



Clinical features, endoscopic and manometric findings in patients with ineffective esophageal motility

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Received 2 Nov. 2022

Accepted 8 Feb. 2023

Published online 17 Feb. 2023

Keywords: Esophageal motility disorder, Gastroesophageal reflux, Manometry, Proton pump inhibitors

Abstract

Introduction: Ineffective esophageal motility (IEM) is an esophageal motility disorder (EMD) and the most prevalent abnormality routinely observed in esophageal manometry.

Objectives: In this study, we investigated the clinical characteristics of IEM patients and the effects of proton pump inhibitors (PPI) and surgical treatments on their conditions.

Patients and Methods: This cross-sectional study was conducted in Isfahan in 2019-2020 on 40 patients diagnosed with IEM. We collected patient demographic information (age, gender, previous medical history, medications, and duration of the current problem) and clinical manifestations (clinical symptoms of patients including dysphagia, heartburn, food and acid regurgitation, chest pain and belching) prior to and following PPI or surgical treatment.

Results: Approximately 65% of patients presented with dysphagia and heartburn, 55% had food and acid regurgitation, 47.5% had belching, and 55% had chest pain. Post-treatment findings revealed that only the recurrence of food and acid regurgitation was significantly lower in the PPI treatment group than in the surgical group. Only dysphagia severity was statistically significant in the surgical group compared to other symptoms ($P=0.042$). In the PPI group, the severity of heartburn ($P=0.007$), dysphagia ($P<0.001$), food and acid regurgitation ($P=0.007$), and chest pain ($P=0.027$) decreased significantly compared to baseline.

Conclusion: This study showed that the common clinical manifestations of IEM were dysphagia, heartburn, food and acid regurgitation, and belching. Moreover, treatment with PPI resulted in more significant improvements than surgical treatment.

Citation: Soheilipour M, Aria A, Momenzadeh M, Tabesh E, Adibi Sedeh P. Clinical features, endoscopic and manometric findings in patients with ineffective esophageal motility. Immunopathol Persa. 2023;x(x):e39451. DOI:10.34172/ipp.2023.39451.

Introduction

High-resolution esophageal pressure topography is a method that combines high-resolution manometry (HRM) and esophageal pressure topography (EPT). Esophageal pressure topography is typically employed to investigate esophageal motility disorders (EMDs) (1,2). The color, encoding, and space-time dimension (spatiotemporal) of esophageal pressure are displayed in EPT images (3).

In studies, criteria such as contraction patterns and esophageal contraction continuity are applied based on the amount of complete relaxation pressure of the lower esophageal sphincter (LES) within four seconds of integrated relaxation pressure (IRP4). There are two groups of EMDs: patients with IRP4 greater than 15 mm Hg (including all types of achalasia) and patients with IRP4 equal to or less than 15 mm Hg (including all non-achalasia motor disorders) (4,5).

Non-achalasia EMDs are more prevalent but have received less attention in research (6). This classification of disorders lacks a

Key point

We evaluated the frequency of clinical features and endoscopic and manometric findings in patients with IEM. We assessed the effects of PPIs and surgical treatments on patients' conditions. Furthermore, we observed that dysphagia, heartburn, food and acid regurgitation, belching, along with chest pain were the most common clinical manifestations of IEM. Our study also showed that PPIs treatment led to more significant improvements than surgical treatments.

definitive treatment or prognosis. Some researchers believe that inflammation and mucosal damage impose a prolonged esophageal translocation due to esophageal motility. The non-achalasia EMDs play a significant role in the return of acid and alkali from the stomach to the esophagus and their prolonged residence in the esophagus, consequently mucosal damage occurs (7).

Manometric criteria define ineffective esophageal motility (IEM) as an EMD (8,9). The muscle contractions follow a normal pattern down the esophagus. Normal manometry is a normal pressure of the LES



of about 15 mm Hg. The pressure is less than 10 mm Hg when the LES relaxes to let food pass into the stomach. In normal manometry, IEM diagnosis is likely if the range of distal esophageal contraction is less than 30 mm Hg and in manometry with HRM, if the distal contraction integral is between 100 and 450 mm Hg/s/cm in more than 50% of swallow activity. The disease affects the esophageal smooth muscles (10,11).

Ineffective esophageal motility is a relatively common abnormality routinely detected by esophageal manometry, with a prevalence of 20% to 30% (12,13). IEM indicates motor dysfunction in 50% of patients with gastroesophageal reflux disease (GERD) and is common in GERD patients with respiratory symptoms (14,15).

Objectives

Despite the significance of IEM as an esophageal disorder, its prevalence concerning this topic and this disease has not been studied in our region to the best of our knowledge, consequently we sought to determine the frequency of clinical characteristics, endoscopic findings, and manometric findings in IEM patients.

Patients and Methods

Study design

This cross-sectional study was conducted at Khorshid hospital, affiliated with Isfahan University of Medical Sciences, between 2019 and 2020. All cases with an HRM-based IEM diagnosis were included in the current investigation.

Inclusion criteria were patients over the age of 18 years with dysphagia or refractory GERD who were diagnosed with IEM through manometry. Patients who did not respond to our questionnaire were excluded.

A checklist was developed for patients who had undergone HRM and were diagnosed with IEM. IEM was diagnosed using HRM based on a standard method. Furthermore, the final diagnosis of patients was based on the Chicago Classification version 3.0 (16). An IEM diagnosis was made if the IRP4 was less than 15 mm Hg and the distal contraction integral was between 100 and 450 mm Hg/s/cm in more than 50% of swallowing activity.

The first section of this checklist included patient demographics (age, gender, previous medical history, medications, and duration of current problem) and clinical information (clinical symptoms of patients including dysphagia, heartburn, food and acid regurgitation, chest pain, or belching). This study evaluated the frequency of esophagitis and hiatal hernia based on the endoscopic findings in patients who had undergone upper gastrointestinal endoscopy. All patients completed the Mayo-GERQ questionnaire (a new questionnaire for GERD). This questionnaire has been previously translated into Persian and its validity and reliability in the Persian population have been confirmed (17).

This questionnaire included sections on demographics,

drug use including H2 blockers and proton pump inhibitor (PPI), history of hiatal hernia, history of gastrointestinal surgery, heart disease, asthma, history of GERD, smoking, tea and coffee. This survey identified four major symptoms of reflux disease: food and acid regurgitation, heartburn, dysphagia, chest pain and minor symptoms such as nausea, sore throat, premature satiety, hiccups and belching.

Six months later, the patients were contacted and asked about their treatment progress and the evolution of their initial symptoms. According to the treating physician, the patients were either treated with PPIs or were surgical candidates for anti-reflux procedures.

Moreover, the demographic information, disease duration and initial symptom of 40 IEM patients were compared to 100 achalasia patients diagnosed by manometry.

Statistical analysis

The obtained data were entered into the Statistical Package for the Social Sciences (SPSS) (version 24, SPSS Inc., Chicago, IL, USA). Quantitative data were reported as mean \pm standard deviation, while qualitative data were presented as frequency distribution (percentage). In addition, an independent *t* test and chi-square were conducted to analyze the data. A *P* value $<$ 0.05 was considered statistically significant.

Results

In this study, data from 40 patients with IEM were analyzed. The mean age of patients was 47.35 ± 14.45 years (range: 19-84 years) and the mean age from disease onset to performing manometry was 6.33 ± 5.33 years (1-20 years). In the study, 57.5% of patients were female. In this investigation, 82.5% of patients consumed tea, 7.5% consumed coffee, and none reported a smoking history. Endoscopic findings showed that 32.5% of patients had a history of hiatal hernia, 30% had esophagitis and 27.5% had gastropathy. No esophageal imaging was conducted on 55% of patients; 32.5% completed imaging once, 10% twice and 2.5% three times (Table 1).

The most common initial symptoms of patients were dysphagia and heartburn (65%), followed by food and acid regurgitation (55%), belching (47.5%) and chest pain (55%) (Table 2).

Table 3 shows 30% of patients had history of coronary artery disease. The other symptoms, included hoarseness (30%), cough (22.5%) and abdominal pain (35%). Administration of aspirin and NSAIDs (non-steroidal anti-inflammatory drugs) were reported in 20% and 30% of the patients, respectively. The severity of abdominal pain ranged from 3-to-10 with the average of 6.57 ± 2.34 .

PPI treatments were administered to 75% (30 patients) of the 40 patients with IEM and anti-reflux surgery was conducted on 25% (10 patients) (Figure 1). As shown in Table 4, the frequency of heartburn and food and acid regurgitation decreased in patients receiving PPI

Table 1. Frequency distribution of the number of physicians referring to the patient, number of endoscopies and esophageal images

Variable	Number of physicians, No. (%)	Number of endoscopies, No. (%)	Number of esophageal images, No. (%)
0	0 (0)	0 (0)	22 (55)
1	5 (12.5)	17 (42)	13 (32.5)
2	20 (50)	13 (32.5)	4 (10)
3	7(17.5)	4 (10)	1 (2.5)
4 and more	8 (20)	6 (15)	0 (0)
Total	40 (100)	40 (100)	40 (100)

treatment after interventions. Notably, all patients in both groups had intermittent dysphagia. Of the 19 patients with chest pain, 55.6% deteriorated with hot or cold fluids, 50% with heavy activity and 33.3% with light activity.

Comparing the symptoms of patients treated medically versus surgically before interventions revealed no significant differences ($P>0.05$); however, the weekly frequency of food and acid regurgitation was higher in patients treated surgically after interventions. Following the administration of PPIs, the severity of symptoms, including heartburn, dysphagia, food and acid regurgitation, chest pain, and the recurrence of dysphagia and food and acid regurgitation weekly, improved significantly ($P<0.05$). Surgical management of patients

Table 2. Frequency distribution of early symptoms before treatment in patients with ineffective esophageal motility

Variable	Symptom, No. (%)
Dysphagia	26 (65)
Heartburn	26(65)
Food and acid regurgitation	22 (55)
Belching	19 (47.5)
Chest pain	22 (55)

Table 3. Frequency distribution of pre-treatment diagnoses and symptoms in patients with IEM

Variable	No. (%)
Diagnosed coronary artery disease	Yes 12 (30)
	No 28 (70)
Aspirin use	Yes 8 (20)
	No 32 (80)
Non-steroidal anti-inflammatory drugs	Yes 12 (30)
	No 28 (70)
Hoarseness	Yes 12 (30)
	No 28 (70)
Cough	Yes 9 (22.5)
	No 31 (77.5)
Abdominal pain	Yes 12 (35)
	No 26 (65)

resulted in only a statistically significant reduction in dysphagia severity ($P=0.042$; [Table 5](#)).

The data of 100 patients with manometry-diagnosed achalasia, including demographic information, time from symptom onset to diagnosis and other most common symptoms, were compared with IEM patients. This comparison revealed that the ages of the groups did not differ significantly ($P=0.120$); however, the duration of symptoms in IEM patients was significantly longer than achalasia group ($P<0.001$). The majority of patients in the IEM group were female (57.5%) and in patients with achalasia were male (63%) that the frequency distribution of gender in the two groups was significantly different ($P=0.027$). In patients with achalasia, dysphagia ($P<0.001$) and food and acid regurgitation ($P=0.020$) were significantly higher and chest pain ($P=0.008$) was significantly lower than IEM patients. There was no significant difference between the two groups regarding cough ($P=0.755$; [Table 6](#)).

Discussion

Our survey aimed to determine the frequency of clinical characteristics, endoscopic and manometric findings and the effects of PPI or surgery in patients with IEM. After analyzing the data from 40 patients, we observed that dysphagia, heartburn, food and acid regurgitation, chest

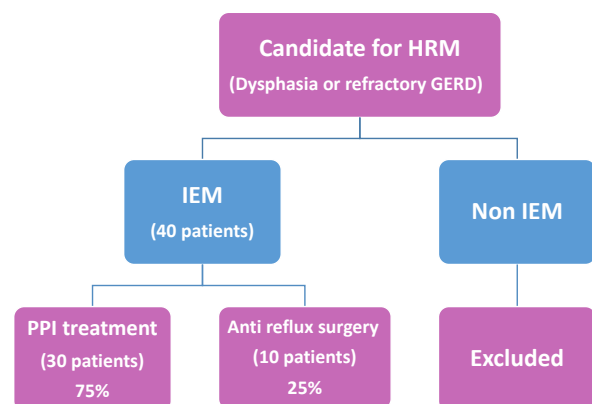
**Figure 1.** Patient's flowchart. IEM; Ineffective esophageal motility, PPI; Proton pump inhibitors, HRM; High-resolution manometry, EPT; Esophageal pressure topography, IRP4; Integrated relaxation pressure, LES; Lower esophageal sphincter, GERD; Gastroesophageal reflux disease

Table 4. Comparison of the frequency distribution of symptoms before and after treatment in patients with IEM

Variable	Time of treatment	PPI, No. (%)	Surgery, No. (%)	P value
Heartburn	Before	22(73.3)	6(60)	0.451
	After	13(43.3)	3(30)	0.711
	P value	0.004	0.250	
Dysphagia	Before	19(63.3)	8(80)	0.451
	After	15(50)	3(30)	0.464
	P value	0.219	0.043	
Food and acid regurgitation	Before	22(73.3)	4(40)	0.123
	After	12(40)	4(40)	-
	P value	0.002	-	
Belching	Before	17(56.7)	3(30)	0.273
	After	11(36.7)	0(0)	0.038
	P value	0.109	0.250	
Chest pain	Before	19(63.3)	6(60)	0.999
	After	15(50)	3(30)	0.464
	P value	0.219	0.250	

pain and belching were the most prevalent complaints. After interventions, the frequency of heartburn and food and acid regurgitation improved in the PPI treatment group.

In addition, we found that PPI treatments consistently benefited our IEM patients over six months, whereas surgical procedures appeared to have a less consistent effect in short-term follow-up.

Furthermore, in the PPI group, the severity of heartburn, dysphagia, food and acid regurgitation and chest pain decreased significantly, while in the surgical treatment group, the severity of dysphagia decreased significantly. These results demonstrated that PPI treatments were significantly more effective than surgical procedures for IEM patients. Additional research is required to identify differences in outcomes.

The clinical characteristics of IEM have been the subject of previous studies. Gyawali et al evaluated the symptoms of IEM patients and found that higher esophageal reflux and dysphagia are the most prevalent symptoms. Furthermore, HRM has been evidenced as one of the best diagnostic tools for IEM (10). Moreover, Mello et al conducted a study that analyzed the data of 68 IEM patients. They reported that dysphagia, heartburn, food and acid reflux and belching are the most prevalent symptoms in patients with a higher distribution at night (18). Our study's findings corroborated these results (10,18). The current study observed that dysphagia, heartburn, food and acid regurgitation and belching were the most prevalent clinical symptoms in IEM patients.

Meanwhile, Abdel Jalil et al conducted a review study of IEM diagnostic and treatment strategies. Based on their findings, more than half of IEM patients with dysphagia had defective bolus transit on multichannel intraluminal impedance testing. This could be a valuable diagnostic technique for IEM. In addition, they noted that the treatment of IEM could be difficult due to the dearth of agents that have a definite effect on esophageal function (8). Based on our research, HRM was conducted to diagnose IEM and both PPI and surgical treatments significantly alleviated patients' symptoms. We observed greater patient symptom relief with PPIs in this cohort compared to surgical procedures, which was the key finding of our study.

Recently, in the study by Jandee et al, the previous reports on IEM treatments were re-examined. The treatment by PPIs were reported to be effective but could not alter the esophagus's motility (19). In addition, there are contradictory reports regarding alleviating patient symptoms with PPI in IEM. While Munitiz et al reported that successful PPI treatments might correct esophagus motility (20), Sandhu et al demonstrated that PPI treatments have no definitive effects (21). These data are not completely consistent with our results (20,21). We

Table 5. Comparison of severity and recurrence of symptoms before and after treatment in patients with IEM

Variable Symptom	Time of treatment	Severity (0-10)			Weekly frequency		
		Surgery	PPI	P value	Surgery	PPI	P value
Heartburn, Mean (SD)	Before	9.75 (0.46)	9.85 (0.36)	0.709	6.75 (0.70)	6.80 (0.61)	0.940
	After	6.5 (1)	4.33 (2.38)	0.133	7.25 (1.89)	6.75 (1.42)	0.862
	P value	0.066	0.007		0.999	0.915	
Dysphagia, Mean (SD)	Before	9.8 (0.44)	9.68 (0.47)	0.694	6.80 (0.44)	6.23 (1.79)	0.976
	After	3.8 (4.23)	2.9 (3.29)	0.713	5.40 (2.19)	3.38 (2.50)	0.117
	P value	0.042	<0.001		0.157	0.011	
Food and acid regurgitation, Mean (SD)	Before	9.83 (0.4)	9.75 (0.44)	0.709	6.83 (0.40)	6.50 (1.31)	0.976
	After	6.25 (1.89)	5.5 (1.31)	0.599	6.75 (0.50)	3.17 (2.25)	0.020
	P value	0.109	0.007		0.317	0.017	
Chest pain, Mean (SD)	Before	9.83 (0.4)	9.84 (0.37)	0.975	5.67 (5.16)	6.47 (1.42)	0.514
	After	7.2 (1.64)	6.38 (1.98)	0.503	4.60 (2.30)	3.92 (2.43)	0.566
	P value	0.102	0.027		0.317	0.116	

Table 6. Comparison of demographic characteristics and in patients with IEM and achalasia

Variable	Symptoms		P value
	IEM (n= 40)	Achalasia (n= 100)	
Age (year), Mean (SD)	47.35 (14.45)	43.48 (8.76)	0.120*
Disease duration (year), Mean (SD)	6.33 (5.58)	1.19 (0.30)	<0.001*
Gender (male), No. (%)	17 (42.5)	63 (63)	0.027**
Dysphagia, No. (%)	27 (67.5)	96 (96)	<0.001**
Heartburn, No. (%)	25 (62.5)	38 (38)	0.008**
Food and acid regurgitation, No. (%)	26 (65)	83 (83)	0.020**
Cough, No. (%)	9 (22.5)	25 (25)	0.755**

*Independent *t* test, ** Chi-square test.

hypothesize that these differences may be attributable to differences in study populations and patient characteristics.

Another significant aspect of the current study was comparing data from 40 IEM patients with 100 achalasia patients. The inability of smooth muscle fibers to relax is the cause of esophageal achalasia, which can cause the LES to remain closed. According to the majority of histopathologic studies, the primary morphologic feature of achalasia is the depletion or absence of ganglion cells in the myenteric plexus (22). According to the available data, symptoms' duration in IEM patients were significantly longer than in achalasia. We observed that most achalasia patients were male, with a higher prevalence of dysphagia, food and acid regurgitation and a lower incidence of heartburn than IEM patients. These data may be useful for providing epidemiologic information on these diseases.

Conclusion

The most common clinical manifestations of IEM were dysphagia, heartburn, regurgitation of food and acid, belching and chest pain. Compared to surgical treatment, treatment with PPI yielded more significant improvements. These findings may have clinical significance. However, further research with larger populations is required.

Limitations of the study

Our study was limited by population size and the fact that it was performed in a single center. Large-scale, multi-centric studies are recommended.

Authors' contribution

Conceptualization: MS.
Methodology: MS, PAS.
Validation: ET.
Formal analysis: AA.
Investigation: AA.
Resources: AA.
Data curation: MS.
Writing—original draft preparation: AA.
Writing—review and editing: AA, MM.
Visualization: PAS.
Supervision: MS.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The study protocol was approved by the Research Committee of Isfahan University of Medical Sciences and the Ethics committee has confirmed it (Ethical code #IR.MUI.MED.RED.1399.1114). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from internal medicine residency thesis of Amir Aria at this university (Thesis #399639). Besides, ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

Funding/Support

None.

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