Observational Study

Medicine®

OPEN

Ineffective esophageal motility assessment in patients with and without pathological esophageal acid reflux

Zehra Betul Pakoz, MD[a,*], Sevil Ozer Sarı, MD[b], Sezgin Vatansever, MD[a], Berna Nilgun Ozgursoy Uran, PhD[c], Hakan Camyar, MD[d], Emine Ozlem Gur, MD[e], Zeynep Zehra Gumus, MD[f], Sabiye Akbulut, MD[g]

Abstract

Ineffective esophageal motility (IEM), defined as minor esophageal motility disorder, is also the most common esophageal motility disorder. The relationship between gastro-esophageal reflux disease is still controversial. Our aim in this study is to evaluate whether there are differences in terms of demographic, endoscopic, or motility findings between IEM patients with pathological esophageal acid reflux and physiological reflux.

Patients diagnosed with IEM according to the Chicago classification v3 with high-resolution manometry (HRM) before acid monitoring constituted the study group of our investigation. The patients were divided into 2 groups as patients with pathological esophageal reflux and patients with physiological reflux according to 24-hour acid monitoring. Demographic data, endoscopic findings, and HRM findings were compared between 2 groups.

A total of 62 patients who were diagnosed with IEM according to the Chicago classification v3 were included in the study. Patients in the physiological reflux group were 7 years younger on average than the pathological reflux group. Esophagitis rates were significantly higher in the pathological reflux group ($P = .033$). Lower esophageal sphincter resting pressure, integrated relaxation pressure, and the presence of hernia were found to be similar in the 2 groups ($P = 392$, $P = 182$, $P = 657$, respectively). The rate of severe IEM was also similar between the 2 groups ($P = .143$).

The fact that the physiological reflux patient group is younger may suggest that the IEM develops in the early period and then reflux accompanies the picture with advancing age.

Abbreviations: DCI = distal contractile integral, EGJ = esophagogastric junction, GERD = gastro-esophageal reflux disease, HRM = high-resolution manometry, IEM = ineffective esophageal motility, IRP = integrated relaxation pressure, LES = lower esophageal sphincter, PPI = proton pump inhibitor.

Keywords: acid reflux, benign esophageal diseases, esophageal dysmotility, motility disorders

Editor: Johannes Mayr.

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The authors have no funding and conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Department of Gastroenterology, Ataturk Training and Research Hospital, [b] Department of Gastroenterology, Tepecik Training and Research Hospital, [c] Internal Medicine Nursing, Health Science Faculty, Katip Celebi University, [d] Department of Gastroenterology, [e] Department of General Surgery, [f] Department of Internal Medicine, Katip Celebi University Faculty of Medicine, Izmir, [g] Department of Gastroenterology, University of Health Sciences, Kartal Kosuyolu High Speciality Training and Research Hospital, Istanbul, Turkey.

[*] Correspondence: Zehra Betul Pakoz, Department of Gastroenterology, Ataturk Training and Research Hospital, Karabaglar, Izmir, Turkey (e-mail: betulpakoz@yahoo.com).

How to cite this article: Pakoz ZB, Sarı SO, Vatansever S, Uran BN, Camyar H, Gur EO, Gumus ZZ, Akbulut S. Ineffective esophageal motility assessment in patients with and without pathological esophageal acid reflux. Medicine 2021;100:20(e26054).

Received: 21 February 2021 / Received in final form: 29 April 2021 / Accepted: 3 May 2021

http://dx.doi.org/10.1097/MD.0000000000026054

1. Introduction

Ineffective esophageal motility (IEM) is an esophageal motility disorder, the clinical significance of which is still controversial. The last definition of IEM was made in the Chicago Classification v3. According to this classification, IEM is defined by the distal contractile integral (DCI) value is below than 450 mm Hg.s.cm in 50% or more of liquid swallows in high-resolution manometry (HRM).[1] IEM, defined as minor esophageal motility disorder, is also the most common esophageal motility disorder and can be detected in 30% of patients who undergo HRM.[2] Symptoms in IEM patients are heterogeneous. Dysphagia or reflux symptoms such as regurgitation and pyrosis may be observed.[3]

Pathophysiological reasons causing IEM are not clear yet. In particular, the relationship between gastro-esophageal reflux disease (GERD) and IEM has been studied in previous studies. It has been reported that esophageal muscle contraction is disrupted by the effect of acid in patients with GERD, and consequently, more severe acid exposure and symptoms are observed.[4] Similar studies reported that the pathological acid exposure time is associated with IEM.[3] Besides, IEM is seen in patients without GERD findings, and there are also studies with no correlation between IEM and GERD.[5]

Our aim in this study is to evaluate whether there are differences in terms of demographic, endoscopic, or motility findings between IEM patients with pathological esophageal acid reflux and physiological reflux.

2. Materials and methods

2.1. Patients

2.1.1. Inclusion criteria. Patients who were admitted to the hospital due to reflux symptoms between February 2017 and February 2020 and underwent 24-hour acid monitoring in our clinic were evaluated in this study. Patients diagnosed with IEM according to the Chicago classification v3 with HRM before acid monitoring constituted the study group of our investigation.

2.1.2. Exclusion criteria. Patients under 18 years of age, patients with non-IEM esophageal motility disorder in HRM, patients with an obstructive esophageal disease such as mass or stricture on endoscopy, patients with rheumatological diseases, history of esophageal surgery or endoscopic treatment, and the patients with acid monitoring for less than 24 hours were excluded from the study.

2.2. Study design

The study was planned as a retrospective cross-sectional study. The demographic information, co-morbid diseases, and endoscopy findings of the patients were obtained from the hospital software system. The patients with any level of esophagitis according to the Los Angeles classification were recorded.[6] Endoscopic hernia data were not recorded because the hernia evaluation was made with HRM.

HRM images were re-evaluated and those with DCI below 450 mm Hg.s.cm in >70% of liquid swallow were evaluated as severe IEM. Lower esophageal sphincter (LES) resting pressure, integrated relaxation pressure (IRP), and esophagogastric junction (EGJ) subtypes were evaluated.

The patients were divided into 2 groups as patients with pathological esophageal reflux and patients with physiological reflux according to 24-hour acid monitoring. Demographic data, endoscopic findings, and HRM findings were compared between 2 groups.

2.2.1. HRM assessment. Esophageal motility tests of the patients were performed with the MMS HRM device (Medical Measurement Systems, the Netherlands). Twenty four-channel water perfusion catheters were used for HRM procedures. The catheter was advanced transnasally and placed in the appropriate position. LES resting pressure was taken in 5 minutes after patient compliance. Then, a total of 10 liquid swallows were obtained by giving 5 mL of drinking water.

The number of swallows with DCI values below 450 mm Hg s, LES resting pressure, IRP levels, and EGJ subtypes were recorded as HRM findings. Hernia assessment was performed by determining the EGJ subtypes of the patients according to the Chicago classification.[1] Accordingly, patients with separation of more than 1 cm between LES and crural diagram considered as patients with hernia.

The procedure was performed in the supine position after 8 hours of fasting. None of the patients were using medication that affected esophageal motility before the procedure.

2.2.2. 24-hour acid monitoring assessment. Twenty four-hour acid monitoring was performed with single sensor impedance catheters. After determining the location of the LES with HRM, the catheter was placed 5 cm proximal to the LES and recorded for a total of 24 hours. GERD diagnosis was made according to the Lyon Consensus criteria.[7]

The procedure was performed after 8 hours of fasting. The proton pump inhibitor (PPI) treatment was stopped 10 days before the procedure. No dietary restrictions were applied to the patients during the 24-hour recording.

The study approval was obtained from the local ethics committee (no: 2020–14-25). Informed consent forms were obtained from all patients.

2.3. Statistical methods

Statistical analyzes were performed using the IBM SPSS Statistics 22 program. Pearson's Chi-Squared test and Fisher exact test were used for categorical distributions of patients, Student *t* test was used for independent samples and Mann–Whitney *U* test was used for non-normal distributions. The results were given as frequency and percentages for categorical variables and mean ± std if the variable was normal for continuous variables. Deviation values were shown with median (minimum-maximum) values if they did not show normal distribution. Statistical significance was considered when the *P* value was below .05.

3. Results

Initially, 215 patients who underwent HRM and 24-hour acid monitoring with reflux symptoms such as regurgitation, non-cardiac chest pain, and heartburn were evaluated. Among these patients, a total of 62 patients who were diagnosed with IEM according to the Chicago classification v3 and without any exclusion criteria were included in the study (Fig. 1).

The patients were divided into 2 groups as those with pathological esophageal reflux and those with physiological esophageal reflux. The main age of 30 patients with pathological reflux was 45.6 ± 13.1 years and 12 of them (40%) were women. The mean age of 32 patients with physiological esophageal reflux was 38.5 ± 10.2 and 20 (37.5%) of them were women. Age was significantly higher in the pathological reflux group ($P = .019$). Patients in the physiological reflux group were 7 years younger on average than the pathological reflux group (Table 1).

Upper gastrointestinal endoscopy results of 54 patients were obtained. In 13 of these patients, varying degrees of esophagitis were detected according to the Los Angeles classification (Grade A in 8 patients, grade B in 4 patients, and grade C in 1 patient). Esophagitis was not detected in 41 of 54 patients and there was no patient with grade D esophagitis. Esophagitis rates were significantly higher in the pathological reflux group ($P = .033$). Endoscopic findings of patients are summarized in Table 2.

When HRM findings were compared between the groups, LES resting pressure, IRP, and the presence of hernia were found to be similar in the 2 groups ($P = 392$, $P = 182$, $P = 657$, respectively). The rate of severe IEM was also similar between the 2 groups ($P = .143$). HRM findings of the patients are summarized in Table 3.

4. Discussion

IEM is the most common esophageal motility disorder, the clinical significance of which is not clearly understood. The relationship between IEM and GERD is controversial, and it is not clear yet whether motor impairment causes gastro-esophageal reflux or gastro-esophageal reflux is the cause of motor impairment. Delayed acid clearance from the esophagus in patients with a diagnosis of IEM is an important reason for the development of GERD.[8]

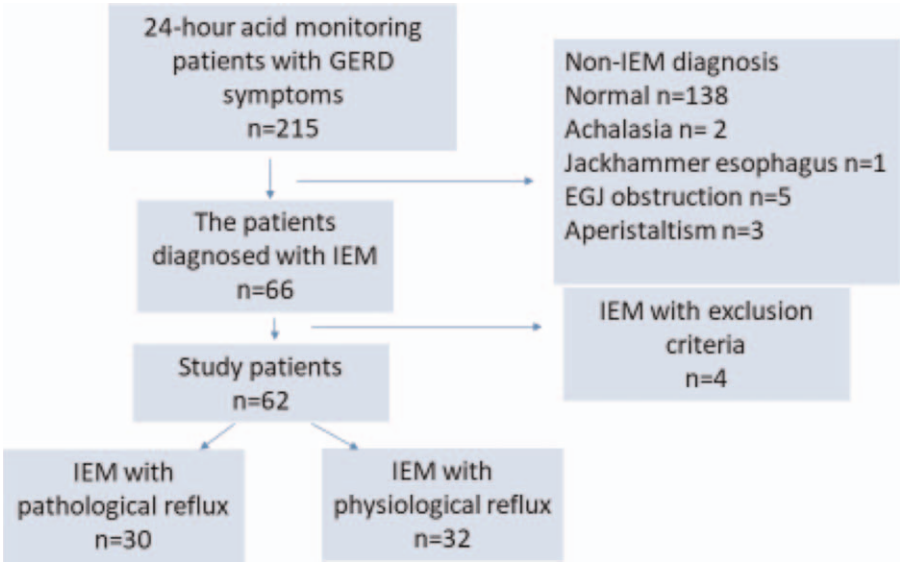

Figure 1. study flow chart.

Besides, IEM is the most common esophageal motility disorder in GERD patients.[9] Nevertheless, while a significant relationship was found between IEM and GERD in some studies, no relationship was found in others.[10–12] As a result, although pathological esophageal acid reflux and IEM are frequently associated, the presence of IEM is not considered pathognomonic for GERD.[7]

Table 1

Characteristics of the study patients.

	IEM patients with pathological reflux (n = 30)	IEM patients with physiological reflux (n = 32)	*P*
Mean age (yr)	45.6 ± 13.1	38.5 ± 10.2	.019
Sex			.076
Female	12 (40%)	20 (62.5%)	
Male	18 (60%)	12 (37.5%)	
Esophagitis	9 (37.5%)	4 (1.9%)	.033
Hiatal hernia	10 (33.3%)	9 (28.1%)	.657

IEM = ineffective esophageal motility.

Table 2

Comparison of esophagitis according to Los Angeles classification between pathological reflux group and physiological reflux group determined by esophago-gastroscopy in 54 of 62 patients.

Esophagitis	IEM patients with pathological reflux (n = 30)	IEM patients with physiological reflux (n = 32)	*P*
No esophagitis	16 (53.3%)	25 (78.1%)	
Grade A	5 (16.6%)	3 (9.3%)	.033
Grade B	3 (10%)	1 (3.1%)	
Grade C	1 (3.3%)		

IEM = ineffective esophageal motility.

Table 3

Comparison of HRM findings between the study groups.

HRM findings	IEM patients with pathological reflux (n = 30)	IEM patients with physiological reflux (n = 32)	*P*
Mean basal LES pressure (mmHg)	13.5 ± 9.1	15.4 ± 8.3	.392
Mean IRP	7.2 ± 4.2	8.7 ± 4.2	.182
EGJ subtype			.657
Type 1	20 (66.7%)	23 (71.9%)	
Type 2	8 (26.6%)	8 (25%)	
Type 3	2 (6.7%)	1 (3.1%)	
Severe IEM	20 (66.7%)	17 (53.1%)	.277

EGJ = esophagogastric junction, HRM = high-resolution manometry, IEM = ineffective esophageal motility, LES = lower esophageal sphincter.

In our study, age was found to be significantly lower in the patient with physiological reflux (45.6 ± 13.1 vs 38.5 ± 10.2; $P = .019$). Shetler et al found in a similar study that the main age was 12 years higher in IEM patients with pathological esophageal reflux.[11] Similar results obtained in both studies may help find an answer to the question of whether reflux is the cause of IEM or IEM exacerbates reflux. The fact that the physiological reflux patient group is younger may suggest that the IEM develops in the early period and then reflux accompanies the picture with advancing age.

It is known that the rate of esophagitis increases in patients with pathological esophageal acid reflux and the degree of esophagitis increases as acid exposure increases.[13] It has been shown in previous studies that the prevalence of IEM increases with the exacerbation of the erosive esophagus.[14–16] Normal endoscopic findings were not related to abnormal DeMeester scores in IEM patients.[17] In our study, we found a significantly higher rate of esophagitis in IEM patients with pathological reflux ($P = .033$). This result in our study is compatible with the literature and is an expected result.

The LES resting pressure was found to be similar between the 2 groups in our study ($P = .392$). Previous studies have shown that as the LES pressure decreases, esophageal acid exposure time increases. A relationship has also been found between hernia size and acid exposure time.[18–20] Jain et al showed that basal LES pressure below 10 mm Hg has a 2.2 likelihood ratio in predicting pathological acid reflux. In the same study, LES pressure (11.9 vs 16.6; $P < .02$) and IRP (5.7 vs 7.4; $P < .01$) were significantly lower, hernia size (1.7 vs 1.4 cm; $P < .003$) was significantly higher in pathological reflux group.[17] On the other hand, similar to the results of our study, some studies showed that hernia size was not related to esophageal motility. In the study conducted by Liu et al, it was reported that low LES resting pressure in patients with hernia caused esophagitis, and esophageal muscle dysfunction in patients without hernia could be the cause of GERD.[13]

Ineffective swallowing in more than 70% of swallows performed during HRM is defined as severe IEM.[21] Some studies have shown that severe IEM is associated with pathological acid exposure and esophageal mucosal damage.[18,22,23] In our study, the rate of severe IEM was similar between the 2 groups ($P = .143$). Thus, there is no relationship between the severity of IEM and pathological esophageal acid reflux according to our study.

Our study has some limitations. First, the study is a retrospective study. Conducting the study with more patients would provide a stronger statistical evaluation. Symptom severity and PPI response evaluation between the 2 groups were not made. Another limitation was that the impedance catheter used in the study was a single-sensor pH probe impedance catheter. Therefore, the concurrent gastric acid evaluation was not performed. Since there may have been patients using PPI before endoscopic evaluation, the esophagitis rate may have been found lower than the actual rate. Also, we did not assess the body mass index between the 2 groups.

In conclusion, no significant difference was found between those with and without pathological esophageal acid reflux between LES resting pressure, hernia size, and IRP levels in our study. The rate of severe IEM was also similar between the 2 groups. Age was found to be significantly lower in the patients with physiological reflux. Although this result suggests that IEM develops first and pathological esophageal acid reflux occurs over the years, it is difficult to reach this conclusion for certain with the present study. Therefore, prospective and longitudinal studies will provide more precise information to show the relationship between GERD and IEM.

Author contributions

Conceptualization: Zehra Betul Pakoz.
Data curation: Zehra Betul Pakoz, Sevil Ozer Sarı, Zeynep Zehra Gumus.
Formal analysis: Sezgin Vatansever, Zeynep Zehra Gumus.
Methodology: Zehra Betul Pakoz, Sezgin Vatansever.
Resources: Berna Nilgun Ozgursoy Uran, Hakan Camyar.
Software: Sezgin Vatansever, Hakan Camyar.
Supervision: Sevil Ozer Sarı, Emine Ozlem Gur, Sabiye Akbulut.
Validation: Berna Nilgun Ozgursoy Uran.
Visualization: Sevil Ozer Sarı.
Writing – original draft: Zehra Betul Pakoz.
Writing – review & editing: Berna Nilgun Ozgursoy Uran, Emine Ozlem Gur, Sabiye Akbulut.

References

[1] Kahrilas PJ, Bredenoord A, Fox M, Gyawali CP, Roman S, Smout AJPM. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil 2015;27:160–74.
[2] Boland K, Abdul-Hussein M, Tutuian R, Castell DO. Characteristics of consecutive esophageal motility diagnoses after a decade of change. J Clin Gastroenterol 2016;50:301–6.
[3] Goyal O, Bansal M, Sood A. Esophageal motility disorders: symptomatic and manometric spectrum in Punjab, northern India. Indian J Gastroenterol 2017;36:202–8.
[4] Diener U, Patti MG, Molena D, Fisichella PM, Way LW. Esophageal dysmotility and gastroesophageal reflux disease. J Gastrointest Surg 2001;5:260–5.
[5] Pandolfino JE, Sifrim D. Evaluation of esophageal contractile propagation using esophageal pressure topography. Neurogastroenterol Motil 2012;24(Suppl 1):20–6.
[6] Sami SS, Ragunath K. The Los Angeles classification of gastroesophageal reflux disease. Video J Encycl GI Endosc 2013;1:103–4.
[7] Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. Gut 2018;67:1351–62.
[8] Jones MP, Sloan SS, Jovanovic B, Kahrilas PJ. Impaired egress rather than increased access: an important independent predictor of erosive oesophagitis. Neurogastroenterol Motil 2002;14:625–31.
[9] Ho SC, Chang CS, Wu CY, Chen GH. Ineffective esophageal motility is a primary motility disorder in gastroesophageal reflux disease. Dig Dis Sci 2002;47:652–6.
[10] Kim KY, Kim GH, Kim DU. Is ineffective esophageal motility associated with gastropharyngeal reflux disease? World J Gastroenterol 2008;14:6030–5.
[11] Shetler KP, Bikhtii S, Triadafilopoulos G. Ineffective esophageal motility: clinical, manometric, and outcome characteristics in patients with and without abnormal esophageal acid exposure. Dis Esophagus 2017;30:1–8.
[12] Kasamatsu S, Matsumura T, Ohta Y, et al. The effect of ineffective esophageal motility on gastroesophageal reflux disease. Digestion 2017;95:221–8.
[13] Liu L, Li S, Zhu K, et al. Relationship between esophageal motility and severity of gastroesophageal reflux disease according to the Los Angeles classification. Medicine (Baltimore) 2019;98:e15543doi: 10.1097/MD.0000000000015543.
[14] Savarino E, Bredenoord AJ, Fox M, Pandolfino JE, Roman S, Gyawali CP. Expert consensus document: advances in the physiological assessment and diagnosis of GERD. Nat Rev GastroenterolHepatol 2017;14:665–76.
[15] Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. Gut 1999;45:172–80.
[16] Wu JCY, Cheung CMY, Wong VW, Sung JJ. Distinct clinical characteristics between patients with nonerosive reflux disease and those with reflux esophagitis. Clin Gastroenterol Hepatol 2007;5:690–5.

[17] Jain M, Srinivas M, Bawane P, Venkataraman J. Basal lower esophageal sphincter pressure in gastroesophageal reflux disease: an ignored metric in high-resolution esophageal manometry. Indian J Gastroenterol 2018;37:446–51.
[18] Reddy CA, Baker JR, Lau J, Chen JW. High resolution manometry diagnosis of ineffective esophageal motility is associated with higher reflux burden. Dig Dis Sci 2019;64:2199–205.
[19] Tsuboi K, Hoshino M, Sundaram A, Yano F, Mittal SK. Role of the lower esophageal sphincter on esophageal acid exposure - a review of over 2000 patients. Trop Gastroenterol 2012;33:107–11.
[20] Tolone S, de Cassan C, de Bortoli N, et al. Esophagogastric junction morphology is associated with a positive impedance-pH monitoring in patients with GERD. Neurogastroenterol Motil 2015;27:1175–82.
[21] Gyawali CP, Sifrim D, Carlson DA, Hawn M, Katzka DA, Pandolfino JE. Ineffective esophageal motility: concepts, future directions, and conclusions from the Stanford 2018 symposium. Neurogastroenterol Motil 2019;31:e13584doi: 10.1111/nmo.13584.
[22] Ribolsi M, Balestrieri P, Emerenziani S, Guarino MP, Cicala M. Weak peristalsis with large breaks is associated with higher acid exposure and delayed reflux clearance in the supine position in GERD patients. Am J Gastroenterol 2014;109:46–51.
[23] Rengarajan A, Bolkhir A, Gor P, Wang D, Munigala S, Gyawali CP. Esophagogastric junction and esophageal body contraction metrics on high resolution manometry predict esophageal acid burden. Neurogastroenterol Motil 2018;30:1647–54.