

ORIGINAL PAPERS

Hypercontractile esophagus: Clinical context and motors findings in high resolution manometry

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ABSTRACT

Background: Hypercontractile esophagus (HE) is a primary hypercontractile disorder of the esophageal musculature not frequently seen in the general population. It is characterized by the presence of at least one contraction with a very high amplitude and duration (DCI > 8,000 mmHg/s/cm) in patients with esophageal symptoms. The aim of our study was to assess the clinical context and manometric characteristics in patients with HE using high-resolution manometry (HRM).

Methods: We thoroughly reviewed the clinical features and manometric findings of a total of 720 patients with esophageal symptoms that were attended in the Department of Gastroenterology of our hospital between June 2011 and June 2013.

Results: We found seven patients that met criteria for HE according to the Chicago Classification (2012). All of the patients were women (100%). Mean age was 64 years old. Most frequent symptoms were: Chest pain, dysphagia and heartburn. In one patient (14%) the HE was related to a gastroesophageal reflux disease (GERD) and gastroesophageal junction (GEJ) outflow obstruction. Three patients (43%) had more than one hypercontractile contraction in the study. Four patient (57%) had multipeaked pattern (Jackhammer esophagus) and two of them were synchronized with respiration. Two patients (29%) were diagnosed with hiatus hernias. Integrated relaxation pressure (IRP) was not higher in hypercontractile contractions than in normal contractions. Only one patient presented a slight alteration of the relaxation (IRP-4s = 15 mmHg) with normal peristalsis, GEJ outflow obstruction and not multipeaked pattern. One patient presented pathological acid exposure (PAE) in 24-hours pH-metry.

Conclusions: HE is a rare disorder and HRM is essential for its correct diagnosis and characterization. The treatment of HE should achieve the disappearance or at least improvement of the patient's symptoms and avoid unnecessary diagnostic testing.

Key words: Hypercontractile esophagus. Jackhammer esophagus. Esophageal motility disorders. High-resolution manometry. Chest pain. Dysphagia.

BACKGROUND

The motor activity of the esophagus is coordinated by the autonomic and central nervous system and by the intrinsic myogenic activity of the esophageal musculature. Hypertensive motility alterations are a heterogeneous entity. They can be produced by primary hyperexcitability of the esophageal muscles caused by a neuromuscular disorder, by hypertrophy of the muscle cells or secondary to other situations. The presence of asynchrony between circular and longitudinal esophageal muscle fibers has also been described, and could be related to excessive cholinergic stimulation (1).

Esophageal manometry tests are the best diagnostic tool for the study of the esophageal motility and the motor activity of the lower esophageal sphincter (LES). With the development of high-resolution manometry (HRM) our knowledge of the physiological and pathophysiological mechanisms of both normal motility and motor disorders has improved a lot. This provides better descriptions of the motor esophageal disorders (2). HRM combined with impedance is a more exact technique to measure variability of pressures throughout the esophagus and sphincters, and to measure bolus progression (3).

The Chicago's International Classification of esophageal motility is based on the results of HRM studies and focused on the lower esophageal sphincter (LES) and esophageal body function parameters obtained from HRM studies, including new parameters such as: contractile front velocity (CFV), the basal LES pressure, integrated relaxation pressure (IRP) and distal contractile integral (DCI). This last index is defined as the contraction volume measure and is estimated multiplying the length of distal segment times the contraction duration, times the integrated pressure amplitude; and the result is expressed as mmHg/s/cm (3-5).

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In Chicago's Classification "motility disorders" are subdivided in distal esophageal spasm (normal average IRP-4s and $\geq 20\%$ premature contractions), hypercontractile esophagus (HE) (at least one swallowing presenting with DCI $> 8,000$ mmHg/s/cm with one peak or multipeaked contractions) and absent peristalsis (normal average IRP, 100% of swallows with failed peristalsis). Hypertensive peristalsis or "Nutcracker esophagus" (average DCI $> 5,000$ mmHg/s/cm, with no swallows with DCI $> 8,000$ mmHg/s/cm) is classified inside the group of "peristaltic disorders" (5). HE is a primary hypercontractile disorder of the esophageal musculature that, although is extremely rare in the general population, is becoming more frequently described in medical literature (6). The 8,000 mmHg/s/cm threshold was chosen because this value was never encountered in healthy volunteers (1,4). Hypercontractility pattern of HE can be multipeaked or not multipeaked. Multipeaked contractions were as defined by Clouse: a) At least 2 peaks; b) pressure trough between the peaks greater than zero; c) the peak of least amplitude was at least 10 mmHg greater than the inter-peak trough; and d) the pressure peaks were separated by at least one second (7).

The aim of the following study is to evaluate the clinical context and manometric findings of patients diagnosed of HE with HRM.

METHODS

Study design

This is an observational and descriptive study where seven hundred twenty manometric studies from patients that suffered varied esophageal symptoms were revised. Patients were attended to the Department of Gastroenterology (Motility Unit) in the Hospital Universitario de La Princesa in Madrid, Spain (HULP) between June 2011 and June 2013.

Patients

A total of seven patients met diagnostic criteria for HE. Variables analyzed were: Age, sex, symptoms suffered, comorbidities, alcohol intake and tobacco use, medication, endoscopic findings and results of 24 hour pH-metry.

Manometric study

A hydropneumocapillary perfusion system of low compliance was used, with a silicone catheter of 4 mm external diameter and 0.8 mm internal diameter and 22 channels opened to laterals holes (that act as manometric sensors) directed radially and separated 1-2 cm from each other. Eight metal ring impedance detectors make 7 impedance channels. The distal manometric sensor is placed in the stomach. The sensors located in sphincters are separated 1 cm apart

and the sensors placed in the esophageal body are separated 2 cm apart from each other.

Each manometric channel is fed by an infusion system of double distilled water. It is connected to an external catheter that turns the pressure register into an electrical sign (solar system GI Manometry-Medical Measurement System: MMS). The electrical signs obtained are sent to a computer that includes specific software that analyses the data obtained.

The patient must have fasted at least 6 hours before the study begins. The manometric catheter was introduced through nasal cavities to stomach and the patient lying in a supine position. Ten fluids swallow of 5 ml, at 20-30 seconds intervals were performed. After removing the manometric tube, the pH-metry catheter was inserted displaying the distal side 5 cm above the superior edge of the LES (its location guided with HRM), and the esophageal pH was registered for 24 hours.

The DCI, IRP-4s, CFV, distal latency and the resting LES pressure at end of expiration were measured in each patient, using the automated function of the program. The contraction pattern (multipeaked or not multipeaked) and its synchrony with respiration was also determined as well as the 24-hours pH-metry and impedance-manometry.

The criteria used for the diagnosis of HE was the appearance of at least one contraction with DCI higher than 8,000 mmHg/s/cm together with normal dissemination (CFV < 9 cm/s and distal lag time > 4.5 s) (according to Chicago's classification 2011).

Statistical analysis

Qualitative results were expressed in percentages and quantitative results as an arithmetic average. Qualitative variables were compared using the Chi Square test and the quantitative variables the Pearson's correlation coefficient, with a significant value of 0.05.

RESULTS

Clinical outcomes

Seven patients met diagnostic criteria for HE, 100% of them being women. Mean age was 64 ± 11 years old. None of them consumed alcohol and only one was a smoker (Table I).

Symptoms frequently presented were: Chest pain in six patients (86%), dysphagia in five patients (71%) and heartburn in five patients (71%) (Fig. 1). Six (86%) of the patients with the diagnosis of HE had comorbidities, the majority being: Hypertension and dyslipidemia. Three patients (43%) were treated with antidepressants and anti-anxiety drugs. Five (71%) were receiving anti-hypertensive drugs: Beta blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists and calcium channel blockers. Six patients (86%) were empirically prescribed a proton pump inhibitors (PPI) in order to treat their gastrointestinal symptoms and/or after discovering gastritis or esophagitis in the endoscopy even if pathological acid exposure (PAE) was absent. Three of

Table I. Clinical characteristics of patients with hypercontractile esophagus

	Total n = 7 (%)
Mean age (years)	64.2
Range (years)	53-75
Sex (M:F)	0:7
Symptoms	
Chest pain	6 (86)
Dysphagia	5 (71)
Heartburn	5 (71)
Paradoxical dysphagia	2 (29)
Epigastralgia	2 (29)
Regurgitation	1 (14)
Dyspnea/cough	1 (14)
Comorbidities	
Hypertension	4 (57)
Dyslipidemia	4 (57)
Fundoplication	1 (14)
Depression	1 (14)
Diabetes	1 (14)
Hypothyroidism	1 (14)
Other	1 (14)
Tobacco	1 (14)
Alcohol	0
Medication	
Benzodiazepine	3 (43)
Beta blockers	3 (43)
ACE inhibitors	2 (29)
Calcium channel blockers	1 (14)
ARBs	1 (14)
Others	1 (14)
PPIs	
Good response	3/6 (50)
No response	3/6 (50)
Endoscopic findings	
Gastritis	6 (86)
Reflux esophagitis	1 (14)
Surgery changes	1 (14)
Gastric polyps	1 (14)
pH-metry	
PAE	1/6 (17)
No-PAE	5/6 (83)

M: Male. F: Female. ACE: Angiotensin-converting enzyme. ARBs: Angiotensin II receptor blocker. PPI: Proton pump inhibitor. PAE: Pathological acid exposure. No-PAE: No pathological acid exposure.

them presented an improvement or disappearance of their chest pain. The remaining three patients did not suffer modifications of their symptoms with the medication, leading to the conclusion of no statistical differences between HE and clinical response to treatment with PPI.

Esophageal pH-metry was practiced in six patients, finding the diagnosis of PAE only in one (17%). When analyzing this patient specifically it was found that she did

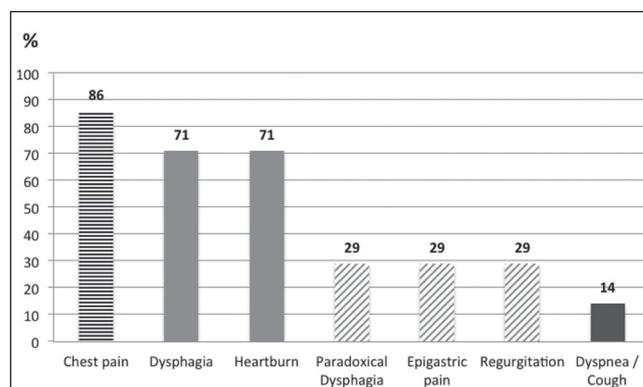


Fig. 1. The most frequent symptoms in patients with hypercontractile esophagus.

not receive PPIs and that the HRM revealed a hiatus hernia and GEJ outflow obstruction. This last parameter is defined by HRM as the absence of relaxation of the GEJ (high IRP) with normal peristalsis of the esophageal body (5).

All the patients included had been given an upper digestive endoscopy, showing presence of gastritis (86%), esophagitis (14%), post-surgical changes due to previous fundoplication (14%) and gastric polyps were observed (14%).

Manometric outcomes

The frequency of HE in our study was of 7/720 (1%) patients sent to the Digestive Motility Unit. The average data of DCI of the hypercontractile contractions was 11,150 mmHg/s/cm, ranging from 8,036 to 20,812 mmHg/s/cm (Table II). In one patient (14%) the HE was related to a gastroesophageal reflux disease (GERD) and gastroesophageal junction (GEJ) outflow obstruction.

Four patients (57%) presented only one hypercontractile contraction in the HRM and three patients (43%) presented more than one hypercontractile wave. In patients presenting one single hypercontractile contraction average DCI was found to be normal (< 5,000 mmHg/s/cm). On the other hand, in patients with more than one hypercontractile contraction, average DCI was higher than 5,000 mmHg/s/cm, it being a positive correlation ($r = 0.96$; $p < 0.05$).

IRP-4s was less than 15 mmHg in six patients and the distal latency was > 4.5 seconds in all the patients included. The average IRP of the hypercontractile contractions was 8.2 mmHg, and 7.7 mmHg in the remaining contractions, without statistical significant differences between both. IRP-4s did not increase in relation to DCI of hypercontractile contractions ($r = -0.04$).

Two patients (29%) were diagnosed with a hiatus hernia (GEJ type III) by HRM. One of these patients presented mild impairment of the relaxation (IRP-4s = 15 mmHg) with normal peristalsis, fulfilling criteria of GEJ outflow obstruction and incomplete bolus transit in two swallows.

Table II. Manometric characteristics in patients with hypercontractile esophagus

	Total, n (%)
Patients with at least a single contraction with DCI > 8,000 mmHg/s/cm	7/720 (1)
DCI average	
Normal	3 (43)
Abnormal (> 5,000 mmHg/s/cm)	4 (57)
Range DCI > 8,000 mmHg/s/cm	8,036 – 20,812
Mean IRP-4s	
Hypercontractile contractions (mmHg)	7.1
Normal contractions (mmHg)	8.3
Basal LES pressure, n (%)	
Normal (10-35 mmHg)	4 (57)
Hypotonic LES (< 10 mmHg)	1 (14)
Hypertensive LES (> 35 mmHg)	2 (29)
Patients with one hypercontractile contraction	4 (57)
Patients with more than one hypercontractile contraction	3 (43)
Type of contraction	
Multi-peaked (Jackhammer)	4 (57)
Not multi-peaked	3 (43)
Hiatus hernia	2 (29)
GEJ outflow obstruction	1 (14)

DCI: Distal contractile integral. IRP: Integrated relaxation pressure. LES: Lower esophageal sphincter. mmHg/s/cm: Millimeters of mercury times second times cm. GEJ: Gastroesophageal junction.

Two patients (29%) were found to have a hypertensive LES (basal LES pressure > 35 mmHg), this parameter being moderate correlated with the symptoms of dysphagia and paradoxical dysphagia ($r = 0.66$). The patient with

the most hypercontractile swallows detected (6/10) had hypertensive LES and had a Nissen fundoplication.

Multi-peaked contractions (Jackhammer esophagus) were observed in 4 patients (57%) (Fig. 2); of whom 50% were synchronized with their respiration without statistical significant differences and with no differences between inspiration and exhalation. Multi-peaked contractions (Jackhammer) were not correlated to a higher IRP-4s or with chest pain or dysphagia ($r = 0.09$ and 0.3).

DISCUSSION

The HE is an extremely rare disorder. Roman et al. (2011) found 4% of cases in a series of 2,000 patients, constantly associated with symptoms of chest pain and dysphagia. However, the appearance of the symptoms directly related to the hypercontractile pathology has not yet been demonstrated. Its clinical presentation is diverse due to a hypercontractility primary disorder of esophageal muscle, but can also be found in association with reflux or GEJ outflow obstruction (1,8).

According to the technical recommendations of the American Gastroenterological Association, in the study of chest pain, patients are submitted to manometry when do not respond to antireflux therapy, based on the fact that GERD is probably the esophageal cause more commonly associated with chest pain. In the study of dysphagia, manometry is indicated after the most common causes of mechanical obstruction (malignant disease, peptic stricture, Schatzki ring) by endoscopy or radiologic studies have been discounted (9). In our series, the predominant symptoms were chest pain and dysphagia. Coinciding with the literature, most patients had received treatment with PPIs without response. Manometry was performed

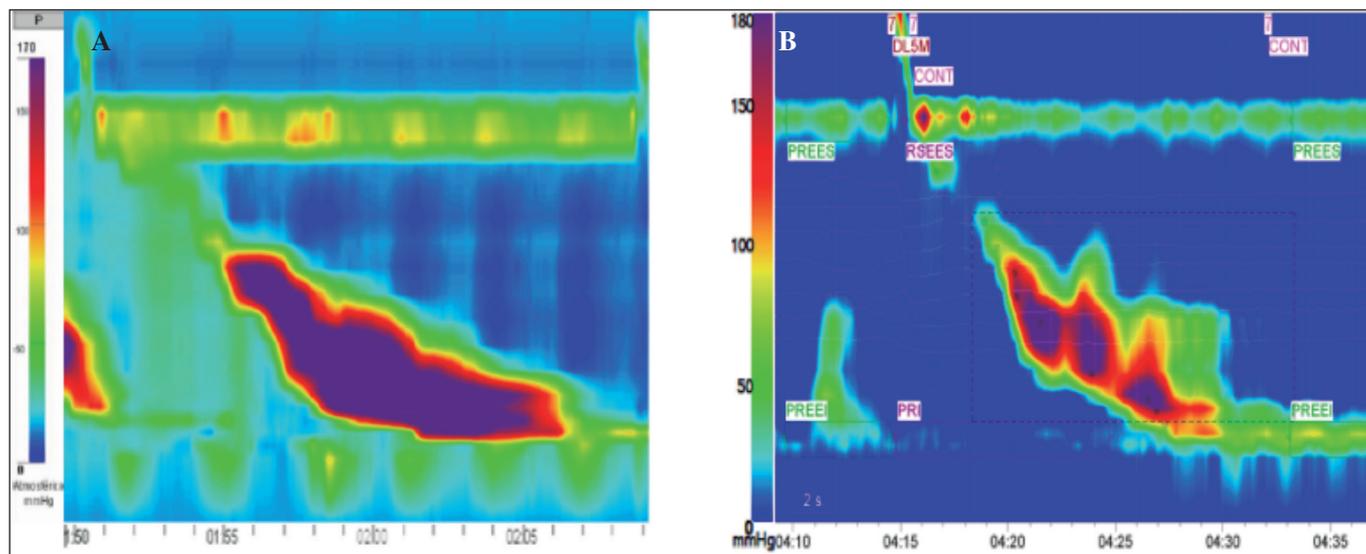


Fig. 2. Contraction patterns. Hypercontractile swallow not multi-peaked (A) and hypercontractile contraction multi-peaked or "Jackhammer esophagus" (B).

following structural pathologies excluded by gastroscopy and cardiovascular disease having previously been ruled out as a cause of chest pain (1).

In contrast to what has been described in the literature, where HE is an isolated phenomenon not usually repeated in manometry, we found that 57% had more than one hypercontractile wave in the same manometry study. This is being taken into consideration for the definition of HE in the latest version of the Classification of Chicago v3.0, 2015 (10). In this group of patients it was also found that the average DCI was greater than 5,000 mmHg/s/cm; this finding suggests that nutcracker esophagus (DCI > 5,000 mmHg/s/cm) and HE may be associated with the same etiological factor or be the same disease in different stages of evolution, which would be studied in the future.

Coexistence of hiatus hernia and GEJ outflow obstruction in the context of patients with HE and symptoms of dysphagia has been described in the literature (8). In the study of Roman et al, the IRP was correlated positively with the DCI in patients with hypercontractility, compared to control subjects (1). Moreover, Gyawali recently found that patients with GEJ outflow obstruction may exhibit spastic pattern, characterized by high amplitude multi-peaked contractions and prolonged duration in the distal esophagus (11). These two studies support the hypothesis that the lack of LES relaxation (IRP-4s > 15 mmHg) may secondarily cause an obstruction to the flow of the GEJ, increasing pressure intrabolus and the phenomenon of hypercontractility with multi-peaked contractions (12).

Regarding the association between hypertensive LES (> 35 mmHg) and hypercontractility disorders of esophageal body (hypercontractile esophagus or hypertensive esophageal peristalsis), remains to be determined whether there is a causal mechanism between the two conditions (1).

Recently Ciriza et al. related the GEJ morphology with manometric alterations and observed that one of the patients with type 1 GEJ presented HE, although didn't find a statistically significant difference with respect to other types of GEJ (13). In our series, we found no correlation between DCI and the type of UEG.

In the study of Barreca et al., 15 patients with GERD or hiatus hernia with chest pain and dysphagia, associated with HE or hypertensive LES, were evaluated. Those patients didn't respond to medical antireflux treatment underwent Nissen fundoplication. They found that surgery reduced esophageal acid exposure, improving most symptoms. However, some patients developed chest pain and dysphagia again after surgery and remained with hypertensive and hypertensive LES contractions. It is hypothesized that the Nissen fundoplication can create a relative obstruction of flow in the distal esophagus, resulting in dilation, stretching, and pain. However not many studies can prove this hypothesis (14).

In our series, the patient that underwent fundoplication showed that the majority of hypercontractile contractions was increased LES pressure and persistent symptoms of

chest pain and dysphagia, even after there was removing the fundoplication. In this patient preoperative manometry had showed decreased peristalsis and hypotensive LES, and HE developed after surgery.

Regarding the pattern of contraction, a higher prevalence of multi-peaked contractions (Jackhammer) than not multi-peaked is described in the literature, showing in our series 57% vs. 43% respectively (8). Remaining under investigation, if the sync with respiration is an artifact caused by the movement of the diaphragm during breathing or it is a phenotypic pattern of hypercontractility disorders (8,15). In our series, two of the four patients (50%) with multi-peaked contractions were synchronized with respiration, without a statistical significant correlation.

Due to the high prevalence of gastroesophageal reflux and chest pain the 24-hour pH-metry may be useful as a complementary test to rule out GERD in these patients. In our study we found that most of our patients with HE had no acid reflux, so the symptoms of chest pain, dysphagia and heartburn are nonspecific. The absence of response to treatment with PPIs should alert the physician to other pathologies.

CONCLUSIONS

The HE is a disorder of very low frequency but with an important clinical relevance for its symptoms of chest pain. Today, the role of manometry in the study of chest pain and dysphagia in patients who have completed the cardiovascular study it's recognized. It's still remains to be determined whether treatment of HE modifies the natural history of the disease but therapy should be oriented to solve or improve the symptoms of these patients, for which it is necessary to have a precise diagnosis, avoiding unnecessary diagnostic testing.

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