis or a completely normal study, rapid drink challenge and multiple rapid swallow test were also executed. Only technically adequate studies were included in the analysis. Manometric findings were evaluated according to the Chicago IV classification

Endoscopy and barium swallow study

Endoscopic data suggestive of an mEMD included esophageal dilation/tortuous esophagus, solids/liquids/saliva in the lumen, and difficulty passing the scope through the lower esophageal sphincter (LES) [15,16]. Delay in barium transit from the esophagus to the stomach (>5 cm at min 1 and > 2 cm at min 5), esophageal dilation/tortuous esophagus, and a bird-like LES appearance were considered as barium swallow findings suggestive of mEMD [17].

Statistical analysis

Statistical analysis was performed using SPSS V23 (SPSS software; SPSS Inc, Chicago, IL, USA). Data were expressed as frequencies, mean ± standard deviation, or median (interquartile range), as appropriate. Quantitative variables were compared between groups using Student's *t*-test or the Mann-Whitney test for normally distributed and non-normally distributed variables, respectively. Qualitative variables were compared using the chi-squared test or Fisher's exact test, as appropriate. The associations between quantitative variables were assessed using Spearman's correlation coefficient. K statistics were used in order to detect the level of agreement between endoscopy data, barium swallow data and their combination with an HRM diagnosis of mEMD. All tests were 2-sided and P-values <0.05 were considered to be significant.

Since this study was a *post hoc* analysis of de-identified previously collected data from esophageal studies, with no

direct link to individual patients, formal ethics approval was not deemed necessary.

Results

We evaluated 302 patients (M/F: 147/155, mean age: 56±17 years). Typical symptoms of some degree were reported by 234 (77.2%) patients, while only atypical symptoms were present in 68 (22.8%). The most common referral symptom was esophageal dysphagia (58.3%; Fig. 1). There was no age or sex predisposition among patients referred for HRM with typical compared to atypical symptoms (56±17 vs. 56±18 years P=0.948 and M: 48.3% vs. 50.0%, P=0.804, respectively). The median time from symptom initiation to HRM submission was 24 months (min: 1 to max: 160 months), and was longer for patients reporting typical symptoms (37±38 months vs. 25±20 months, P=0.027).

A diagnosis of mEMD in HRM was established in 175/302 (57.9%), and was more common when typical symptoms were present (163/234, 69.9% vs. 12/68, 17.6%, P<0.001). The mean age of patients diagnosed with mEMD was 56±18 years, and 94 (53.7%) were male. There was no age- or sex-related difference between patients with typical symptoms diagnosed with mEMD and those with atypical symptoms (56±18 vs. 58±22 years, P=0.735, and M: 53.4% vs. 58.3%, P=0.740, respectively).

Among patients with typical symptoms, achalasia was the most common mEMD diagnosis, while DES and HE were rather uncommon, a finding also observed in patients with non-typical symptoms. The distribution of HRM diagnoses among patients with typical and non-typical symptoms are given in Fig. 2. The rate of achalasia diagnosis among patients with a conclusive mEMD diagnosis was higher, although

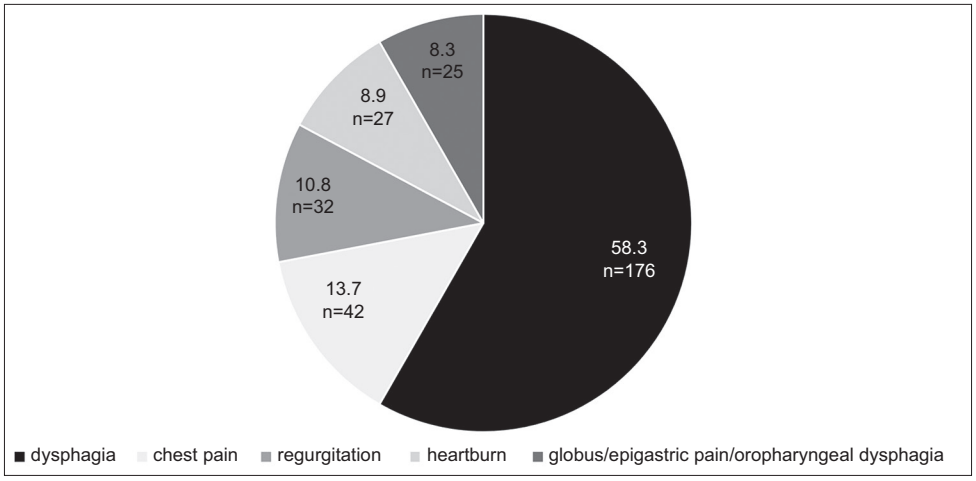

Figure 1 Referral symptoms

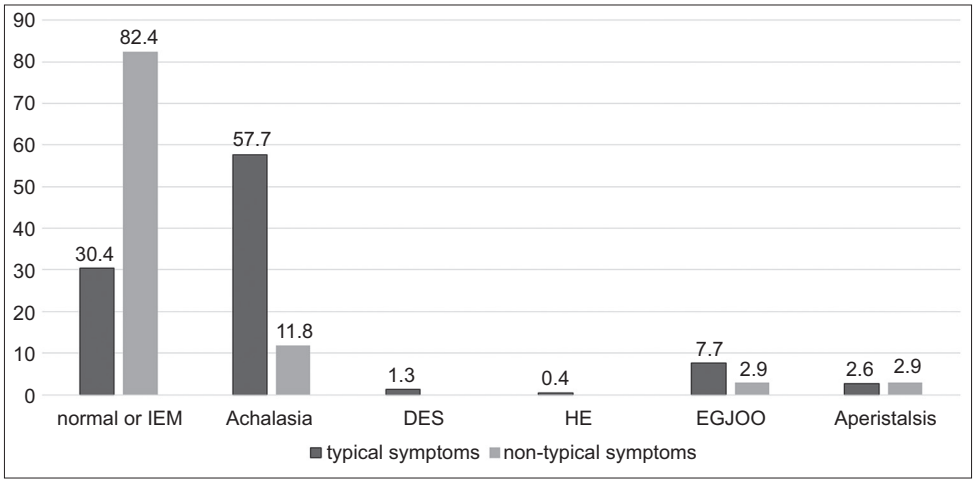

Figure 2 High-resolution manometry (HRM) diagnosis among patients with typical or atypical symptoms
IEM, ineffective esophageal motility; DES, diffuse esophageal spasm; HE, hypercontractile esophagus; EGJOO, esophago-gastric junction outflow obstruction

not statistically significantly so, among patients with typical symptoms compared to patients with a conclusive mEMD diagnosis and non-typical symptoms (135/163 (82.8%) vs. 8/12 (66.6%), P=0.162). Among all the patients with an achalasia diagnosis, type II achalasia was the most common diagnosis (134/143, 93.7%) in both patients with typical and those with non-typical symptoms (127/135, 94.8% vs. 7/8 87.5%, P=0.457)

Endoscopy data

In our total cohort, endoscopic data compatible with mEMD were observed in 113/263 (43%), and were more common among patients with typical symptoms (108/207, 52.2% vs. 5/56, 8.9%, P<0.001). Specific endoscopic data for the whole study group, as well as patients with a diagnosis of mEMD, are given in Table 1.

Among patients finally diagnosed with mEMD by HRM, endoscopic data compatible with mEMD were found more frequently in patients with typical symptoms (103/149, 69.1% vs. 4/10, 40%, P=0.057). Among patients with achalasia, 75.8% had compatible endoscopy findings. The rate of specific endoscopic findings among patients with achalasia is given in Fig. 3. Among patients with mEMD apart from achalasia, suggestive endoscopic findings were observed in 7/30 (23.3%)

The level of agreement between endoscopic data compatible with mEMD and a positive HRM diagnosis was significant, but not high (Table 2).

Barium swallow data

Barium swallow data compatible with mEMD were observed in 136/176 (77.3%), and were more common in patients with typical symptoms (119/146, 81.5% vs. 17/30, 56.6%, P=0.003). Specific barium swallow data for the total study group and for patients with a diagnosis of mEMD are given in Table 1.

Among patients with an HRM diagnosis positive for mEMD, no difference was found in the rate of barium swallow data compatible with mEMD between patients with typical and those with atypical symptoms (110/116, 94.8% vs. 9/9, 100%, P=0.633 respectively). Among patients with achalasia, almost every patient (97.3%) presented barium swallow findings compatible with achalasia. The rate of specific barium swallow study findings among patients diagnosed with achalasia by HRM is given in Fig. 3. Among patients with mEMD apart from achalasia diagnosed by HRM, suggestive barium swallow esophagogram findings were observed in 16/19 (84.2%)

The level of agreement between a barium swallow study compatible with mEMD and a positive HRM diagnosis was significant, and higher than that of endoscopy, but still suboptimal (Table 2).

Table 1 Specific barium swallow and endoscopy data among the total study group and in patients with mEMD

Data	Total cohort	All patients with a mEMD diagnosis
Endoscopy data compatible with mEMD	113/263 (43%)	107/159 (67.3%)
Esophageal dilation/ tortuous esophagus	37/263 (14.1%)	36/159 (22.6%)
Solids/liquids/saliva in the lumen	86/263 (32.7%)	82/159 (51.6%)
Difficulty passing the scope through the LES	44/263 (16.7%)	42/159 (26.4%)
Barium swallow findings compatible with mEMD	136/176 (77.3%)	119/125 (95.2%)
Delay in barium transit from esophagus to the stomach	105/176 (59.7%)	92/125 (73.6%)
Esophageal dilation/ tortuous esophagus	86/176 (48.9%)	84/125 (67.2%)
Bird-like appearance of LES	65/176 (36.9%)	63/125 (50.4%)

Endoscopy data were available in 263/302 and 159/175 respectively and barium swallow data in 176/302 and 125/175 respectively

mEMD, major esophageal motility disorders; LES, lower esophageal sphincter

Combination of endoscopic and/or barium swallow data and their agreement with HRM diagnosis

HRM diagnosis of mEMD among patients with compatible findings from either barium swallow or endoscopy was found more frequently among patients with typical symptoms (134/145, 92.4% vs. 10/19, 52.6%, P<0.001). Most importantly, among 43 patients with non-typical symptoms and normal endoscopy and barium swallow study, only 1 (2.3%) had an mEMD diagnosis by HRM (EGJOO findings in a patient with GERD symptoms; an EGJOO diagnosis could not be established because of non-typical symptoms and a negative barium study). The level of agreement between endoscopy data, barium swallow data and their combination with HRM diagnosis of a mEMD for the total cohort, as well as among patients with typical and atypical symptoms, are given in Table 2. The same table also shows the sensitivity, specificity, and positive and negative predictive values of endoscopy and barium swallow, and their combination, for the diagnosis of an mEMD by HRM.

Discussion

Our study was the first to compare the diagnosis of mEMD between patients with typical and non-typical esophageal symptoms. We showed that achalasia is the most common mEMD diagnosis among patients with typical symptoms of motility disorders, such as dysphagia and retrosternal pain. As expected, the rate of mEMD diagnosis was significantly lower among patients with non-typical symptoms, and the vast majority of such patients had a normal HRM study, though when it was abnormal, once again achalasia was the most common diagnosis, in two thirds of patients. Additionally, although low, the rate of mEMD diagnosis (15.4%) among patients with non-typical symptoms found in our study was

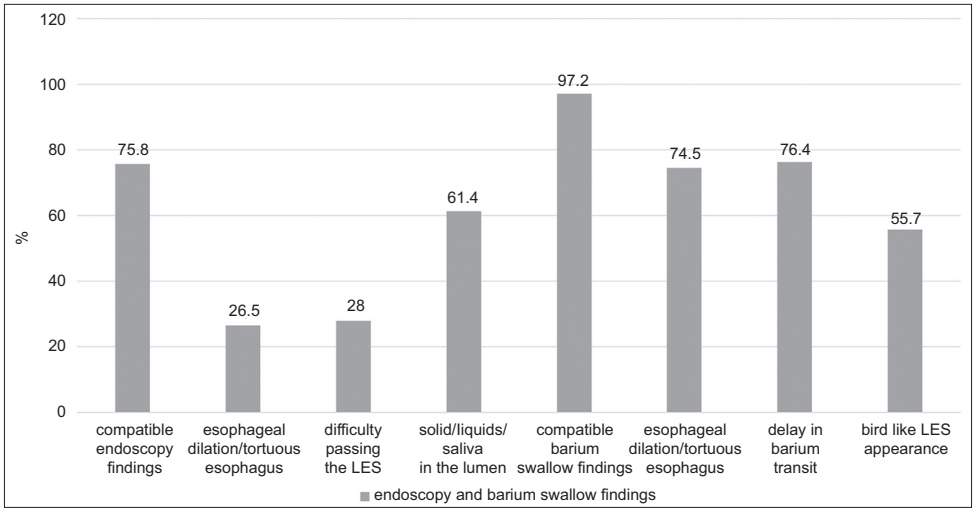

Figure 3 Endoscopic and barium swallow findings patients with a diagnosis of achalasia
LES, lower esophageal sphincter

not negligible, and HRM should be offered to such patients in the correct setting.

Our study showed that, among patients with typical symptoms (i.e., dysphagia and retrosternal chest pain), achalasia is the most common HRM diagnosis, and more specifically, achalasia type II. This finding is in agreement with previously published data from studies including patients with typical esophageal symptoms [18,19]. However, the rate of specific types of achalasia found in our cohort differ when compared to older studies [19,20]. We believe that the difference between our rate of 95% and the 70% reported in other studies is not so high, since the number of HRM studies in each publication shows a high variation [19].

The rate of DES and HE diagnoses in our cohort was extremely low, even lower than previously reported [7,8]. The rate of DES diagnosis was calculated to be below 1%, one that is in agreement with a previous study by Almansa *et al*, who reported a rate close to 0.5%—although in this study patients with non-typical symptoms were also included [21]. The low rate of HE observed in our cohort is in agreement with a recent report by Hani *et al*, who also reported an HE diagnosis rate of 0.4% [22]. Keeping in mind these low rates of DES and HE diagnosis, confirmed in our study, clinicians should exclude other entities before attributing symptoms of non-cardiac pain to such disorders. Regarding the EGJOO diagnosis in particular, its diagnosis rate in our cohort amounted to 11.4% among patients with typical symptoms. The prevalence of EGJOO in our cohort was lower than the one previously reported [9]. This could be attributed to the fact that Chicago IV classification has made the EGJOO diagnosis criteria stricter, requiring agreement of findings in both supine and upright positions, as well as verification of the findings by complementary manometric testing, such as a rapid drink challenge [12].

Once again, our study proved the great value of a TBE in the diagnosis of mEMD, and especially achalasia. Almost all patients diagnosed with achalasia in our study had findings compatible with a motility disorder in TBE, even when presenting with non-typical symptoms. Our results are in agreement with previous studies showing that TBE studies can diagnose achalasia with great accuracy [17,23]. In a recent study by Hoshino *et al*, only 2.4% of patients with achalasia had normal esophageal clearance by TBE and no esophageal dilatation [23]. However, as pointed out in our analysis, among patients diagnosed finally by HRM with mEMD other than achalasia, TBE's diagnostic efficacy, even among patients with typical symptoms, is suboptimal because of its comparatively low specificity. Our findings come in accordance with a previous study aiming to compare the barium esophagram with HRM results in order to determine whether the esophagram is an adequate screening examination for esophageal motility disorders among patients either typical or atypical symptoms. The study reported that the sensitivity of esophagram for detecting esophageal dysmotility was 0.69, and the specificity was 0.50 [24]. Additionally, Blonski *et al*, though reporting a great sensitivity of TBE in the diagnosis of achalasia in their study, also pointed out that the combined liquid barium and tablet barium esophagogram diagnostic yield was only 60% in EGJOO patients [23]. Our fair k statistic agreement between TBE and HRM in general, and not solely in patients with achalasia, is in agreement with those previous reports. In our study we chose to use k statistics in order to evaluate the level of agreement between TBE findings (as well as endoscopic findings) and HRM. We elected not to perform ROC curve analysis, as both TBE and endoscopic findings, in our study, were expressed as dichotomous discrete variables, and ROC curve analysis in such instances, even if mathematically feasible, is statistically problematic [25,26]. In conclusion, TBE is an excellent adjuvant modality, but its use is limited by the high number of false positive results, especially in patients who do not have achalasia.

On the other hand, we once more showed that up to 75% of patients with achalasia presented with endoscopic

Table 2 Agreement, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of barium study, endoscopy, and their combination, with an mEMD diagnosis by HRM among the total cohort (To) and patients with typical (T) or atypical (A) symptoms

Parameters	P-value			k-statistics			Sensitivity (%)			Specificity (%)			PPV (%)			NPV (%)		
	To	T	A	To	T	A	To	T	A	To	T	A	To	T	A	To	T	A
Barium swallow compatible with EMD	<0.001	<0.001	0.002	0.661	0.673	0.494	95.2	94.8	100	66.7	70	61.9	87.5	92.4	52.9	85	77.8	100
Endoscopy compatible with EMD	<0.001	<0.001	<0.01	0.572	0.494	0.472	67.3	95.2	40	94.2	53.1	97.9	94.7	95.4	80	65.3	53.1	88.5
Barium or endoscopy compatible with EMD	<0.001	<0.001	<0.001	0.698	0.666	0.570	87.8	87.6	90.9	82	81.7	82.4	87.7	92.4	52.6	82	72.1	82.4
Barium and endoscopy compatible with EMD	<0.001	<0.001	0.007	0.491	0.418	0.449	68.3	70.5	37.5	93.2	88.9	100	96.3	95.5	100	51.9	42.1	77.3

mEMD, major esophageal motility disorders; HRM, high-resolution manometry

findings compatible with mEMD when undergoing upper gastrointestinal endoscopy, a rate which dropped to 25% among patients diagnosed with mEMD other than achalasia. In relatively old studies focusing on achalasia, the reported rates of suggestive endoscopic findings ranged from 38-96% [27,28]. In a recent study by Matsubara *et al*, which included only patients with dysphagia, the authors reported that 64.4% of patients with a motility disorder showed compatible endoscopic findings, a rate which does not differ from ours (67.3%) [15]. As also observed in our study, the rates reported by Matsubara were significantly higher among patients with achalasia (91.3%), and were lower among patients with other types of mEMD (14.3% for EGJOO, 66.7% for DES and 60% for HE) [15]. Nevertheless, it should be stated that, whereas even among patients who are ultimately diagnosed with mEMD other than achalasia 80% have an abnormal TBE, compatible endoscopic findings are observed in a minority of patients with either typical or non-typical symptoms and mEMD other than achalasia. Such a difference may be attributed to the fact, that with the exception of achalasia, no specific, objective, well-validated endoscopic criteria exist for the diagnosis of motility disorders, as by definition no visible epithelial abnormalities can be seen by endoscopists during the natural history of motility disorders until the very end. Finally, our fair k statistic agreement between endoscopy and HRM over our whole cohort highlights the low diagnostic yield of endoscopy when addressing mEMD in general, and comes in agreement with the above previous reports.

Our study also found a difference between patients with typical and non-typical findings in the time from symptom initiation to mEMD diagnosis. This may be explained by the fact that patients with symptoms that are non-typical for motility disorders may be to a large extent finally diagnosed with disorders of the gut–brain interaction [13]. Such patients show increased levels of anxiety, which may lead them to put pressure on clinicians for a quicker diagnosis [29].

Finally, one of the most important findings of our study was that no patient who had non-typical symptoms, and showed no compatible TBE and endoscopic findings, was finally diagnosed with mEMD. Consequently, since practically all patients with non-typical upper gastrointestinal symptoms will have undergone upper gastrointestinal endoscopy before being referred for HRM, before referring a patient with no endoscopic evidence of a motility disorder for HRM, it is more rational to order a timed barium swallow esophagogram, a procedure less expensive and more comfortable for the patient. As highlighted by the moderate to fair k-statistics found in our analysis, the combination of endoscopy and TBE is not correlated with a positive mEMD HRM diagnosis; however, if both are negative, HRM will not add anything to the diagnostic approach in patients with non-typical upper gastrointestinal symptoms.

The main limitation of our study was the fact that it was a retrospective one. Moreover, our study was a single-center practice study and further validation of our results from multicenter studies is required.

In conclusion, more than half of the patients referred for HRM will be diagnosed with mEMD, and the rate will

be higher when typical symptoms are reported. In these patients, achalasia, and more specifically achalasia type II, is the commonest diagnosis. In patients with typical symptoms, the esophagogram alone can provide extremely important diagnostic information, while endoscopy has little to offer besides excluding other non-motility entities that might be blamed for the patient's symptoms. In the absence of typical symptoms, a lack of compatible endoscopic and TBE findings almost completely rules out a diagnosis of mEMD.

Summary Box

What is already known:

- Dysphagia and retrosternal chest pain are considered typical manifestations of major esophageal motility disorders, although in many patients with non-typical symptoms motility disorders are suspected as the origin of their symptoms
- High-resolution manometry (HRM) is the gold standard for the diagnosis of motility disorders
- There are insufficient data regarding the findings of endoscopy and barium studies in patients with non-typical esophageal symptoms referred for HRM

What the new findings are:

- In the absence of typical symptoms, a lack of compatible endoscopic and timed-barium swallow findings almost completely rules out a diagnosis of major esophageal motility disorders (mEMD)
- More than half of the patients referred for HRM will be diagnosed with mEMD, and the rate will be higher when typical symptoms are reported
- Achalasia, and especially type II achalasia, is the most commonly diagnosed major motility disorder, even among patients with non-typical esophageal symptoms

References

1. Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. *Neurogastroenterol Motil* 2021;**33**:e14058.
2. Wilkins T, Gillies RA, Thomas AM, Wagner PJ. The prevalence of dysphagia in primary care patients: a HamesNet Research Network study. *J Am Board Fam Med* 2007;**20**:144-150.
3. Fass R, Achem SR. Noncardiac chest pain: epidemiology, natural course and pathogenesis. *J Neurogastroenterol Motil* 2011;**17**:110-123.
4. Yamasaki T, Fass R. Noncardiac chest pain: diagnosis and management. *Curr Opin Gastroenterol* 2017;**33**:293-300.
5. van Hoeij FB, Ponds FA, Smout AJ, Bredenoord AJ. Incidence and costs of achalasia in The Netherlands. *Neurogastroenterol Motil* 2018;**30**(2).
6. Samo S, Carlson DA, Gregory DL, Gawel SH, Pandolfino JE, Kahrilas PJ. incidence and prevalence of achalasia in central Chicago, 2004-2014, since the widespread use of high-resolution manometry. *Clin Gastroenterol Hepatol* 2017;**15**:366-373.
7. Zaher EA, Patel P, Atia G, Sigdel S. Distal esophageal spasm: an updated review. *Cureus* 2023;**15**:e41504.
8. Clément M, Zhu WJ, Neshkova E, Bouin M. Jackhammer esophagus: from manometric diagnosis to clinical presentation. *Can J Gastroenterol Hepatol* 2019;**2019**:5036160.
9. Beveridge C, Lynch K. Diagnosis and management of esophagogastric junction outflow obstruction. *Gastroenterol Hepatol (N Y)* 2020;**16**:131-138.
10. Chen JW, Savarino E, Smout A, et al. Chicago Classification Update (v4.0): technical review on diagnostic criteria for hypercontractile esophagus. *Neurogastroenterol Motil* 2021;**33**:e14115.
11. Roman S, Hebbard G, Jung KW, et al. Chicago Classification Update (v4.0): technical review on diagnostic criteria for distal esophageal spasm. *Neurogastroenterol Motil* 2021;**33**:e14119.
12. Bredenoord AJ, Babaei A, Carlson D, et al. Esophagogastric junction outflow obstruction. *Neurogastroenterol Motil* 2021;**33**:e14193.
13. Aziz Q, Fass R, Gyawali CP, et al. Functional esophageal disorders. *Gastroenterology* 2016;**150**:1368-1379.
14. Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ.ACG clinical guideline for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol* 2022:**117**:27-56.
15. Matsubara M, Manabe N, Ayaki M, et al. Clinical significance of esophagogastroduodenoscopy in patients with esophageal motility disorders. *Dig Endosc* 2021;**33**:753-760.
16. Kuribayashi S, Hosaka H, Uraoka T. Usefulness of endoscopy for the detection and diagnosis of primary esophageal motility disorders and diseases relating to abnormal esophageal motility. *Diagnostics (Basel)* 2023;**13**:.
17. Blonski W, Kumar A, Feldman J, Richter JE. Timed barium swallow: diagnostic role and predictive value in untreated achalasia, esophagogastric junction outflow obstruction, and non-achalasia dysphagia. *Am J Gastroenterol* 2018;**113**:196-203.
18. Assadian M, Momayez Sanat Z, Asl Soleimani H, Mikaeli J. Prevalence of different types of primary esophageal motility disorders and their associated factors in patients referring to Shariati hospital during 2018-2019. *Middle East J Dig Dis* 2022;**14**:70-76.
19. Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: a new clinically relevant classification by high-resolution manometry. *Gastroenterology* 2008;**135**:1526-1533.
20. Zhou MJ, Kamal A, Freedberg DE, Markowitz D, Clarke JO, Jodorkovsky D. Type II Achalasia Is Increasing in Prevalence. *Dig Dis Sci* 2021;**66**:3490-3494.
21. Almansa C, Heckman MG, DeVault KR, Bouras E, Achem SR. Esophageal spasm: demographic, clinical, radiographic, and manometric features in 108 patients. *Dis Esophagus* 2012;**25**:214-221.
22. Hani A, Zuluaga C, Costa V, et al. Jackhammer esophagus: Prevalence and demographic, clinical, and manometric characteristics. *Rev Gastroenterol Mex (Engl Ed)* 2020;**85**:421-427.
23. Hoshino M, Omura N, Yano F, et al. Is esophageal manometry essential for the diagnosis of achalasia? Identifying patients with achalasia by the esophageal clearance method. *Esophagus* 2021;**18**:163-168.
24. O'Rourke AK, Lazar A, Murphy B, Castell DO, Martin-Harris B. Utility of esophagram versus high-resolution manometry in the detection of esophageal dysmotility. *Otolaryngol Head Neck Surg* 2016;**154**:888-891.
25. Muschelli J. ROC and AUC with a binary predictor: a potentially misleading metric. *J Classif* 2020;**37**:696-708.

26. Mbizvo GK, Larner AJ. Receiver operating characteristic plot and area under the curve with binary classifiers: pragmatic analysis of cognitive screening instruments. *Neurodegener Dis Manag* 2021;**11**:353-360.
27. Howard PJ, Maher L, Pryde A, Cameron EW, Heading RC. Five year prospective study of the incidence, clinical features, and diagnosis of achalasia in Edinburgh. *Gut* 1992;**33**:1011-1015.
28. Cameron AJ, Malcolm A, Prather CM, Phillips SF. Videoendoscopic diagnosis of esophageal motility disorders. *Gastrointest Endosc* 1999;**49**:62-69.
29. Caballero-Mateos AM, López-Hidalgo JL, Torres-Parejo Ú, et al. Risk factors for functional dyspepsia, erosive and non-erosive gastroesophageal reflux disease: a cross-sectional study. *Gastroenterol Hepatol* 2023;**46**:542-552.