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COMPARISON OF MOTOR DIAGNOSES BY CHICAGO CLASSIFICATION VERSIONS 2.0 AND 3.0 ON ESOPHAGEAL HIGH-RESOLUTION MANOMETRY

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SUMMARY

Background—The Chicago Classification (CC) uses high-resolution manometry (HRM) software tools to designate esophageal motor diagnoses. We evaluated changes in diagnostic designations between two CC versions, and determined motor patterns not identified by either version.

Methods—In this observational cohort study of consecutive patients undergoing esophageal HRM over a 6-year period, proportions meeting CC 2.0 and 3.0 criteria were segregated into esophageal outflow obstruction, hypermotility, and hypomotility disorders. Contraction wave abnormalities (CWA), and ‘normal’ cohorts were recorded. Symptom burden was characterized using dominant symptom intensity and global symptom severity. Motor diagnoses, presenting symptoms, and symptom burden were compared between CC 2.0 and 3.0, and in cohorts not meeting CC diagnoses.

Results—Of 2569 eligible studies, 49.9% met CC 2.0 criteria, but only 40.3% met CC 3.0 criteria ($p < 0.0001$). Between CC 2.0 and 3.0, 82.8% of diagnoses were concordant. Discordance resulted from decreasing proportions of hypermotility (4.4%) and hypomotility (9.0%) disorders, and increase in ‘normal’ designations (13.0%); esophageal outflow obstruction showed the least

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the classification into the 'normal' category with this update⁷. For instance, rapid contractions (contraction velocity >8 cm/s) and hypertensive contractions (DCI>5000 mmHg.cm.s) were replaced by premature contractions (DL<4.5 s) and hypercontractile peristalsis (DCI>8000 mmHg.cm.s). New motor designations, such as ineffective esophageal motility (IEM) and fragmented peristalsis, were introduced. The impact of this changing landscape of esophageal motor disorders on motor diagnosis and symptom burden are unclear. Further, contraction wave abnormalities (CWA), including multiple peaked waves, prolonged wave duration, simultaneous contractions, and exaggerated contraction amplitudes, may not be identified by the averaging process incorporated into these software tools within the CC⁸⁹.

In this study, we assessed the impact of CC versions 2.0 and 3.0 on the proportions of motor diagnoses made in clinical esophageal HRM studies. Further, we assessed the impact of the averaging process of motor data during analysis of esophageal HRM, by determining the proportions of CWA that do and do not result in abnormal CC designations on versions 2.0 and 3.0. Finally, we compared symptom burden in patients with and without abnormal CC designations on versions 2.0 and 3.0.

METHODS

Subjects

This retrospective cohort study evaluated consecutive HRM studies performed over a 6-year period (2006-2011) at the motility laboratory at the Washington University School of Medicine and Barnes-Jewish Hospital in Saint Louis. All patients undergoing esophageal HRM (Given Imaging/Covidien/Medtronic, Duluth, GA) were eligible for this study; patients with uninterpretable or critically imperfect HRM studies were excluded from analysis. Symptom burden, extracted from symptom questionnaires completed by patients at the time of esophageal HRM, was compared between cohorts with and without motor diagnoses under CC versions 2.0 and 3.0. The study protocol and review of esophageal HRM were approved by the Human Research Protection Office (Institutional Review Board) at the Washington University School of Medicine.

Esophageal HRM

All patients were studied after an overnight fast and after discontinuing medications that can affect esophageal motor function (metoclopramide, anticholinergic medication, smooth muscle relaxants) for 5-7 days prior to the study, as previously described⁸. Briefly, a solid-state HRM catheter assembly (36 solid-state sensors spaced at 1-cm intervals, 4.2 mm diameter) was placed transnasally after topical anesthesia to the nasal passages. Studies were performed with the patient supine and slightly tilted to the left for ease of swallowing. A 20-second swallow-free period (landmark phase) was obtained after the patient was settled and resting quietly. Esophageal peristaltic function was assessed with 10 wet swallows of 5 mL ambient temperature water, administered 20 seconds apart. Pressure data was acquired using dedicated HRM software (Manoview, Given Imaging/Covidien/Medtronic, Duluth, GA).

Analysis of HRM Data

The esophageal HRM studies were first interpreted clinically using Chicago Classification 2.0⁶ by investigators not involved in the initial interpretation or clinical management of the study patients. Each study was analyzed using Manoview ESO 3.0 (Given Imaging/Covidien/Medtronic, Duluth, GA), which allows for automated designation of CC diagnoses after anatomic landmarks are reviewed to ensure accurate placement. After manual review to confirm accurate placement of anatomic landmarks and identification of swallows, CC 2.0 diagnoses were recorded, following which CC version 3.0 criteria were applied⁷ and each study was interpreted a second time. Subsequently, these designations were further segregated into four categories as follows⁹: a) outflow obstruction with elevated IRP (2.0 and 3.0: achalasia, esophageal outflow obstruction, including achalasia spectrum), b) hypermotility or spastic disorders (2.0: distal esophageal spasm (DES), hypercontractile or jackhammer esophagus, hypertensive peristalsis or nutcracker esophagus, rapid contractions with normal latency; 3.0: DES, hypercontractile or jackhammer esophagus), c) hypomotility disorders (2.0: absent peristalsis, weak peristalsis with small or large peristaltic defects, frequent failed peristalsis; 3.0: absent contractility, ineffective esophageal motility (IEM), fragmented peristalsis), and d) “normal” according to each version of CC^{6, 7}.

Contraction wave abnormalities (CWA) were identified in the esophageal body as follows⁹⁻¹¹: a) averaged esophageal body contraction amplitudes ≥ 180 mmHg in the distal esophagus (nutcracker esophagus, NE), b) $>20\%$ simultaneous contractions (SC), identified by contraction front velocity >6.8 cm/s, c) any multiple peaked waves with or without broad contraction wave >5.7 s (MPW/BW), d) $>15\%$ double peaked waves (DPW), and e) distal shift in contraction vigor, for which averaged distal contraction amplitudes of 150-179 mmHg were used as a surrogate marker^{8, 10} (Figure 1). Proportions of individual CWA, and overall CWA proportions were compared between cohorts meeting CC diagnoses and those designated ‘normal’ by CC.

Symptom Assessment

Whenever possible, patients presenting for esophageal HRM at our center are asked to complete symptom questionnaires. In these questionnaires, patients self-report their dominant and secondary symptom frequency and severity, as well as a global esophageal symptom assessment^{12, 13}. The frequency and severity for each symptom are rated on 5-point Likert scales generated *a priori* for esophageal physiologic studies at our institution, utilized in prior publications, and validated for assessment of esophageal symptoms in both esophageal motor disorders and gastroesophageal reflux disease^{10, 13, 14}. On these Likert scales, patients rate symptom frequency from 0 (no symptoms) to 4 (multiple daily episodes) and symptom severity from 0 (no symptoms) to 4 (very severe symptoms). The corresponding dominant symptom intensity (DSI) is then calculated as the product of the symptom frequency and symptom severity, for a total score from 0 to 16. The patient's global symptomatic state pertaining to the esophagus over the previous two weeks is queried on a 10-cm visual analog scale (VAS). On this scale, 0 designates no symptoms, and 10 indicates disabling symptoms interfering with activities of daily living (global symptom severity, GSS). The DSI and GSS represented our symptom burden metrics for the purposes of this study.

Statistical Methods

Data are reported as mean $\pm$ standard error of mean (SEM) unless otherwise noted. Proportions of cohorts with and without CC 2.0 and 3.0 designations and their motor patterns were determined and compared using the Chi-square test for categorical data. Demographics (age and gender) and symptom burden metrics (DSI and GSS) were compared between and within cohorts and motor patterns meeting CC 2.0 and 3.0 criteria, CWA, and true normal HRM studies, using Student's *t*-test or ANOVA, as appropriate, for continuous data. All analyses were two-tailed and $p < 0.05$ was required for statistical significance. Analyses were performed using IBM SPSS Statistics V.22.0 (Armonk, NY).

RESULTS

Study Cohort

The 6-year study period yielded a total of 2634 patients undergoing HRM studies. Of these, 65 (2.5%) were incomplete or critically imperfect and were excluded from further analysis (Figure 2). The remaining 2569 patients (54.6 ± 0.3 years, 63.5% female) fulfilled study inclusion criteria, and represented the study cohort. Based on available symptom questionnaire data, the study cohort had moderate-to-severe symptom burden, with DSI of 10.4 ± 0.1 (out of 16) and GSS of 6.0 ± 0.1 (out of 10). The most frequent presenting symptoms were heartburn (23.7%) and dysphagia (16.8%).

CC 2.0 and 3.0 Diagnoses

With both CC 2.0 and 3.0, hypermotility disorders were the least common diagnosis made, while the majority – more than half the studies – did not fulfil criteria for a CC motor diagnosis (Figure 2). There was a significant decrease in total proportions with a motor diagnosis between CC 2.0 (49.9%) and CC 3.0 (40.3%, $p < 0.0001$). This decrease was driven by a reduction in proportions with predominantly hypomotility and, to some extent, hypermotility diagnoses with CC 3.0 ($p < 0.0001$ for both comparisons), while proportions with esophageal outflow obstruction remained stable ($p = 0.93$, Figure 2). Concomitantly, proportions without a CC diagnosis increased significantly with CC 3.0 ($p < 0.0001$). The likelihood of a CC diagnosis was highest in patients with dysphagia (CC 2.0: 67.4%; CC 3.0: 57.6%) compared to all other symptoms combined (CC 2.0: 47.9%, CC 3.0: 37.5%, $p < 0.0001$ for each comparison).

Discordance Between CC 2.0 and 3.0

Taking all motor diagnoses including lack of a CC diagnosis into consideration, CC 2.0 and 3.0 diagnoses were concordant in 82.8%, while 17.2% of diagnoses were discordant (Figure 3). There were 333 patients (13.0%, age: 54.3 ± 0.8 years, 61.2% female) who made CC 2.0 diagnoses but did not meet CC 3.0 diagnostic criteria. On the other hand, 87 patients (3.4%, age: 54.9 ± 1.5 years, 64.8% female) met CC 3.0 but not CC 2.0 diagnostic criteria. Esophageal outflow obstruction was the most stable diagnosis between the two CC versions, with only 6.9% discordant diagnoses. In contrast, there was a 49.1% decline in hypermotility diagnoses, and a 31.6% decline in hypomotility diagnoses with CC 3.0 in comparison to CC

2.0. There were comparatively smaller gains in hypermotility (7.9%) and hypomotility diagnoses (14.7%) as well with CC 3.0 from changed criteria for some of these disorders.

Symptom Burden by CC Diagnoses and Motor Patterns

Patients meeting CC 2.0 criteria had similar DSI (10.6 ± 0.2 vs 10.2 ± 0.2 , $p=0.10$) and GSS (6.0 ± 0.1 vs 5.9 ± 0.1 , $p=0.17$) compared to those not meeting CC 2.0 criteria. In contrast, patients meeting CC 3.0 diagnoses had higher DSI (10.9 ± 0.2 vs 10.0 ± 0.2 , $p<0.0001$) and GSS (6.2 ± 0.1 vs 5.8 ± 0.1 , $p=0.005$) compared to those not meeting CC 3.0 criteria. When symptom burden metrics were compared between CC diagnostic designations (outflow obstruction, hypermotility, and hypomotility), these three groups were similar for both CC 2.0 (DSI: $p=0.16$, GSS: $p=0.42$) and CC 3.0 diagnoses (DSI: $p=0.57$, GSS: $p=0.51$; Table 1).

Contraction Wave Abnormalities

Of the study cohort, 884 patients (34.4%, 57.7 ± 0.5 years, 67.1% female) were identified with CWA, of which 472 (53.4%) and 329 (37.2%) met CC 2.0 and 3.0 criteria for a motor diagnosis, respectively. When compared to patients with a “normal” study (no CC 2.0 and 3.0 diagnoses), patients with CWA but without a CC diagnosis had higher proportions of presenting symptoms of dysphagia, heartburn, and regurgitation (Figures 4A and 4B, $p=0.01$ for all comparisons). The proportions of patients meeting CC 2.0 and 3.0 diagnoses were higher for those presenting with dysphagia (66.5% and 52.4%, respectively) compared to patients with other symptoms ($p<0.001$ for both comparisons). In the setting of dysphagia, patients with criteria for both CWA and a CC diagnosis were most prevalent, followed by those with CWA but not a CC diagnosis. Symptom burden was similar within CWA cohorts with or without a CC diagnosis (DSI: 10.3 ± 0.2 vs 10.4 ± 0.2 , $p=0.77$; GSS: 5.9 ± 0.1 vs 6.0 ± 0.1 , $p=0.23$). In contrast to CWA in the setting of CC 2.0 criteria, those meeting CC 3.0 criteria trended towards higher symptom burden compared to those not meeting CC 3.0 criteria (DSI: 10.9 ± 0.3 vs 10.0 ± 0.3 , $p=0.044$; GSS: 6.1 ± 0.2 vs 5.7 ± 0.1 , $p=0.080$).

Within the CWA cohorts, the presence of criteria for CC 2.0 and 3.0 diagnoses were highest for ‘nutcracker esophagus’ (89.4% and 67.3%, respectively) and simultaneous contractions (76.1% and 54.0%, respectively); prevalence was lowest for double peaked waves (39.7% and 27.8%, respectively; Table 2). The proportions of patients meeting CC 2.0 for each CWA designation were higher than those meeting CC 3.0 ($p=0.045$).

DISCUSSION

In this report evaluating over 2500 esophageal motility studies using both CC 2.0 and 3.0, we demonstrate that the CC 3.0 classification is more selective than CC 2.0, with significantly fewer patients meeting CC 3.0 criteria compared to CC 2.0. While the proportions with esophageal outflow obstruction are similar, the attrition of motor diagnoses with CC 3.0 is primarily from excluding patients meeting CC 2.0 hypermotility and hypomotility disorders based upon changes in the definitions of motor disorders within these categories. Further, our data demonstrates CC 3.0 selects patients with higher symptom burden, in contrast to CC 2.0, where symptom burden metrics were similar between patients meeting and not meeting criteria for a motor diagnosis. Finally, we demonstrate that certain

CWA do not fulfill criteria for a CC diagnosis, especially with CC 3.0. Despite this, within these 'normal cohorts' not meeting CC criteria, more symptomatic patients have CWA than a truly normal study. These differences were most striking for dysphagia as a presenting symptom, and suggest the importance of inspecting the motility study and potentially recording the presence of CWA in addition to making a CC diagnosis.

For the purpose of this study, we have grouped esophageal body motor disorders by pathophysiologic designation, rather than by their original CC characterization into major and minor motor disorders. We have previously demonstrated that pathophysiologic designation into esophageal outflow obstruction, hypermotility, and hypomotility disorders facilitates comparison of symptom burden between disorders, and better representation of symptoms⁹. Specifically, absent contractility aligns better with the two CC 3.0 minor disorders (IEM and fragmented peristalsis) in that reflux burden is higher with these hypomotility disorders, while dysphagia prevalence is lower compared to the major disorders (hypercontractile disorder and DES). Further, this grouping was necessary to compare motor disorders across the two classification systems.

With the transition from CC 2.0 to 3.0, several key modifications contributed to new diagnostic designations in the CC 3.0 criteria⁷. Within esophageal outflow obstruction, mean IRP was replaced by median IRP. Within hypermotility disorders, hypercontractile disorder (DCI>8000 mmHg.cm.s on at least 20% sequences) replaced all disorders with exaggerated contraction, and criteria for DES (DL<4.5 s on at least 20% sequences) replaced prior criteria based on contraction front velocity. The most profound changes were within hypomotility disorders, where two new designations, IEM (DCI<450 mmHg.cm.s on at least 50% sequences) and fragmented peristalsis (breaks >5 cm with DCI>450 mmHg.cm.s on at least 50% sequences) were introduced. These modifications, developed by consensus based on new evidence and expert opinion, appear to better extract motor diagnoses with increased symptomatic burden. Therefore, as many as 17.2% of motor diagnoses changed between CC 2.0 and 3.0, mostly from a loss of hypermotility (4.4%) and hypomotility (9.0%) designations, resulting in a gain in the 'no CC diagnosis' category of 13.0% in CC 3.0 (Figure 3).

Our data suggest that a 'normal' study according to either version of CC does not preclude abnormalities in the peristaltic wave, lumped together and termed CWA for the purpose of this study. Supporting the existing data available from prior reports in the literature, our data suggest that CWA may be clinically relevant, especially when dysphagia is a presenting symptom. In past studies evaluating patients with non-obstructive dysphagia, CWA, especially simultaneous contractions, were more evident compared to normal volunteers, both with routine conventional manometry and with provocative studies using esophageal air or fluid infusion^{15, 16}. Simultaneous (or rapid) peristalsis has been reported to have similar implications as DES according to CC 3.0¹⁷, with significant dysphagia rates regardless of whether CC 3.0 criteria were fulfilled. Simultaneous and retrograde contractions have been induced by balloon distension studies, both using conventional manometry where typical symptoms were reproduced with balloon distension¹⁸, and more recently, using the functional luminal imaging probe and evaluating esophageal luminal diameter changes in response to balloon distension¹⁹. In some symptomatic patients, limited data suggests that

asynchrony between esophageal circular and longitudinal muscle contraction can potentially explain bolus transit abnormalities²⁰. Therefore, CWA could potentially increase the suspicion for obstructive esophageal pathophysiology in the setting of dysphagia²¹, and lead the clinician towards further evaluation for obstruction, or empiric dilation.

Alternatively, increased esophageal sensitivity and hypervigilance are also reported in conjunction with contraction wave abnormalities, especially in the setting of perceptive symptoms like heartburn and chest pain^{11, 22, 23}. Esophageal perceptive thresholds are lower in the presence of CWA^{23, 24}, CWA may participate in esophageal acid sensitivity¹⁰, and the presence of CWA contributes to persisting esophageal symptoms following successful antireflux surgery¹¹. Moreover, our group has demonstrated that exaggerated esophageal body contraction patterns (distal shift in contraction vigor, merged esophageal body contraction segments) represent a continuum in terms of esophageal symptoms, and only the most extreme of these patterns are identified by CC designations⁸. Many of the CWA have been linked to abnormal esophageal inhibitory function²⁵, with an inverse relationship between the degree of inhibition and the propagation velocity of deglutitive contraction, as well as an absence of inhibition in simultaneous contractions²⁵. Finally, functional magneto-electroencephalographic studies demonstrate activation of cortical areas depicting vigilance and self-monitoring in perceptive esophageal symptoms like dysphagia, which in turn may interfere with downstream sensorimotor control of deglutition and generation of abnormal motor patterns²⁶. These data suggest that CWA could represent a minor motor disorder which may not be pathognomonic for a defined motor diagnosis, but one which can potentially explain esophageal symptoms, particularly transit symptoms like dysphagia. Therefore, we believe it is important to recognize abnormalities in the contraction wave before designating a motility study as normal, using either of CC 2.0 and 3.0. The clinical utility of identification of CWA in these settings is that this could lead to further evaluation for a subtle structural or motor explanation for dysphagia, or treatment for hypervigilance, in contrast to a completely normal manometry devoid of CWA, where the manometry study does not explain the symptomatic presentation.

This study has limitations inherent to its retrospective cohort study design. Processes such as gastroesophageal reflux or functional esophageal syndromes may have contributed to symptom burden in these patients, but were not uniformly assessed in this study. Outcome data from therapy arising from the motor assessments would have added further value to our analysis, but were not available. There remains the possibility of referral bias to our tertiary referral academic center, potentially limiting the generalizability of our findings. Outcome data would have further enhanced our report, which was not available in this patient cohort. Finally, results from provocative testing (multiple rapid swallows) were not utilized to further evaluate or characterize CWA in this report, since data collection predated routine use of provocative testing in our institution. Nonetheless, on the strength of its large sample size, our study offers valuable information that CC 3.0 is more specific compared to CC 2.0, and that CWA are clinically relevant and deserve recognition in reporting of esophageal motor function. Our findings could lead to further prospective studies evaluating the relationship between esophageal motor patterns and symptom burden.

In conclusion, we demonstrate that 82.8% of motor diagnoses are generally concordant between CC 2.0 and 3.0. CC 3.0 identifies the more extreme motor disorders with higher symptom burden, and is more specific within the diagnoses made when compared to its predecessor CC 2.0. The averaging process used with CC software tools pertaining to the esophageal body results in the lack of designation of several motor patterns (CWA), previously identified in relationship to esophageal symptoms. These motor patterns can be associated with esophageal symptoms, and could represent an additional minor disorder of esophageal body peristalsis.

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Key Points

- High resolution manometry (HRM) algorithms for interrogation of esophageal motor phenomena vary between Chicago Classification (CC) versions 2.0 and 3.0. We evaluated 2569 HRM studies using both CC 2.0 and 3.0 criteria.
- 82.8% of motor diagnoses are concordant between CC 2.0 and 3.0.
- CC 3.0 criteria are less sensitive, but identify motor disorders with highest symptom burden compared to CC 2.0.
- A 'normal' designation on both CC 2.0 and 3.0 remains compatible with abnormalities of the contraction wave, which are associated with a higher likelihood of esophageal symptoms compared to true normal studies.

Figure 1.

Examples of contraction wave abnormalities (CWA) not meeting Chicago Classification 3.0 diagnoses. A) Nutcracker esophagus with distal esophageal contraction amplitude >180 mmHg, but DCI <8000 mmHg.cm.s; B) Simultaneous contraction with contractile front velocity >8 cm/s, but DL >4.5 s; C) Double peaked wave with DCI <8000 mmHg.cm.s; D) Multiple peaked wave with broad wave duration, DCI <8000 mmHg.cm.s.

Figure 2.

Schematic flow diagram of study design. Although similar proportions of outflow obstruction were found on CC 2.0 and 3.0, there were lower proportions of HRM studies meeting hypermotility and hypomotility diagnostic criteria on CC 3.0 compared to CC 2.0. Consequently, proportions designated 'normal' were higher with CC 3.0.

		CC 3.0					
Concordant diagnoses		Outflow Obstruction	Hypermotility	Hypomotility	No diagnosis	Totals	Discordant (loss from 2.0)
CC 2.0	Outflow Obstruction	310	3	1	6	320	10 (0.4%)
	Hypermotility	4	117	8	101	230	113 (4.4%)
	Hypomotility	2	3	500	226	731	231 (9.0%)
	No diagnosis	6	4	77	1201	1288	87 (3.4%)
	Totals	322	127	586	1534	2569	441 (17.2%)
	Discordant (gain to 3.0)	12 (0.5%)	10 (0.4%)	86 (3.4%)	333 (13.0%)	441 (17.2%)	2128 (82.8%)

Figure 3.

Comparison of pathophysiologic diagnostic categories between CC 2.0 and 3.0. Esophageal outflow obstruction (including achalasia spectrum diagnoses) were the most stable and concordant diagnoses. There were diminishing proportions of both hypermotility and hypomotility disorders, with a consequent increase in ‘normal’ diagnoses with CC 3.0 compared to CC 2.0.

Figure 4.

Comparison of dominant presenting symptoms across diagnostic groups for CC 2.0 (A) and CC 3.0 (B). The diagnostic groups include normal HRM studies without CC diagnoses or contraction wave abnormalities (CWA), CWA without CC diagnoses, and CWA meeting CC diagnostic criteria. Patients with CWA but without CC diagnoses were more likely to present with dysphagia, heartburn, or regurgitation, compared to those with normal HRM studies ($p < 0.01$). In patients presenting with dysphagia, those with CWA meeting CC diagnostic criteria were most prevalent, followed by those with CWA without CC diagnoses, and only then by those without CWA or CC diagnoses.

Table 1

Symptom Burden by Motor Patterns for CC 2.0 and 3.0 Diagnoses

	DSI	p value *	GSS	p value *
CC 2.0		0.16		0.42
Outflow obstruction	11.1±0.3		6.1±0.2	
Hypermotility disorders	10.2±0.4		5.8±0.2	
Hypomotility disorders	10.5±0.2		6.1±0.1	
CC 3.0		0.57		0.51
Outflow obstruction	11.0±0.3		6.1±0.2	
Hypermotility disorders	10.4±0.5		5.9±0.3	
Hypomotility disorders	11.0±0.2		6.3±0.1	

* ANOVA between different motor patterns within each CC version

Table 2**CWA Cohorts**

	NE N=113	SC N=113	MPW/BW N=131	DPW N=421	Distal shift N=106	P values *
DSI	10.9±0.5	10.6±0.6	10.3±0.5	10.3±0.3	9.8±0.5	0.679
GSS	6.1±0.2	6.2±0.3	5.5±0.3	5.8±0.1	5.8±0.3	0.436
Heartburn	30.6%	27.7%	27.1%	33.6%	20.8%	0.145
Dysphagia	26.5%	30.7%	21.5%	20.2%	31.3%	0.061
Number meeting CC 2.0	101 (89.4%)	86 (76.1%)	73 (55.7%)	167 (39.7%)	45 (42.5%)	<0.001
Outflow obstruction	19.8%	24.4%	27.4%	18.6%	26.7%	0.473
Hypermotility	78.2%	31.4%	49.3%	22.2%	62.2%	<0.001
Hypomotility	2.0%	44.2%	23.3%	59.3%	11.1%	<0.001
Number not meeting CC 2.0	12 (10.6%)	27 (23.9%)	58 (44.3%)	254 (60.3%)	61 (57.5%)	<0.001
Number meeting CC 3.0	76 (67.3%)	64 (56.6%)	42 (32.1%)	117 (27.8%)	30 (28.3%)	<0.001
Outflow obstruction	25.0%	34.4%	45.2%	28.2%	50.0%	0.036
Hypermotility	75.0%	26.6%	38.1%	13.7%	43.3%	<0.001
Hypomotility	0.0%	39.1%	16.7%	58.1%	6.7%	<0.001
Number not meeting CC 3.0	37 (32.7%)	49 (43.4%)	89 (67.9%)	304 (72.2%)	76 (71.7%)	<0.001

NE: nutcracker esophagus; SC: simultaneous contractions; MPW/BW: multiple peaked waves and/or broad waves; DPW: double peaked waves; distal shift: distal shift in contraction vigor to the third contraction segment

* ANOVA or Chi-square tests, as appropriate