

# Impact of Objective Colonic and Whole Gut Motility Data as Measured by Wireless Motility Capsule on Outcomes of Antireflux Surgery

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- BACKGROUND:** Studies show higher rates of dissatisfaction with antireflux surgery (ARS) outcomes in patients with chronic constipation. This suggests a relationship between colonic dysmotility and suboptimal surgical outcome. However, due to limitations in technology, there is no objective data available examining this relationship. The wireless motility capsule (WMC) is a novel technology consisting of an ingestible capsule equipped with pH, temperature, and pressure sensors, which provide information regarding regional and whole gut transit times, pH and motility. The aim of this study was to assess the impact of objective regional and whole gut motility data on the outcomes of ARS.
- STUDY DESIGN:** This was a retrospective review of patients who underwent WMC testing before ARS. Transit times, motility, and pH data obtained from different gastrointestinal tract regions were used in analysis to determine factors that impact surgical outcome. A favorable outcome was defined as complete resolution of the predominant reflux symptom and freedom from antisecretory medications.
- RESULTS:** The final study population consisted of 48 patients (fundoplication [n = 29] and magnetic sphincter augmentation [n = 19]). Of those patients, 87.5% were females and the mean age  $\pm$  SD was  $51.8 \pm 14.5$  years. At follow-up (mean  $\pm$  SD,  $16.8 \pm 13.2$  months), 87.5% of all patients achieved favorable outcomes. Patients with unfavorable outcomes had longer mean whole gut transit times (92.0 hours vs 55.7 hours;  $p = 0.024$ ) and colonic transit times (78.6 hours vs 47.3 hours;  $p = 0.028$ ), higher mean peak colonic pH (8.8 vs 8.15;  $p = 0.009$ ), and higher mean antral motility indexes (310 vs 90.1;  $p = 0.050$ ).
- CONCLUSIONS:** This is the first study to demonstrate that objective colonic dysmotility leads to suboptimal outcomes after ARS. WMC testing can assist with preoperative risk assessment and counseling for patients seeking ARS. (J Am Coll Surg 2023;236:305–315. © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American College of Surgeons. This is an open-access article distributed under the terms of the [Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 \[CCBY-NC-ND\]](https://creativecommons.org/licenses/by-nc-nd/4.0/), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.)

An optimal antireflux surgery (ARS) aims to provide long-term relief from reflux symptoms, while minimizing complications and complaints induced by the operation. Achieving this goal can be a challenge and is highly

dependent on identifying the patients who will benefit from surgery the most. Several studies have examined preoperative factors associated with surgical outcomes to guide patient selection, risk stratification, and preoperative

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### Abbreviations and Acronyms

ARS	= antireflux surgery
CTT	= colonic transfer time
GERD-HRQL	= GERD Health-related Quality of Life questionnaire
IBS	= irritable bowel syndrome
IRP	= integrated relaxation pressure
MSA	= magnetic sphincter augmentation
WMC	= wireless motility capsule

counselling. Previous studies have shown that presence of an abnormal pH score, a typical primary GERD symptom (eg heartburn, regurgitation, dysphagia), and a significant response to acid suppression therapy predict a favorable outcome.<sup>1,2</sup> In contrast, there is some inconsistency in the results of studies on factors predicting an unfavorable outcome, with obesity, esophageal dysmotility, and delayed gastric emptying among factors found to be associated with complications or complaints related to surgery.<sup>3,4</sup> The focus of all these studies has been on clinical and physiologic foregut factors linked to the outcome. However, despite up to 71% of GERD patients reporting symptoms consistent with irritable bowel syndrome (IBS) and other function bowel disorders of the hindgut, there is limited data on the impact of hindgut physiology on ARS outcomes.<sup>5-8</sup>

Colonic dysmotility has been implicated as a potential predictor of unfavorable outcome after ARS. This suggestion is based on studies demonstrating an association

between poor outcomes and subjective functional bowel disorder symptoms, such as constipation.<sup>9-12</sup> However, an objective measure of colonic dysmotility has never been used to confirm this relationship.

Endoscopic and radiologic foregut evaluation, assessment of esophageal motility by high resolution manometry, and pH monitoring are essential parts of workup before ARS.<sup>13,14</sup> Objective colonic and whole gut physiology testing are rarely added to this regimen. As a result, there is a paucity of objective data linking colonic dysmotility to ARS outcomes. The wireless motility capsule (WMC) is a novel technology which may prove to be a practical method of measuring colonic dysmotility in addition to regional and whole gut physiology.<sup>15</sup> The WMC consists of an ingestible capsule equipped with pH, temperature, and pressure sensors.<sup>15</sup> The data collected from these sensors can be used to determine the time spent in each part of the GI tract.<sup>15</sup> Using the data recorded during each of these transit times, the WMC is able to provide information on regional and whole gut pH and motility. We designed the current study to evaluate the impact of objective regional and whole GI tract motility, as measured by WMC, on the outcomes of ARS.

## METHODS

### Study population

This is a retrospective review of prospectively collected data from patients who underwent WMC testing before ARS at Allegheny Health Network hospitals (Pittsburgh, PA) between 2017 and 2021. Inclusion criteria were patients who were 18 years or older that completed WMC testing before ARS, and had adequate follow-up of at least 6 months after surgery. This study was evaluated and approved by the Institutional Review Board of the Allegheny Health Network (No. 2021-224).

### Preoperative assessment

All patients underwent complete foregut evaluation before surgery, consisting of a detailed clinical examination, esophagogastroduodenoscopy, video esophagram, and esophageal functioning testing. Additionally, patients were asked to complete standardized questionnaires including the GERD Health-related Quality of Life (GERD-HRQL). The GERD-HRQL assesses reflux symptom severity using a 0 to 5 rating scale.<sup>16</sup> Esophageal motility was assessed by high-resolution manometry (Medtronic Inc, Shoreview, MN). Once off proton pump inhibitors for 10 days, patients underwent ambulatory wireless 48-hour Bravo pH monitoring (Medtronic).<sup>17</sup> A DeMeester score >14.7 was considered abnormal acid exposure of the distal esophagus.

## WMC protocol

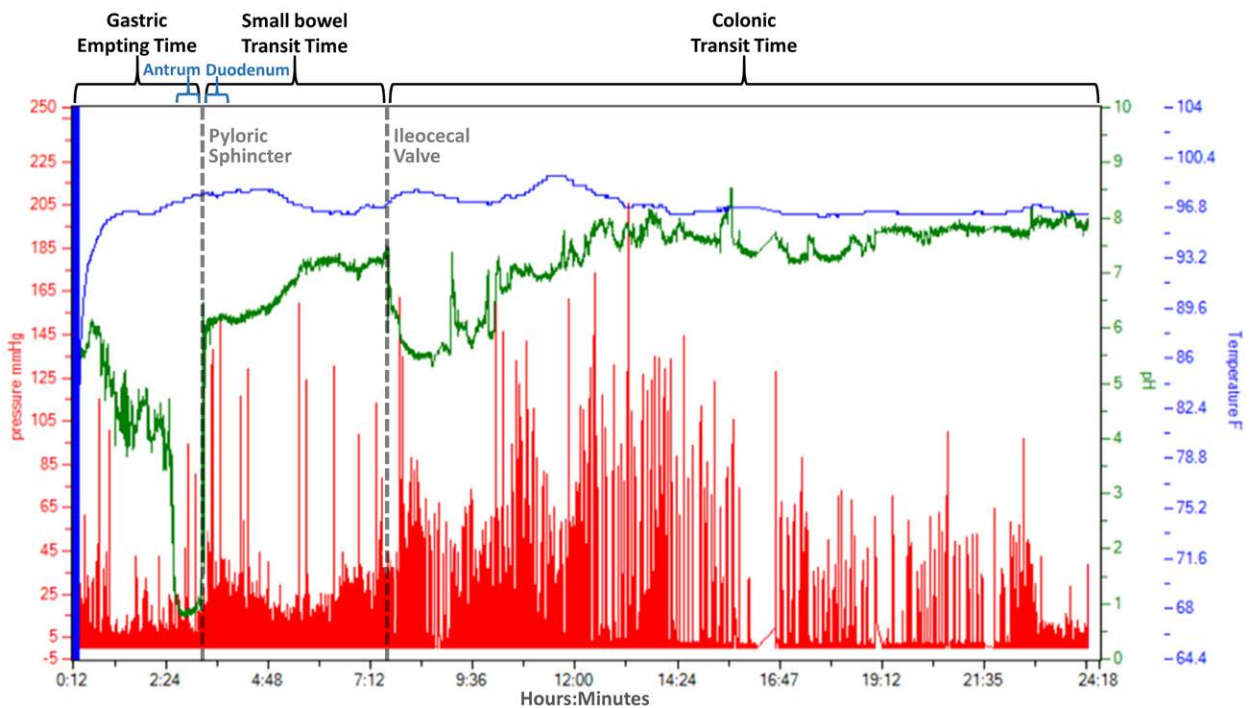
Patients undergoing SmartPill Motility Capsule testing (Medtronic) were instructed to discontinue the following before testing: proton pump inhibitors (7 days before testing); motility medications, antiemetics, and H2 channel blockers (2 days before testing); antacids, pre-/probiotics, laxatives, antidiarrheals, stool softeners, and alcohol (1 day before testing); and food, drink, and nicotine (8 hours before testing). These medications were also held for the duration of the test. On the day of the procedure, patients were given a standardized meal within 15 minutes of ingesting the WMC. Patients were instructed to wait an additional 6 hours before resuming their normal diet. Information collected from the WMC was transmitted from pH, temperature, and pressure sensors via radiofrequency to the monitor worn by the patient for the duration of the test. The end of the test was determined by loss of signal between capsule and monitor. Analysis of the temperature data at the end of recording confirmed capsule exit.

Temperature (°C), pH, and pressure (mmHg) data were recorded continuously from activation of the WMC until the signal was lost. Data was analyzed using a manufacturer provided software, MotiliGI (Medtronic), and divided anatomically by regional transit times defined by characteristic physiological changes within the GI tract. The gastric emptying time begins at ingestion and ends

with the detection of a sharp rise (>3) in pH corresponding to the transition between the stomach and duodenum. The small bowel transit time begins at this point and continues until the pH plateaus and then decreases by 0.5 to 1.0 units without returning to the plateau pH within 10 minutes, corresponding to the change in pH at the ileocecal junction. The colonic transit time (CTT) begins at this point and continues until a sharp decrease in temperature is detected, signifying the transition from internal body temperature to environmental temperature. The sum of these intervals are recorded as the whole gut transit time. Previous studies have validated these measurements against concurrent scintigraphy.<sup>15,18-26</sup> The antrum and duodenum do not have clear beginning or end points, respectively. However, previous antroduodenal studies have validated that the period 30 minutes before and 30 minutes after the increase in pH that marks the pyloroduodenal junction is an accurate approximation of capsule transit through these areas of the GI tract.<sup>27</sup> Regional motility is recorded as a pressure amplitude and number of contractions.

Figure 1 shows a sample tracing from a WMC test. The software calculates motility indexes for the antrum and duodenum defined by the following equation:

$$\text{Motility Index} = \text{Ln} (\text{sum of pressure amplitudes} \times \text{number of contractions} + 1)$$



**Figure 1.** Sample wireless motility capsule tracing showing the temperature (blue), pH (green), and pressure (red) tracings. The temporal locations of the pyloric sphincter and ileocecal valve are shown in gray. Regional transit time periods are labeled.

### Surgical technique and hospital stay

Patients either underwent Nissen fundoplication or magnetic sphincter augmentation (MSA), performed laparoscopically by experienced foregut surgeons using standardized surgical techniques as previously described.<sup>13,28</sup> The majority of discharges from the hospital occurred on the day of surgery for MSA patients and on the first postoperative day after Nissen fundoplication.

### Postoperative assessment

Postoperative follow-up visits were scheduled at 2 weeks, 6 weeks, 6 months, 1 year, and annually thereafter. Patients were assessed for clinical resolution of their predominant reflux symptoms, freedom from antisecretory medications, bloating, and constipation at each visit. At 1 year, patients were approached to repeat their objective esophageal physiologic testing.

### Outcomes assessment and statistical analysis

Favorable outcome was defined as complete resolution of predominant reflux symptoms and freedom from antisecretory medications. Unfavorable surgical outcome was defined as failure to meet either of these criteria. Clinically significant bloating was defined as a score >3 on GERD-HRQL “gas or bloating” item. Patients were then divided into two groups based on these outcomes and WMC parameters were compared between groups. A subanalysis was performed comparing WMC data to esophageal physiology data.

Data are expressed as median (interquartile range) or mean  $\pm$  SD. Values for categorical variables are presented as frequency and percentage. Statistical analysis was performed by means of nonparametric tests, including Mann–Whitney and Fisher exact tests. Correlation analyses were performed using Spearman test and expressed as the correlation coefficient *R* with 95% CI. A *p* value <0.05 was considered to be statistically significant. All statistical

analyses were performed using SAS software (version 9.4; SAS Institute).

### RESULTS

The final study population consisted of 48 patients. Of these, 29 underwent Nissen fundoplication and 19 underwent MSA. The baseline demographic and clinical characteristics of the study population and each surgical group are shown in [Table 1](#).

At follow-up (mean  $\pm$  SD 16.8  $\pm$  13.2 months), 89.6% of patients had complete resolution of their predominant symptom and 93.7% were free from use of antisecretory medications. Favorable outcomes were achieved in 87.5% of all patients. There were no significant differences in surgical outcomes (*p* = 0.381) or follow-up duration (*p* = 0.992) between the Nissen fundoplication and MSA groups. The median (interquartile range) GERD-HRQL total score improved from 37 (23.5 to 55) to 6 (3 to 14) (*p* < 0.001). Pre- and postoperative bloating and constipation for each outcome group are shown in [Table 2](#). Normalization of esophageal pH was achieved by 18 (75.0%) of patients who completed postoperative pH monitoring test.

### WMC and preoperative objective data

Patients with a hiatal hernia >3 cm had significantly longer CTTs (64.3 [52.4 to 91.6] vs 25.2 [18.7 to 38.5]; *p* = 0.008) and whole-gut transit times (70.0 [58.7 to 97.8] vs 32.6 [27.0 to 47.9]; *p* = 0.011) compared to those with a <3 cm hiatal hernia. Correlation analysis revealed a direct correlation between hiatal hernia size and CTT ([Figure 2](#)). There was also a strong direct correlation between antral pressure and integrated relaxation pressure ([IRP] *R* = 0.76; 95% CI 0.61 to 0.86; *p* < 0.0001).

The colonic pH was inversely correlated with DeMeester score. Longest reflux episode (min) was the component of

**Table 1.** Baseline Demographics and Clinical Characteristics

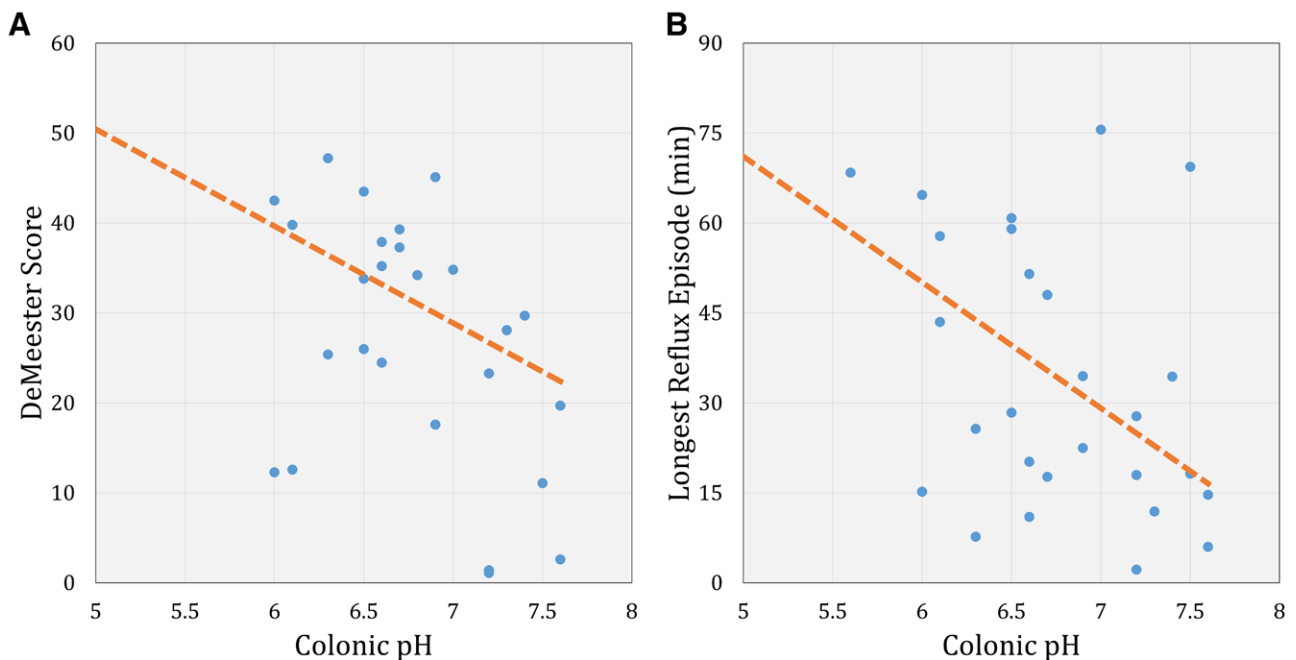
Characteristic	Study population (n = 48)	Nissen fundoplication (n = 29)	MSA (n = 19)	<i>p</i> Value
Age, y, median (IQR)	53.0 (40.3-65.5)	57.0 (50.0-68.0)	44.0 (34.0-55.0)	0.004
Sex, n (%)				
Male	7 (14.6)	3 (42.9)	4 (57.1)	0.412
Female	41 (85.4)	26 (63.4)	15 (36.6)	
BMI, kg/m <sup>2</sup> , median (IQR)	29.4 (26.8-32.0)	28.8 (25.8-31.5)	29.6 (27.2-33.1)	0.359
DeMeester score, median (IQR)	35.4 (24.1-40.9)	37.2 (26.3-55.9)	31.5 (16.9-38.0)	0.204
Hiatal hernia, n (%)	33 (68.8)	20 (69.0)	13 (68.4)	0.999
Esophagitis, n (%)	15 (31.3)	9 (31.0)	6 (31.6)	0.999

IQR, interquartile range; MSA, magnetic sphincter augmentation.

**Table 2.** Comparison of Pre- and Postoperative Bloating and Constipation Symptom Prevalence Between the Favorable and Unfavorable Outcomes Groups

Variable measurement	Favorable outcomes, % (n = 42)	Unfavorable outcomes, % (n = 6)	p Value
Preoperative			
GERD-HRQL bloating score >3	50.0	100	0.0287
Constipation	52.4	100	0.0339
Postoperative			
GERD-HRQL bloating score >3	15.6	100.0	0.0008
Constipation	35.7	100	0.0044

GERD-HRQL, GERD Health-related Quality-of-Life questionnaire.

**Figure 2.** Inverse correlation between colonic pH and (A) DeMeester score ( $R = -0.48$ ; 95% CI  $-0.67$  to  $-0.22$ ;  $p = 0.009$ ), and (B) longest reflux episode (min) ( $R = -0.72$ , 95% CI  $-0.83$  to  $-0.55$ ;  $p < 0.0001$ ).

esophageal pH monitoring with the strongest inverse correlation with colonic pH (Figure 3).

### Surgical outcomes in relation to WMC data

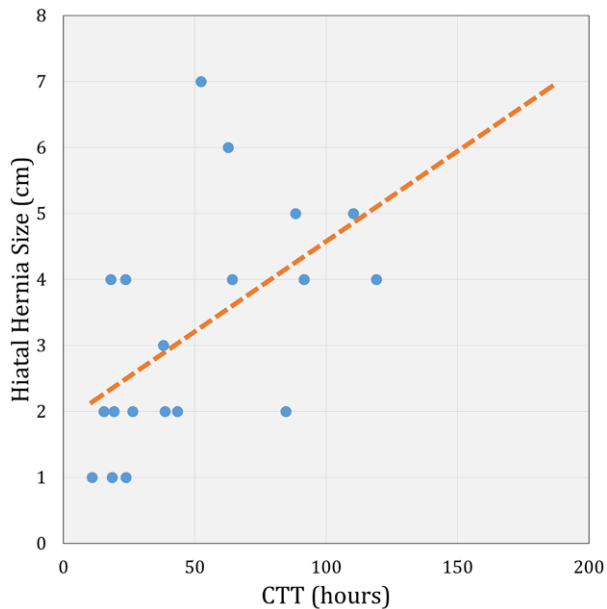
A comparison of regional and whole gut transit times between outcome groups is shown in Table 3. Patients who failed to achieve favorable outcomes criteria had significantly longer median (interquartile range) whole gut transit times (76.9 [56.7 to 127.7] vs 47.8 [26.8 to 65.8] hours;  $p = 0.024$ ). Of the components contributing to whole gut transit time, unfavorable outcomes were only associated with longer CTT (Table 3). Patients with delayed colonic transit time (>59 hours) were more likely to have postoperative bloating and constipation (Figure 4).

Comparison of regional mean pressures, contractions per minute, and antroduodenal motility indexes are shown in Table 4. Patients with unfavorable surgical outcomes had higher antral motility index, but the difference did not reach statistical significance ( $p = 0.05$ ).

Comparison of peak, median, and trough pH data for each region of the GI tract are shown in Table 5. Patients with unfavorable outcomes had higher peak colonic pH measurements.

### DISCUSSION

Foregut and hindgut are two distinct parts of the digestive tract, but several studies have suggested a common pathophysiologic link between the diseases of these two



**Figure 3.** Correlation between colonic transit time (CTT) and preoperative hiatal hernia size (cm) ( $R = 0.54$ ; 95% CI 0.11 to 0.80;  $p = 0.018$ ).

anatomic regions.<sup>12</sup> Lower abdominal complaints are present in 60% of patients with GERD<sup>29</sup> and patients with IBS frequently complain of esophageal symptoms.<sup>5,7,8</sup> Studies have also shown a higher rate of dissatisfaction with outcomes of ARS in patients with symptoms suggestive of colonic dysmotility.<sup>9,10</sup> This study is the first to use an objective measure of hindgut physiology to demonstrate that patients with colonic dysmotility are less likely to derive significant improvement in their symptoms after ARS. We also demonstrated that elevated colonic pH is associated with higher rate of unfavorable outcome.

The main finding of this study was that colonic transit times were significantly longer in patients who failed to achieve a favorable ARS outcome. This finding is consistent with previous studies that have associated poor ARS outcomes with subjective measures of colonic dysmotility such as constipation and other IBS-like symptoms.<sup>9,10</sup> Zeman and Tihanyi<sup>10</sup> followed a cohort of 41 patients

undergoing ARS and found that patients with high preoperative constipation severity scores were more likely to report dissatisfaction with their surgical outcome. This association was present despite intact fundoplication on endoscopy and normal distal esophageal acid exposure on postoperative testing.<sup>10</sup> They suggested that the colonic motility disorder contributes to postoperative symptomatology associated with dissatisfaction. Similarly, we found that postoperative bloating and constipation was associated with delayed colonic transit time and unfavorable outcome. Axelrod and colleagues<sup>9</sup> made a similar observation in their study of 155 patients undergoing ARS. They reported that patients with preoperative symptoms consistent with IBS and other functional bowel disorders were more likely to report a poor surgical outcome.<sup>9</sup> By contrast, Raftopoulos and colleagues<sup>11</sup> reported no difference in ARS outcomes between 32 patients who met Rome II criteria for IBS and 70 non-IBS patients. These three studies relied on subjective measures to draw their conclusions. The inconsistency in their findings highlights the need for objective measures of colonic motility, as was provided by the WMC in our study.

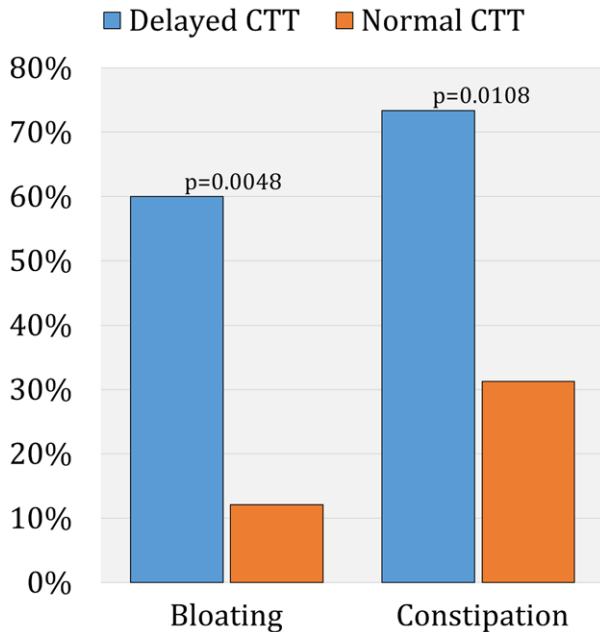
One mechanism by which colonic dysmotility may negatively impact ARS outcomes is by markedly increasing the intraabdominal pressure and diaphragmatic tension. Slow-transit constipation leads to colonic dilation and abdominal distention.<sup>6</sup> Evacuation difficulties and excessive strain also increase the intraabdominal pressure.<sup>6</sup> This explanation is further supported by our finding that colonic transit time was correlated with preoperative hiatal hernia size. Others have reported that increased intraabdominal pressure caused by a constipated or redundant colon is one of the mechanisms that fosters the development of hiatal hernia.<sup>30</sup>

If the relationship between colonic dysmotility and the foregut is causal in nature, then there must be a physiologic pathway connecting hindgut physiology to the function of foregut. The existence of such a pathway was demonstrated in a randomized crossover study by Piche and colleagues<sup>31</sup> They showed that colonic fermentation of indigestible carbohydrates increases the

**Table 3.** Wireless Motility Capsule Transit Time Data Between the Favorable and Unfavorable Outcomes Groups

Anatomic Region	Favorable outcomes	Unfavorable outcomes	Odds ratio	p Value
Gastric	3.3 (2.5-4.0)	3.7 (3.1-3.7)	0.530	0.607
Small bowel	4.0 (2.9-4.9)	4.5 (3.0-3.7)	0.530	0.607
Colon	37.5 (19.5-60.2)	69.3 (50.8-101.3)	2.213	0.028
Whole gut	47.8 (26.8-65.8)	76.9 (56.7-127.7)	2.276	0.024

Data presented as transit time, h, median (IQR).  
IQR, interquartile range.



**Figure 4.** Histogram comparing postoperative bloating (GERD-HRQL bloating score >3) and constipation between patients with a delayed (>59 hours) and normal colonic transit time (CTT). Patients with delayed colonic transit had significantly higher rates of postoperative bloating (60.0 vs 12.1%; p = 0.0048) and constipation (73.3 vs 31.3%; p = 0.0108). GERD-HRQL, GERD Health-related Quality of Life questionnaire.

rate of transient lower esophageal sphincter relaxations, the number of acid reflux episodes, and the symptoms of GERD. They also reported a marked elevation of glucagon-like peptide-1 (GLP-1) after a test meal in

GERD patients.<sup>31</sup> Similarly, our results showed that colonic pH was inversely correlated with preoperative DeMeester score. Interestingly, longest reflux episode was the component of esophageal pH monitoring with the strongest inverse correlation with colonic pH. It is likely that high colonic pH results in a neurohormonal phenomenon that is associated with long reflux events. Several studies have shown that both GLP-1 and peptide YY (PYY) possess inhibitory effects on gastrointestinal motility.<sup>32,33</sup> The effect of GLP-1 on LES motility is through an effect on the proximal stomach (ie gastric relaxation).<sup>34</sup> In fact, GLP-1 is a physiologic inhibitory regulator of gastric emptying and fundus motility.<sup>34</sup> Since fundoplication preserves the transient lower esophageal sphincter relaxation capability, this proposed neurohormonal mechanism is a potential explanation for the association between higher rates of unfavorable surgical outcomes in patients with higher peak colonic pH in our cohort.

Similar to surgical outcome, the response to anti-acid secretion medications is also associated with colonic conditions. Miyamoto and colleagues<sup>35</sup> studied 467 patients with typical reflux symptoms and endoscopic evidence of GERD and found that patients with constipation were twice as likely to fail to respond to PPI therapy. They also found that adding a prokinetic agent resulted in improvement in PPI response in these patients with chronic constipation.<sup>35</sup> This finding suggests that the untreated colonic motility disorder likely contributed to the poor response to antacid medication. Similarly, a study of laxative use in GERD patients reported that a

**Table 4.** Comparison of Wireless Motility Capsule Motility Data Between the Favorable and Unfavorable Outcomes Groups

Anatomic region measurement	Favorable outcomes	Unfavorable outcomes	Odds ratio	p Value
Pressure, mmHg, median (IQR)				
Gastric	3.3 (2.8-4.0)	3.2 (3.1-5.2)	0.797	0.437
Antrum	3.5 (2.4-5.1)	3.2 (3.0-7.0)	0.602	0.560
Duodenum	3.8 (2.5-4.4)	4.3 (3.9-4.5)	0.933	0.361
Small bowel	4.6 (3.8-5.4)	3.2 (3.0-4.2)	1.654	0.102
Colon	4.0 (3.2-5.2)	3.4 (3.0-4.4)	0.525	0.613
Contractions per minute, median (IQR)				
Gastric	2.0 (1.1-2.8)	2.7 (1.8-4.3)	1.225	0.228
Antrum	1.5 (0.8-2.3)	2.0 (1.5-2.4)	0.698	0.498
Duodenum	3.0 (1.6-4.5)	4.3 (2.3-4.9)	0.447	0.669
Small bowel	4.3 (3.4-5.6)	3.2 (2.8-3.6)	1.595	0.115
Colon	1.8 (1.6-2.1)	1.5 (1.1-2.3)	0.659	0.523
Motility Index, median (IQR)				
Antrum	61.0 (40.8-107.1)	92.0 (77.9-175.9)	1.952	0.050
Duodenum	95.7 (60.2-164.5)	148.3 (116.0-168.4)	1.394	0.296

IQR, interquartile range.

**Table 5.** Comparison of Wireless Motility Capsule pH Data Between the Favorable and Unfavorable Outcomes Groups

Anatomic region measurement	Favorable outcomes	Unfavorable outcomes	Odds ratio	p Value
pH peak, median (IQR)				
Gastric	6.2 (5.6-6.9)	6.4 (4.4-6.5)	0.914	0.371
Antrum	3.3 (1.6-6.0)	2.9 (2.7-6.5)	0.737	0.348
Duodenum	7.0 (6.5-7.1)	6.8 (6.7-7.0)	0.260	0.811
Small bowel	7.6 (7.5-7.8)	7.8 (7.6-7.9)	0.782	0.446
Colon	8.1 (7.7-8.4)	8.7 (8.5-8.7)	2.631	0.009
pH median, median (IQR)				
Gastric	1.5 (1.2-2.4)	1.9 (1.3-4.2)	0.933	0.331
Antrum	1.1 (0.8-1.6)	1.4 (0.9-2.0)	1.032	0.104
Duodenum	6.1 (5.7-6.3)	6.4 (6.0-6.6)	0.819	0.424
Small bowel	6.8 (6.5-7.2)	7.2 (6.9-7.4)	1.060	0.298
Colon	6.5 (6.1-7.0)	6.9 (6.8-7.1)	1.888	0.062
pH trough, median (IQR)				
Gastric	0.6 (0.5-0.8)	0.9 (0.5-0.9)	1.147	0.292
Antrum	0.8 (0.5-0.9)	1.0 (0.9-1.5)	1.814	0.938
Duodenum	1.2 (0.8-1.9)	2.5 (1.0-6.2)	1.377	0.175
Small bowel	1.2 (0.8-1.9)	2.5 (1.0-6.2)	1.357	0.181
Colon	5.4 (5.1-5.8)	5.8 (5.6-6.0)	1.140	0.263

IQR, interquartile range.

subset of patients achieve reflux symptom resolution and freedom from PPIs with adequate constipation control alone.<sup>6</sup>

We found a strong correlation between antral motility and IRP. The IRP is a manometric marker for resistance at the esophagogastric junction.<sup>36</sup> An elevated residual pressure during lower esophageal sphincter relaxation would likely interfere with belching and expelling air from the stomach. Studies have reported difficulty with belching in patients with esophagogastric junction outflow obstruction and showed an association between bloating symptoms and elevated IRP.<sup>37</sup> We postulate that elevated antral pressure in patients with raised IRP is a compensatory mechanism in patients with inability to belch, a function that is compromised even further after ARS (Figure 5). This hypothesis is also a plausible explanation for the non-significant trend that we found for a high antral motility index in patients with worse ARS outcomes in our cohort. However, the full implications of the antral measurements require further investigation as they are subject to unique limitations and have never been applied to this patient population before the present study.

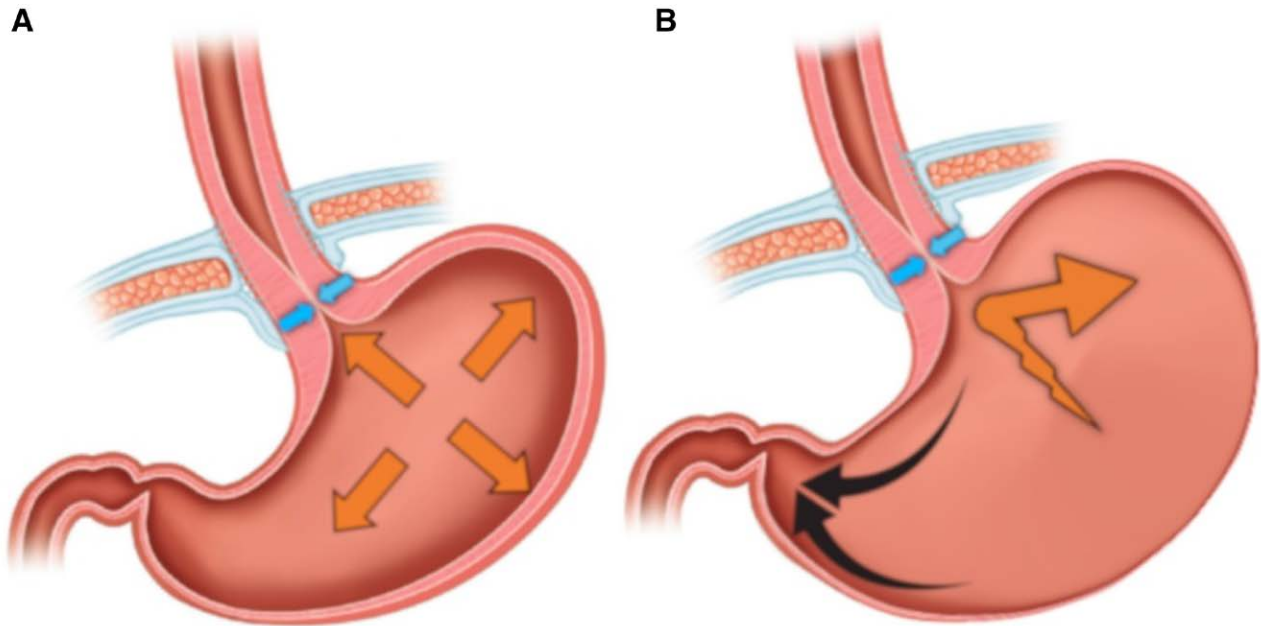
The major limitation of WMC duodenal and antral measurements is that, unlike the regional transit times, there are no predictable pH or temperature changes to bookend these anatomical regions. The antrum and duodenum are arbitrarily defined by the manufacturer as 30 minutes before or after the pH change that marks the

pyloroduodenal junction, respectfully. However, studies validating this method of approximating the duodenal and antral regions have used 60-minute windows.<sup>27</sup> Therefore, the normal values established in the literature are not comparable to the manufacturer defined values.

A novel test is only useful if its results are valid, accurate, and reliably comparable to the previous gold standard. The WMC relies on characteristic changes in temperature and pH to determine its location within the GI tract. This localization method was validated in a study of healthy individuals who underwent concurrent WMC testing and whole gut scintigraphy.<sup>20</sup> Similarly, Camilleri and colleagues<sup>18</sup> studied 158 patients who underwent concurrent WMC and Sitz marker tests to validate CTT as a measure of colonic motility. They found 87% agreement between the tests.<sup>18</sup> Most relevant to our results, Rao and colleagues<sup>21</sup> found 88% agreement between WMC CTT and Sitz marker testing for the presence of clinically significant constipation. Other studies have validated the WMC for diagnosing gastroparesis and predicting the development of small intestinal bacterial overgrowth.<sup>19,22</sup> Therefore, the WMC is an effective alternative to a number of different testing modalities, and provides additional information on intraluminal pressures and pH, which is not available through conventional motility tests.

We acknowledge the limitations of this study including its limited sample size and retrospective nature.





**Figure 5.** Compensatory increase in antral motility in response to elevated integrated relaxation pressure. (A) An elevated esophagogastric junctional outflow resistance as measured by the integrated relaxation pressure (blue arrows) may interfere with retrograde venting and belching resulting in increased intragastric pressure (orange arrows). (B) The stomach becomes distended and compensatory increase in antral motility (black arrows) is proposed to develop as a means of enhancing gastric emptying in these patients.

WMC motility testing was not randomly offered to the patients in this study. In our practice WMC is most frequently used in patients with symptoms suggestive of motility disorders like gastroparesis or IBS, which may have introduced an element of bias. However, these symptoms are non-specific and are seen in the majority of GERD patients.<sup>29</sup> Furthermore, 87.5% of the patients in this study reported typical primary GERD symptoms. Patients were not randomized to MSA or laparoscopic Nissen fundoplication. However, there was no significant difference in outcomes between surgical procedures, which is consistent with previous studies comparing MSA and laparoscopic Nissen fundoplication outcomes.<sup>38</sup> WMC is a novel technology and the findings of this study are promising for its use in assessing patients considering ARS. Randomized control trials and large volume studies are necessary to fully assess its utility in practice.

Colonic dysmotility may be a predictor of unfavorable outcome, but should not be considered as a contraindication to ARS. Up to 71% of patients with GERD report symptoms consistent with colonic dysmotility disorders.<sup>7,12,29</sup> However, large volume studies have shown that at 5 years after ARS only 17.7% of patients require antisecretory medications.<sup>39</sup> Therefore, while colonic dysmotility is associated with a higher risk of a suboptimal outcome, many patients derive significant benefit from

ARS. Consequently, the findings of this study should not be used to determine surgical candidacy. However, patients with evidence of colonic dysmotility should be informed of their risk. Foregut and hindgut factors that affect surgical outcomes should be evaluated collectively for appropriate risk stratification. Surgeons should tailor expectation management discussions based on risk during patient selection and pre- and postoperative counselling. WMC testing can provide valuable information to aid these discussions.

## CONCLUSION

In this study we used an objective measure of colonic physiology to demonstrate that delayed colonic motility is associated with suboptimal outcomes after ARS. Additionally, we found that high colonic pH was associated with unfavorable outcomes. Colonic dysmotility should not be treated as a contraindication to ARS. However, surgeons should counsel these patients that they are less likely to have complete resolution of their symptoms postoperatively, and manage their expectations accordingly. Clinical and physiologic foregut factors should be evaluated in conjunction with hindgut factors during risk stratification. WMC testing has a role in assessing objective GI pathophysiology and provides valuable information for preoperative discussions of risk

stratification and expectation management for patients seeking ARS.

### Author Contributions

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### REFERENCES

- Campos GM, Peters JH, DeMeester TR, et al. Multivariate analysis of factors predicting outcome after laparoscopic Nissen fundoplication. *J Gastrointest Surg* 1999;3:292–300.
- Ayazi S, Zheng P, Zaidi AH, et al. Clinical outcomes and predictors of favorable result after laparoscopic magnetic sphincter augmentation: Single-institution experience with more than 500 patients. *J Am Coll Surg* 2020;230:733–743.
- Pauwels A, Boeckstaens V, Andrews CN, et al. How to select patients for antireflux surgery? The ICARUS guidelines (international consensus regarding preoperative examinations and clinical characteristics assessment to select adult patients for antireflux surgery). *Gut* 2019;68:1928–1941.
- Stefanidis D, Hope WW, Kohn GP, et al. Guidelines for surgical treatment of gastroesophageal reflux disease. *Surg Endosc* 2010;24:2647–2669.
- de Bortoli N, Tolone S, Frazzoni M, et al. Gastroesophageal reflux disease, functional dyspepsia and irritable bowel syndrome: Common overlapping gastrointestinal disorders. *Ann Gastroenterol* 2018;31:639–648.
- Momma E, Koeda M, Tanabe T, et al. Relationship between gastroesophageal reflux disease (GERD) and constipation: Laxative use is common in GERD patients. *Esophagus* 2021;18:152–155.
- Zimmerman J, Hershovici T. Bowel symptoms in nonerosive gastroesophageal reflux disease: Nature, prevalence, and relation to acid reflux. *J Clin Gastroenterol* 2008;42:261–265.
- Pimentel M, Rossi F, Chow EJ, et al. Increased prevalence of irritable bowel syndrome in patients with gastroesophageal reflux. *J Clin Gastroenterol* 2002;34:221–224.
- Axelrod DA, Divi V, Ajluni MM, et al. Influence of functional bowel disease on outcome of surgical antireflux procedures. *J Gastrointest Surg* 2002;6:632–637.
- Zeman Z, Tihanyi T. Quality of life and patient satisfaction after laparoscopic antireflux surgery using the QOLARS questionnaire. *Surg Endosc* 2007;21:1418–1422.
- Raftopoulos Y, Pappasavvas P, Landreneau R, et al. Clinical outcome of laparoscopic antireflux surgery for patients with irritable bowel syndrome. *Surg Endosc* 2004;18:655–659.
- Gasiorowska A, Poh CH, Fass R. Gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS)—Is it one disease or an overlap of two disorders? *Dig Dis Sci* 2009;54:1829–1834.
- Ayazi S, Zheng P, Zaidi AH, et al. Magnetic sphincter augmentation and postoperative dysphagia: Characterization, clinical risk factors, and management. *J Gastrointest Surg* 2019;24:39–49.
- Ayazi S. Esophageal manometry testing and anti-reflux surgery: The preoperative necessity and prognostic utility. *Foregut* 2021;1:216–226.
- Farmer AD, Scott SM, Hobson AR. Gastrointestinal motility revisited: The wireless motility capsule. *United European Gastroenterol J* 2013;1:413–421.
- Velanovich V. The development of the GERD-HRQL symptom severity instrument. *Dis Esophagus* 2007;20:130–134.
- Ayazi S, Crookes PF. High-resolution esophageal manometry: Using technical advances for clinical advantages. *J Gastrointest Surg* 2010;14(Suppl 1):S24–S32.
- Camilleri M, Thorne NK, Ringel Y, et al. Wireless pH-motility capsule for colonic transit: prospective comparison with radiopaque markers in chronic constipation. *Neurogastroenterol Motil* 2010;22:874–82, e233.
- Lee AA, Rao S, Nguyen LA, et al. Validation of diagnostic and performance characteristics of the wireless motility capsule in patients with suspected gastroparesis. *Clin Gastroenterol Hepatol* 2019;17:1770–1779.e2.
- Maqbool S, Parkman HP, Friedenberg FK. Wireless capsule motility: comparison of the SmartPill GI monitoring system with scintigraphy for measuring whole gut transit. *Dig Dis Sci* 2009;54:2167–2174.
- Rao SS, Coss-Adame E, Valestin J, Mysore K. Evaluation of constipation in older adults: Radioopaque markers (ROMs) versus wireless motility capsule (WMC). *Arch Gerontol Geriatr* 2012;55:289–294.
- Roland BC, Ciarleglio MM, Clarke JO, et al. Low ileocecal valve pressure is significantly associated with small intestinal bacterial overgrowth (SIBO). *Dig Dis Sci* 2014;59:1269–1277.
- Roland BC, Ciarleglio MM, Clarke JO, et al. Small intestinal transit time is delayed in small intestinal bacterial overgrowth. *J Clin Gastroenterol* 2015;49:571–576.
- Tran K, Brun R, Kuo B. Evaluation of regional and whole gut motility using the wireless motility capsule: Relevance in clinical practice. *Therap Adv Gastroenterol* 2012;5:249–260.
- Kuo B, McCallum RW, Koch KL, et al. Comparison of gastric emptying of a nondigestible capsule to a radio-labelled meal in healthy and gastroparetic subjects. *Aliment Pharmacol Ther* 2008;27:186–196.
- Zarate N, Mohammed SD, O’Shaughnessy E, et al. Accurate localization of a fall in pH within the ileocecal region: Validation using a dual-scintigraphic technique. *Am J Physiol Gastrointest Liver Physiol* 2010;299:G1276–G1286.
- Kloetzer L, Chey WD, McCallum RW, et al. Motility of the antroduodenum in healthy and gastroparetic characterized by wireless motility capsule. *Neurogastroenterol Motil* 2010;22:527–33, e117.

28. Hinder RA, Filipi CJ, Wetscher G, et al. Laparoscopic Nissen fundoplication is an effective treatment for gastroesophageal reflux disease. *Ann Surg* 1994;220:472–81; discussion 481–3.
29. Fass R, Stanghellini V, Monnikes H, et al. Baseline analysis of symptom spectrum in GERD clinical trial patients: Results from the ReQuest (TM) database. *Gastroenterology* 2006;130:A6–29-A.
30. De Luca L, Di Giorgio P, Signoriello G, et al. Relationship between hiatal hernia and inguinal hernia. *Dig Dis Sci* 2004;49:243–247.
31. Piche T, des Varannes SB, Sacher-Huvelin S, et al. Colonic fermentation influences lower esophageal sphincter function in gastroesophageal reflux disease. *Gastroenterology* 2003;124:894–902.
32. Allen JM, Fitzpatrick ML, Yeats JC, et al. Effects of peptide YY and neuropeptide Y on gastric emptying in man. *Digestion* 1984;30:255–262.
33. Naslund E, Gryback P, Backman L, et al. Distal small bowel hormones: Correlation with fasting antroduodenal motility and gastric emptying. *Dig Dis Sci* 1998;43:945–952.
34. Schirra J, Wank U, Arnold R, et al. Effects of glucagon-like peptide-1(7-36)amide on motility and sensation of the proximal stomach in humans. *Gut* 2002;50:341–348.
35. Miyamoto M, Manabe N, Haruma K. Efficacy of the addition of prokinetics for proton pump inhibitor (PPI) resistant non-erosive reflux disease (NERD) patients: Significance of frequency scale for the symptom of GERD (FSSG) on decision of treatment strategy. *Intern Med* 2010;49:1469–1476.
36. Ayazi S, Grubic AD, Zheng P, et al. Measurement of outflow resistance imposed by magnetic sphincter augmentation: defining normal values and clinical implication. *Surg Endosc* 2021;35:5787–5795.
37. Liu X, Wang H, Wang L, et al. Clinical features and esophageal motility characteristics of patients with esophagogastric junction outflow obstruction. *Chinese Journal of Digestion* 2019;7–11.
38. Reynolds JL, Zehetner J, Wu P, et al. Laparoscopic magnetic sphincter augmentation vs laparoscopic Nissen fundoplication: A matched-pair analysis of 100 patients. *J Am Coll Surg* 2015;221:123–128.
39. Maret-Ouda J, Wahlin K, El-Serag HB, Lagergren J. Association between laparoscopic antireflux surgery and recurrence of gastroesophageal reflux. *JAMA* 2017;318:939–946.

## Invited Commentary

### Antireflux Surgery and Colonic Motility

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The gastrointestinal (GI) tract is a hollow viscus that extends from oral to aboral ends with a series of valves interspersed throughout. GERD is a common upper

GI tract disorder presenting with excessive backflow of gastric contents via an incompetent lower esophageal sphincter (LES). Many patients with GERD also report symptoms that overlap with irritable bowel syndrome (IBS), such as bloating and constipation. While some have considered GERD and IBS to belong on the same spectrum of functional bowel disorders,<sup>1</sup> the underlying mechanisms remain unclear.<sup>2,3</sup> Antireflux surgery (ARS), which aims to restore the lower esophageal sphincter barrier, is often held as the culprit for postoperative bloating and associated patient dissatisfaction. Although overall bloating scores generally improve after surgery, several authors have reported decreased satisfaction after ARS in patients who report bloating and constipation before surgery.<sup>4</sup>

In general, surgeons have been wary of offering ARS to patients with considerable constipation and bloating,<sup>5,6</sup> presumably because this complaint is “frequently blamed on the surgery,” thus, negatively impacting the patient’s satisfaction with the procedure.<sup>7</sup> In a new study, Eriksson and associates<sup>8</sup> use an objective test to quantify gut motility and correlate it with patient-reported dissatisfaction after ARS. They use a novel wireless motility capsule to measure whole-gut transit time (WGTT) and colon transit time (CTT). They show that patients with slower WGTT and CTT have significantly higher rates of postoperative bloating and decreased satisfaction after ARS, confirming the logic that if you have downstream issues, upstream symptoms may develop as well.

Postoperative bloating and the inability to belch are unwelcome sequelae, especially after conventional ARS. Recent studies have reported that postoperative gas bloat did not vary among the different surgical approaches in short- and long-term follow-up,<sup>9</sup> and more specifically, that there was no significant difference between traditional fundoplication and magnetic sphincter augmentation, even though magnetic sphincter augmentation allows for “venting.”<sup>9</sup> This underscores the argument that bloating is likely due to multifactorial gut motility issues beyond the restored lower esophageal sphincter barrier.

Methodologically, we found some shortcomings in the design of the study.<sup>8</sup> First, the authors fail to describe how the patients with colonic gut motility testing were selected, and second, we believe that the preoperative evaluation of bloating and other symptoms, such as constipation, should be broader and not limited to a single question on the GERD Health-Related Quality of Life questionnaire. A more specific IBS or general GI Health-Related Quality of Life score may be more useful.<sup>10,11</sup>

The authors have opened an exciting avenue to help us further understand the association between GI motility, as measured by WGTT and CTT, and dissatisfaction after