Published in final edited form as:

J Clin Gastroenterol. 2018 October ; 52(9): e73–e81. doi:10.1097/MCG.0000000000000949.

Roles of High-resolution Manometry in Predicting Incomplete Bolus Transit in Patients With Dysphagia

Zhaohong Shi, MD^{*,†}, Jie Guo, MD^{*,†}, John Clarke, MD^{*}, Haifeng Jin, MD^{*,‡}, Xinjun Wang, MD^{*}, Nina Zhang, MD^{*}, Ellen Stein, MD^{*}, Sameer Dhalla, MD^{*}, Pankaj J. Pasricha, MD^{*}, and Jiande D.Z. Chen, PhD^{*}

^{*}Division of Gastroenterology and Hepatology, Johns Hopkins Center for Neurogastroenterology, Baltimore, MD

[†]The First Hospital of Wuhan, Wuhan

[‡]The First Affiliated Hospital of Zhejiang Traditional Chinese Medicine University, Hangzhou, China.

Abstract

Background: High-resolution manometry (HRM) is used to assess esophageal motility diseases. Abnormalities in a number of HRM parameters have been reported in patients with dysphagia. However, it is unclear whether some of abnormal HRM parameters are predictive of dysphagia. The aim of this retrospective study was to investigate the roles of HRM parameters in predicting incomplete bolus clearance (IBC) in patients with dysphagia using high-resolution impedance manometry.

Methods: A total of 644 wet swallows were reviewed and analyzed in 63 patients with symptoms of dysphagia or reflux who underwent a clinical high-resolution impedance manometry test. IBC was defined based on impedance measurement. The relationship of each of abnormal HRM parameters with IBC was analyzed and their roles in predicting IBC were determined.

Results: Patients with symptoms of both dysphagia and reflux showed the highest IBC rate, and patients with symptoms of reflux had the lowest IBC rate. The IBC was more prevalent in the distal esophagus. Premature contractions and peristalsis with large breaks were associated with a higher IBC rate in the proximal esophagus ($P < 0.05$); large breaks, ineffective peristalsis, and abnormalities of the esophageal gastric junction functions were associated with higher IBC rates in the distal esophagus ($P < 0.05$). Abnormalities in a number of motility parameters were able to predict IBC with high specificities and/or high sensitivity, such as pan esophageal pressurization, ineffective peristalsis, and large breaks. Abnormal integrative relaxation pressure of the lower

Address correspondence to: Jiande D.Z. Chen, PhD, Division of Gastroenterology and Hepatology, Johns Hopkins Center for Neurogastroenterology, Baltimore, MD 21224 (jchen184@jhmi.edu). Z.S. and J.G. are co-first authors and they contributed equally.

J.D.Z.C.: designed the research study. Z.S. and J.G.: performed the research, analyzed the data, and wrote the paper. H.J., X.W., and N.Z.: analyzed a part of the data. J.D.Z.C., J.C., E.S., S.D., and P.P. are responsible for the revision of the manuscript. J.D.Z.C.: is responsible for the critical revision of the manuscript.

The authors declare that they have nothing to disclose.

esophageal sphincter with concurrent pan esophageal pressurization, ineffective peristalsis, or large breaks is predictive of IBC with nearly 100% of specificity.

Conclusions: Abnormalities in a number of HRM parameters are not only useful in diagnosing esophageal motility diseases, but also valuable in predicting IBC during swallowing.

Keywords

high-resolution esophageal impedance manometer (HRIM); bolus transit; esophageal motility abnormalities; dysphagia; gastrointestinal motility

The primary function of the esophagus is to facilitate bolus transport to the stomach. Complete bolus clearance (CBC) during swallowing results from a delicate balance between the esophageal body peristaltic function and the esophageal gastric junction (EGJ) relaxing function.^{1,2} High-resolution manometry (HRM) is an important method used to assess the functions of esophageal body peristalsis and EGJ relaxation.³ Armed with the technology of HRM, esophageal pressure topography (EPT) is used to assess the integrity of peristalsis using motility parameters, such as small and large breaks, distal contractile integral (DCI), and distal latency (DL). EPT is also used to assess functions of EGJ with basal pressure of lower esophageal sphincter (LES) (BPL), integrated relaxation pressure (IRP), and hiatal hernia (HH). All these motility parameters have their definitions and normal ranges according to the Chicago Classification and are used to diagnose esophageal motility disorders.⁴ However, HRM cannot be used to assess the clearance of bolus transit through the esophagus and it is unclear whether esophageal HRM is predictive of incomplete bolus clearance (IBC).

Simultaneous recordings of esophageal manometry and impedance, a technique called, high-resolution impedance manometry (HRIM) provide an opportunity to study the correlation between bolus transit and esophageal motility abnormalities. Bredenoord et al reported that in individuals with normal EGJ relaxation and morphology, peristaltic contractions with breaks <2 cm in the 20 mm Hg isobaric contour or <3 cm in the 30 mm Hg isobaric contour were associated with CBC, whereas, longer breaks were predictive of IBC.⁵ However, correlations of IBC with other motility abnormalities were left unexplored. A number of previous studies have reported impaired bolus transit in patients with nonobstructive dysphagia⁶⁻⁹ and patients with globus symptoms.¹⁰ Cho et al¹¹ reported that patients with symptoms of reflux showed mild peristaltic dysfunction and incomplete bolus transit and these conditions predisposed them to prolonged acid contact with the esophagus. Our literature review has suggested that there is lack of systematic studies investigating the relationship between IBC and various esophageal motility abnormalities in patients with different symptoms. Moreover, it is unclear whether the relationship is different between the proximal esophagus and the distal esophagus. Most importantly, it is unknown whether abnormal HRM parameters could predict IBC.

Accordingly, the aims of this study were (i) to assess the IBC rate in the proximal and distal esophagus in patients with different symptoms (dysphagia, reflux, or both); (ii) to study correlation of IBC with abnormalities of esophageal motility parameters based on 2015

Chicago Classification; (iii) to determine roles of various esophageal motility parameters in predicting impaired bolus transit.

METHODS

Subjects

This was a retrospective chart review study including 63 patients (21 male, 42 female, mean age of 55, ranging from 18 to 79 y) who underwent an HRIM test from January 5, 2014 to September 30, 2014 at the Johns Hopkins Bayview Medical Center. We analyzed available data, including symptoms, endoscopy, and HRIM of every patient. Patients were excluded if they had esophageal stricture, esophagitis, or other abnormal esophageal anatomy by endoscopic evidence. Patients included in the analysis had at least one of the following symptoms at the time of initial clinic visit: dysphagia, gastroesophageal reflux, and dysphagia plus reflux. Reflux symptoms used were typical. Patients with only atypical symptoms of reflux were excluded. Patients with achalasia were not excluded. To avoid overlap in symptoms as much as possible, we classified patients into 3 groups based on their major complaints: dysphagia (18/63, 28.6%, major symptoms of dysphagia without typical reflux symptoms except difficult swallowing), reflux (28/63, 39.7%, major typical symptoms of reflux with no symptoms of dysphagia or difficult swallowing), and mixed symptoms of dysphagia and reflux (17/63, 31.8%). The assessment of esophageal motility disorders was based on the 2015 Chicago Classification.⁵

HRIM

The HRIM catheter used in these patients was assembled with 36 circumferential sensors spaced at 1 cm intervals (Given Imaging, Los Angeles, CA) and 8 impedance sensors spaced at 5 cm intervals. The patient was fasted for at least 6 hours before the transnasal placement of the HRIM assembly. The HRIM test was conducted with the subject in a supine position, and the HRIM assembly was positioned to record from the hypopharynx to the proximal stomach; the impedance sensors were positioned to record from the upper esophageal sphincter through the distal esophagus and into the proximal stomach with ~2 intragastric impedance measurements.¹² The manometric protocol included 20 to 30 stable recording without swallows for assessing basal EGJ pressure and morphology followed with ten 5 mL swallows of 0.3% saline solution. Saline solution was chosen because its conductivity allowed it to be easily distinguished from esophageal mucosa during impedance monitoring.¹³ HRIM data were analyzed using the ManoView software (version 2.0; Sierra Scientific Instruments Inc.) by 1 investigator who was blinded to patients' symptoms and diagnosis.

EPT Analysis

High-resolution EPT was applied to derive 8 major parameters.^{14,15} The information reflecting the function of the LES included BPL, IRP, and HH. The contraction amplitude of the esophageal body was assessed with the DCI. Contraction integrity of the esophageal body was assessed with small/large breaks and ineffective peristalsis on 20 mm Hg isobaric contour. The propagation of contractions along the esophageal body was assessed with contractile front velocity (CFV) and DL.

The normal range of every parameter was established based on the 2015 Chicago Classification criteria.^{5,12,16} The normal range of BPL was from 13 to 43 mm Hg, hypertension and hypotension of LES was defined as BPL > 43 and <13 mm Hg, respectively. The normal IRP was lower than 15 mm Hg and the abnormal IRP was higher than 15 mm Hg. HH was defined as ≥ 2 cm separation between the LES and the crural diaphragm. The normal range of DCI was from 500 to 8000 mm Hg.s.cm-s and hypercontraction was defined as DCI ≥ 8000 mm Hg.s.cm. Large break and small break was defined as > 5 cm defect and 2 to 5 cm defect in length on 20 mm Hg isobaric contour, respectively. Ineffective peristalsis was defined as weak or failed peristalsis. The normal DL was > 4.5 and < 4.5 s was defined as premature contraction. The normal CFV was < 9 and > 9 cm/s was defined as rapid contraction. Pan esophageal pressurization was defined as uniform pressurization of > 30 mm Hg extending from the upper esophageal sphincter to the EGJ.

Impedance Assessment of IBC

Bolus transit was assessed using the impedance tracing and colorized contour functions of ManoView.^{17–21} Colorization was adjusted to the threshold at which pink colorization corresponded to bolus presence on impedance tracings (Fig. 1). Bolus transit was considered complete if colorization was followed by color disappearance and incomplete if this was not the case. Impedance tracings of all instances of IBC were assessed according to the following criteria: (i) the basic value of saline is 1100 Ω /cm, so the impedance value was around 1.1 k Ω /cm. (ii) The impedance color scale was adjusted to ensure that the impedance tracing did not show the pink color reflecting swallows during the baseline recording without swallows but displayed the pink color and swallowing tracing during known regular swallows (perfect esophageal peristalsis upon saline ingestion). (iii) To be more objective, we analyzed the bolus transit of each swallow without knowing corresponding motility parameters. (iv) To minimize bias, 3 researchers analyzed the data and swallows with inconsistent judgements among the 3 were abandoned. Each swallow was classified as CBC or IBC according to these definitions and methods.

Statistical Analysis

Statistical analyses were performed using the SPSS 17.0 (Chicago, IL). Multiple linear regression analyses were used to assess correlations between IBC and various esophagus motility parameters. The χ^2 test was used to determine the difference in the IBC rate between normal and abnormal esophageal motility parameters. A $P < 0.05$ was considered statistically significant.

RESULTS

IBC Rate and Relationship With Major Symptoms

The IBC rate in the proximal and distal esophagus in different patient groups was analyzed and is presented in Figure 2. In patients with major symptoms of dysphagia, the IBC rate was 17.0% (34/200) in the proximal esophagus and 23.5% (47/200) in the distal esophagus. The IBC rate was slightly lower in patients with major symptoms of reflux: 9.5% (26/275) in the proximal esophagus and 16.7% (46/275) in the distal esophagus. The highest IBC rate was observed in patients with the mixed symptoms of dysphagia and reflux: 26.0% (44/169)

in the proximal esophagus and 33.7% (57/169) in the distal esophagus. No significant difference was noted in the percentage of swallows associated with IBC per patient among the 3 groups of patients (or symptom presentations), neither in the proximal nor in the distal esophagus ($P > 0.05$, ANOVA). The distal esophagus exhibited uniformly a higher IBC rate than the proximal esophagus in all 3 groups of patients; however, the difference was significant only in patients with symptoms of reflux ($P < 0.05$).

Esophageal motility disorders were diagnosed using the 2015 Chicago Classification with following results: 2 cases of achalasia with a 95% of IBC, 6 cases of EGJ outflow obstruction with a 15% of IBC, 6 cases of ineffective peristalsis with a 50% of IBC, 4 cases of HH with a 10% of IBC, etc. Although it seemed apparent that a higher IBC rate was associated with achalasia and ineffective peristalsis, and a lower IBC rate with EGJ outflow obstruction and HH, statistical difference could not be established due to a small number of cases with each motility disorder.

Association of IBC With Esophagus Motility Parameters

The abnormality of a number of esophageal motility parameters was found to be associated with IBC in patients with dysphagia. In the distal esophagus of patients with dysphagia, IBC was observed in 23.5% of swallows (Table 1). Hypertension of the LES (LES basal pressure > 43 mm Hg) was associated with a higher IBC percentage (49.3% vs. 28.8% under normal LES pressure, $P < 0.01$). Abnormal IRP (> 15 mm Hg) was shown to be associated with the increased IBC percentage (30.3% vs. 19.0% with normal IRP, $P < 0.01$). Pan esophageal pressurization and ineffective peristalsis were both associated with a higher IBC percentage than normal peristaltic contractions (100% vs. 13.8% with normal contraction, $P < 0.001$ and 85% vs. 13.8% with normal contraction, $P < 0.001$). On the 20 mm Hg isobaric contours, large breaks (> 5 cm) were associated with a higher IBC percentage than normal contractions (47.6% vs. 20.4%, $P < 0.01$). The premature contraction (DL < 4.5 s) and rapid contraction (CFV > 9 cm/s) were both associated with a higher IBC percentage than normal swallows (38.9% vs. 17.9%, $P < 0.001$ and 77.8% vs. 17.0%, $P < 0.001$).

Regression coefficients of these abnormal motility parameters in association with IBC are shown in Table 2. From these data, we can see that ineffective peristalsis, abnormal IRP, large breaks, HH, and hypertensive BPL were important contributing factors to IBC in the distal esophagus of patients with major symptom of dysphagia ($P < 0.05$). According to the value of the regression coefficient, abnormal IRP was mostly correlated with IBC in the distal esophagus. On contrary, the regression coefficient of DCI was negative, suggesting that elevated DCI was associated with a reduced IBC percentage in distal esophagus of patients with symptoms of dysphagia.

Similarly, in patients with symptoms of reflux and patients with mixed symptoms, there were also a number of abnormal esophageal motility parameters that were associated with IBC (Tables 2–4). Findings different from those in patients with symptoms of dysphagia are as follows: (1) in the distal esophagus in patients with symptoms of reflux, abnormal IRP was found to be associated with a lower IBC incidence than normal IRP (6.8% vs. 19.4%, $P < 0.05$); hypotensive LES (basal pressure < 13 mm Hg) was associated with a higher IBC incidence than normal BPL (50% vs. 14.2%, $P < 0.001$); (2) in the distal esophagus in

patients with mixed symptoms, no significant difference was noted in the prevalence of IBC between abnormal and normal IRPs. Hypertension of LES (basal pressure > 43 mm Hg) was associated with a higher IBC incidence than normal basal pressure (76.7% vs. 24.8%, $P < 0.001$).

In the proximal esophagus, the associations of abnormal esophageal motility parameters with IBC were different from those in the distal esophagus. It can be seen from Tables 1–3 that (1) the large break was associated with IBC in all 3 groups of patients ($P < 0.05$); (2) the rapidly propagated contraction (CFV > 9 cm/s) was associated with IBC in patients with symptoms of dysphagia and patients with symptoms of reflux ($P < 0.05$). The regression analysis revealed similar results in the proximal esophagus with those in the distal esophagus. For example, the regression coefficients of DCI and DL were negative, indicating that a lower DL was associated with an increased IBC percentage, and elevated DCI was associated with a decreased IBC percentage.

Prediction of IBC Based on Abnormal Esophageal Motility Parameters

Our further analyses revealed that a number of abnormal esophageal motility parameters were predictive of IBC (Table 5). Multiple impairments (LES impairment plus one of esophageal body impairment) were found to be associated with a higher predictive rate of IBC than single abnormality. As it can be seen from Table 5, abnormal IRP plus ineffective peristalsis or large breaks could predict IBC in the distal esophagus with a sensitivity of 100%.

Table 6 shows sensitivities and specificities of each abnormal motility parameter in predicting IBC in 3 subgroups of patients. In patients with major symptoms of dysphagia, ineffective peristalsis and pan esophageal pressurization predicted IBC with sensitivities higher than other abnormal motility parameters: 85% and 100%, respectively. Meanwhile, hypercontraction, ineffective peristalsis, premature contractions (DL < 4.5 s), abnormally fast propagation (CFV > 9 cm/s), and abnormal IRP predicted IBC with high specificities: 91.5%, 83.3%, 81.6%, 83.0% and 81.0%, respectively. In patients with major symptoms of reflux, almost all abnormal motility parameters predicted IBC with high specificities. In contrast, however, in patients with mixed symptoms, almost all abnormal motility parameters predicted IBC with low specificities (< 75%).

The receiver operating characteristic analysis was performed on a number of major HRM parameters, including IRP, ineffective peristalsis and DCI in predicting IBC and the results are presented in Figure 3. It is seen that the DCI yielded the highest area under curve (0.81) and the IRP resulted in the lowest area under curve (0.44) among these 3 parameters.

DISCUSSION

Esophageal motility disorders and IBC were frequently observed in patients with dysphagia and reflux symptoms. In this study, we found that (1) the prevalence of IBC was highest in patients with combined symptoms of reflux and dysphagia, followed by patients with dysphagia and lowest in patients with symptoms of reflux; (2) most of abnormal esophageal motility parameters, such as ineffective contractions, pan esophageal pressurization,

contractions with large breaks and abnormal IRP, were found to be associated with a higher incidence of IBC; (3) certain abnormal motility parameters, especially combination of abnormal IRP with impaired contractions were able to predict IBC with high specificities and/or sensitivities, suggesting clinical values of abnormal esophageal motility parameters in assessing swallowing abnormalities.

The prevalence of IBC was found to be uniformly higher in the distal esophagus than the proximal esophagus in all 3 subgroups of patients. Another interesting finding was that the patients with mixed symptoms of both dysphagia and reflux, not those with dysphagia only, showed the highest IBC prevalence. Recent high-resolution esophageal manometric studies have shown that esophageal peristalsis actually comprises 2 distinct contractile waves, corresponding to distinct muscle types and neural control mechanisms of the proximal and distal esophagus,^{22–25} and that the bolus transit time was longer in the distal esophagus for both primary peristalsis and secondary peristalsis.²⁶ This might partially contribute to the higher IBC prevalence in the distal esophagus observed in the present study. The other major contributing factor we believe is the impairment of the LES, that is, the impaired relaxation and/or elevated BPL.

Previous impedance manometry studies reported that IBC was associated with dysphagia.^{27–29} In a study of 350 patients, IBC occurred in 51% of patients with dysphagia compared with 30% of patients without dysphagia.¹⁸ The normative data in Figure 2 generally support that finding. In this study we found that impaired integrity of esophageal contractions (break > 5 cm or ineffective peristalsis) and EGJ functional disorders (elevated BPL, impaired IRP, or HH) were associated with a higher prevalence of IBC in the distal esophagus in patients with dysphagia. Tutuian and Castell¹⁸ suggested that normal bolus transit could occur in the context of a poorly relaxing EGJ if peristalsis could generate a sufficient intrabolus pressure to overcome EGJ obstruction pressure. One of our findings, the association of increased DCI with a lower IBC incidence, indirectly supported that opinion. Weak peristalsis (large/small breaks) was reported to be associated with a higher IBC incidence than the normal contractions.^{30–32} We found that large breaks but not small breaks were associated with a higher IBC percentage than normal contractions in the distal esophagus in all subgroups of patients. The relationship between abnormal motility parameters and the IBC percentage in patients with mixed symptoms was similar to the patients with dysphagia. However, different findings in this relationship were noted in patients with reflux: abnormal IRP and hypertension of LES were associated with a lower IBC incidence than the normal condition. This was in disagreement with the findings in patients with dysphagia. The probable reason was that abnormal IRP and hypertension of LES might help decreasing the reflux of bolus; further studies are needed to explore the mechanisms associated with this finding. Interestingly, we found that although elevated DCI was associated with a lower IBC rate in the patients with reflux or mixed symptoms, this was not the case for the patients with dysphagia. A possible reason to this is that elevated DCI in patients with dysphagia is often accompanied with dysfunction of the LES (impaired IRP or hypertensive LES).

In the proximal esophagus, rapid contraction (CFV > 9 cm/s) was associated with a higher IBC incidence in the patients with symptoms of dysphagia and patients with symptoms of reflux; weak peristalsis (break > 5 cm) was associated with a higher IBC incidence in the

patients with mixed symptoms. To the best of knowledge, no previous studies have investigated the association of abnormal esophageal motility parameters with IBC in the proximal esophagus.

Most interestingly and importantly, the findings of this study revealed that certain abnormal esophageal motility parameters, especially the combination of abnormalities in the esophageal body with the LES, were found to be able to predict IBC with high specificities and/or sensitivities. This is of great clinical significance and provides important swallowing information in case esophageal manometry was performed without impedance measurement. In all patients, abnormal IRP with concurrent large breaks or ineffective peristalsis predicted IBC in the distal esophagus with a 100% sensitivity and specificities of 91.4% or 84.5%. In patients with symptoms of dysphagia, ineffective peristalsis was able to predict IBC in the distal esophagus with both high specificity and high sensitivity, demonstrating a crucial role of distal esophageal peristalsis in bolus transit. Pan esophageal pressurization predicted IBC in the distal esophagus with a high sensitivity, whereas premature contractions, contractions with rapid velocity, and abnormal IRP predicted IBC in the distal esophagus with higher specificities. There has been limited research on the relationship between esophageal motility parameters and IBC. Bulsiewicz et al¹² reported that weak peristalsis with breaks <2 cm in the 20 mm Hg isobaric contour or <3 cm in the 30 mm Hg isobaric contour was associated with CBC, whereas longer breaks were predictive of IBC. Ribolsi et al³³ showed that GERD patients with esophageal peristalsis of large breaks were characterized by a significantly prolonged reflux clearance. These 2 previous studies were focused only on the weak peristalsis. Bogte et al²⁹ studied a few more esophageal motility parameters and believed that motility patterns could predict the effectiveness of bolus transit and level of stasis to some degree but concluded that “the relationship between esophageal motility and transit is complex and far from perfect.” We believe that the present study is so far the most comprehensive in investigating the relationship between each of major motility parameters and bolus transit, and establishing the role of abnormal esophageal motility parameters in predicting IBC.

There were several limitations in this study. One of them was the potential age bias among the 3 groups of patients: patients with symptoms of dysphagia (mean, 47 y; range, 18 to 63 y), of reflux (mean, 58 y; range, 25 to 76 y) and of mixed symptoms (mean, 61 y; range, 22 to 79 y). Subdividing the reflux group and the mixed symptoms group into 2 groups of above 45 years and below 45 years, we found no significant age effect, but the possibility of bias remains. Retrospective design was another drawback of the study. In addition, pooled analysis of all swallows in the 63 patients could potentially resulted in biased findings as swallows occurring in a same patient were not independent observation and theoretically results could be driven by 1 subject in a group. Finally, no healthy controls were included in the study to determine whether IBC was in fact more frequent in patients with esophageal symptoms. However, a literature search revealed that such a comparison (IBC between patients and healthy controls) was carried out in a previous study.³⁴ In that particular study, the impedance outcome was defined as transit or stasis; the stasis rate was 42% (42/99) in healthy controls and 54% (43/80) in patients with dysphagia. These findings suggested that IBC or bolus stasis was not uncommon even in healthy controls. In our study, the IBC rate

was lower. This discrepancy was apparently attributed to different definitions of IBC or bolus stasis.

Recently, sophisticated pressure-flow analysis algorithms have been developed for analysis of esophageal pressure-impedance recordings, integrating pressure, and impedance measurements to derive new metrics linked to pressures occurring within and around the bolus.^{35,36} This novel method has been shown to enhance the esophageal motility evaluation and provide complementary/additional diagnostic information to Chicago Classification,^{37,38} whereas the findings of the present study suggested predictive values of certain HRM parameters for IBC.

In conclusion, abnormal IRP with concurrent pan esophageal pressurization, ineffective peristalsis, or large breaks results in IBC in the distal esophagus of patients with dysphagia. In contrast, elevated DCI may help transporting bolus from the distal esophagus into the stomach even when IRP was abnormal. Abnormalities in a few of esophageal parameters defined in Chicago Classification are not only useful in diagnosing esophageal motility diseases, but also valuable in assessing bolus transit during swallowing.

REFERENCES

1. Ren J, Massey BT, Dodds WJ. Determinants of intrabolar pressure during esophageal peristaltic bolus transport. *Am J Physiol*. 1993;264:407–413.
2. Pal A, Williams RB, Cook IJ, et al. Intrabolar pressure gradient identifies pathological constriction in the upper esophageal sphincter during flow. *Am J Physiol Gastrointest Liver Physiol*. 2003;285:1037–1048.
3. Fox M, Hebbard G, Janiak P, et al. High-resolution manometry predicts the success of oesophageal bolus transport and identifies clinically important abnormalities not detected by conventional manometry. *Neurogastroenterol Motil*. 2004;16:533–542. [PubMed: 15500509]
4. Bredenoord AJ, Fox M, Kahrilas PJ, et al. International High Resolution Manometry Working Group. Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography. *Neurogastroenterol Motil*. 2012;24(suppl 1):57–65. [PubMed: 22248109]
5. Kahrilas PJ, Bredenoord AJ, Fox M, et al. The Chicago Classification of esophageal motility disorders, v3.0. *Neurogastroenterol Motil*. 2015;27:160–174. [PubMed: 25469569]
6. Clayton SB, Rife C, Kalbfleisch JH, et al. Viscous impedance is an important indicator of abnormal esophageal motility. *Neurogastroenterol Motil*. 2013;25:563–572. [PubMed: 23621545]
7. Chen CL, Yi CH, Liu TT, et al. Characterization of esophageal pressure-flow abnormalities in patients with non-obstructive dysphagia and normal manometry findings. *J Gastroenterol Hepatol*. 2013;28:946–953. [PubMed: 23432518]
8. Chen CL, Szczesniak MM, Cook IJ. Identification of impaired oesophageal bolus transit and clearance by secondary peristalsis in patients with non-obstructive dysphagia. *Neurogastroenterol Motil*. 2008;20:980–988. [PubMed: 18492025]
9. Bogte A, Bredenoord AJ, Oors J, et al. Sensation of stasis is poorly correlated with impaired esophageal bolus transport. *Neurogastroenterol Motil*. 2014;26:538–545. [PubMed: 24372856]
10. Chen CL, Yi CH, Liu TT. Association between swallow perception and esophageal bolus clearance in patients with globus sensation. *Dig Dis Sci*. 2013;58:1042–1048. [PubMed: 23108530]
11. Cho YK, Choi MG, Lim CH, et al. Impaired esophageal bolus transit in patients with gastroesophageal reflux disease and abnormal esophageal acid exposure. *Gut Liver*. 2012;4:440–445.

12. Bulsiewicz WJ, Kahrilas PJ, Kwiatek MA, et al. Esophageal pressure topography criteria indicative of incomplete bolus clearance: a study using high-resolution impedance manometry. *Am J Gastroenterol.* 2009;104:2721–2728. [PubMed: 19690527]
13. Roman S, Lin ZY, Monika A, et al. Weak peristalsis in esophageal pressure topography: classification and association with dysphagia. *Am J Gastroenterol.* 2011;106:349–356. [PubMed: 20924368]
14. Sloan S, Kahrilas PJ. Impairment of esophageal emptying with hiatal hernia. *Gastroenterology.* 1991;100:596–605. [PubMed: 1993483]
15. Pandolfino JE, Ghosh SK, Lodhia N, et al. Utilizing intraluminal pressure gradients to predict esophageal clearance: a validation study. *Am J Gastroenterol.* 2008;103:1898–1905. [PubMed: 18637086]
16. Kahrilas PJ, Ghosh SK, Pandolfino JE. Esophageal motility disorders in terms of pressure topography: the Chicago Classification. *J Clin Gastroenterol.* 2008;42:627–635. [PubMed: 18364587]
17. Tutuian R, Elton JP, Castell DO, et al. Effects of position on oesophageal function: studies using combined manometry and multichannel intraluminal impedance. *Neurogastroenterol Motil.* 2003;15:63–67. [PubMed: 12588470]
18. Tutuian R, Castell DO. Combined multichannel intraluminal impedance and manometry clarifies esophageal function abnormalities: study in 350 patients. *Am J Gastroenterol.* 2004; 99:1011–1019. [PubMed: 15180718]
19. Simrén M, Silny J, Holloway R, et al. Relevance of ineffective oesophageal motility during oesophageal acid clearance. *Gut.* 2003;52:784–790. [PubMed: 12740331]
20. Sifrim D, Castell D, Dent J, et al. Gastro-oesophageal reflux monitoring: review and consensus report on detection and definitions of acid, non-acid, and gas reflux. *Gut.* 2004;53: 1024–1031. [PubMed: 15194656]
21. Sifrim D, Silny J, Holloway RH, et al. Patterns of gas and liquid reflux during transient lower esophageal sphincter relaxation: a study using intraluminal electrical impedance. *Gut.* 1999;44:47–54. [PubMed: 9862825]
22. Crist J, Gidda JS, Goyal RK. Intramural mechanism of esophageal peristalsis: roles of cholinergic and noncholinergic nerves. *Proc Natl Acad Sci U S A.* 1984;81:3595–3599. [PubMed: 6587375]
23. Ghosh SK, Janiak P, Schwizer W, et al. Physiology of the esophageal pressure transition zone: separate contraction waves above and below. *Am J Physiol Gastrointest Liver Physiol.* 2006;290:568–576.
24. Meyer GW, Austin RM, Brady CE III, et al. Muscle anatomy of the human esophagus. *J Clin Gastroenterol.* 1986;8:131–134. [PubMed: 3745845]
25. Roman C, Gonella J. *Extrinsic Control of Digestive Tract Motility*, 2nd ed. New York, NY: Raven Press; 1987.
26. Chen CL, Cook IJ. Proximal versus distal oesophageal motility as assessed by combined impedance and manometry. *Dig Liver Dis.* 2009;41:104–109. [PubMed: 18760980]
27. Cho YK, Lipowska AM, Nicodème F, et al. Assessing bolus retention in achalasia using high-resolution manometry with impedance: a comparator study with timed barium esophagram. *Am J Gastroenterol.* 2014;109:829–835. [PubMed: 24710506]
28. Chen CL, Yi CH. Clinical correlates of dysphagia to oesophageal dysmotility: studies using combined manometry and impedance. *Neurogastroenterol Motil.* 2008;20:611–617. [PubMed: 18298439]
29. Bogte A, Bredenoord AJ, Oors J, et al. Relationship between esophageal contraction patterns and clearance of swallowed liquid and solid boluses in healthy controls and patients with dysphagia. *Neurogastroenterol Motil.* 2012;24:364–372.
30. Almansa C, Smith JA, Morris J, et al. Weak peristalsis with large breaks in chronic cough: association with poor esophageal clearance. *Neurogastroenterol Motil.* 2015;27:431–442. [PubMed: 25628004]
31. Lee TH, Lee JS, Park JW, et al. High-resolution impedance manometry facilitates assessment of pharyngeal residue and oropharyngeal dysphagic mechanisms. *Dis Esophagus.* 2014;27: 220–229. [PubMed: 23855892]

32. Roman S, Kahrilas PJ. Challenges in the swallowing mechanism: nonobstructive dysphagia in the era of high-resolution manometry and impedance. *Gastroenterol Clin North Am*. 2011; 40:823–835. [PubMed: 22100120]
33. Ribolsi M, Balestrieri P, Emerenziani S, et al. Weak peristalsis with large breaks is associated with higher acid exposure and delayed reflux clearance in the supine position in GERD patients. *Am J Gastroenterol*. 2014;109:46–51. [PubMed: 24189712]
34. Bogte A, Bredenoord AJ, Oors J, et al. Assessment of bolus transit with intraluminal impedance measurement in patients with esophageal motility disorders. *Neurogastroenterol Motil*. 2015;27:1446–1452. [PubMed: 26284688]
35. Omari T, Tack J, Rommel N. Impedance as an adjunct to manometric testing to investigate symptoms of dysphagia: What it has failed to do and what it may tell us in the future. *United European Gastroenterol J*. 2014;2:355–366.
36. Rommel N, Van Oudenhove L, Tack J, et al. Automated impedance manometry analysis as a method to assess esophageal function. *Neurogastroenterol Motil*. 2014;26:636–645. [PubMed: 24447538]
37. Carlson DA, Omari T, Lin Z, et al. High-resolution impedance manometry parameters enhance the esophageal motility evaluation in non-obstructive dysphagia patients without a major Chicago Classification motility disorder. *Neurogastroenterol Motil*. 2017;29:176–189.
38. Rommel N, Omari TI, Selleslagh M, et al. High-resolution manometry combined with impedance measurements discriminates the cause of dysphagia in children. *Eur J Pediatr*. 2015; 174:1629–1637. [PubMed: 26105773]

FIGURE 1.

EPT and impedance tracings in HRIM study. A, Example of intact peristalsis associated with complete bolus clearance. Impedance tracings are superimposed to EPT and impedance data are also displayed by overlaid pink colorization. The pink shaded area indicates bolus presence. Complete bolus clearance was observed with the onset of contraction at each esophageal level corresponding to the clearance of pink colorization and the upward inflection in the impedance tracings. B, Example of weak peristalsis associated with IBC in proximal esophagus. C, Example of weak peristalsis associated with IBC in distal esophagus. D, Example of ineffective peristalsis (weak contraction and reduced DL) plus with abnormal IRP (> 15 mm Hg) associated with IBC in the whole esophagus. DL indicates distal latency; EPT, esophageal pressure topography; HRIM, high-resolution impedance manometry; IBC, incomplete bolus clearance; IRP, integrated relaxation pressure.

FIGURE 2.

Incomplete bolus clearance rate in the proximal and distal esophagus of patients with different symptoms (dysphagia, reflux, or dysphagia and reflux). * $P < 0.05$ versus proximal; # $P < 0.05$ versus proximal esophagus of patients with symptoms of reflux; & $P < 0.05$ versus distal esophagus of patients with symptoms of reflux.

FIGURE 3.

ROC analysis of using IRP, ineffective peristalsis, and DCI to predict incomplete bolus transit. DCI indicates distal contractile integral; IRP, integrated relaxation pressure; ROC, receiver operating characteristic.

TABLE 1.
Prevalence of IBC in Association With Esophageal Motility Parameters in Patients With Symptom of Dysphagia

Motility Parameters	Proximal Esophagus			Distal Esophagus		
	IBC % (n = 34)	CBC % (n = 166)	P	IBC % (n = 47)	CBC % (n = 153)	P
Basal LES pressure						
Normal	19.9	80.1	—	28.8	71.2	—
Hypotensive	0.0	100.0	0.10	9.1	90.9	0.16
Hypertensive	11.6	88.4	0.21	49.3	50.7	<0.01
IRP						
Normal	12.4	87.6	—	19.1	80.9	—
Abnormal	24.1	75.9	<0.05	30.4	69.6	<0.01
DCI						
Normal	18.3	71.7	—	22.3	77.7	—
Hyper	5.0	95.0	0.26	11.4	88.6	0.63
Peristalsis						
Normal	13.3	86.7	—	13.7	86.3	—
Ineffective	35.0	65.0	<0.01	85.0	15.0	<0.001
Pan esophageal pressurization	57.1	42.9	<0.001	100.0	0.0	<0.001
Breaks						
No break	14.3	85.7	—	20.4	79.6	—
Small break	18.7	81.3	0.52	21.9	78.1	0.85
Large break	33.3	66.7	<0.05	47.6	52.4	<0.01
DL						
Normal	12.7	87.3	—	17.9	82.1	—
Premature	55.6	44.4	<0.05	38.9	61.1	<0.001
CFV						
Normal	13.3	86.7	—	17.1	82.9	—
Rapid	77.8	22.2	<0.001	77.8	22.2	<0.001
Hiatal hernia						
Absent	12.9	87.1	—	16.8	83.2	—
Present	48.2	51.8	<0.001	51.9	48.1	<0.001

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

P -values were calculated using the χ^2 test against the corresponding normal value.

Bold value indicates $P < 0.05$ vs. normal motility parameters.

CBC indicates complete bolus clearance; CFV, contractile front velocity; DCI, distal contractile integral; DL, distal latency; IBC, incomplete bolus clearance; IRP, integrated relaxation pressure; LES, lower esophageal sphincter.

TABLE 2.

The Regression Coefficient of Esophageal Motility Parameters

Location	IBC (%)	P*	LES (Basal Pressure)			IRP			DCI			Ineffective Peristalsis			Defect Size			CFV			HH Size		
			P	RC	P	RC	P*	P	RC	P	P	RC	P	P	RC	P	P	RC	P	P	RC	P	
Patients with the symptom of dysphagia (n = 18, 200 swallows)																							
Proximal	17.00	<0.05	0.12	0.052	0.16	0.01	-0.09	0.29	0.11	0.15	0.07	0.16	0.28	<0.001*	0.06	0.13							
Distal	23.50	<0.05	0.13	*0.04	0.28	<0.001	-0.07	0.47	0.20	0.001*	0.13	0.016*	0.07	0.41	0.19	0.002*							
Patients with mixed symptoms (n = 17, 169 swallows)																							
Proximal	9.45	<0.05	0.036	0.44	0.042	0.384	0.012	0.723	0.14	0.055	0.12	<0.001*	-0.09	0.23	0.28	<0.001*	0.003	0.89					
Distal	16.73	<0.05	-0.32	<0.001*	-0.09	0.17	-0.256	0.091	0.21	0.018*	0.29	0.013*	-0.27	<0.001*	0.16	0.14	0.22	0.028*					
Patients with the symptom of reflux (n = 28, 275 swallows)																							
Proximal	26.04	<0.05	0.017	0.21	0.023	0.061	-0.045	0.41	0.30	0.005*	0.19	0.042*	0.13	0.362	0.11	0.367	0.035	0.281					
Distal	33.73	<0.05	0.44	<0.001*	0.023	0.72	-0.388	0.001*	0.24	0.036*	0.12	0.29	-0.129	0.317	0.289	0.006*	0.07	0.19					

* P-values were calculated using multivariate analysis with SPSS 17.0 software.

CFV indicates contractile front velocity; DCI, distal contractile integral; DCI, distal latency; HH, hiatal hernia; IBC, incomplete bolus clearance; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; RC, regression coefficient.

TABLE 3.

Correlation of Esophageal Motility With Bolus Clearance in Patients With the Mixed Symptoms

Motility Parameters	Proximal Esophagus		Distal Esophagus		P
	IBC % (n = 44)	CBC % (n = 125)	IBC % (n = 57)	CBC % (n = 112)	
Basal LES pressure					
Normal	18.6	81.4	24.8	75.2	—
Hypotensive	0.0	100.0	20.0	80.0	0.73
Hypertensive	66.7	33.3	76.7	23.3	<0.001
IRP					
Normal	14.1	85.9	29.8	70.3	—
Abnormal	56.2	43.8	43.8	56.2	0.083
DCI					
Normal	25	75	28.9	71.1	—
Hyper	54.5	45.5	0.0	100.0	<0.001
Peristalsis					
Normal	21.4	78.6	15.9	84.1	—
Ineffective	100.0	0.0	80.8	19.2	<0.01
Pan esophageal pressurization	88.2	11.8	94.1	5.9	<0.001
Breaks					
No break	14.3	85.7	14.3	85.7	—
Small break	27.1	72.9	33.3	66.7	0.27
Large break	31.6	68.4	57.9	42.1	<0.01
DL					
Normal	28.5	71.5	28.5	71.5	—
Premature	50.0	50.0	50.0	50.0	0.50
CFV					
Normal	19.3	80.7	17.1	82.9	—
Rapid	76.2	23.8	77.8	22.2	<0.001
Hiatal hernia					
Absent	26.9	73.1	24.3	75.7	—
Present	80.0	20.0	44.9	55.1	<0.05

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

P-values were calculated using the χ^2 test against the corresponding normal value.

Bold value indicates *P* < 0.05 vs. normal motility parameters.

CBC indicates complete bolus clearance; CFV, contractile front velocity; DCI, distal contractile integral; DL, distal latency; IBC, incomplete bolus clearance; IRP, integrated relaxation pressure; LES, lower esophageal sphincter.

TABLE 4.
Correlation of Esophageal Motility With Bolus Clearance in Patients With Symptoms of Gastroesophageal Reflux

Motility Parameters	Proximal Esophagus			Distal Esophagus		
	IBC % (n = 26)	CBC % (n = 249)	P	IBC % (n = 46)	CBC % (n = 229)	P
Basal LES pressure						
Normal	6.2	93.8	—	14.2	85.8	—
Hypotensive	15.0	85.0	0.14	50.0	50.0	< 0.001
Hypertensive	34.5	65.5	< 0.001	13.8	86.2	0.96
IRP						
Normal	9.1	90.9	—	19.4	80.5	—
Abnormal	11.2	88.8	0.56	6.7	93.3	< 0.05
DCI						
Normal	9.3	90.7	—	17.8	82.2	—
Hyper	10.2	90.8	0.18	0	100.0	< 0.001
Peristalsis						
Normal	8.8	91.2	—	11.2	88.8	—
Ineffective	18.2	81.8	0.15	77.3	22.7	< 0.001
Pan esophageal pressurization	17.1	82.9	0.26	50.0	50.0	0.086
Breaks						
No break	2.5	97.5	—	12.4	87.6	—
Small break	21.7	78.3	< 0.01	15.7	84.3	0.54
Large break	31.4	68.6	< 0.01	56.5	43.5	< 0.001
DL						
Normal	8.9	91.1	—	12.8	87.2	—
Premature	16.7	83.3	0.28	72.2	27.8	< 0.001
CFV						
Normal	8.7	91.3	—	15.8	84.2	—
Rapid	33.3	66.7	< 0.05	44.4	55.6	< 0.05
Hiatal hernia						
Absent	8.7	91.3	—	13.0	86.9	—
Present	9.6	90.4	0.85	32.3	67.7	< 0.05

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

P -values were calculated using the χ^2 test against the corresponding normal value.

Bold value indicates $P < 0.05$ vs. normal motility parameters.

CBC indicates complete bolus clearance; CFV, contractile front velocity; DCI, distal contractile integral; DL, distal latency; IBC, incomplete bolus clearance; IRP, integrated relaxation pressure; LES, lower esophageal sphincter.

TABLE 5.

Sensitivity and Specificity of Motility Parameters in Predicting IBC in All Patients

	Ab. IRP	Ineffective Peristalsis	Pan Esophageal.	Hypercontraction	Large Breaks	Small Breaks	Abnormal IRP+ Ineffective Peristalsis	Abnormal IRP+ Pan Esophageal.	Abnormal IRP+ Hypercontraction	Abnormal IRP + Large Breaks	Abnormal IRP + Small Breaks
Sensitivity	18.4	77.3	88.5	4.7	31.6	23.6	100	93.3	66.7	100	6.7
Specificity	85.8	84.5	79.3	90.7	86.1	85.5	84.5	81.6	98.6	91.4	85.9

Bold value indicates $P < 0.05$ vs. normal motility parameters.

Ab. indicates abnormal; IBC, incomplete bolus clearance; IRP, integrated relaxation pressure; Pan esophageal., Pan esophageal pressurization.

TABLE 6.

Sensitivity and Specificity of Abnormal Motility Parameters in Predicting IBC in Subgroups of Patients

	Ab. IRP	LES <13	LES >43	DCI 8000	Ineffective Peristalsis	Pan Esophageal.	Small Breaks	Large Breaks	DL < 4.5	CFV > 9	HH
Dysphagia											
Sensitivity	30.4	9.1	9.3	14.9	85	100	21.9	47.6	38.9	77.8	43.8
Specificity	81	75.7	72.6	91.5	83.3	78.9	76.2	79.3	81.6	82.9	77.9
Reflux											
Sensitivity	6.8	54.5	37.9	0	81.8	50	15.7	56.5	72.2	44.4	56.5
Specificity	80.6	82.7	83.5	93	88.5	83.5	83.1	86.9	87.2	84.2	82.5
Mixed symptoms											
Sensitivity	43.8	20	76.7	0	80.8	94.1	14.3	57.9	50	76.2	75.7
Specificity	70.2	65.4	75.5	84.8	74.8	73.1	63.5	69.3	71.5	73.1	59.6

Bold value indicates $P < 0.05$ vs. normal motility parameters.

Ab. indicates abnormal; CFV, contractile front velocity; DCI, distal contractile integral; DL, distal latency; HH, hiatal hernia; IBC, incomplete bolus clearance; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; Pan esophageal., Pan esophageal pressurization.