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Phenotypes and clinical context of hypercontractility in high resolution esophageal pressure topography (EPT)

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Abstract

Backgrounds & Aims—This study aimed to refine the criteria for esophageal hypercontractility in high resolution esophageal pressure topography (EPT) and examine the clinical context in which it occurs.

Subjects & Methods—72 control subjects were used to define the threshold for hypercontractility as a distal contractile integral (DCI) greater than observed in normals. 2,000 consecutive EPT studies were reviewed to find patients exceeding this threshold. Concomitant EPT and clinical variables were explored.

Results—The greatest DCI value observed in any swallow among the control subjects was 7,732 mmHg-s-cm; the threshold for hypercontractility was established as a swallow with DCI >8,000 mmHg-s-cm. 44 patients were identified with a median maximal DCI of 11,077 mmHg-s-cm, all with normal contractile propagation and normal distal contractile latency, thereby excluding achalasia and distal esophageal spasm. Hypercontractility was associated with multipeaked contractions in 82% of instances leading to the name Jackhammer Esophagus. Dysphagia was the dominant symptom although subsets of patients had hypercontractility in the context of EGJ outflow obstruction, reflux disease, or as an apparent primary motility disorder.

Conclusion—We describe an extreme phenotype of hypercontractility characterized in EPT by the occurrence of at least a single contraction with DCI > 8,000 mmHg-s-cm, a value not encountered in control subjects. This phenomenon, branded Jackhammer Esophagus was usually accompanied by dysphagia and occurred both in association with other esophageal pathology (EGJ outflow obstruction, reflux disease) or as an isolated motility disturbance. Further studies are required to define the pathophysiology and treatment of this disorder.

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Sabine Roman has served as consultant for Given Imaging.

Keywords

esophageal pressure topography; jackhammer esophagus; distal contractile integral; dysphagia; esophageal motility disorders; nutcracker esophagus

Introduction

Hypertensive esophageal peristaltic contractions are among the most common reported findings in clinical manometric studies, usually classified as “nutcracker esophagus” (1). However, whereas it was initially hypothesized that nutcracker esophagus might represent a causal explanation for unexplained chest pain or dysphagia, subsequent analyses have concluded that, most often, this was not the case (2–3). The finding lacked specificity, frequently encountered in reflux patients (4), patients with hypersensitivity (5), and normal controls. However, the concept persists that there is a pattern of esophageal hypercontractility causally linked to dysphagia or pain that is not consistent with achalasia or spasm. Additional manometric features that may be relevant include prolonged or repetitive contractions (6). However, the cardinal criterion of mean peristaltic amplitude has persisted, albeit with a progressively increasing threshold of what constitutes “nutcracker esophagus”. The most recent published criterion for nutcracker esophagus applicable to conventional manometry suggests a mean peristaltic amplitude of 180 mmHg measured 3 and 8 cm proximal to the lower esophageal sphincter (LES) measured in 10 test swallows (6).

A major recent advancement in clinical manometry has been the adoption of high resolution systems with esophageal pressure topography (EPT) plotting (7–8). In parallel with that evolution, the Chicago Classification of esophageal motility disorders has been devised to classify motility disorders in EPT-specific metrics. The Chicago Classification continually evolves through the workings of an international working group (9). With respect to hypercontractility, the relevant EPT metric is the distal contractile integral (DCI) expressed as the product of the mean amplitude of contraction in the distal esophagus (mmHg) times the duration of contraction (s) times the length of the distal esophageal segment (cm). The upper limit of normal for DCI in 75 asymptomatic controls was a mean of 5,000 mmHg-s-cm calculated only for test swallows with an intact peristaltic contraction. In the current Chicago Classification two DCI-based diagnoses are recognized: hypertensive peristalsis with a mean DCI >5,000 mmHg-s-cm and “spastic nutcracker” with a mean DCI greater than 8,000 mmHg-s-cm. In the original report of 400 patients, hypertensive peristalsis was relatively common, found in 12% of individuals with normal esophagogastric junction (EGJ) relaxation whereas spastic nutcracker was unusual, found in only 6 individuals (1.5%) with “repetitive high-amplitude contractions...uniformly associated with dysphagia or chest pain” (10). For comparison, the same series included 73 (18.4%) patients with achalasia.

With widespread adoption and a continuing consensus process, the Chicago Classification has been honed over the past few years with new criteria for achalasia (11), weak peristalsis (12), and DES (13). Along with this process, there has been increasing dissatisfaction with the “spastic nutcracker” designation for a number of reasons: 1) the criterion of a mean DCI threshold was arbitrary and ignored the possibility of a single extremely abnormal contraction, 2) no definition was provided for a “repetitive” contraction, and 3) the nomenclature, alluding to two other nebulous entities, has encountered widespread disapproval. However, despite these limitations, there has been persistent strong consensus behind the existence of a pattern of esophageal hypercontractility causally linked to dysphagia or chest pain, but inconsistent with a diagnosis of achalasia or spasm. Consequently, the aim of this study was to refine the criteria for an extreme phenotype of

hypercontractile esophagus though detailed analysis of a large clinical experience with EPT studies and, in the process, to rename it.

Methods

Subjects

High resolution manometry (HRM) studies of 72 healthy volunteers (38 males, mean age 27 years, range 19–48 years) and a series of 2,000 consecutive clinical EPT studies performed from January 2007 until May 2010 were reviewed for this study. Volunteers were recruited by advertisement or word of mouth and had no history of esophageal symptoms (heartburn, regurgitation, dysphagia), previous surgery, or significant medical conditions (10, 14–15). Patients presented with diverse conditions consistent with an esophageal referral practice. Individuals with previous upper gastro intestinal surgery, duplicate studies, technically limited studies and subjects with fewer than 70% of analyzable swallows were excluded from the series leaving 1070 unique patients. The study protocols were approved by the Northwestern University Institutional Review Board and informed consent was obtained from each subject.

Study protocol

HRM studies were done in a supine position after at least a 6-hr fast. The HRM catheter was 4.2 mm outer diameter solid-state assemblies with 36 circumferential sensors at 1-cm intervals (Given Imaging, Los Angeles, CA). Transducers were calibrated at 0 and 300 mmHg using externally applied pressure. The manometry assembly was placed transnasally and positioned to record from the hypopharynx to the stomach with about 3 intra-gastric sensors. The study protocol included at least 30-s baseline recording and ten 5-ml swallows.

EPT analysis

EPT data were analyzed using ManoView™ analysis software (Given Imaging, Los Angeles, CA). The DCI was assessed using the automated function of ManoView™ measured between the proximal (P) pressure trough and esophagogastric junction or distal (D) pressure trough. Only the pressures greater than 20 mmHg contributed to the calculation of DCI, expressed in mmHg-s-cm (15). In each study, the swallow with the greatest DCI was further characterized for maximal peristaltic amplitude, integrated relaxation pressure (IRP) (14), contractile front velocity (CFV) (16), distal contractile latency (DL) (17), and multi-peaked contractions (18). Multi-peaked contractions were scored as defined by Clouse: i) at least 2 peaks, ii) pressure trough between the peaks greater than zero, iii) the peak of least amplitude was at least 10 mmHg greater than the inter-peak trough, and iv) the pressure peaks were separated by at least one second (18). The synchrony of pressure peaks in multi-peaked contractions with respiration was also explored (19) (Figure 1). Inspiration was identified by the diaphragmatic contraction and/or a decrease of intra-esophageal pressure with corresponding increase of abdominal pressure. Multi-peaked contractions were independently scored as in synchrony or out of synchrony with respiration by two observers (SR and LB) with disagreement arbitrated in a blinded manner by JEP.

Clinical Data

Patients with hypercontractility on the basis of a maximal DCI value exceeding the greatest value observed in normal controls were grouped according to whether or not they had multi-peaked contractions and whether or not multi-peaked contractions were synchronized with respiration. Clinical data were then explored on these subsets of patients to look for similarities within groups and differences among groups in dominant symptoms. Dysphagia was evaluated using the Impaction Dysphagia Questionnaire (IDQ, Table 1) at the time of

initial EPT study. Although this questionnaire has not been validated in control subjects, we consider a score greater than 3 to be pathological. Subsequently, a phone survey was done in May – June 2011 to update clinical data in patients with hypercontractile esophagus. All patients diagnosed with hypercontractile esophagus from June 2010 to May 2011 were included in the phone survey.

Statistical analysis

For the analysis of the swallows with the greatest DCI, EPT metrics (IRP, CFV, DL) were expressed as median (interquartile range) and compared using Mann Whitney and Kruskal Wallis tests. DCI was also correlated with IRP using Pearson correlation coefficient. Qualitative data were expressed as a percentage and compared using Chi-square test.

For each subject the metrics (IRP, CFV, DCI, DL) were then calculated as a mean of all analyzable test swallows and expressed as median (interquartile range) for controls and patients with at least one high-DCI swallow. Qualitative data were expressed as a percentage. The groups were compared using Mann Whitney and Kruskal Wallis tests for quantitative data and using Chi-square test for qualitative data.

Results

High-DCI swallows: control subjects versus patients with hypercontractility

The median (5–95th percentile) for the greatest single DCI value in the control subjects was 2073 (757–5946) mmHg-s-cm with the maximal observed value in the group being 7,732 mmHg-s-cm. Consequently, hypercontractility was defined in the patient group by the occurrence of a swallow with DCI value greater than 8,000 mmHg-s-cm. As such, 44 patients were identified with hypercontractility in the context of normal propagation (less than 20% of swallow with a CFV > 9 cm/s and/or a DL < 4.5 s). Table 2 contrasts the characteristics of the greatest DCI swallow in the control subjects and patients with hypercontractility.

Significant differentiating features in the hypercontractile swallows included increased peak peristaltic amplitude (309 vs 134 mmHg), increased localization of peak peristaltic amplitude in the distal versus the middle contractile segment (86% vs 65%), and an increased incidence of multi-peaked contractions (82% vs 3%). Although significant, differences in IRP, CFV, and DL were slight. Even though the IRP was higher for the contractions with the greatest DCI compared to controls, the correlation between DCI and IRP was weak ($r=0.28$, $p<0.01$) (Figure 2). Restricting the analysis to patients with hypercontractility, the correlation between DCI and IRP was negligible ($r=0.05$, $p=0.77$).

Phenotypes of hypercontractility: single vs multi-peaked contractions

Figure 3 displays three patterns of hypercontractile swallows: multi-peaked synchronized with respiration, multi-peaked not synchronized with respiration and not multi-peaked. These phenotypes were encountered in 20 (1.9%), 16 (1.5%) and 8 patients (0.8%), respectively. The EPT characteristics of patients with hypercontractility are compared to control subjects in Table 3. The mean IRP was significantly greater in the group of patients without multi-peaked contractions ($p<0.01$) and the concomitant finding of impaired deglutitive EGJ relaxation was higher in this group of patients. Hence, hypercontractility without multi-peaked contractions might be associated with EGJ outflow obstruction while multi-peaked contractions, whether or not synchronized with respiration, seem to be a unique abnormality of contractility, independent of EGJ outflow obstruction. As hypercontractility was commonly associated with multi-peaked contractions, we propose the name,

Jackhammer Esophagus . Other EPT metrics were similar among the three phenotypes of hypercontractility.

Clinical characteristics

Clinical data on patients with hypercontractility are summarized in Table 4. The most common symptom was dysphagia (75% of subjects), which had similar prevalence among the three hypercontractility phenotypes. An IDQ score from the time of the EPT study was available in 17 patients; the median was 10 (range 0 – 36). Only 1 patient had an IDQ score of less than 3; she presented with reflux symptoms. Esophagogastroduodenoscopy and barium swallow were available for 41 and 18 patients respectively. Esophagitis was observed in about 10% of each group with no other specific findings. Endoscopic ultrasound was done in one patient from each subgroup; both patients with multipeaked contractions exhibited thickening of the muscularis propria in the distal esophagus. The one patient without multipeaked contractions was eventually determined to have pseudoachalasia from a squamous cell cancer. Computerized tomography studies were done in nine patients and were without significant findings in all cases.

Long-term follow-up was obtained in 33 patients (24 completed the phone survey) after a mean of 26 months (range 8–51). Anti-reflux therapy was pursued in 12 patients (10 proton pump inhibitors (PPI) and 2 Nissen fundoplication); 7 of these improved significantly (5 PPI and 2 Nissen fundoplication). Post PPI manometry was realized in 2 patients: the Jackhammer pattern was persistent in one patient who remained symptomatic on PPI and normalized in 1 patient whose symptoms resolved on PPI (pH-metry also normalized). Anticholinergic therapy significantly improved symptoms in all three patients so treated. Botulinum toxin injection into the distal esophagus was done in two patients and into the LES in one patient. Dysphagia regressed in both patients in whom Botox™ was injected in the distal esophagus; an EPT study two months after Botox™ injection normalized in one of these patients (Figure 4A, 4B). Dysphagia persisted for the patient in whom Botox™ was injected into the LES.

Finally, since the end of the 2,000 patient series, 11 new patients were diagnosed as Jackhammer Esophagus in the past year. Phone survey was available in eight of them with a median follow up of 5 months (range 1–11). The one patient with a score below 3 presented chest pain as dominant symptom. One patient received sildenafil with a significant decrease in chest pain and dysphagia associated with decreased contraction amplitude (Figure 4C, 4D). One patient with muscularis propria thickening on EUS had a partial improvement after Botox™ injection into the thickened area. One patient treated with PPI was significantly improved as well as 1 patient treated with an anticholinergic. Symptoms remained unchanged in 4 patients (two treated with PPI, one with imipramine, and one with nitrates).

Discussion

The major objective of this study was to refine the diagnostic criteria for hypercontractile peristalsis, drawing from a large clinical experience with EPT studies. Based on an analysis of 72 control subjects, the threshold DCI value for hypercontractility was established to be a single contraction with a DCI value greater than 8,000 mmHg-s-cm, thereby exceeding any value encountered in control subjects. Thereafter, hypercontractility was subgrouped into that with and without multipeaked contractions. These different groups presented similar characteristics (normal distal contractile latency, normal peristaltic contractile velocity) and similar outcomes. Since the repetitive, high amplitude contractions evoke the action of a jackhammer, we coined the descriptive term Jackhammer Esophagus with the defining criterion of at least one peristaltic contraction with a DCI value greater than 8,000 mmHg-s-cm. In this series of 1,070 consecutive patients encountered in a tertiary esophageal referral

practice, Jackhammer Esophagus was decidedly rare, seen in only 44 (4.1%) with the dominant symptom being dysphagia about 70% of the time. The clinical presentation was diverse; some Jackhammer Esophagus cases were clearly associated with mechanical EGJ outflow obstruction, others secondary to reflux disease, and some attributable to primary esophageal muscle hypercontractility.

The development of EPT has greatly clarified our understanding of the segmental architecture of peristalsis (20). Rather than occurring as a seamless process, peristalsis occurs through the sequential activation of four discrete contractile segments spanning from the proximal striated muscle to the lower esophageal sphincter. After realizing this architecture, Clouse observed that double peaked contractions occurred as a consequence of the overlap and imperfect coordination between the adjacent second and third contractile segments. He further observed that although double peaked contractions could occur normally, they were more likely to occur in swallows with strong contraction in the third segment (18). Those observations are borne out in the current series, evident by the occurrence of multi peaked contractions in 3% of control subjects and by the dominant localization of hypercontractility to the third contractile segment detailed in Table 2. In this paradigm, Jackhammer esophagus is best conceptualized as extreme hypercontractility in the third contractile segment.

The Clouse hypothesis of the genesis of multi peaked contractions detailed above is not universally accepted. Alternatively, it has recently been proposed that multiple peaked swallows might be an artifact (19). Indeed, the distal esophagus and diaphragm are attached at the EGJ causing them to move in unison during respiration, which could cause the appearance of a multi peaked pattern of contraction attributable to oscillatory movement of the contracting esophagus relative to the sensor recording that contraction. This was proposed by Sampath *et al.* in a study of the synchrony between respiration and pressure peaks in patients with multi peaked contractions (19). Suspended breathing and hyperventilation modified the esophageal contraction waveform morphology accordingly. In view of those observations, we systematically explored the synchrony between multi peaked contractions and respiration. Multi peaked contractions were synchronized with respiration in roughly half of the Jackhammer patients whereas in the other half they were not. There was no apparent clinical difference between these subsets (Tables 3 and 4). Furthermore, although the respiratory oscillation hypothesis may suffice to explain a multi peaked contraction at the spatial margins of the contractile segment in some instances, this explanation is clearly insufficient to explain the extreme oscillations spanning the entire contractile segment illustrated in Figures 1 and 3.

Hypercontractility may also result from EGJ obstruction. Experimental EGJ obstruction caused esophageal smooth muscle hypertrophy and excitability in the opossum (21). In humans, gastric banding represents a model of EGJ obstruction and band inflation can induce hypertensive and repetitive esophageal contractions (22). Finally Gyawali recently showed that patients with EGJ outflow obstruction might exhibit a spastic motor pattern characterized by multi peaked contractions, high distal esophageal amplitude and prolonged contraction duration (23). This may have been the cause of hypercontractility in some of our patients evident by the abnormal IRP values observed in 8 of them (19%) (Table 3). However, there was minimal correlation between DCI and IRP within the Jackhammer group.

The pathophysiology of Jackhammer Esophagus is largely unknown beyond that patients with hypertensive contractions have been noted to have increased esophageal muscle thickness on ultrasound (24) and exhibit an atropine-sensitive asynchrony between the circular and the longitudinal muscle contraction (25–26). Consequently, excess cholinergic

drive may be a distinguishing feature. Another argument for a role of the cholinergic pathway in the genesis of multi-peaked contractions comes from observations in diabetics with autonomic neuropathy. Loo *et al.* reported that a higher frequency of multi-peaked waves in diabetics with autonomic neuropathy than in diabetics without neuropathy or controls (27). These multi-peaked contractions occurred in a context of normal peristaltic amplitude and were converted to single peaked contractions after atropine injection. We also observed instances of Jackhammer Esophagus in GERD patients consistent with prior reports of hypercontractility in patients with reflux disease (4, 28). Relatively few patients in our series had pH monitoring studies done, but about 10% had reflux esophagitis on endoscopy and anti-reflux therapy was also associated with the resolution of symptoms in 8 of 15 patients and normalization of EPT studies in 1 of 2 cases who had follow-up studies. Further studies are required to evaluate the respective roles of EGJ obstruction, reflux disease and cholinergic modulation in patients with Jackhammer Esophagus.

This study has some limitations attributable to its retrospective design. No validated dysphagia questionnaire was used leaving us without a precise symptom profile of Jackhammer patients. There was also no controlled approach to treatment of this decidedly rare disorder (only 4.1% of our series). A variety of treatments were proposed based on individual patient characteristics with variable success. This variability emphasizes the heterogeneity of the patient population exhibiting esophageal hypercontractility.

In conclusion, we described an extreme phenotype of esophageal hypercontractility characterized in EPT by the occurrence of at least a single contraction with DCI >8,000 mmHg-s-cm. This phenomenon, branded Jackhammer Esophagus, was never encountered in control subjects and was usually accompanied by a dominant symptom of dysphagia. Further studies are required to define the pathophysiology and treatment of this disorder.

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Abbreviations

CFV	contractile front velocity
DCI	distal contractile integral
DL	distal contractile latency
EPT	esophageal pressure topography
EGJ	esophago-gastric junction
HRM	high resolution manometry
IRP	integrated relaxation pressure

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What is current knowledge?

- Hypertensive peristalsis (“nutcracker esophagus”) is defined by high amplitude peristaltic contractions and can be associated with dysphagia and/or chest pain
- As conventionally defined, nutcracker esophagus is a relatively common heterogeneous condition encountered in normal controls, dysphagic patients and patients with reflux disease

What is new here?

- Esophageal hypercontractility is defined in esophageal pressure topography (EPT) by the occurrence of a propagated swallow-induced contraction with distal contractile integral (DCI) > 8,000 mmHg-s-cm, a magnitude never encountered in control subjects
- Hypercontractility, nicknamed Jackhammer esophagus because it is usually associated with multi-peaked contractions, is rare (4.1% of a referral practice) and is usually associated with dysphagia
- Subsets of patients with Jackhammer Esophagus had this associated with EGJ outflow obstruction, reflux disease, or as an apparent primary abnormality of hypercontractility

Figure 1.

Esophageal pressure topography (EPT) of swallows with extreme DCI and multi-peaked contractions. The white bold line represents the pressure tracing 3 cm proximal to the EGJ. The white arrows indicate inspiration as signaled by diaphragmatic contraction. The white dashed lines indicate the timing of interpeak pressure troughs. In Panel A the pressure troughs are synchronized with inspiration whereas in Panel B they are not.

Figure 2.

Correlation between Distal Contractile Integral (DCI) and Integrative Relaxation Pressure (IRP) for each subject's greatest DCI swallow. For the control subjects (gray diamonds) the coefficient correlation was 0.05 ($p=0.70$). For the hypercontractile swallows (dots) the Pearson coefficient correlation was 0.05 ($p=0.77$). No significant correlation was observed in any subgroup (multi-peaked synchronized with respiration, $r=0.15$, $p=0.54$; multi-peaked not synchronized with respiration, $r=0.20$, $p=0.47$); and not multi-peaked, $r=-0.2$, $p=0.97$).

Figure 3. 3-D landscape plots illustrating examples of (A) multi-peaked hypercontractility (jackhammer) synchronized with inspiration, (B) multi-peaked hypercontractility not synchronized with inspiration, and (C) non-multi-peaked hypercontractility.

Figure 4.

Examples of patients with Jackhammer Esophagus. Panels A and B are from a 76-year old woman with a complaint of dysphagia and chest pain. The first EPT study revealed Jackhammer Esophagus with a DCI of 9,530 mmHg-s-cm. The patient received PPI therapy without symptom improvement. One year later a second EPT study (Panel A) included a swallow with a DCI of 12,560 mmHg-s-cm. EUS demonstrated a 6-cm distal segment of thickened esophageal wall and BotoxTM was injected in this area. Symptoms improved and a third EPT study 2 months later (Panel B) showed normalization (greatest DCI = 4,165 mmHg-s-cm). The patient illustrated in Panels C and D, was a 26-year old woman with a complaint of chest pain and dysphagia. Upper endoscopy was normal. EPT study demonstrated Jackhammer Esophagus (greatest DCI = 18,655 mmHg-s-cm, Panel C) and EUS showed wall thickening (12 mm) in the lower third of the esophagus. Symptoms rapidly improved after treatment with sildenafil. Nine months later the patient was still taking sildenafil (25 mg qd) with minimal symptoms and a normalized EPT study (greatest DCI = 3,810 mmHg-s-cm, Panel D).

Table 1

Impaction Dysphagia Questionnaire. Each question was scored 0 to 5. Results for each patient are expressed as a total (0 to 50)

Questions	Score 0 to 5
Over the past 30 days, on average, how often have you had the following? a- Trouble eating solid food (meat, bread) b- Trouble swallowing liquids c- Pain while swallowing d- Trouble eating soft foods (yogurt, jello, pudding) e- Coughing or choking when swallowing foods	never (0) less than once a month (1) 1–9 times a month (2) 10–19 times a month (3) 20–29 times a month (4) daily (5)
Over the past year, how often have you had the following? f- Food stuck in throat or esophagus for more than 30 minutes g- An emergency room visit because of food being stuck in the throat or esophagus	never (0) 1 time in the past year (1) 2 times in the past year (2) 3 times in the past year (3) 4 times in the past year (4) more than 4 times in the past year (5)
Over the past 6 months, on average, how would you rate your discomfort or pain during swallowing? a1- Eating solids (meat, bread) a2- Eating soft foods (yogurt, jello, pudding) a3- Drinking liquid	none (0) very mild (1) mild (2) moderate (3) moderately severe (4) severe (5)

Table 2

Characteristics of the swallow with the greatest DCI in control subjects and patients with hypercontractility. Data presented as median (IQR).

	Controls (n=72)	Patients with hypercontractility (n=44)	p
Maximum DCI (mmHg-s-cm)	2073 (1445–2624)	11077 (9264–16357)	<0.01
Maximal peristaltic amplitude (mmHg)	134 (112–169)	309 (258–405)	<0.01
Location of maximal amplitude			
Middle segment	25 (35%)	6 (14%)	0.01
Distal segment	47 (65%)	38 (86%)	
IRP (mmHg)	7.9 (5.8–10.8)	9.6 (6.8–14.3)	0.02
CFV (cm/s)	4.5 (3.5–5.8)	3.7 (2.9–5.2)	0.02
Distal latency (s)	6.8 (6.1–7.6)	7.3 (6.4–7.8)	0.34
Multipeaked contractions			
- Total	2 (3%)	36 (82%)	<0.01
- Not synchronized with respiration	2 (3%)	16 (36%)	<0.01

Table 3
EPT characteristics of patients with hypercontractility and controls. Data presented as median (IQR).

	Patients with hypercontractility			Controls (n=72)	p
	Multipeaked synchronized with respiration (n=20)	Multipeaked not synchronized with respiration (n=16)	Not multipeaked (n=8)		
Greatest DCI (mmHg-s-cm)	11569 (9230–17064) [‡]	10342 (9012–15952) [‡]	10613 (9661–11841) [‡]	2073 (1445–2624)	<0.01
Mean IRP (mmHg)	9.3 (6.9–11.9)	8.4 (6.8–13.9)	17.2 (10.5–36.3) ^{‡†}	8.0 (5.3–10.0)	<0.01
Abnormal mean IRP, n (%)	2 (10%)	1 (6%)	5 (63%) ^{‡†}	3 (4%)	<0.01
Mean DCI (mmHg-s-cm)	6290 (3902–7479) [‡]	5479 (3902–7704) [‡]	6648 (5267–8737) [‡]	1600 (1063–2179)	<0.01
Mean CFV (cm/s)	4.0 (3.1–5.0) [‡]	4.1 (3.3–5.5)	4.0 (3.3–4.7)	4.8 (3.7–6.2)	<0.01
Mean DL (s)	7.1 (6.8–7.7)	7.2 (6.6–8.1)	6.6 (6.1–7.5)	6.9 (6.3–7.5)	0.21

[‡] p<0.05 vs both multipeaked groups;

[†] p<0.01 vs controls

Table 4

Clinical characteristics of patients with hypercontractility.

	Multipeaked synchronized with respiration (n=20)	Multipeaked not synchronized with respiration (n=16)	Not multipeaked (n=8)
Mean age (range) yrs	54 (28–69)	57 (28–78)	68 (48–82)
Gender (M/F)	7/13	7/9	5/3
Dysphagia, n (%)	13 (65%)	12 (75%)	7 (88%)
Reflux, n (%)	6 (30%)	5 (31%)	2 (25%)
Chest pain, n (%)	3 (15%)	1 (6%)	1 (13%)
Endoscopic findings	n=18	n=15	n=8
Normal	10	5	4
Hiatal hernia	3	3	1
Eosinophilic inflammation	0	2	1
Reflux esophagitis	2	1	1
Other (Schatzki ring, etc)	3	4	1
Barium swallow	n=6	n=7	n=5
Slightly delayed transit	0	1	0
Delay transit of barium tablet	1	1	1
Follow-up obtained	n=16	n=12	n=5
Good treatment response	11 [¶]	7 [‡]	4 [*]

[¶] PPI (1), Nissen (1), antidepressant (2), PPI and antidepressant (2), anticholinergic (2), botulinum toxin injection in esophageal muscle under EUS guidance (1), spontaneous (2)

[‡] PPI (3), Nissen (1), antidepressant (1), fluticasone (1), botulinum toxin injection in esophageal muscle under EUS guidance (1)

^{*} anticholinergic (1), calcium channel blockers (1), PPI (1), spontaneous (1)