

Classifying Esophageal Motility by Pressure Topography Characteristics: A Study of 400 Patients and 75 Controls

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- AIM:** This study aimed to devise a scheme for the systematic analysis of esophageal high-resolution manometry (HRM) studies displayed using topographic plotting.
- METHODS:** A total of 400 patients and 75 control subjects were studied with a 36-channel HRM assembly. Studies were analyzed in a stepwise fashion for: (a) the adequacy of deglutitive esophagogastric junction (EGJ) relaxation, (b) the presence and propagation characteristics of distal esophageal persistalsis, and (c) an integral of the magnitude and span of the distal esophageal contraction.
- RESULTS:** Two strengths of pressure topography plots compared to conventional manometric recordings were: (a) the ability to delineate the spatial limits, vigor, and integrity of individual contractile segments along the esophagus, and (b) the ability to distinguish between loci of compartmentalized intraesophageal pressurization and rapidly propagated contractions. Making these distinctions objectified the identification of distal esophageal spasm (DES), vigorous achalasia, functional obstruction, and nutcracker esophagus subtypes. Applying these distinctions made the diagnosis of spastic disorders quite rare: (a) DES in 1.5% patients, (b) vigorous achalasia in 1.5%, and (c) a newly defined entity, spastic nutcracker, in 1.5%.
- CONCLUSION:** We developed a systematic approach to analyzing esophageal motility using HRM and pressure topography plots. The resultant scheme is consistent with conventional classifications with the caveats that: (a) hypercontractile conditions are more specifically defined, (b) distinctions are made between rapidly propagated contractions and compartmentalized esophageal pressurization, and (c) there is no "nonspecific esophageal motor disorder" classification. We expect that pressure topography analysis, with its well-defined functional implications, will prove valuable in the clinical management of esophageal motility disorders.

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INTRODUCTION

Conventional esophageal manometry uses 3–8 pressure sensors with variable spacing positioned within the esophageal lumen to monitor pressure changes following water swallows. There is no agreed upon convention regarding an optimal array of pressure sensors and, depending on the type and number of sensors used, the recording assembly may need to be repositioned in the course of the study to focus on a particular area of interest. Individual pressure tracings are analyzed for pressure onset, amplitude, and duration of contraction usually referring sensor position in cm from the lower esophageal sphincter (LES). Peristaltic velocity is estimated by analyzing the relative timing of the pressure upstroke at adjacent transducers in proximity to the LES (1–4). Resultant diagnoses of esophageal motor disorders derived from these studies are summarized in Table 1 (2).

A recent evolution in manometric methodology has been the introduction of solid-state high-resolution manometry

(HRM), the basic concept being that by vastly increasing the number of high-fidelity recording sites and decreasing the spacing between them, one can more completely define the intraluminal pressure environment of the esophagus with minimal spatial gaps between recording sites and, consequently, with minimal movement-related artifact (5, 6). Coupled with the introduction of HRM have come sophisticated algorithms to display the expanded manometric data set as pressure topography plots, usually with isobaric conditions among sensors indicated by color (Fig. 1). However, this being a relatively new methodology, there is currently no uniform scheme to analyze HRM pressure topography plots. In an attempt to help fill this void, we recently performed a comprehensive characterization of esophageal HRM data in 75 normal subjects using new analysis paradigms unique to pressure topography interpretation (7, 8). At the very least, the technical advancements inherent in solid-state HRM coupled with pressure topography analysis should simplify manometric technique and the interpretation of esophageal motor

Table 1. Conventional Classification of Esophageal Motility

Conventional Manometric Diagnoses	
Aperistalsis	<ul style="list-style-type: none"> Absent or simultaneous contractions (<30 mmHg)
Ineffective esophageal motility (IEM)	<ul style="list-style-type: none"> ≥ 3 peristaltic contractions with failure of wave progression due to an ineffective distal contraction amplitude (>30 mmHg) or failed peristalsis over a segment of the distal esophagus
Normal	<ul style="list-style-type: none"> Normal velocity Normal peristaltic amplitude ≥ 7 peristaltic contractions with an intact wave progression (amplitude >30 mmHg)
Nutcracker esophagus	<ul style="list-style-type: none"> Average peristaltic amplitude >180 mmHg over pressure sensors 3 and 8 cm above LES
Isolated hypertensive LES	<ul style="list-style-type: none"> Basal LES pressure greater than 45 mmHg (mid-respiratory pressure)
Distal esophageal spasm (DES)	<ul style="list-style-type: none"> Contractile velocity >8 cm/s mmHg over pressure sensors 3 and 8 cm above LES in ≥ 2 swallows
Atypical disorders of LES relaxation	<ul style="list-style-type: none"> Abnormal LES relaxation, with some normal, may have simultaneous or absent peristalsis
Achalasia	<ul style="list-style-type: none"> Abnormal LES relaxation Absent or simultaneous contractions

Modified from Spechler and Castell (2).

dysfunction. Thus, the goal of this study was to develop a systematic, pressure topography-oriented analysis to a large series of HRM clinical studies to analyze and categorize motor disorders of the distal esophagus (8, 9). In addition, we hypothesize that the detail provided by pressure isocontour plots analysis could enhance description of clinically relevant abnormalities of peristaltic function, such as achalasia and spasm.

METHODS

Patients

HRM studies done between February 2003 and July 2005 on 400 consecutive patients (248 men, age 18–87) referred to the Northwestern Memorial Hospital manometry laboratory for evaluation were analyzed. These patients presented with a diverse set of pathological conditions to a tertiary-care practice specializing in the management of esophageal disease. Patients were interviewed and examined to assess symptoms and to make anthropometric measurements. Manometric findings from the patient group were compared to those of 75 asymptomatic control subjects (7, 8). HRM paradigms developed and reported for the normal subjects were directly applied to the patient groups.

Patients were initially categorized by their dominant clinical symptom. One hundred seventy-eight patients were undergoing evaluation for dysphagia, 144 for predominantly gastroesophageal reflux disease (GERD) symptoms (heartburn, regurgitation), 54 for chest pain, and 22 for miscellaneous complaints or follow-up. Typical of a referral practice,

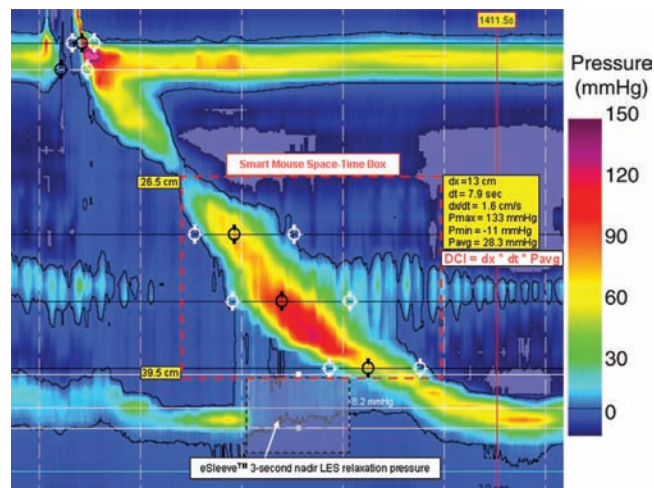


Figure 1. Measurement of EGJ relaxation using an automated measurement of the lowest mean residual pressure over a 3-s interval within the postdeglutitive period available in ManoView™. The eSleeve™ measurement tool is illustrated by the gray box that identifies the 3-s interval within which the mean residual pressure is measured. In this example, the 3-s nadir eSleeve™ measurement was 8.2 mmHg. The Smart Mouse tool in ManoView™ analysis software can also be used to calculate the distal contractile integral (DCI) by creating a Space-Time box starting at the transition zone and extending distal to the proximal aspect of the EGJ and bound temporally at the end of peristalsis or 15 s if no peristaltic wave is noted. The values for distance of the esophageal segment (dx), time duration of the contraction measured (ds), and mean pressure (Pavg) over the entire Space-Time box are provided by the Smart Mouse tool (yellow box). DCI is calculated by multiplying these values together and is expressed as mmHg·s·cm. In this example, the mean pressure is 28.3 mmHg and the time and length of the Space-Time box are 7.9 s and 13 cm, respectively. Thus, the DCI is 2,906.4 mmHg·s·cm.

some patients had already undergone treatment for their condition: 35 patients had prior fundoplication and 38 patients had undergone treatment for achalasia (pneumatic dilation, Heller myotomy, or both). Only four patients were excluded from the final analysis: two with pseudo-achalasia due to cancer and two with paraesophageal hernia that prevented intubation of the stomach. The study protocol was approved by the Northwestern University Institutional Review Board.

High-Resolution Manometry

A solid-state HRM assembly with 36 solid-state sensors spaced at 1-cm intervals (O.D. 4.2 mm) was used (Sierra Scientific Instruments Inc., Los Angeles, CA). The response characteristics of this device, calibration procedure, and post-study thermal correction algorithm have been described in detail elsewhere (10), but to summarize, each sensor is circumferentially sensitive, accurate to within 1 mmHg, capable of recording transient pressure changes in excess of 6,000 mmHg/s, and zeroed to atmospheric pressure. Studies were done in a supine position after at least a 6-h fast. The HRM assembly was passed transnasally and positioned to record from the hypopharynx to the stomach with about 5 intragastric sensors. The catheter was fixed in place by taping it to the

nose. The manometric protocol included a 5-min period to assess basal sphincter pressure and ten 5-mL water swallows.

Subsequently, the data were analyzed using both ManoView™ analysis software (Sierra Scientific Instruments Inc.) and custom programs written in Matlab™ (The MathWorks Inc., Natick, MA). Manometry data files were analyzed in Matlab™ by exporting the data from ManoView™ in ASCII format and then converting them for storage and processing. Although pressure topography plots can be generated using ManoView™, Matlab™ was preferentially used because of greater flexibility in customizing isobaric contour and spatial pressure variation plots as well as providing a tool with which to devise and refine computer programs to explore novel HRM paradigms. Once written, these Matlab™ programs could systematically analyze each of the nearly 5,000 swallows in the manometric data set under analysis.

Characterization of Esophageal Motility Using Pressure Topography Parameters

Recognizing that esophageal bolus transport is effected by the interaction of resistance through the esophagogastric junction (EGJ), intrabolus pressure, and esophageal closure pressure behind the bolus (11), we devised a stepwise HRM analysis algorithm that focused on each of these three key functional variables. Patients were first characterized by the presence or absence of impaired deglutitive EGJ relaxation using an automated measurement tool in ManoView™ of the lowest mean residual pressure over a 3-s interval within the postdeglutitive period (ManoView eSleeve™ 3-s nadir) (7) (Fig. 1).

Following the analysis of deglutitive EGJ relaxation, patient studies were further categorized by the dominant characteristics of the distal esophageal contraction after swallows. This analysis was facilitated by the generation of isobaric contour plots of the distal esophageal segment and EGJ at a 30-mmHg threshold pressure, given previous data suggesting that pressures greater than this are almost uniformly associated with complete bolus transit (12, 13). Pressurization front velocity (PFV) was calculated from the 30-mmHg isobaric contour plots by marking the distal temporal margin of the transition zone and the superior margin of the EGJ on the 30-mmHg isobaric contour and then calculating the slope between the two, expressed in cm/s (Fig. 2). Although this value was calculated using a Matlab™ program, this measurement can be made manually using the Smart Mouse tool in ManoView™. From prior analysis of 75 normal subjects, we had determined that the upper limit of normal for mean PFV (95th percentile) was 4.5 cm/s (8). Each swallow was thus characterized by conventional manometric parameters of peristaltic function (2). Swallows were characterized as normal (intact 30-mmHg isobaric contour and a PFV <8 cm/s), failed (complete failure of contraction with no pressure domain above 30 mmHg), hypotensive (≥ 2 -cm defect in the 30-mmHg isobaric contour), or rapidly conducted (PFV ≥ 8 cm/s) (Fig. 2). The ≥ 2 -cm defect in the 30-mmHg isobaric contour is an arbitrary cutoff that focuses on previous data

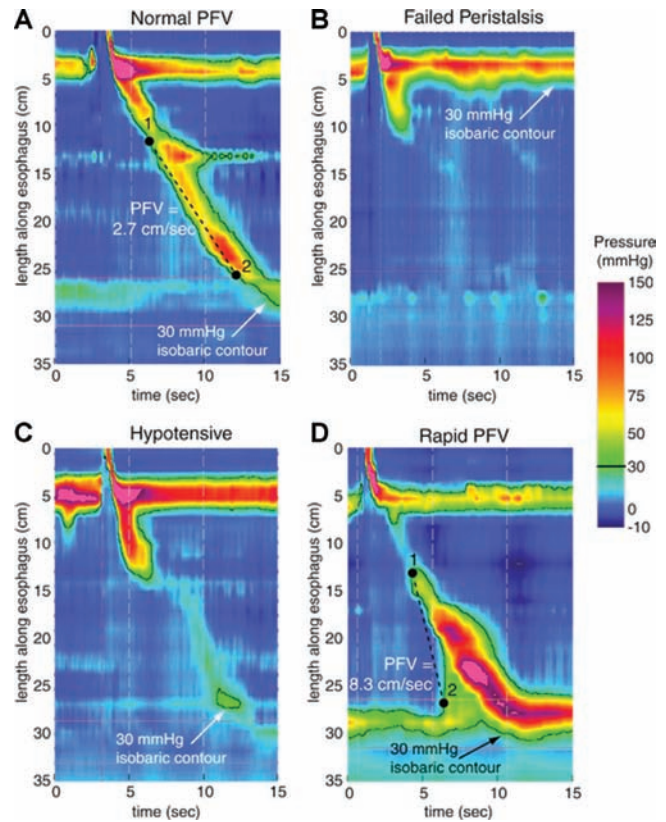


Figure 2. Derivation of the pressurization front velocity (PFV) from 30 mmHg isobaric contour plots. The heavy black line delineates the pressure domain ≥ 30 mmHg. Four representative swallows are shown to illustrate a normal PFV (A), aperistalsis (B), hypotensive peristalsis (C), and a rapid PFV (D). In order to calculate the PFV, the distal temporal margin of the transition zone (point 1) and the proximal margin of the EGJ on the 30-mmHg isobaric contour (point 2) were localized by hand. The slope of the line connecting the two points was the PFV, expressed in cm/s. The Smart Mouse™ tool available in ManoView™ can be used to calculate the slope. Note that in the example of panel D, the rapid PFV is attributable to compartmentalized esophageal pressurization in the setting of obviously impaired deglutitive EGJ relaxation (3-s nadir eSleeve™ > 30 mmHg).

supporting that a continuous 30-mmHg wave front is almost always associated with complete bolus transit (12, 13). In addition, swallows with a rapid PFV were further characterized based on the distinction between a compartmentalized esophageal pressurization and a rapidly conducted contraction (spasm) (Fig. 3).

Swallows with a quantifiable PFV were also characterized by the vigor of the associated distal esophageal pressurization using the distal contractile integral (DCI) that was calculated using MatLab™ (8) (Fig. 4). The DCI quantified the length, vigor, and persistence of postdeglutitive pressurization in the distal esophageal segment, expressed as mmHg·s·cm. Using data from 75 asymptomatic controls, a DCI value greater than 5,000 mmHg·s·cm was considered elevated. Alternatively, the DCI can be assessed using the Smart Mouse tool in ManoView™ by first outlining a Space-Time box that

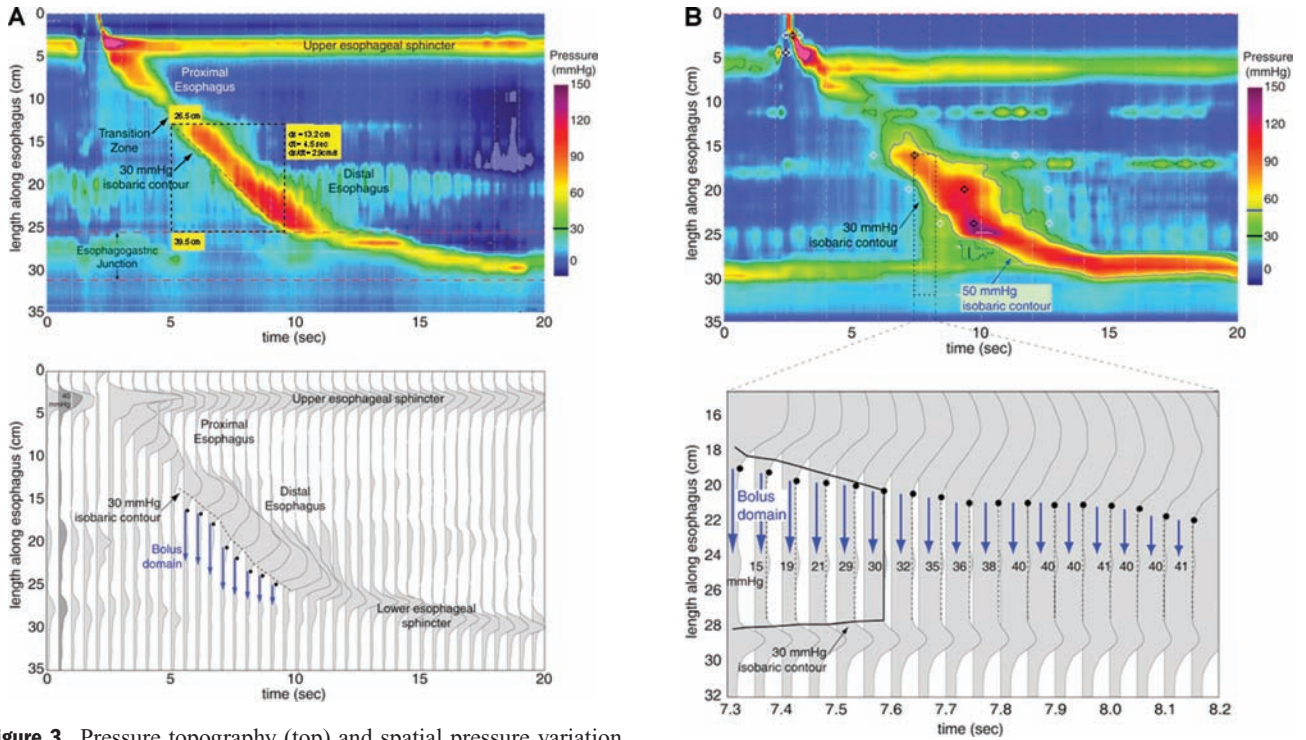


Figure 3. Pressure topography (top) and spatial pressure variation plots (bottom) differentiating normal (A) from compartmentalized esophageal pressurization (B) from a rapidly propagated contraction (C). Figure 3A represents a simultaneous pressure isocontour plot and spatial pressure variation plot during a normal swallow. The pressure topography plots easily distinguish the upper esophageal sphincter (UES), proximal esophagus, transition zone, distal esophagus, and EGJ. The dashed black box on the pressure isocontour plot (A, top) illustrates the measurement of the PFV using a 30-mmHg isobaric contour (black line) and the Smart Mouse tool in ManoView™ Analysis software (dashed box). The PFV is indicated in the yellow box as ds/dt in cm/s. The lower panel illustrates a series of spatial pressure variation plots at 0.5-s intervals of the same swallow. The darkened line (0.5 s) indicates the pressure scaling. These plots provide a convenient means to visualize intraluminal pressure gradients. The dashed line (A, bottom) indicates the demarcation of the 30-mmHg isobaric contour domain noted in the pressure topography plot (A, top) while the black dots indicate the locus of luminal closure along the contractile wave front. The blue arrows thus represent the bolus domain ahead of the contractile wave front. Figure 3B illustrates a swallow with functional obstruction at the EGJ. Note that the 30-mmHg isobaric contour domain (black) deviates quickly from the propagating contractile wave front highlighted by the 50-mmHg isobaric contour line (blue). Thus, the PFV of the 30-mmHg isobaric contour domain is 8.2 cm/s and would fit criteria for a rapid contraction. Analyzing the small segment outlined by the dashed box in the pressure isocontour plot (B, top) and exploding this to a series of spatial pressure variation plots at 0.05-s intervals (B, bottom) distinguished compartmentalized esophageal pressurization from the contractile wave front. Note that the compartmentalized esophageal pressurization between the peristaltic wave front (delineated by upstroke of the intraluminal pressure variation, black dots) and the EGJ is uniform between these closure points and defines a rapid PFV when the pressure exceeds 30 mmHg. In this context, the rapid PFV is attributable to pseudo-spasm. In contrast, Figure 3C represents a swallow with rapid PFV attributable to spasm. The 30-mmHg and 50-mmHg isobaric contours parallel each other, indicating that no compartmentalized esophageal pressurization has occurred. Evident in the spatial pressure variation plots (C, lower), the entire distal esophagus is contracting simultaneously.

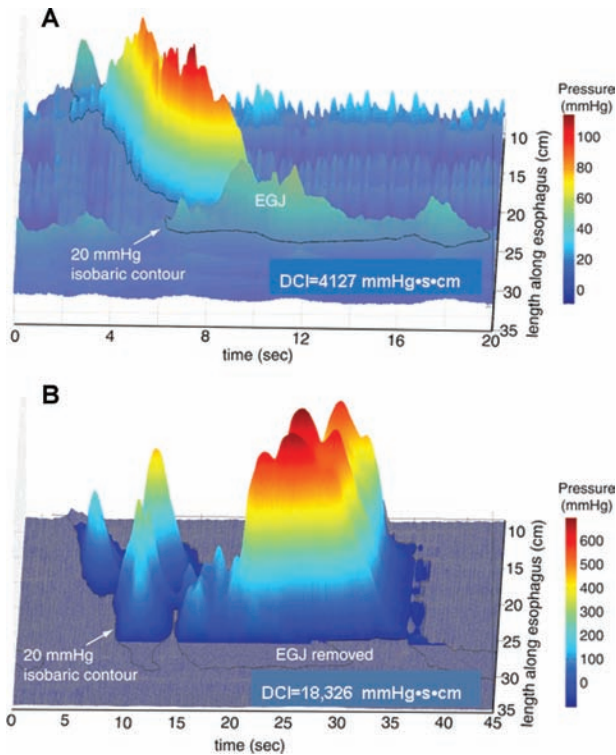


Figure 4. Derivation of the distal contractile integral (DCI). Two examples are illustrated, a normal DCI (*A*) and a greatly increased DCI (*B*). Conceptually, if the isobaric contour map of distal esophageal pressurization is envisioned as a three-dimensional solid, the footprint of the solid is time multiplied by the length of the distal esophageal segment (cm) and the height of the solid is pressure. The DCI is the volume of that solid spanning from 20 mmHg at the base to its peak, expressed as mmHg·s·cm. The patient illustrated in panel B was an extreme example of a spastic nutcracker pattern as the PFV value is normal (3.0 cm/s).

encompasses the distal peristaltic wave (Fig. 1). The Space-Time box starts at the transition zone and extends distal to the proximal aspect of the EGJ and it is bound temporally at the end of peristalsis or at 15 s if no peristaltic wave is noted (Fig. 1). The DCI can then be calculated by multiplying the mean pressure in the Space-Time box by the length and duration of the Space-Time box.

After each patient's 10 swallows were analyzed and categorized, their overall motility pattern was classified using a scheme adapted to topographic metrics from conventional manometric criteria (2) as detailed in Table 2. Patients with failed peristalsis in all test swallows were classified as aperistalsis. Patients with failed peristalsis or hypotensive peristalsis in $\geq 30\%$ but $< 70\%$ of test swallows were classified as mild peristaltic dysfunction while those with $\geq 70\%$ of swallows with these patterns had severe peristaltic dysfunction. Patients with a PFV < 8 cm/s in $> 90\%$ of swallows and a DCI greater than 5,000 were considered to have hypertensive peristalsis and this was stratified based on the magnitude of the DCI and the locus of the hypercontractile segment (Table 2). Patients with a PFV > 8 cm/s in $\geq 20\%$ of swallows

were classified as having rapidly propagated pressurization. These patients were further classified as spasm or compartmentalized pressurization based on the distinction between a rapidly propagated contractile wave front and compartmentalized esophageal pressurization (Fig. 3).

Statistical Analysis

The high-resolution manometric parameters (eSleeve™ 3-s nadir pressure, PFV, DCI) were summarized using mean and standard error (SE). Analysis of variance (ANOVA) was used to compare the mean values of these parameters between patient groups defined by HRM.

RESULTS

Evaluable studies were obtained in 396 of the 400 patients (99%). A total of 279 (70%) had normal deglutitive EGJ relaxation while 117 (30%) had impaired deglutitive EGJ relaxation based on an eSleeve™ 3-s nadir value > 14.0 mmHg. Among the patients with impaired deglutitive EGJ relaxation, 77 (66%) had aperistalsis or a PFV < 8 cm/s in $> 90\%$ of swallows while 40 (34%) patients had pan-esophageal pressurization or a PFV > 8 cm/s in $\geq 20\%$ of swallows (Fig. 5A). In contrast, almost all of the patients with normal deglutitive EGJ relaxation had a normal PFV (98%), with only 6 (2%) patients characterized as spasm on the basis of having a PFV with greater than 8 cm/s for $\geq 20\%$ of their swallows (Fig. 5B)

Incomplete Deglutitive EGJ Relaxation

ACHALASIA. Seventy-three of the 117 (62%) patients with abnormal deglutitive EGJ relaxation met criteria for achalasia, with 40 having aperistalsis and 33 having either a pattern of pan-esophageal pressurization (Fig. 6A) or a PFV greater than 8 cm/s with $\geq 20\%$ of swallows related to a spastic contraction (Fig. 6B). Although the patients with pan-esophageal pressurization would fit conventional criteria for vigorous achalasia, they had no focal contraction within the esophageal body; rather, the increased intraesophageal pressure was attributable to compartmentalization of the entire esophageal body between the two sphincters. Only four patients exhibited the pattern of Figure 6B with the combination of both impaired deglutitive EGJ relaxation and spasm of the distal esophageal segment; we restrict the label of vigorous achalasia to this much less common subtype.

FUNCTIONAL OBSTRUCTION. Thirty-seven patients had impaired EGJ relaxation with a normal PFV (mild functional obstruction) and seven had severe functional obstruction evident by impaired EGJ relaxation with a compartmentalized pressurization pattern (Fig. 3B). Although either pattern is consistent with evolving or variant achalasia, they are also associated with mechanical abnormalities of the EGJ leading to outflow obstruction: 15 were postfundoplication (Fig. 7), 5 had peptic stricture, 3 had eosinophilic

Table 2. Esophageal Motility Classification Based on Pressure Topography Criteria

Diagnostic Criteria for Esophageal Motility	# Cases (%)
Normal	91 (23.0%)
<ul style="list-style-type: none"> • Propagation front velocity (PFV) <8 cm/s in >90% of swallows • Mean DCI <5,000 mmHg·s·cm • Normal EGJ pressure (10–35 mmHg) and deglutitive relaxation (eSleeve™ 3-s nadir <15 mmHg) 	
Peristaltic dysfunction	73 (18.4%)
<ul style="list-style-type: none"> • Mild: ≥3 and <7 swallows with either failed peristalsis or a ≥2-cm defect in the 30-mmHg isobaric contour of the distal esophageal segment 	–45 (11.4%)
<ul style="list-style-type: none"> • Severe: ≥7 swallows with either failed peristalsis or a ≥2-cm defect in the 30-mmHg isobaric contour of the distal esophageal segment 	–28 (7.0%)
Aperistalsis	29 (7.3%)
<ul style="list-style-type: none"> • No continuous pressure domain above an isobaric contour of 30 mmHg in the distal esophageal segment in any swallow • Scleroderma pattern: no continuous pressure domain above an isobaric contour of 30 mmHg in the distal esophageal segment in any swallow and a mean LES pressure <10 mmHg 	–14 (3.5%)
Hypertensive peristalsis	37 (9.3%)
<ul style="list-style-type: none"> • PFV <8 cm/s in >90% of swallows • Mean DCI: >5,000 mmHg·s·cm • Nutcracker: mean DCI >5,000 and <8,000 mmHg·s·cm • Segmental nutcracker: mean DCI >5,000 with only one segmental focus of hypertensive contraction (>180 mmHg) • Spastic nutcracker: mean DCI >8,000 mmHg·s·cm • Nutcracker LES: mean DCI >5,000 mmHg·s·cm with the focus of hypertensive contraction (>180 mmHg) limited to the LES after-contraction. 	–16 (4%) –12 (3%) –6 (1.5%) –3 (0.8%)
Rapidly propagated pressurization	10 (2.5%)
<ul style="list-style-type: none"> • PFV >8 cm/s in ≥20% of swallows • Spasm (increased PFV attributable to rapid contractile wave front) • Compartmentalized pressurization (increased PFV attributable to distal compartmentalized esophageal pressurization) 	–6 (1.5%) –4 (1.0%)
Abnormal LES tone (end-expiratory)	39 (9.9%)
<ul style="list-style-type: none"> • Hypotensive: mean <10 mmHg with normal peristaltic function and EGJ relaxation • Hypertensive: mean >35 mmHg with normal peristaltic function and EGJ relaxation 	–24 (6.1%) –15 (3.8%)
Achalasia	73 (18.4%)
<ul style="list-style-type: none"> • Impaired deglutitive EGJ relaxation • Aperistalsis • Classic: aperistalsis or pan-esophageal pressurization with no identifiable segmental contractile activity with all swallows • Vigorous: with distal spasm 	–69 (17.4%) 4 (1.0%)
Functional obstruction	44 (11.1%)
<ul style="list-style-type: none"> • Impaired deglutitive EGJ relaxation • Mild: PFV <8 cm/s in >90% of swallows with a mild elevation (15–30 mmHg) of distal esophageal pressurization • Severe: PFV >8 cm/s in ≥20% of swallows with compartmentalized pressurization 	–37 (9.3%) –7 (1.8%)

PFV = pressurization front velocity; DCI = distal contractile integral.

esophagitis, while the remainder had no defined pathology and were treated as achalasia.

Normal Deglutitive EGJ Relaxation

SPASM. After distinguishing between a rapid PFV attributable to compartmentalized esophageal pressurization and that attributable to a rapidly conducted contraction, very few patients met the criteria for distal esophageal spasm (DES). In fact, only six patients (1.5%) had a PFV >8 cm/s in ≥20% of their swallows and met the criteria for a rapidly propagated contraction (Fig. 8A). Of the four patients who had normal EGJ relaxation and compartmentalized pressurization, two had eosinophilic esophagitis (Fig. 8B) and the other two had GERD symptoms without a pathologic diagnosis on biopsy.

HYPERTENSIVE PERISTALSIS. Thirty-seven of the 297 patients with normal deglutitive EGJ relaxation (12%) had a DCI >5,000 mmHg·s·cm, thereby defining hypertensive peri-

stalsis. However, there was substantial heterogeneity among this group. Although a DCI value >5,000 mmHg·s·cm exceeded the 95th percentile of normal, thereby meeting the usual criterion for nutcracker esophagus, a threshold value of 8,000 mmHg·s·cm distinguished a spastic nutcracker subgroup (N = 12) characterized by repetitive high-amplitude contractions that was uniformly associated with dysphagia or chest pain (Fig. 9). An additional six subjects with a DCI >5,000 had a locus of hypertensive peristalsis isolated within one of the distal esophageal contractile segments that would likely have gone undetected using conventional methods and criteria.

LES function was variable among the nutcracker group. Of the 22 patients with a mean basal end-expiratory LES pressure >35 mmHg (hypertensive LES), seven met criteria for nutcracker esophagus. In addition, three of these patients had a segmental focus of hypertensive peristalsis limited to the LES after-contraction and were thus classified as nutcracker LES.

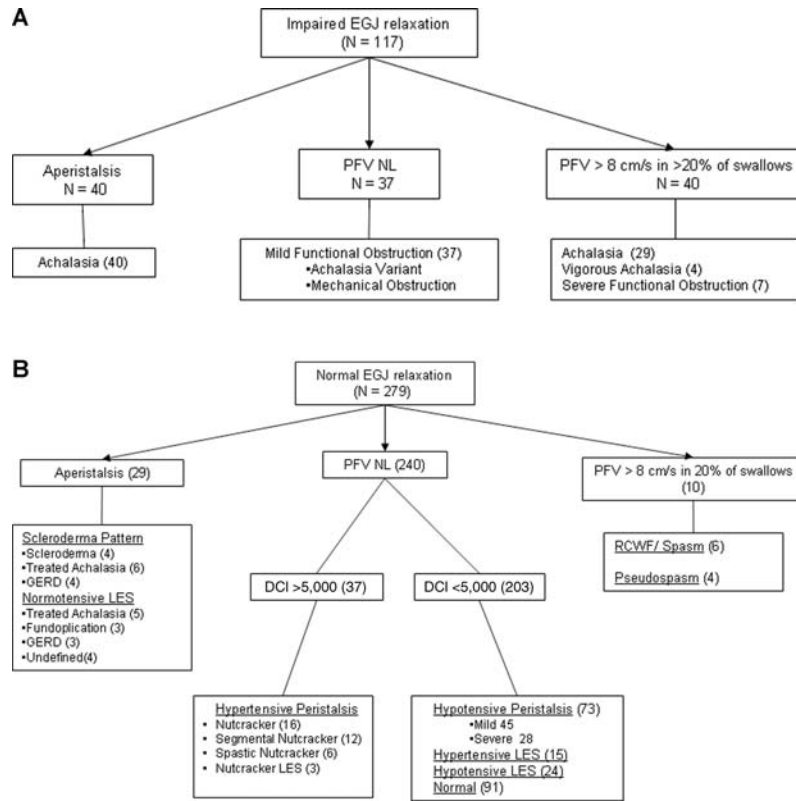


Figure 5. Flowchart illustrating the classification of patients with impaired deglutitive EGJ relaxation (A) and normal EGJ relaxation (B).

PERISTALTIC DYSFUNCTION. Twenty-nine subjects had normal deglutitive EGJ relaxation and aperistalsis. Fourteen of these patients had a mean basal end-expiratory LES pressure <10 mmHg, fulfilling criteria for a scleroderma pattern while the remaining fifteen had normal basal end-

expiratory LES pressure. Six of the scleroderma pattern patients were treated achalasics while four had a confirmed diagnosis of scleroderma and four had only GERD symptoms. Patients with aperistalsis and normal basal end-expiratory LES pressure were comprised of partially treated achalasics

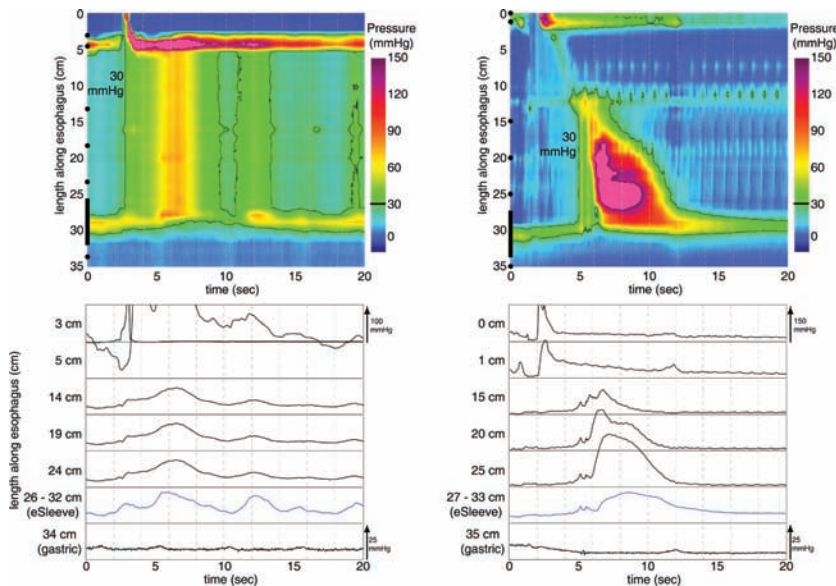


Figure 6. The difficult distinction between achalasia associated with pan-esophageal pressurization (left) and vigorous achalasia (right). In each case, the black line indicates the 30-mmHg isobaric pressure contour and both examples have an abnormal eSleeve™ 3-s nadir LES relaxation measurement. Note the characteristic pan-esophageal pressurization on the pressure topography plot in panel A and the spastic contraction in panel B. This differentiation is more difficult using conventional pressure tracings displayed on the bottom of panels A and B.

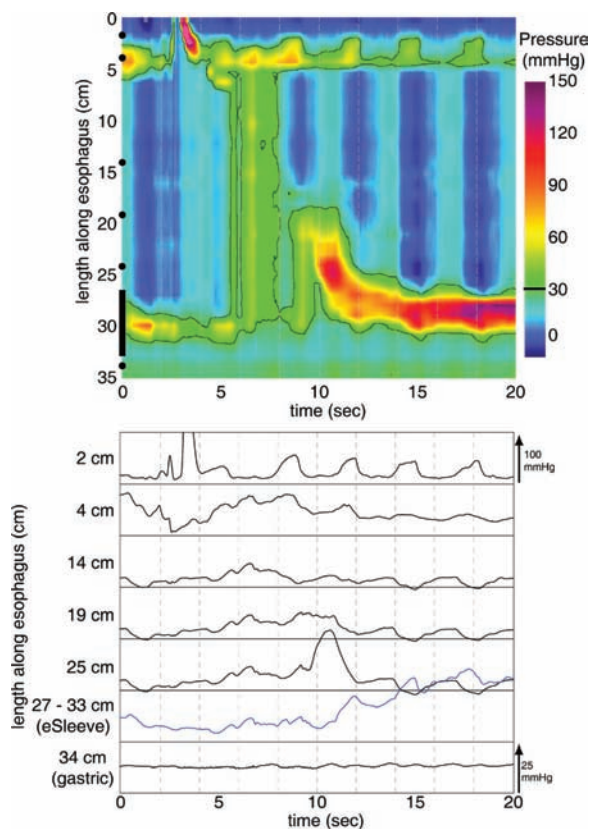


Figure 7. Pressure topography plot illustrating functional obstruction in a postfundoplication patient. The PFV is >8 cm/s and preceded by a period of pan-esophageal pressurization. The compartmentalized esophageal pressurization associated with this functional obstruction is difficult to appreciate using conventional pressure tracings (bottom panel).

(5), postfundoplication patients with dysphagia (3), GERD (3), and undefined dysphagia (4). Lesser degrees of peristaltic dysfunction were seen in 73 patients, severe in 28 patients, and mild in 45.

Symptom Association With Pressure Topography Variables

There was a significant increase in the mean DCI in patients with chest pain (DCI 3,813.0 mmHg·s·cm, SE 328.4) and dysphagia (DCI 4,146 mmHg·s·cm, SE 345.0) compared to patients with GERD (DCI 2,658.1 mmHg·s·cm, SE 158.7) (ANOVA, $P < 0.05$). In addition, patients with dysphagia had an elevated PFV (7.5 cm/s, SE 0.3) compared to both chest pain patients (3.4 cm/s, SE 0.2) and GERD patients (3.6 cm/s, SE 0.3) (ANOVA, $P < 0.05$).

DISCUSSION

The introduction of solid-state HRM capable of simultaneously monitoring the entire axial pressure profile from the pharynx to the proximal stomach along with the application of sophisticated topographic plotting algorithms rep-

resent an unquestionable evolution in the methodology of esophageal manometry. The major goal of this study was to devise a scheme for the systematic analysis of these pressure topography plots based on a large clinical series and normative data from 75 controls. In doing so, we found two major strengths of pressure topography plots compared to conventional manometric recordings: (a) the ability to easily delineate the spatial limits and contractile characteristics of individual contractile segments along the esophagus, and (b) the ability to easily distinguish between loci of compartmentalized intraesophageal pressurization and rapidly propagated esophageal contractions. Making these distinctions was of great utility in identifying DES, vigorous achalasia, functional obstruction, and subtypes of nutcracker esophagus. Applying an analysis algorithm that recognized these distinctions to a 400 patient clinical series led to the conclusion that these spastic motility disorders were quite rare: (a) DES was found in 6 (1.5%) patients, (b) vigorous achalasia in 6 (1.5%), and (c) a newly defined entity, spastic nutcracker, in 6 (1.5%).

The application of HRM with topographic plots for assessment of esophageal motor function was first described by Clouse and Staiano in 1991 along with the observation that the propagation of esophageal peristalsis was not seamless (14). Rather, topographic plotting demonstrated the existence of distinct transition zones: (a) between the striated and smooth muscle segments, (b) between the proximal and distal aspects of the smooth muscle esophagus, and (c) between the distal smooth muscle esophagus and the LES, which contracted with vigor and persistence quite dissimilar to the adjacent esophagus. More recently, Fox *et al.* combined HRM pressure topography plots with simultaneous videofluoroscopy to establish the correspondence between specific pressure topography signatures and impaired bolus transit (6). They concluded that HRM with pressure topography plotting was more accurate than conventional manometry in identifying impaired bolus transit attributable to either focal breaks in the peristaltic wave front or impaired EGJ relaxation. Although prior studies had established intrabolus pressure to be an important determinant of effective peristalsis (15), delineating the limits and magnitude of intrabolus pressure on conventional manometric tracings depends upon defining the “ramp-up,” or pressure inflexion point, in line tracings, something that is difficult to achieve on more than a qualitative basis and difficult to temporarily relate among recording sites. A major advantage of pressure topography plotting is in precisely quantifying the magnitude and spatial domain of compartmentalized intraesophageal pressurization by recognizing a characteristic pressure signature in an isobaric contour analysis (Figs. 2 and 3).

Conventional classification of esophageal motility recognizes the significance of simultaneous contractions at adjacent intraesophageal recording sites but makes no distinction between “simultaneous contractions” attributable to rapidly propagated lumen-obliterating events and those

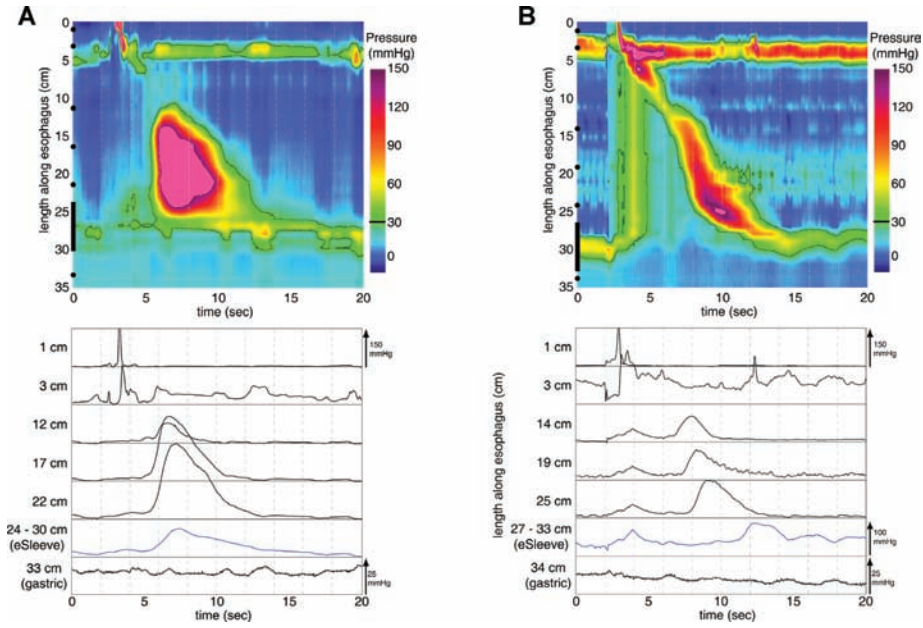


Figure 8. Differentiating spasm from pseudo-spasm. Panel A illustrates a swallow with rapid PFV due to a spastic contraction. In contrast, panel B illustrates a swallow with a normal PFV that is preceded by a period of pan-esophageal pressurization in a patient diagnosed with eosinophilic esophagitis and a normal endoscopy. Although this is evident on careful analysis of the conventional pressure tracings below, it may be confused with a double-peaked contraction or artifactual pressurization.

attributable to downstream obstruction with resultant compartmentalized intraesophageal pressurization (2, 16, 17). This void, along with the ability to easily make this distinction with HRM and isobaric contour analysis, mandates that

esophageal motility classification be readdressed to accommodate it. In doing so, the interdependency between the interpretation of “simultaneous contractions” and the adequacy of EGJ relaxation also mandate that the systematic analysis of

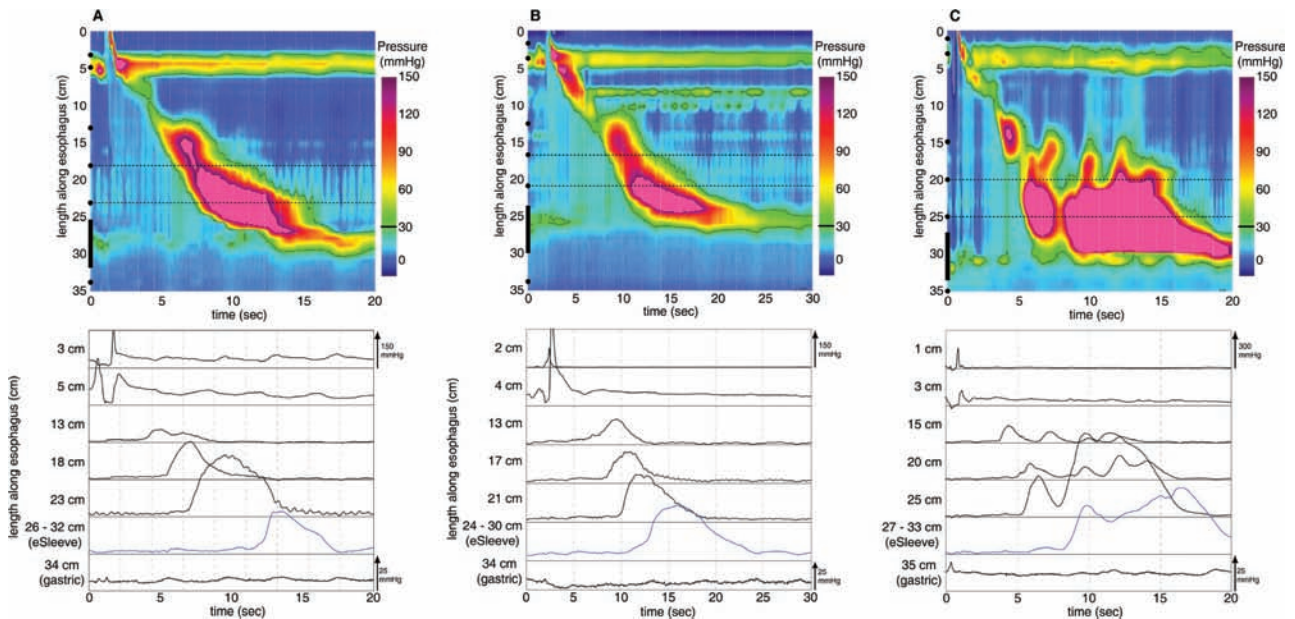


Figure 9. Heterogeneity of hypertensive peristalsis. Panel A represents nutcracker esophagus defined as a DCI greater than 5,000 mmHg-s-cm and a normal PFV. The dashed lines represent the conventional measurement points of 3 and 8 cm above the LES and this patient would fulfill conventional criteria for nutcracker esophagus (tracing). Panel B represents another patient with a DCI greater than 5,000 mmHg-s-cm; however, this patient would have been missed by conventional measurement, as the hypercontractile focus is limited to a short segment in the distal esophagus. Panel C illustrates the less common spastic variant of hypertensive peristalsis (spastic nutcracker) identifiable by a DCI value greater than 8,000 mmHg-s-cm. In this example, the contraction does not meet PFV criteria for spasm (8 cm/s) and the contraction has a spastic component that occurs after the wave front propagates to the EGJ.

motility progresses in the sequence: (a) quantification of EGJ relaxation, (b) evaluation of integrity and propagation velocity of peristalsis, and (c) characterization of the peristaltic contraction (if present). A key outcome of this approach is in drawing a distinction between spasm (a rapidly propagated lumen obliterating contraction) and a compartmentalized pressurization, a phenomenon attributable to regional intraesophageal pressurization be it confined to the distal esophagus in the setting of preserved peristalsis or pan-esophageal as commonly observed with achalasia. Table 2 reflects our best effort at incorporating pressure topography analysis concepts into the classification of esophageal motility.

In examining Table 2, the differentiation between it and existing conventional criteria for classifying motility disorders (Table 1) is in defining the spastic disorders: DES, vigorous achalasia, and spastic nutcracker. In each case, applying topographic criteria leads to a more restrictive diagnosis of the spastic condition. In the case of DES, the basic concept of requiring that $\geq 20\%$ of swallow be characterized by rapidly propagated pressurization (PFV > 8 cm/s) is maintained, but eliminating cases ultimately attributable to functional obstruction at the EGJ reclassifies 4/10 (40%) cases to compartmentalized pressurization, an entity best dealt with by treatments directed at the EGJ. Similarly, an additional 40 patients with severe outflow obstruction causing the PFV to be greater than 8 cm/s in at least two swallows may have been classified as DES or “nonspecific” depending on the interpreter. With respect to vigorous achalasia, the pattern of pan-esophageal pressurization, seen in 29 cases, would typically be interpreted as “simultaneous contractions” on conventional line tracings as it is not unusual for the amplitude of these to exceed 60 mmHg. However, after recognizing those for what they were and classifying them as classical achalasia, only four achalasia cases (10% of achalasia overall) exhibited rapidly propagating contractions with PFV > 8 cm/s with $\geq 20\%$ of swallows (the criterion of spasm), making this an unusual variant.

In the case of nutcracker esophagus, this was a relatively common diagnosis when loosely defined as a locus of hypertensive peristalsis (mean amplitude > 180 mmHg). However, using an isobaric contour analysis it becomes evident that hypertensive peristalsis can be localized to 1, 2, or all 3 (including the LES) smooth muscle segments. The meaning of these foci of hypertension is still the object of investigation but current thinking is that they are epiphenomena associated with esophageal hypersensitivity (18). On the other hand, topographic analysis clearly identifies a variant of nutcracker, characterized by normal peristaltic propagation but extraordinarily high DCI more akin to DES than to nutcracker (Figs. 4B and 9C). However, since it does not meet what has become the hallmark of DES (a rapidly propagated contraction), we named this entity spastic nutcracker. To our knowledge, this group has not been previously characterized, although other investigators have suggested that the definition of nutcracker be revised to stratify patients on the degree of contractile abnormalities (19).

In summary, we have used a large clinical experience of 400 consecutive patients and 75 control subjects to develop a systematic approach to classifying esophageal motility using HRM and pressure topography plots. The resultant scheme (Table 2) is consistent with conventional classifications with the caveats that: (a) hypercontractile conditions are more specifically defined, (b) distinctions are made between “simultaneous contractions” attributable to rapidly propagated contractions and those attributable to compartmentalized esophageal pressurization, and (c) there is no “nonspecific esophageal motor disorder” classification. Ultimately, further clinical experience will be the judge, but it is our expectation that pressure topography analysis of HRM data, along with its well-defined functional implications, will prove valuable in the clinical management of esophageal motility disorders.

STUDY HIGHLIGHTS

What Is Current Knowledge

- Esophageal manometry is the best method to characterize esophageal motility.
- High-resolution esophageal manometry analyzed with pressure topography plots provides greater detail regarding the characteristics of individual contractile segments along the esophagus.
- High-resolution manometry (HRM) incorporating pressure topography plotting either is or soon will be commercially available from most manufacturers.

What Is New Here

- The first classification system for defining esophageal motility using a scheme adapted to HRM with pressure topographic metrics.
- Isobaric contour analysis provides a means to easily distinguish between loci of compartmentalized intraesophageal pressurization (pseudo-spasm) and rapidly propagated esophageal contractions (spasm).
- Diffuse esophageal spasm and vigorous achalasia with spastic contractions are quite rare such that the majority of patients so classified by conventional criteria actually exhibit a pseudo-spasm pattern.
- A subset of nutcracker esophagus patients has a pattern of contractility akin to distal esophageal spasm (DES).

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CONFLICT OF INTEREST

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Specific author contributions: John Pandolfino: hypothesis, data analysis, statistics, main coauthor; Sudip Ghosh: developed analysis software, created figures, data analysis-statistics; John Rice: performed studies, created database for analysis; John O’Clarke: data analysis, performed studies; Monica Kwiatek: data analysis, performed studies; Peter Kahrilas: hypothesis, data analysis, main coauthor.

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