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The value of multiple rapid swallows during preoperative esophageal manometry before laparoscopic antireflux surgery

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Abstract

Background—When multiple swallows are rapidly administered, esophageal peristalsis is inhibited, and pronounced lower esophageal sphincter relaxation ensues. After the last swallow of the series, a robust contraction sequence results. The authors hypothesize that multiple rapid swallows (MRS) may have value in predicting esophageal transit symptoms in patients undergoing laparoscopic antireflux surgery (LARS).

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Methods—Records of patients undergoing esophageal high-resolution manometry (HRM) before LARS were evaluated. The evaluation of MRS included adequate inhibitory response during swallows and the contraction pattern after MRS. Dysphagia was scored based on a product of symptom frequency and severity using 5-point Likert scales. A composite dysphagia score comprised the sum of scores for solid and liquid dysphagia, and a score of 4 or higher was considered clinically significant. The normal and abnormal MRS responses of patients with preoperative, early, and late postoperative dysphagia were compared with those of patients with no dysphagia.

Results—In this study, 63 patients (mean age, 60.3 ± 1.7 years, 48 women) undergoing HRM before LARS successfully performed MRS (median, 5 swallows; longest interval between swallows, 3.2 ± 0.1 s). After MRS, 14 patients (22.2 %) had an intact peristaltic sequence. Complete failure of peristalsis was seen in 21 (33.3 %), and incomplete esophageal inhibition in 25 (39.7 %) of the remaining patients. When stratified by presence or absence of dysphagia, 58.3 % of the subjects without dysphagia had a normal MRS response, whereas 83.3 % had formation of peristaltic segments after MRS. In contrast, only 14 % of the subjects with dysphagia had a normal MRS response ($p = 0.003$ vs. the subjects with no dysphagia). Abnormal MRS responses were more prevalent in the patients with any preoperative and late postoperative dysphagia ($p = 0.04$ across groups) and in those with clinically significant dysphagia ($p = 0.08$ across groups).

Conclusions—High-resolution manometry with MRS helps to predict dysphagia in subjects undergoing preoperative esophageal function testing before LARS.

Keywords

Dysphagia; Esophageal manometry; Laparoscopic antireflux surgery; Multiple rapid swallows

Dysphagia is one of the most problematic complications after laparoscopic antireflux surgery (LARS). The incidence of dysphagia after LARS is reported to be 15–20 % in the early postoperative period, with a 10 % incidence of chronic dysphagia [1]. Factors that may have an impact on the occurrence of dysphagia after LARS include the nature of the wrap performed, the preoperative esophageal motor function, and the skill of the operator.

Preoperative esophageal manometry can identify situations in which obvious esophageal peristaltic defects exist, [e.g., achalasia, abnormal lower esophageal sphincter (LES) relaxation, extreme hypomotility with minimal or no propagated motor sequences]. In such cases, LARS may be modified to include a myotomy or to limit the circumference of the esophagus that is wrapped (i.e., Toupet or Dor funduplications). However, in many instances, intermittent transmitted sequences with low or modest contraction amplitudes are noted, interspersed with failed sequences [2]. To date, these intermittent hypomotility features have not been systematically assessed to determine whether postoperative transit symptoms can be predicted.

Provocative testing during esophageal manometry is an area of ongoing research. The simplest provocative maneuver that can be incorporated into the esophageal manometry protocol is the use of multiple rapid swallows (MRS). When multiple swallows are rapidly administered, esophageal peristalsis is inhibited, and pronounced LES relaxation ensues [3].

After the last swallow of the series, a robust contraction sequence results (Fig. 1). Abnormal responses consist of incomplete inhibition (when contraction fragments are seen during the period of expected inhibition) or suboptimal contraction (when the sequence after the last swallow of the MRS series fails to demonstrate augmentation of contraction).

In a series of 157 patients, 70 % of symptomatic patients with normal manometry demonstrated an abnormal response after MRS [3]. We speculate that MRS may have value in addressing peristaltic reserve in esophageal motor function and that the motor response after MRS may have value in predicting whether peristaltic vigor can escalate when the esophagus is challenged with an obstructive intervention (i.e., LARS).

In this study, we tested the hypothesis that improved peristaltic vigor after MRS is associated with less dysphagia after LARS. Patients who underwent LARS with preoperative esophageal function testing that included MRS were objectively and prospectively evaluated with symptom questionnaires to determine the development of dysphagia. The study was limited to a single surgeon's practice to ensure uniformity in surgical technique and consistency in pre- and postoperative symptom score documentation. The primary aim was to determine whether preoperative esophageal manometry, specifically the motor response to MRS, could predict esophageal dysphagia. Secondary aims were to determine whether specific motor patterns could predict pre- and postoperative dysphagia.

Methods

All patients referred for LARS to a single surgeon (L.M.B.) over a 36-month period were eligible for inclusion in this study. The inclusion criteria specified subjects who had undergone preoperative high-resolution manometry (HRM) with an adequately performed MRS sequence (at least 4 swallows of water [2 mL] performed in rapid succession with a <4-s interval between swallows). The exclusion criteria ruled out surgery for indications other than gastroesophageal reflux disease (GERD) or hiatal hernia repair, prior foregut resections (Billroth 1 or 2 surgery, gastric bypass, gastrectomy), unintelligible studies with artifacts limiting evaluation, and lack of either pre- or postoperative symptom assessment. The study protocol for this retrospective observational study was approved by the Human Research Protection Office (institutional review board) at Washington University School of Medicine.

Preoperative esophageal physiologic testing

All the patients underwent esophageal HRM using a 36-sensor solid state system (Sierra Scientific/Given Imaging, Los Angeles, CA, USA) capable of generating spatiotemporal Clouse plots of esophageal peristalsis [4]. Studies were reviewed by an investigator (J.E.D.) not involved with patient management or clinical analysis of manometric studies.

The adequacy of MRS was first established by determining the number of swallows and the interval between swallows during the MRS series. Peristaltic performance (% peristaltic sequences using 30-mmHg isobaric contour), averaged contraction amplitudes (3 and 8 cm above the LES), and wave duration were computed for the routine water swallows performed during the study. Additionally, peak contraction amplitudes in the proximal (S2)

and distal (S3) contraction segments were determined for the wet swallows. Assessment of LES relaxation used both the 3-s nadir (3SN) and integrated relaxation pressure (IRP) methods. Additional findings on preoperative HRM (including the presence of hiatal hernia, shortened esophagus, named esophageal motor disorders) were recorded.

The motor response to MRS was addressed for normal or abnormal inhibition and contractile response. Abnormal inhibition was designated when contraction segments longer than 3 cm were noted instead of the expected inhibition (i.e., during the course of the multiple swallows). Abnormal contraction consisted of complete contractile failure (no contraction seen using the 30-mmHg isobaric contour tool), partial contractile failure (absence of S2 or S3), or an intersegmental trough (IST) consisting of more than a 3-cm separation between skeletal and smooth muscle contraction segments. The averaged amplitude of the peristaltic response and the peak amplitudes for S2 and S3 were determined for wet swallows, as described earlier. Again, LES relaxation was assessed with both 3SN and IRP methods.

When available, results of other esophageal function tests including ambulatory pH testing, contrast esophagograms, and upper endoscopy procedures also were collected. These were not required for subject inclusion in the study.

Symptom assessment

All the patients completed a symptom assessment questionnaire. This symptom questionnaire, developed a priori for use with patients undergoing esophageal function studies at our institution, has previously been used in similar outcome assessments [5, 6]. On the symptom questionnaire, five symptoms (dysphagia for solids, dysphagia for liquids, heartburn, chest pain, regurgitation) are individually scored by subjects for frequency and severity using 5-point Likert scales: 0 (no symptoms or not severe) to 4 (very frequent symptoms or extremely severe).

In this study, the product of symptom frequency and severity constituted the symptom score (maximum score, 16). For the purpose of this study, only dysphagia was evaluated, and a composite symptom score was calculated as the sum of the scores for dysphagia with solids and liquids. A composite symptom score of 4 or higher constituted clinically relevant dysphagia for this study (maximum score, 32). Symptom questionnaires were administered at the time of preoperative esophageal function testing and at each office visit with the surgeon (L.M.B.).

Surgical technique

LARS was performed as previously described [7]. In all cases, the short gastric vessels were divided, and the fundus of the stomach was fully mobilized. A 360° wrap was performed over a 54-Fr bougie comprising three interrupted sutures of 0-polyester suture. Two of the three sutures incorporated the anterior esophageal muscle, whereas the last stitch (lowest) was to the stomach only.

Statistical analysis

Data are reported as mean $\pm$ standard error of mean or median (interquartile range [IQR]) as appropriate. Intergroup differences were compared using the chi-square test or Fisher's exact test for categorical values and Student's *t* test for continuous values. A *p* value <0.05 was required for statistical significance.

Results

A total of 63 patients (mean age, 60 ± 1.7 years, 48 women) undergoing HRM before LARS successfully performed MRS (median swallows, 5; IQR, 1; longest interval between swallows, 3.2 ± 0.1 s). Preoperative symptom information was available for all 63 subjects, obtained 2.1 ± 0.2 months before LARS (Table 1).

At presentation, all the patients had heartburn or regurgitation, with 31 patients (49.2 %) reporting dysphagia of any degree, whereas 22 patients (34.9 % of the total; Fig. 2) had a composite dysphagia score of 4 or higher (median score, 12). The mean LES end-expiratory pressure was low (11.5 ± 1.3 mmHg), with 16 patients showing values lower than 5 mmHg.

The mean post-swallow residual pressure (IRP) was 6.2 ± 0.7 mmHg. With HRM wet swallows, patients had a mean of 86.4 % transmitted sequences. Two patients had a peristaltic failure of 50 % or more. The mean averaged contraction amplitude in the smooth muscle esophagus was 74.3 ± 4.1 mmHg. The mean esophageal length was 20 ± 0.5 cm, and 39 patients (61.9 %) had a hiatal hernia suspected or identified on HRM.

During MRS, profound relaxation of the LES ensued, with an LES residual pressure (IRP) of 4.1 ± 0.6 mmHg ($p = 0.04$ vs. IRP during routine wet swallows). After MRS, esophageal body contraction segments failed to form, with complete failure of peristalsis in one-third of the patients. Contraction segments formed in the remaining patients (Table 1). Despite formation of contraction segments, esophageal inhibition was incomplete in almost 40 % of the patients, and only the third contraction segment (S3) formed with failure of S2 in 9.5 %. Some patients had overlapping abnormalities. A normal MRS response was seen in only 14 patients (22.2 %). When averaged, peak contraction amplitudes were similar during wet swallows (S2, 92.8 mmHg; S3, 119.2 mmHg) and after MRS (S2, 82.4 mmHg; S3, 122.83 mmHg; nonsignificant difference) for patients who had retained a contraction response after MRS.

All the patients underwent LARS. Early preoperative symptom data (1.0 ± 0.03 months after LARS) were available for 56 patients, and late symptom data (14.5 ± 0.8 months after LARS; Table 1) were available for 54 subjects. In the early postoperative period, 67.9 % of the patients reported dysphagia of any degree, whereas 32.1 % had a composite dysphagia score of 4 or higher (median score, 11.5) (Fig. 2). Late postoperative dysphagia of any degree was reported by 33.3 % of the patients, and 13 % had a composite dysphagia score of 4 or higher (median score, 5.5). Whereas 19 % of the entire cohort had no dysphagia at any time point, 66.7 % with late postoperative dysphagia of any degree and 71.4 % with late postoperative dysphagia scores of 4 or higher also had preoperative dysphagia.

When stratified by the presence or absence of dysphagia, 58.3 % of the subjects without dysphagia had a normal MRS response, and 83.3 % had formation of peristaltic segments after MRS (Fig. 3). In contrast, only 14 % of the subjects with any dysphagia had a normal MRS response ($p = 0.003$ vs. subjects with no dysphagia), and 56 % had formation of peristaltic segments ($p = 0.1$).

Further comparisons were made between the subjects with dysphagia scores of 4 or higher in the pre- and postoperative dysphagia groups and the subjects with no dysphagia (Fig. 3). Abnormal MRS responses were the most prevalent among the patients with preoperative dysphagia and late postoperative dysphagia and least prevalent among those without dysphagia ($p = 0.08$ across groups).

Similar results were seen when comparisons were made among the patients with any dysphagia ($p = 0.04$ across groups). The proportion of patients with normal MRS responses was highest in the absence of dysphagia compared with groups that had any grade of dysphagia at any time point before and after LARS ($p = 0.02$ across groups). Abnormal inhibition as a dominant abnormality was proportionately most frequent among the patients with preoperative dysphagia (Fig. 3), but this difference with other dysphagia groups did not reach statistical significance ($p = 0.26$).

Performance characteristics of MRS findings were compared with those of preoperative dysphagia in predicting late postoperative dysphagia. Preoperative dysphagia had a sensitivity of 66.7 % and a specificity of 57.8 % in predicting late postoperative dysphagia. Any abnormal MRS response had a much higher sensitivity (88.9 %) at the cost of specificity (28.9 %), whereas failure of peristalsis after MRS had a lower sensitivity (61.1 %) and a higher specificity (64.4 %). The positive predictive value for postoperative dysphagia was highest with failure after MRS (40.7 %), and the negative predictive value was highest with any MRS response (86.7 %). Both were higher than that of preoperative dysphagia alone.

Discussion

In this observational study with prospective outcome assessments, we demonstrate that preoperative HRM with MRS helps to predict dysphagia in subjects undergoing LARS. We show varying proportions of abnormal inhibition and abnormal contraction response in patients with pre- and postoperative dysphagia, indicating differing pathophysiologic mechanisms in these patients. Our results suggest that the contractile response after MRS may indicate esophageal peristaltic reserve. Subjects with inadequate reserve, as identified by a failed response to MRS, are more likely to experience transit symptoms (i.e., dysphagia) after esophageal outflow obstruction is generated with LARS.

The MRS technique expands upon the known esophageal physiology that occurs after a swallow [3]. At the end of a swallow, a wave of inhibition (deglutitive inhibition) transitions into a contraction sequence (deglutitive excitation). The period of inhibition courses along the length of the esophagus and is controlled by both central and peripheral mechanisms. The central portion involves activation of vagal fibers that leads to inhibition of the entire

esophagus. The adjunct peripheral mechanism involves myenteric inhibitory neurons that release nitric oxide, which inhibits contraction of smooth muscle. A rebound contraction occurs that is not cholinergically mediated but is overlapped by deglutitive excitation, which is cholinergically mediated.

Because multiple swallows in succession cause continued inhibition and relaxation of the LES until the last swallow, there is a robust peristalsis of the esophagus (deglutitive excitation phase) with a post-relaxation contraction of the LES. Normal responses to MRS require intact neural pathways and an appropriate esophageal muscle response to stimulation. Therefore, abnormalities in inhibition are secondary to dysfunction of either central or peripheral inhibitory nerve pathways, and abnormal contraction is due either to inadequate nerve input for muscle contraction or to an inability of the muscle to generate an adequate muscle response [3].

The potential clinical value of performing MRS as part of the preoperative peristaltic evaluation is that this may identify patients that have underlying esophageal dysmotility or inadequate esophageal motility reserve with the aim to overcome the relative mechanical obstruction that occurs when the distal esophageal pressure gradient is recreated at the LES through fundoplication.

The data describing improved esophageal function after fundoplication are limited. Anvari and Allen [8] compared their series of patients with manometry performed after LARS at 6- and 24-month intervals. In general, 76 % of the patients had improved dysphagia scores at 6 and 24 months. When esophageal peristaltic performance was evaluated, scores were improved by using fundoplication for patients with resolved dysphagia and those with persistent dysphagia postoperatively. The only difference was that the group with continued symptoms had significantly higher LES basal and nadir pressures. This led to the authors' conclusions that fundoplication overall improves esophageal function, but the explanation for dysphagia was multifactorial and could not be based on manometry alone. They also determined that wrap tightness played a large role in causing chronic postoperative dysphagia [8].

Hunter et al [9] described similar results for patients with poor preoperative esophageal motility. In their series, 75 % of the patients had improved motility after LARS. Interestingly, 10 % had worsening peristalsis, and 13 % had worsening body pressure. In the group of patients with normal manometry results preoperatively, 9 % had diminished motility postoperatively. Dysphagia rates overall decreased, but there was a 10 % incidence of new dysphagia postoperatively. Manometry once again did not correlate with dysphagia symptoms [9].

Both of the aforementioned studies imply improved esophageal function after LARS but do not demonstrate predictability of dysphagia. Improved peristaltic function can potentially be explained by changes in esophageal peristaltic function that result after esophageal obstruction, as described by Gyawali and Kushnir [5]. In their series, these authors focused on comparing the segmental characteristics of peristalsis between a group of patients with nonachalasic mechanical obstruction and patients who had elevated pressure gradients

without the presence of mechanical obstruction. Overall pressure shifts occurred in the second and third segments. The patients with mechanical obstruction had a significant shift in contraction vigor to the second segment, whereas the patients with functional obstruction had a significant shift to the third segment [5]. The improvement in peristalsis after LARS could represent an attempt by the esophageal body, particularly the second segment, to overcome the obstructive effect of the fundoplication in the patients with peristaltic reserve.

Despite general improvement of esophageal motility after LARS, a correlation with dysphagia still is elusive. MRS may provide a further layer of understanding in that they may identify patients with peristaltic reserve because it is a provocative maneuver that displays the ability of the esophageal body to respond in terms of both inhibition and contraction.

Our results show that the patients with either pre- or postoperative dysphagia were more likely to have an abnormal MRS than those with no dysphagia ($p = 0.003$). Because LARS increases the LES pressure mechanically, MRS may identify those patients who are able to augment esophageal smooth muscle contraction in response to a relative distal esophageal outflow obstruction, thereby predicting those patients less likely to experience postoperative dysphagia.

Equally intriguing were the patterns of abnormal MRS responses in the pre- and postoperative groups with dysphagia. Abnormal inhibition was the dominant characteristic of the patients with preoperative dysphagia, whereas absent peristalsis was the dominant characteristic of the postoperative group.

Although no one has previously used MRS as a tool to describe motility characteristics in the surgical population, the significance of nonspecific spastic disorders (NSSD) of the esophagus (thought to be related to abnormal esophageal inhibition) has previously been described during conventional manometric evaluations. Winslow et al. [10] found that patients with NSSD were more likely to have persistent postoperative symptoms such as heartburn, waterbrash, and medication usage [10]. These persistent symptoms were hypothesized to be associated with heightened esophageal perception seen in the setting of abnormal inhibition [10], a finding supported by original work with patients who had spastic motor disorders and noncardiac chest pain [11–13].

Because abnormal inhibition was seen during MRS in a proportion of patients, it is possible that heightened esophageal perception could have contributed to the sensation of dysphagia in at least some of the patients. Evaluation of performance characteristics suggests that the components of the MRS response may improve on the current practice of using preoperative dysphagia in predicting late postoperative dysphagia. However, because the pathophysiologic mechanisms being tested by the components of the MRS response may have specific perceptive versus peristaltic implications, further research is needed to better define the best metric to use in reporting an adequate MRS response, especially in the attempt to predict postoperative dysphagia.

Evaluation of postoperative dysphagia symptoms can be difficult, especially in the acute postoperative period. Postoperative dysphagia can be divided into two groups (acute and

chronic) that likely have different etiologies. Acute postoperative dysphagia (dysphagia occurring within 6 weeks after surgery) can be secondary not only to esophageal dysmotility but also to edema and swelling of the operative site. Chronic dysphagia (>6 weeks) is more likely to be associated with failure of sufficient esophageal contraction in the distal esophagus to overcome the relative mechanical obstruction caused by fundoplication, inherent esophageal sensorimotor dysfunction from abnormal inhibition, variation in wrap construction, wrap dysfunction, or combinations thereof. Previous studies, unable to draw correlations clearly between abnormal manometry and dysphagia, have vaguely concluded that the etiology of postoperative dysphagia is multifactorial [8, 9].

In this report, we conclude that a normal MRS response may better identify patients who are less likely to have chronic dysphagia symptoms. Conversely, abnormal MRS responses may predict transit symptoms. The low prevalence of a completely normal MRS response likely reflects the fact that GERD patients requiring antireflux surgery have advanced esophageal hypomotility. In contrast, preliminary results for a cohort of 18 healthy volunteers from our institution demonstrated a peristaltic response after MRS in 94.4 % of the patients, with profound inhibition of contraction during the MRS sequence in 52.8 % (authors' unpublished data).

Our report has a few limitations. Although the use of MRS has tremendous potential as a tool to evaluate esophageal motility, it has not been well standardized, and normal values are not clearly established. This study was further limited by the retrospective nature of the case series and by the fact that not all patients could perform an adequate MRS sequence. Because of these two limitations, performance characteristics of the MRS response in predicting postoperative dysphagia could not be better characterized. The reproducibility of the MRS response with repeated MRS maneuvers also is unknown because the MRS maneuver was not repeated in any of our patients. Furthermore, dysphagia symptoms also could have been associated with structural esophageal issues in both the preoperative period (e.g., hiatal hernia, reflux esophagitis) and the postoperative period (e.g., wrap dysfunction, recurrent hiatal hernia).

Despite these limitations, MRS responses do appear to have value in the evaluation of esophageal motor function before LARS. Additional prospective studies are warranted to further explore the value of MRS in esophageal function testing.

Conclusions

Abnormal MRS responses during high-resolution manometry help to predict dysphagia in patients undergoing pre-operative manometric evaluation for LARS. Therefore, MRS is a valuable adjunct to the standard HRM protocol for preoperative esophageal function testing before LARS. Further research is needed to characterize further the gamut of esophageal motor abnormalities during routine wet swallows and after MRS in the preoperative setting.

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Fig. 1.

Esophageal body and LES response to MRS. **A** Normal response showing inhibition of esophageal body peristalsis with profound LES relaxation during the five swallows in rapid succession followed by a robust contraction response in both the esophageal body and the LES after the last swallow of the sequence. **B** Abnormal inhibition showing contraction activity during the MRS (*arrow*). **C** Failure of contraction after MRS, with no esophageal body contraction response. *UES* upper esophageal sphincter

Fig. 2.

Proportions of patients with dysphagia before and after LARS. The proportions were lower during the late postoperative period (mean, 14.5 ± 0.8 months after LARS) than during the preoperative (2.1 ± 0.2 months before LARS) and early postoperative (1.0 ± 0.03 months after LARS) periods. These differences in proportion also held true when only patients with significant dysphagia (dysphagia score, ≥ 4.0) were considered (*black bars*)

Fig. 3.

Esophageal body contraction response after MRS in subgroups with significant dysphagia (dysphagia score, 4.0) versus patients without dysphagia. The proportion of patients with normal MRS response was highest in the absence of dysphagia and lowest in preoperative and late postoperative dysphagia ($p = 0.02$ across groups). The proportions of patients with failed responses and abnormal inhibition also were higher among patients with dysphagia than among those without dysphagia ($p = 0.08$ across groups). Similar results were obtained when patients with any dysphagia were compared

Table 1

Clinical characteristics and MRS response

	<i>n</i> = 63 <i>n</i> (%)
Age (years)	60 ± 1.7
Female gender	48 (76.2)
Timing of symptom assessment	
Preoperative (months before LARS)	2.1 ± 0.2
Early postoperative (months after LARS)	1.0 ± 0.03
Late postoperative (months after LARS)	14.5 ± 0.8
Normal MRS response	14 (22.2)
Abnormal MRS response ^a	
Complete failure of contraction	21 (33.3)
Partial failure of contraction	6 (9.5)
Abnormal inhibition	25 (39.7)

LARS, laparoscopic antireflux surgery

^aSome patients had overlapping abnormalities