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Prevalence of Different Types of Primary Esophageal Motility Disorders and Their Associated Factors in Patients Referring to Shariati Hospital during 2018-2019

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ABSTRACT

BACKGROUND:
Esophageal motility disorders (EMDs) are common in patients with dysphagia and are effectively diagnosed with high-resolution manometry (HREM). In this study, we aimed to evaluate the prevalence of different types of primary EMDs in patients referred for HREM and to further investigate the factors associated with EMDs.

METHODS:
In this cross-sectional study, all patients referred to the endoscopy section of Shariati Hospital during 2018-2019 (279 patients) were subjected to HREM and were evaluated according to their diagnosis, and the effect of each factor and each symptom on motility disorders was investigated.

RESULTS:
84.5% (235) of the participants were diagnosed with at least one esophageal motility disorder; of them, achalasia was the most common form (52.6%). None of the predictive factors showed a statistically significant correlation with EMDs. However, regarding the symptoms, regurgitation and nocturnal cough were significantly more common in patients with EMD ($P=0.001$ and 0.009, respectively).

CONCLUSION:
This study demonstrates the high prevalence of EMDs in patients undergoing manometry. None of the factors studied, such as age, sex, diabetes, hypothyroidism, smoking, and alcohol and opium consumption, had a statistically significant correlation with EMDs.

KEYWORDS:
Achalasia; Esophageal motility disorders; Manometry; Risk factors

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INTRODUCTION

The esophagus is a tubular structure consisting of a two-layer combination of striated and smooth muscles. The coordinated contraction of the esophageal muscles organizes the peristalsis, which pushes the food content through the

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esophagus into the stomach. The proximal and distal parts of the esophagus contain two sphincters, the upper esophageal sphincter (UES) and the lower esophageal sphincter (LES).[1] Any disturbance in the coordination of peristalsis or UES and LES function leads to a spectrum of disorders known as esophageal motility disorders (EMDs).[2] EMDs can be a consequence of primary esophageal disease or secondary to other systemic diseases.[3] EMDs cause various symptoms such as dysphagia, retrosternal pain or discomfort, regurgitation, bolus obstruction, hoarseness, chronic cough, and weight loss.[4] In the past, conventional manometry was known for six decades as the gold standard diagnostic method for EMDs. However, the development of high-resolution esophageal manometry (HREM) allowed for improved pressure resolution and more sensitive objective measurements, resulting in a more accurate assessment of EMDs.[5-8] HREM has largely replaced conventional manometry due to its higher diagnostic accuracy and 50% shorter intervention time.[5,9] The last updated version (version 3.0) of the Chicago Classification of Esophageal Motility Disorders introduced a hierarchical approach to interpret manometric findings and to facilitate the diagnosis of EMDs.[7,10,11] The key metrics of Chicago Classification are integrated relaxation pressure (IRP), distal contractile integral (DCI), and distal latency (DL).[4] The treatment of EMDs currently includes medical and endoscopic therapies and rarely surgical intervention in more severe cases that do not respond to first-line treatment.[12,13] Based on the Chicago Classification version 3.0, frequent EMDs include disturbances of the outflow of the esophagogastric junction (achalasia with minimal esophageal pressure (type I, classical), achalasia with esophageal compression (type II), achalasia with spasm (type III), and obstruction of the outflow of the esophagogastric junction), major disorders of peristalsis (distal or diffuse esophageal spasm (DES), hypercontractile esophagus, and lack of contractility) and minor disorders of peristalsis (ineffective esophageal motility and fragmented peristalsis).[3,4,7,14,15]

Achalasia is a primary esophageal motility disorder caused by the failure of complete relaxation of LES during swallowing and ineffective peristalsis. The exact mechanism of achalasia is unknown, but it is believed that this disorder is caused by the denervation of the smooth muscles of the esophagus. Achalasia is demonstrated by the bird beak-like sign in barium swallowing study and by aperistalsis and elevated IRP of LES in classic manometry. DES is associated with intermittent chest pain and dysphagia. Pain associated with DES is a consequence of abnormal simultaneous contractions of the esophageal body (a normal median IRP = 20% premature contractions and DL = 4.5 seconds) and usually occurs when taking very cold or very warm foods. A pattern of irregular simultaneous contractions of the esophageal body is the classic anomaly observed in esophageal manometry in patients with DES. The corkscrew or pink pearl appearance of the esophageal body is also usually observed in a barium swallow study.[12]

Abnormal LES relaxation (IRP 15 mmHg) with normal or weak peristalsis leads to obstruction of the esophagogastric outflow. A hypercontractile esophagus or jackhammer esophagus is characterized by a DCI 8000 mmHg/s/cm in at least 20% of swallows and a normal DL, while a lack of contractility is described by an aperistalsis in the presence of a normal LES relaxation (IRP 10 mmHg). Minor peristaltic disturbances, ineffective esophageal motility, and fragmented peristalsis cause >= 50% ineffective swallowing and >= 50% fragmented contractions; however, in contrast to ineffective esophageal motility, fragmented peristalsis has a normal contractile force.[15]

The etiology and pathophysiology of primary EMDs (with the exception of achalasia) have remained unclear.[1] It is hypothesized that clinical features such as advanced age, obesity, gastroesophageal reflux disease, hypercholesterolemia, diabetes, and a history of alcohol and tobacco consumption are also possible predictive factors for EMDs and play a role in the patients' response to treatment.[2,13,16,17] Although primary EMDs are common in patients undergoing HREM, few studies have investigated the prevalence of EMDs and possible associated risk factors. In this study, we aimed to identify the prevalence of EMDs and potential risk factors. We also evaluated the association between the participants' symptoms such as dysphagia to solids, liquids, regurgitation, and nocturnal cough and their diagnoses in an attempt to identify the symptoms that were strong predictors of motility disorders in the patients' history.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of Tehran University of Medical Sciences (approval

number IR.TUMS. MEDICINE. REC.1399.012) and has been conducted according to the Helsinki Declaration principles of 1964 and its subsequent amendments. After a full explanation of the study objectives, methods, benefits, and risks, written informed consent was obtained from the participants.

In this cross-sectional study, we enrolled a total of 279 patients with possible EMDs referred to the manometry section of Shariati Hospital, Tehran, Iran, from 2018 to 2019. The patients complained of clinical symptoms such as dysphagia, non-cardiac chest pain, food regurgitation, retrosternal chest pain or discomfort, hoarseness, asthma, vomiting, and weight loss.

The participants were qualified for HREM analysis after a full examination, appropriate imaging studies, and upper esophagogastroscopy to rule out other differential diagnoses. Exclusion criteria were history of any malignancy, history of upper gastrointestinal tract surgery, cardiovascular disease, grade C and D esophagitis in upper endoscopy, and Barrett's esophagus in histopathological findings. All medications affecting esophageal motility, such as metoclopramide, anticholinergics, and muscle relaxants, were discontinued 5 to 7 days before the procedure. All participants were asked to complete a detailed questionnaire on age, sex, height, weight, medication, symptoms, duration of symptoms, history of weight loss, underlying diseases, history of smoking, and opiate abuse. Regarding smoking status, alcohol, and opiate consumption, a consumer was defined as an individual who used them on a weekly basis for at least six-month.

Finally, the data of demographic characteristics, clinical features, manometric data, and final diagnosis were collected retrospectively.

Statistical Analysis

The data were coded, manually entered, and statistically analyzed using SPSS software (version 20.0; IBM Corp, Armonk, NY, USA). The categorical variables were represented by descriptive statistics (frequency and percentage), while range, mean and standard deviation were used to describe continuous data. We used the Pearson's Chi-square test to analyze the categorical data and to test differences between groups with and without motility disorders to determine possible risk factors. P value < 0.05 was considered statistically significant.

RESULTS

All 279 participants were included. None of the participants met the exclusion criteria. 49.5% (138) of the participants were female, and 50.5% (141) were male. The mean age of the participants was 47.75 ± 15.09 years. The mean weight loss of the participants was 4.93 ± 6.53kg, and the mean duration of symptoms was 36.4 ± 45.6 months. The mean weight loss of the participants who were diagnosed as having motility disorders was higher (5.21 kg) than those without motility disorder (3.41 kg). The disorder with the highest mean weight loss was achalasia (6.50 kg). The most common chief complaint among the participants was dysphagia (94.6%). Also, in the previous six months, 21, 5, and 5 patients reported using cigarettes, alcohol, and opioids, respectively on a weekly basis.

In order to evaluate the association between the symptoms and motility disorders, we gave scores to symptoms such as dysphagia to liquids and solids, regurgitation, and chest pain from zero to 3 based on the frequency of symptoms (zero for never, 1 for occasionally, 2 for daily, and 3 for symptom with every meal) and compared the symptoms between the patients who had at least one motility disorder and those who had none. Regurgitation and nocturnal cough were significantly more common in patients with EMD, as presented in table 1 ($P = 0.001$ and 0.009, respectively).

We also evaluated the association between the symptoms and achalasia. Dysphagia to solids, liquids, nocturnal cough, and regurgitation were all significantly more common in achalasia as presented in table 2 (all P values were 0.000). Most of the participants diagnosed as having achalasia had dysphagia to liquids (89.11%), and the most common motility disorder among the participants with dysphagia to liquids was achalasia (60.93%).

84.5% (235) of the participants were diagnosed as having at least one esophageal motility disorder, and 15.4% (44) had no esophageal dysmotility in HREM. The prevalence of EMDs was 22.58%, 25.08%, 4.65%, 14.3%, 5.7%, 10.4%. 2.5%, and 0.70% for type 1 achalasia, type 2 achalasia, type 3 achalasia, Ineffective esophageal motility, DES, absent contractility, esophagogastric junction outflow obstruction, and fragmented peristalsis, respectively (table 3). We divided the participants into three

Table 1: Statistical analysis of data of patients with symptoms of EMD

Symptoms		EMD present 235	No EMD 44	*P* value
Dysphagia to solids	0	8	1	0.183
	1	34	12	
	2	34	7	
	3	159	24	
Dysphagia to liquids	0	51	13	0.708
	1	60	11	
	2	42	7	
	3	82	13	
Nocturnal cough		91	8	0.009
Regurgitation	0	93	31	0.001
	1	89	4	
	2	39	7	
	3	14	2	
Chest pain	0	127	27	0.455
	1	83	11	
	2	19	4	
	3	6	2	

EMD : esophageal motility disorder

Table 2: Statistical analysis of symptoms of data of patients with achalasi

Symptoms	Groups	achalasia present (n=147)	No achalasia (n=132)	*P* value
Dysphagia to solids	0	1	8	0.000
	1	15	31	
	2	22	19	
	3	109	74	
Dysphagia to liquids	0	16	48	0.000
	1	39	32	
	2	33	16	
	3	59	36	
Nocturnal cough		72	27	0.000
Regurgitation	0	38	86	0.000
	1	66	27	
	2	31	15	
	3	12	4	
Chest pain	0	86	68	0.609
	1	47	47	
	2	11	12	
	3	3	5	

EMD: esophageal motility disorder

age groups: Group 1 (<=30 years), group 2 (31-60 years), and group 3 (>=61 years). The results of the statistical analysis for EMDs considering age group, sex, diabetes, smoking, alcohol and opium consumption, hypothyroidism, and hypertension are presented in tables 4-8.

DISCUSSION

Table 3: Prevalence of each esophageal motility disorder

Type of EMD	Prevalence
Type 1 achalasia	63 (22.58%)
Type 2 achalasia	70 (25.08%)
Type 3 achalasia	13 (4.65%)
IEM	40 (14.3%)
DES	16 (5.7%)
Absent contractility	29 (10.39%)
EGJ outflow obstruction	7 (2.5%)
Fragmented peristalsis	2 (0.70%)

EMD: esophageal motility disorder
IEM: Ineffective esophageal motility
DES: Diffuse esophageal spasm
EGJ: Esophagogastric junction

Table 4: Statistical analysis of data of patients with achalasia

Factors	Achalasia present (n=147)	No achalasia (n=132)	*P* value
Diabetes	15	8	0.209
Age groups			
1	18	21	0.628
2	97	81	
3	32	30	
Sex			
Male	75	66	0.865
Female	72	66	
Smoking	12	14	0.483
Alcohol	4	3	1.000
Opium	5	3	0.726
Hypothyroidism	7	4	0.458
Hypertension	16	13	0.777

We conducted a cross-sectional study to evaluate the prevalence of EMDs and potentially associated factors that could be useful for physicians to more accurately diagnose EMDs in patients with esophageal symptoms.

In this study, achalasia was more common than non-achalasia motility disorders (IEM, DES, absent contractility, esophagogastric junction outflow obstruction, and fragmented peristalsis). This result was consistent with an HREM study in 155 patients that revealed achalasia, hypermotility disorders (DES), and hypomotility disorders (absent contractility, IEM, and fragmented peristalsis) were the most common EMDs in patients. EMDs were also not significantly related to

Table 5: Statistical analysis of data of patients with IEM

Factors	IEM present (n=40)	No IEM (n=239)	*P* value
Diabetes	1	22	0.218
Age groups	6 26 8	33 152 54	0.928
Sex			
Male	15	126	0.075
Female	25	113	
Smoking	5	21	0.554
Alcohol	1	6	1.000
Opium	3	5	0.091
Hypothyroidism	2	9	0.661
Hypertension	5	24	0.583

IEM : Ineffective esophageal motility

Table 6: Statistical analysis of data of patients with absent contractility

Factors	Absent contractility present (n=29)	No absent contractility (n=250)	*P* value
Diabetes	3	20	0.718
Age groups			
1	6	33	
2	17	161	0.545
3	6	56	
Sex			
Male	12	129	
Female	17	121	0.297
Smoking	2	24	1.000
Alcohol	0	7	1.000
Opium	0	8	1.000
Hypothyroidism	2	9	0.388
Hypertension	4	25	0.520

Table 7: Statistical analysis of data of patients with EGJ outflow obstruction

Factors	EGJ outflow obstruction present (n=7)	No EGJ outflow obstruction (n=272)	*P* value
Diabetes	2	21	0.106
Age groups	1 2 4	38 176 58	0.069
Sex Male Female	4 3	137 135	1.000
Smoking	1	25	0.500
Alcohol	0	7	1.000
Opium	0	8	1.000
Hypothyroidism	0	11	1.000
Hypertension	2	27	0.158

EGJ : Esophagogastric junction

Table 8: Statistical analysis of data of patients with DES

Factors	DES Present (n=16)	No DES (n=263)	*P* value
Diabetes	1	22	1.000
Age groups	2 9 5	37 169 57	0.670
Sex			
Male	10	131	0.324
Female	6	132	
Smoking	1	25	1.000
Alcohol	1	6	0.342
Opium	0	8	1.000
Hypothyroidism	0	11	1.000
Hypertension	1	28	1.000

DES: Diffuse esophageal spasm

age, smoking status, alcohol and opiate consumption, hypertension, and diabetes; however, a significantly higher prevalence of EMDs was discovered in male patients.[18] Another cross-sectional study by Goyal and colleagues found ineffective esophageal motility and achalasia the most common EMDs in 412 patients with esophageal symptoms.[4] Fakhre Yaseri and co-workers also reported that non-achalasia motility disorders were more common in patients with upper gastrointestinal tract symptoms.[19]

We found no significant difference between individuals with and without esophageal symptoms based on their age group ($P>0.05$ for all). Preliminary studies showed more evidence of EMDs in healthy adults over 80 years of age compared with younger healthy individuals.[16]

Another study suggested that in the older population (>60 years) with esophageal symptoms, the reduction in UES pressure, distal esophageal motility, and peristaltic velocity might be correlated with esophageal symptoms using HREM.[20] Nevertheless, Jadiri and colleagues reported no significant difference between young and old patients with dysphagia.[21]

Furthermore, we found no correlation between smoking status and alcohol and opiate consumption and EMDs prevalence ($P>0.05$). In contrast, a retrospective study in chronic opioid users, when opioid medication was discontinued in half of the patients at least 24 hours before HREM, showed a significantly higher prevalence of esophagogastric junction outflow obstruction, longer integrated relaxation pressure, higher resting LES and lower DL.[22] Meanwhile, Bhandarkar and colleagues performed conventional manometry in 36 patients to investigate the effects of acute and long-term tobacco use on esophageal motility and LES pressure. This study found no significant relationship between the LES baseline pressure and velocity, amplitude, and duration of contraction at the distal esophageal body in tobacco users compared with non-tobacco users.[23]

We investigated the association between EMDs and underlying diseases such as hypothyroidism, diabetes, and hypertension and found no significant correlation. Unlike our result, Emami and others showed a possible association of achalasia and thyroid diseases such as hypothyroidism (13.3%), hyperthyroidism (6.7%), and non-functional thyroid nodule (3.3%) among their 30 patients with achalasia.[24] In a previous study of patients with and without diabetes with esophageal symptoms, 60% of patients with diabetes had EMDs and lower median values for DCI, CFV, and IRP compared with patients without diabetes, indicating higher gastric pressure and poor esophageal clearance in patients with diabetes.[25] Another study also claimed the presence of EMDs in almost half of the diabetic patients with dysphagia. Failed swallow attempts were more common in patients with diabetes and dysphagia, and those who received insulin treatment had a greater chance of swallowing problems and weakness compared with patients without diabetes.[26, 27]

Limitations

There were some limitations in this study. First, our study was conducted in a single tertiary center with a population of mostly referred patients, and therefore our results could not be generalized to a normal population. Second, it was a retrospective cross-sectional study and did not show any definitive causal relationships between the predictors and EMDs.

CONCLUSION

We found a high prevalence of EMDs in patients undergoing HREM, confirming the important role of HREM in the diagnosis of EMDs. Achalasia was the most common motility disorder, followed by IEM and absent contractility. However, none of the predictive factors evaluated, including age, sex, history of diabetes, hypothyroidism, smoking, alcohol, and opium consumption, showed a statistically significant correlation with EMDs. Evaluation of the association between the participants' symptoms and their diagnoses showed a correlation between nocturnal cough and regurgitation and motility disorders and a significant association between achalasia and nocturnal cough, regurgitation, and dysphagia to solids and liquids. These findings highlight the importance of these symptoms in patient's history as possible predictors and tools to aid us in suspecting and diagnosing EMDs.

ETHICAL APPROVAL

There is nothing to be declared.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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