Original Article

Clinical, Endoscopic, and Radiologic Features of Three Subtypes of Achalasia, Classified Using High-Resolution Manometry

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ABSTRACT

Background/Aims: High-resolution manometry (HRM) has improved the accuracy of manometry in detecting achalasia and determining its subtypes. However, the correlation of achalasia subtypes with clinical, endoscopic, and radiologic findings has not been assessed. We aimed to evaluate and compare the clinical, endoscopic, and fluoroscopy findings associated with three subtypes of achalasia using HRM. **Patients and Methods:** The retrospective clinical data, HRM, endoscopy, and radiologic findings were obtained from the medical records of untreated achalasia patients. **Results:** From 2011 to 2013, 374 patients underwent HRM. Fifty-two patients (14%) were diagnosed with achalasia, but only 32 (8.5%) of these patients had not received treatment and were therefore included in this study. The endoscopy results were normal in 28% of the patients, and a barium swallow was inconclusive in 31% of the achalasia patients. Ten patients (31%) were classified as having type I achalasia, 17 (53%) were classified as type II, and 5 (16%) were classified as type III. Among the three subtypes, type I patients were on average the youngest and had the longest history of dysphagia, mildest chest pain, most significant weight loss, and most dilated esophagus with residual food. Chest pain was most common in type III patients, and frequently had normal fluoroscopic and endoscopic results. **Conclusion:** The clinical, radiologic, and endoscopic findings were not significantly different between patients with type I and type II untreated achalasia. Type III patients had the most severe symptoms and were the most difficult to diagnose based on varied clinical, radiologic, and endoscopic findings.

Key Words: Achalasia, Chicago classification, high-resolution manometry

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Achalasia is a relatively rare esophageal motility disorder characterized by impaired gastroesophageal junction relaxation and the absence of normally propagated peristaltic contractions without a structural explanation.[1] High-resolution esophageal pressure topography, a revolutionary technology combining high-resolution manometry (HRM) and pressure topography plotting in the form of Clouse plots, was introduced in the year 2000 for the clinical evaluation of esophageal motility.[2] Based on the presence of contractile activity and pressurization, Pandolfino *et al.*[3] described three distinct subtypes of achalasia using HRM. The differentiating criteria were recently revised by the international HRM working group.[4] *Type I achalasia* (classic achalasia) is defined as having a mean integrated relaxation pressure (IRP) greater than the upper limit of normal with 100% failed peristalsis. *Type II achalasia* (compressive achalasia) is achalasia with esophageal compression with a mean IRP greater than the upper limit of normal with no normal peristalsis and a panesophageal pressurization with at least 20% of swallows. *Type III achalasia* (spastic achalasia) is characterized by a mean IRP greater than the upper limit of normal, no normal peristalsis, and preserved fragments of distal peristalsis or premature (spastic) contractions with at least 20% of swallows.

Almost all untreated achalasia patients present with moderate-to-severe dysphagia for both solids and liquids; however, it is unclear whether chest pain, heartburn, and regurgitation are more common in certain subtypes of achalasia. Recently, Lee *et al.*[5] reported no statistical difference in symptoms of dysphagia, chest pain, regurgitation, and weight loss among the three subtypes of achalasia in a

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Korean population but demonstrated that patients with type I achalasia showed marked dilatation and food stasis, whereas patients with type II or III achalasia had near-normal upper gastrointestinal endoscopy results. Radiologic esophageal emptying studies have shown that esophageal emptying in patients with achalasia is incomplete,[6] but the diagnostic accuracy of radiologic abnormality in the three subtypes of achalasia is not known.

The primary role of upper gastrointestinal endoscopy in diagnosing achalasia is to rule out a mechanical obstruction or pseudoachalasia,[7] which can mimic achalasia both clinically and radiologically. However, endoscopic findings in patients with achalasia may range from normal to a puckered gastroesophageal junction (GEJ) with mild resistance and tortuous dilated sigmoid esophagus with retained food and secretions. Thus, endoscopic findings for a referred patient require a careful evaluation of the GEJ and gastric cardia on a retroflexed view for all subtypes of achalasia. Thus, the aim of this study was to evaluate and compare the clinical features, endoscopic findings, and radiologic changes found in patients with the three subtypes of achalasia using HRM.

PATIENTS AND METHODS

Patients

The medical records of all adult patients (>16 years of age) who underwent HRM (*n* = 374) at King Faisal Specialist Hospital and Research Center (KFSH and RC) from June 2011 to June 2013 were searched to identify patients who met the diagnostic criteria of achalasia. This cross-sectional retrospective study protocol was approved by the research advisory council and the ethics committee of our institution. Written informed consent was obtained as a routine practice before the esophageal HRM. The presence of dysphagia, heartburn, chest pain, regurgitation, vomiting, and/or weight loss was recorded, noting the length of time from the onset of the symptoms to the time of the patient's first visit to the hospital.

Using a recognized and established[4] HRM diagnostic criterion, 52 (14%) consecutive patients were diagnosed with achalasia. Twenty (5.5%) achalasia patients were excluded from the study because they had received endoscopic (endoscopic balloon dilation or botulinum toxin injection) or surgical (Heller's myotomy) treatment at a referring hospital in the past. The patients with a past history of previous foregut surgery, bariatric surgery, or Nissen fundoplication were also excluded. The remaining 32 patients (8.5%) in the untreated achalasia cohort were included in this study. The clinical features, HRM data, endoscopic findings, and radiologic assessments were obtained from each patient's medical records for retrospective review.

Timed barium esophagram

A timed barium esophagram was performed with the patient in the upright position to obtain frontal spot films of the esophagus at baseline and at 1, 2, and 5 min after ingestion of 200 mL (sometimes limited by patient tolerance) of low-density (45% weight to volume) barium sulfate. The maximal esophageal diameter was measured at the barium–air interface in the standard anteroposterior image along the esophageal body perpendicular to the axial plane of the esophagus. Significant esophageal dilatation was considered when the diameter was >6 cm. The typical "bird's beak" appearance was defined as a smooth tapering of the distal esophagus with minimal lower esophageal sphincter (LES) opening and proximal aperistalsis esophageal dilation, also called a "rat tail appearance."

Upper gastrointestinal endoscopy

An upper gastrointestinal endoscopy was performed by the authors (MQK, HA, FA, and KA) after the patient had fasted for 12 h to check the amount of food residue, the degree of esophageal dilatation, reflux esophagitis, esophageal candidiasis, and specifically to rule out pseudoachalasia.

Equipment and HRM protocol

A solid-state HRM was performed after the patient had fasted for at least 12 h (some patients had significant residual food and required 48 h of restriction to a liquid diet to avoid any coiling of the catheter in the esophagus). HRM was performed with a 4.2-mm-diameter catheter (Sandhill Scientific Inc.,® Highlands Ranch, CO, USA), 32 solid-state pressure sensors placed 1 cm apart, four dual impedance sensors placed 5 cm apart, and the patient in the semi-recumbent position. Esophageal body function was assessed through 10 saline (5 cc) swallows at 20–30 s intervals. The HRM tracings were analyzed using Bio VIEW analysis software (Version M, Sandhill Scientific Inc.). The pressure topography parameters were analyzed using the Chicago classifications for liquid swallows. Achalasia was diagnosed as an impaired LES relaxation on deglutition (mean IRP ≥ 15 mmHg) and the absence of peristalsis of the esophageal body. The distal esophageal amplitude (the average of contraction amplitude 5 and 10 cm above the LES), IRP (mean of the lowest relaxation pressures measured within the LES for a minimum of 4 s during a swallow), and mean LES resting pressure (end expiratory) were recorded.

Statistical analyses

The data were recorded initially in a Microsoft Excel worksheet and then transferred to IBM SPSS (version 20, SPSS Inc., Chicago, IL, USA). The mean ± SD is presented for each continuous variable, and the number and percentage (n [%]) are shown for each categorical variable. To determine whether the differences between variables were significant, a parametric analysis of variance statistical analysis was used for the normal distribution variables and a nonparametric Kruskal–Wallis *post hoc* test was used for the non-normal distribution variables. For categorical variables, the Pearson Chi-square test or Fisher's exact test was used. A *P* value less than or equal to 0.05 was considered significant.

RESULTS

The mean age of the patients was 46.8 ± 18.9 years with a 15:17 ratio of males to females. Twenty-seven (84%) of the 32 patients had used proton pump inhibitors (PPIs) prior to their first visit to our institution, believing that gastro-esophageal reflux disease (GERD) was the cause of their heartburn and regurgitation. The type I patients were younger in age than the type II or III patients, whereas type III patients were typically older than patients with types I or II. In our cohort, 17 patients (53%) had type II achalasia, 10 (31%) had type I, and 5 (16%) had type III. The mean duration of symptoms was 3.5 years with type I patients having the longest mean duration (5.9 years). The type III patients reported having prominent chest pain, but none of them had experienced weight loss [Table 1]. Vomiting was common in type III patients but infrequent in type I patients. In the cohort of type I achalasia patients, weight loss was the most common symptom and chest pain the least common symptom. Chest pain was intriguingly more common in type II achalasia patients than type I patients [Figure 1].

All 32 patients underwent an upper gastrointestinal endoscopy to rule out secondary achalasia or pseudoachalasia. The Esophago-gastro-duodenoscopy (EGD) results [Table 2] did not show any significant abnormalities in 28% of the achalasia patients, which included the majority of the type III patients (80%). In spite of the overnight fast, 43.7% of the achalasia patients had residual food in their esophagus; in contrast, only 20% of the type III patients had residual food. Esophageal candidiasis was found in only two cases and reflux esophagitis, in three cases.

The barium swallow studies suggested a diagnosis of achalasia in 68.7% of the achalasia cases confirmed by HRM. Surprisingly, the results of the barium swallow tests suggested either GERD or nonspecific esophageal motility disorders but not achalasia in 80% of the type III patients. The barium swallow studies showed the classic radiologic sign of a bird's beak appearance of the distal esophagus in 59.3% of the total cases. Esophageal dilatation (>6 cm) due to the narrowing of the LES was evident in all of the patients with type I achalasia but only observed in 76.4% of the type II achalasia patients. The bird's beak appearance, esophageal dilatation, and food residue were not apparent in any of the type III achalasia patients [Table 2].

Characteristic HRM pictures of each subtype of achalasia are shown in Figure 2. The LES resting pressure was between 25 and 42 mmHg in 13 patients (40.6%) and was > 45 mmHg in 19 patients (59.3%). The type III achalasia patients had the highest mean LES resting pressure (76.9 mmHg). A high mean IRP (>15 mmHg) was noted in all of the achalasia patients; the highest mean IRP was observed in the type I patients, and the lowest mean IRP was found in the type III patients. The mean distal esophageal amplitude (DEA) was higher in type II patients than in type I patients; however, in type III patients, a stronger distal esophageal contraction led to the highest amplitude during 10 wet swallows [Table 3].

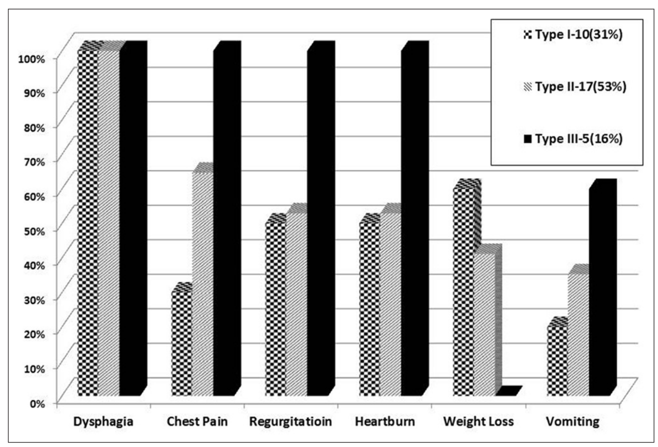

Figure 1: Comparison of various presenting symptoms among the three subtypes of achalasia

Table 1: Baseline clinical characteristics of the three subtypes of achalasia

Basic characteristics	Total	Chicago classification			*P*
		Type I (*n*=10)	Type II (*n*=17)	Type III (*n*=5)	
Age (mean±SD)	46.89±18.90	34.83±12.24	49.07±20.01	54±17.93	0.172
Gender (M: F)	15:17	3:7	9:8	3:2	0.217
Duration of symptoms in years (mean±SD)	3.51±1.90	5.90±0.72	3.28±2.00	2.1±2.0	0.084
Dysphagia	32 (100%)	10/10 (100%)	17/17 (100%)	5/5 (100%)	
Chest pain	19/32 (59.4%)	3/10 (30%)	11/17 (64.7%)	5/5 (100%)	0.019
Regurgitation	17/32 (53.1%)	5/10 (50%)	9/17 (52.9%)	3/5 (60%)	0.512
Heartburn	17/32 (53.1%)	5/10 (50%)	9/17 (52.9%)	3/5 (60%)	0.423
Weight loss	13/32 (40.6%)	6/10 (60%)	7/17 (41.1%)	None	0.111
Vomiting	11/32 (34.4%)	2/10 (20%)	6/17 (35.3%)	3/5 (60%)	0.155

Table 2: EGD and barium swallow study in the three subtypes of achalasia

Procedure and results	Total	Chicago classification			*P*
		Type I	Type II	Type III	
No. of patients	32	10	17	5	-
Upper GI endoscopy (*n* (%))					
Normal esophagus	9 (28.1)	1 (10)	4 (23.5)	4 (80)	0.143
Food residue	14 (43.7)	6 (60)	7 (41.1)	1 (20)	0.638
High LES resistance	22 (68.8)	6 (60)	13 (76.5)	3 (60)	0.630
Esophagitis	3 (9.4)	0 (0)	2 (11.8)	1 (20)	0.395
Barium swallow (*n* (%))					
Barium study suggestive of achalasia	22 (68.7)	8 (80.0)	13 (76.4)	1 (20.0)	0.004
Bird beak appearance	19 (59.3)	8 (80.0)	11 (64.7)	None	0.062
Esophageal dilatation	23 (71.8)	10 (100%)	13 (76.4)	None	0.001
Food residue	13 (40.6)	8 (80.0)	5 (29.4)	None	0.437

EGD: Esophago-gastro-duodenoscopy, LES: Lower esophageal sphincter, GI: Gastrointestinal

Table 3: High-resolution manometry values in three subtypes of achalasia patients

HRM data values (mmHg)	Total	Chicago classification (mean±SD)			*P*
		Type I (*n*=10)	Type II (*n*=17)	Type III (*n*=5)	
LES resting pressure	56.07±30.19	48.07±16.45	52.78±22.67	76.86±55.47	0.420
Integrated relaxation pressure	28.23±15.87	32.93±10.98	27.50±14.86	25.04±24.85	0.532
Distal esophageal amplitude	49.25±50.59	26.17±14.80	33.29±18.58	131.20±73.09	<0.001

LES: Lower esophageal sphincter, HRM: High-resolution manometry

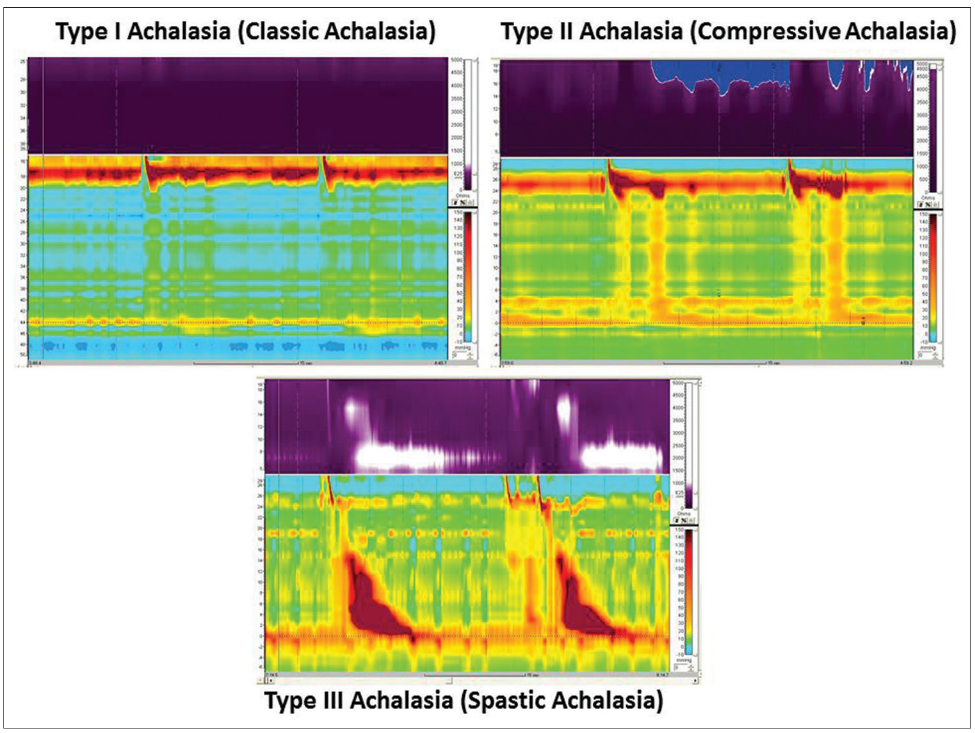

Figure 2: Three subtypes of achalasia diagnosed by high-resolution impedance manometry

DISCUSSION

Using the HRM-based Chicago classification proposed in 2008, achalasia can be categorized into three subtypes that are distinct with respect to their response to treatment;[8] however, to the best of our knowledge, insufficient data exist to correlate clinical characteristics, endoscopic profiles, and radiologic changes with these achalasia subtypes. Lee *et al*.[5] performed a similar study to ours in which 40 of 55 Korean patients were diagnosed with achalasia using water-perfused conventional manometry (CM) with a sleeve sensor; HRM was not available in their center prior to 2011. However, HRM offers improved sensitivity and greater accuracy in detecting achalasia compared with CM.[9] In addition, the classification of achalasia subtypes based on HRM is more precise than the CM-based classification, and the HRM-based categorization correlates with treatment responsiveness. Thus, HRM technology was intended to replace rather than complement CM.

In the present study, type II achalasia was reported to be predominant in our Saudi achalasia cohort. Type II achalasia has been reported to be the most common type of achalasia in other studies as well,[5,9,10] although Pratap *et al*.[11] found types I and II to occur with the same frequency in an Indian population using water-perfused HRM.

A recent European study[12] described some correlation of symptoms with the manometric subtypes of achalasia using a pneumohydraulic perfusion system and a 6- to 10-channel esophageal manometry catheter with a sleeve sensor incorporated at the distal end. They reported that a significant greater percentage of type III achalasia patients complained of chest pain than type I or type II patients; other symptoms (dysphagia, regurgitation, and weight loss) were similar among all three achalasia groups. In agreement with this European report, in our cohort, chest pain was the predominant symptom in type III achalasia (occurred in 100% of type III patients), was less common in type II, and least common in type I patients. Salvador *et al*.[13] confirmed the predictive value of high chest pain scores and spastic contractions with respect to a negative outcome after surgery. Both of these factors are most likely related (chest pain was reported by 80% of type III achalasia patients), although exactly how they are related to various achalasia subtypes remains to be determined. It was hypothesized that chest pain is evoked mainly by high-amplitude esophageal contractions rather than esophageal stretching secondary to dilatation. Consistent with this hypothesis, we found that of the three achalasia subtypes, type III patients had the highest mean DEA and no significant esophageal dilatation (>6 cm), whereas substantial esophageal dilatation, complete aperistalsis and greater amounts of food residue were more evident in type I patients.

In the present study, the average length of time from the onset of symptoms until diagnosis was 3.7 years, shorter than the 5.2 years reported in a French study[14] and longer than the 2 years reported by a Scottish study.[15] These differences could be explained by referral bias. In particular, the diagnostic delay in our study was very long (5.9 years) for patients with type I achalasia, most likely due to the slow onset of symptoms. In the Scottish study, using water-perfused CM, 6.3% of the patients referred for esophageal manometry were diagnosed with achalasia. In contrast, at our center, 14% patients referred for HRM were diagnosed as having achalasia, perhaps due to the higher diagnostic accuracy of HRM as compared with CM.

Achalasia patients frequently report having experienced heartburn, chest pain, and regurgitation, all thought to be related to gastroesophageal reflux (GER). However, in untreated achalasia patients, these symptoms are believed to be caused by the stasis and fermentation of residual food in the esophagus secondary to the impaired esophageal emptying, rather than by real GER.[16] Approximately 86% of our referred patients were taking PPIs to suppress their GER symptoms. In 80% of the type III achalasia cases, a barium swallow did not result in a diagnosis of achalasia, and a diagnosis of either GERD or a nonspecific esophageal motility disorder was made. One-fourth of our untreated achalasia patients had normal EGD findings. These findings demonstrate that suspected achalasia patients may present with GERD-like symptoms and have inconclusive barium swallow and endoscopy results, especially patients with type III achalasia, thereby delaying diagnosis and treatment. If HRM is not performed early on, there is a risk that some patients may be advised to undergo a fundoplication after responding poorly to proton pump inhibitors (PPIs) and being labeled as refractory GERD. Therefore, we believe that even without endoscopic or radiologic evidence of achalasia, HRM testing before antireflux surgery should be highly recommended and may be especially helpful in ruling out type III achalasia, in which symptoms suggest a GERD diagnosis.

Although frequently observed in achalasia patients, a high resting LES pressure does not establish a diagnosis. In our series, the LES resting pressure was normal (<42 mmHg) in 45% of the patients. A common misconception is that the LES is hypertensive in all patients with esophageal achalasia.[17] Our findings contradict this general belief; only 55% of our untreated achalasia patients had a hypertensive LES (>42 mmHg). Fisichella *et al*.[18] reported hypotensive LES (<14 mmHg) in 25% of achalasia patients, among whom esophageal pressure was measured by water-perfused conventional manometry and the normal range for LES-resting pressure was found to be limited (14–24 mmHg). In contrast, using HRM, Jee *et al*.[19] found a normal LES pressure in up to 45% of achalasia patients and concluded that a low LES pressure is never observed in patients with untreated achalasia. In the present study, none of the achalasia patients had an LES pressure <25 mmHg (normal range 11–42 mmHg), and the type III patients had the highest LES pressures among the three subtypes, as reported earlier,[20] with maximal peristaltic contractions of the lower esophagus.

A weakness of the study is its retrospective nature and relatively small number of untreated achalasia cases. The results of the barium swallow and subjective endoscopy were inconsistent, most likely because the procedures were performed and reported by different individuals.

In summary, in our group of untreated achalasia patients, type II achalasia was the most common type, followed by type I and then type III. Barium swallow testing and endoscopy had low sensitivity in diagnosing achalasia and did not permit differentiation between the various subtypes. The diagnosis of type III achalasia was often difficult and delayed due to vague GERD-like symptoms, unclear endoscopic findings and nonspecific radiologic images. However, barium swallow testing played a complementary role in the diagnosis of type I and type II achalasia, whereas EGD had a negligible role in differentiating various achalasia subtypes but was still required to rule out pseudoachalasia.

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