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Surgical and endoscopic management options for patients with GERD based on proton pump inhibitors symptom response: recommendations from an expert U.S. panel

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Abstract

Background and Aims: The objective of this study was to examine expert opinion and agreement on the treatment of distinct GERD profiles, from a surgical and therapeutic endoscopy perspective.

Methods: We used the RAND/University of California, Los Angeles Appropriateness Method over 6 months (July 2018 to January 2019) to assess the appropriateness of antireflux interventions among foregut surgeons and therapeutic gastroenterologists. Patients with primary atypical or extraesophageal symptoms were not considered. Patient scenarios were grouped according to their symptom response to PPI therapy. The primary outcome was appropriateness of an intervention.

Results: Antireflux surgery with laparoscopic fundoplication (LF) and magnetic sphincter augmentation (MSA) were ranked as appropriate for all complete and partial PPI responder scenarios. Transoral incisionless fundoplication (TIF) was ranked as appropriate in complete and partial PPI responders without a hiatal hernia. Radiofrequency energy was not ranked as appropriate for complete or partial responders. There was lack of agreement between surgery and interventional gastroenterology groups on the appropriateness of LF and MSA for PPI nonresponders. Rankings for PPI nonresponders were similar when results from impedance-pH testing on PPI therapy were available, except that LF and MSA were not ranked as appropriate for PPI nonresponders if the impedance-pH study was negative.

Conclusions: This work highlights areas of agreement for invasive therapeutic approaches for GERD and provides impetus for further interdisciplinary collaboration and trials to compare and generate novel and effective treatment approaches and care pathways, including the role of impedance-pH testing in PPI nonresponders.

Keywords

gastroesophageal reflux disease; proton-pump inhibitors; ambulatory reflux monitoring

INTRODUCTION

Gastroesophageal reflux disease (GERD) is the most frequent gastrointestinal diagnosis in ambulatory care.[1] Antireflux medication, particularly proton pump inhibitors (PPIs), are the first line of therapy for symptoms attributed to GERD. Consequently, PPIs are the most widely prescribed class of medications in the United States and account for over 50% of prescriptions for all digestive diseases.[2,3] Up to 40% of patients treated with PPIs may have incomplete or no symptom response to therapy.[4] Thus, patients with GERD and related symptoms are often referred to specialists, including foregut surgeons and gastroenterologists who offer surgical and endoscopic treatment options.[5]

Patients with GERD symptoms can be classified based on multiple criteria including clinical history, PPI symptom response (absent or incomplete), endoscopic findings (eg, hiatal

hernia, esophagitis), ambulatory esophageal pH/impedance monitoring, and esophageal function. A series of recent consensus documents propose a global approach to the "modern diagnosis" of GERD in efforts to standardize care and more accurately triage patients for therapy.[6–9] This approach accounts for the different and overlapping mechanisms of GERD symptoms (increased esophageal acid exposure, reflux burden, and esophageal hypersensitivity). Effective management of patients on long-term therapy and with chronic symptoms not responsive to PPI therapy can be difficult and costly.

Heterogeneity of GERD phenotypes can lead to confusion about appropriate therapeutic options and variable care for patients.[10] Recent work has assessed agreement by a panel of expert esophageal diagnosticians on appropriate treatment options for patients with documented GERD and persistent symptoms on PPI, using RAND methodology.[11] The primary conclusion was that invasive therapy (surgery or endoscopy) should only be offered to patients with abnormal esophageal reflux burden in the form of elevated acid exposure and/or increased reflux events (with or without hernia) or regurgitation with positive symptom association and a large hiatal hernia. A recognized limitation of this prior work included its sole focus on PPI nonresponders and lack of surgery or therapeutic endoscopy perspective. Thus, the objective of the present initiative was to examine expert opinion on the treatment of distinct GERD profiles (heartburn and regurgitation), from a surgical and therapeutic endoscopy perspective, using a validated prospective process.

METHODS

Study Design

A prospective study used the RAND/University of California, Los Angeles Appropriateness Method over 6 months (July 2018 to January 2019) to assess the appropriateness of antireflux interventions.[12]

Sixteen key opinion leaders were invited to participate as expert panelists, 8 foregut surgeons and 8 interventional/therapeutic gastroenterologists. Invitation criteria included leadership in the field of GERD, prior involvement with GERD management consensus development, and experience with performing one or more of the antireflux procedures under consideration. REDCap (University of Colorado) was used to electronically distribute surveys and collect data.

Expert panelists participated in a 2-round process. The process was moderated by 2 health-services researchers experienced in the RAND Appropriateness Method (R.Y. and A.J.G.). The American Foregut Society facilitated the meeting.

Round 1: Baseline Survey—In round 1 panelists completed 2 surveys. The first assessed baseline characteristics. In the second survey panelists individually ranked the appropriateness of interventions for distinct hypothetical patient scenarios described below (Table 1).

Round 2: Group Discussion and Re-Ranking—In round 2 panelists convened for an in-person meeting (January 2019, Denver, Colo, USA). Before round 2 panelists received a

comprehensive literature review and the search strategy as outlined below. At the in-person round 2 meeting panelists agreed upon definitions for hypothetical patient scenarios, reviewed the round 1 results, discussed personal experiences and the literature, and re-ranked the appropriateness of antireflux interventions for hypothetical patient scenarios.

Hypothetical Patient Scenarios

For each scenario, all hypothetical patients met the following baseline criteria: (1) age of 18 years or older, (2) presence of objective GERD evidenced by reflux esophagitis (Los Angeles Grade B or higher), Barrett's esophagus, and/or elevated esophageal acid exposure (EAE) on pH monitoring performed off acid-suppression, (3) treatment with maximum dose of PPI therapy defined as the maximum FDA approved or clinically indicated dosing, including twice daily, for PPI formulations, (4) troublesome symptoms of heartburn or regurgitation per Montreal Classification.[13] Each hypothetical patient was without contraindication to potential antireflux interventions, prior foregut surgery, paraesophageal hernia, or body mass index (BMI) >35 kg/m^2. Patients with primary atypical or extraesophageal symptoms were not considered similar to the previous study involving diagnostic esophageal physicians.[11] Further, we acknowledged that patients with atypical and extraesophageal reflux symptoms reflect opportunites for future multidisciplinary work beyond the scope of this initiative.

Patient scenarios were grouped according to their symptom response to PPI therapy (complete, partial, or none). For the purposes of voting on the scenarios, nonresponders were defined as patients with no resolution of symptoms on PPI therapy. A partial responder was defined as someone with any partial resolution of symptoms; for example 25% improvement would be a partial responder. For patients with PPI nonresponse, a further discussion was held based on additional testing results from multichannel impedance-pH testing performed on PPI, similar to the process with esophageal gastroenterologists published in 2017.[11] Esophageal function testing (eg, high resolution manometry) was not considered in the scenarios, similar to previous work[11], due to the unwieldy number of scenarios and permutations this would have created. It was acknowledged that many centers incorporate this for determining surgical approach. Each patient scenario was separated based on presence or absence of a clinically significant type I (axial) hiatal hernia. A clinically significant hernia was one in which the crural component to the reflux barrier was lacking, mechanical features of reflux predominated, and failure to perform hiatal hernia repair (cruroplasty) could impact clinical outcomes. Additionally, a hernia of >2 cm in axial or transverse dimension is technically challenging and hence clinically significant for successful, purely transoral techniques. A total of 24 hypothetical patient scenarios were considered (Table 1).

Six interventions were discussed for each patient scenario: LF with crural repair, laparoscopic MSA with crural repair, TIF, TIF with laparoscopic crural repair, radiofrequency energy delivery, and optimization of medical therapy. Optimization of medical therapy included addition of adjunctive pharmacologics used for GERD (H2 receptor antagonist, GABA agonist, alginate antacid, low-dose antidepressants) or

behavioral interventions (cognitive behavioral therapy, hypnosis), as well as continuation of the same or increased dose of PPI.

Literature Review

Three systematic literature searches and narrative reviews were performed by 3 members of the study team (R.Y., A.J.G., Z.V.). Foci of the literature search and review were (1) MSA, (2) TIF, and (3) radiofrequency energy delivery. The initial search strategy was a literature search in Medline with the following criteria: articles published between 2008 to 2018, available as full-text English, involving human adult subjects only, related to gastroesophageal reflux disease. The initial search yielded 212 articles (68 MSA, 93 TIF, 51 radiofrequency energy delivery). The study team reviewed the title and abstract of the 212 articles to exclude case reports, case series, systematic reviews, and narrative reviews, as well as articles that did not fulfill the initial search criteria. In this process 154 articles were excluded and 58 articles remained (19 MSA, 26 TIF, 13 radiofrequency energy delivery).

Each article was reviewed by the study team and the following details were tabulated: author, date of publication, study design, subject inclusion criteria, and outcomes. The outcomes of interest were patient-reported health-related quality of life, distal EAE time, independence from PPI therapy, and safety profile.

Outcomes from Ranking

The primary outcome was appropriateness of an intervention, defined according to the RAND appropriateness method, as an intervention in which the expected health benefit exceeds the expected negative consequences by a sufficiently wide margin that the procedure is worth doing, exclusive of cost. Ranking for appropriateness was on a nine-point scale. Per RAND constructs, agreement was present when 80% or more of panelists' rankings fell in the same 3-point range: not appropriate (1–3), equivocal (4–6), or appropriate (7–9). If more than 20% of the rankings were in disparate categories this was indicative of disagreement.

RESULTS

Overall 16 of 16 invited panelists accepted the invitation and 15 of 16 participated in both rounds 1 and 2. Therefore, results from 15 panelists are included in the analysis (Table 2). The 15 panelists represented a mean of 20.7 years in practice (SD 7.8) and included 8 foregut surgeons and 7 interventional gastroenterologists from diverse practice settings (9 (60%) academic, 2 (13%) community, and 4 (27%) hybrid of academic and community).

Complete PPI Responder (Table 3)

A complete PPI responder is an adult patient with a prior objective diagnosis of GERD off PPI with complete or near complete resolution of symptoms with PPI therapy. Four patient scenarios for a complete PPI responder were considered: (1 & 2) heartburn or regurgitation symptoms responsive to PPI therapy with a clinically significant hiatal hernia, (3 & 4) heartburn or regurgitation symptoms responsive to PPI therapy without a clinically significant hiatal hernia.

Ranked as Appropriate—LF and MSA were ranked as appropriate interventions with agreement across all 4 complete PPI responder patient scenarios. During the round 2 discussion panelists specifically referenced high quality evidence supporting the role of laparoscopic antireflux surgery for complete PPI responders with heartburn or regurgitation and clinically insignificant hernia.[14,15] More than 80% of panelists ranked TIF as an appropriate intervention for complete PPI responder patient scenarios without a clinically significant hiatal hernia. All 15 panelists ranked optimization of medical therapy as appropriate for the patient with heartburn exhibiting a complete PPI response and without a clinically significant hiatal hernia, remarking that in this scenario optimization of medical therapy would be to continue PPI and attempt to eventually reduce to lowest effective PPI dose.

Rankings for TIF with crural repair for patient scenarios with a clinically significant hiatal hernia were high although did not meet criteria for agreement, likely due to lack of high quality evidence per panelists. Further, there was a lack of agreement (uncertain appropriateness) for the role of radiofrequency energy delivery for patient scenarios without a clinically significant hiatal hernia. Some panelists asserted that radiofrequency energy delivery should not be discounted as it is a therapeutic option that does not preclude surgical options for future management.

All panelists asserted during the round table discussion that continuation of PPI should always be considered for patients with a complete response to PPI. In general TIF options were ranked higher by the interventional gastroenterology group compared with the foregut surgery group.

Partial PPI Responder (Table 4)

A partial PPI responder is an adult patient with a prior objective diagnosis of GERD off PPI with some resolution of symptoms with PPI therapy. Four patient scenarios for a partial PPI responder were considered: (1 & 2) heartburn or regurgitation symptoms with some response to PPI with a clinically significant hiatal hernia, (3 & 4) heartburn or regurgitation symptoms with some response to PPI without a clinically significant hiatal hernia.

Ranked as Appropriate—Similar to rankings for the complete PPI responder patient scenarios, LF and MSA were ranked with agreement as appropriate interventions across all 4 partial PPI responder patient scenarios. Similarly, a vast majority ranked TIF as an appropriate intervention for partial PPI responder patient scenarios without a clinically significant hiatal hernia yet inappropriate for patients with a clinically significant hernia.

Overall, TIF with crural repair did not meet criteria for agreement for all 4 partial PPI responder patient scenarios.

Indeterminate Rankings—Compared with the rankings for the complete PPI responder, optimization of medical therapy was ranked lower for the partial PPI responder. Radiofrequency energy delivery was also ranked as indeterminate for the partial PPI responder with heartburn or regurgitation without a clinically significant hiatal hernia. Panelists discussed that randomized controlled trials demonstrate the data for radiofrequency

energy delivery for partial PPI responders is variable and low quality, and as such radiofrequency energy delivery is likely not the best practice for partial PPI response, however, is not inappropriate.

PPI Nonresponder

A PPI nonresponder is an adult patient with a prior objective diagnosis of GERD off PPI with lack of symptom improvement with PPI therapy. Twenty patient scenarios for a PPI nonresponder were considered.

PPI Nonresponder Without Further Impedance-pH Testing (Table 5)

The first 4 patient scenarios for a PPI nonresponder did not include consideration of further reflux testing: (1 & 2) heartburn or regurgitation symptoms with no response to PPI therapy with a clinically significant hiatal hernia, (3 & 4) heartburn or regurgitation symptoms with no response to PPI therapy without a clinically significant hiatal hernia.

Ranked as Appropriate—Eighty percent ranked LF as appropriate for nonresponder scenarios with a clinically significant hernia, with uncertain agreement in scenarios without a hernia. Eighty percent ranked MSA as appropriate for the PPI no-responders with regurgitation regardless of presence of hernia. TIF without crural repair was ranked as an appropriate intervention for the 2 PPI nonresponder patient scenarios without a clinically significant hernia. Further discussion was nuanced and panelists voiced that although high level data is lacking, TIF may be a more conservative option for this challenging patient phenotype as opposed to LF.

There was lack of agreement between the foregut surgery and interventional gastroenterology groups for the appropriateness of surgical interventions for PPI nonresponders. For instance, all 8 foregut surgeons ranked LF and MSA as appropriate for all PPI nonresponder patient scenarios. Interventional gastroenterologists did not find consensus that LF or MSA are appropriate for any of the PPI nonresponder patient scenarios. Panelists discussed that although high level data exist supporting LF for PPI responders, one RCT supports MSA in PPI nonresponders with regurgitation[16], and otherwise there are a lack of high-level data to support its role in PPI nonresponders. Radiofrequency energy delivery was ranked high and nearly met criteria for agreement as an appropriate intervention for PPI nonresponder scenarios without a clinically significant hernia. Some panelists expressed that radiofrequency energy delivery would be their first consideration for these particular PPI nonresponder patient scenarios.

Ranked as Inappropriate—Optimization of medical therapy was ranked as inappropriate with near agreement across all 4 PPI nonresponder patient scenarios. Panelists remarked that continuing PPI therapy for these patients without additional intervention is inappropriate. However, medical optimization with the addition of other pharmacologic or behavioral interventions (ie, alginate antacid, GABA agonist, cognitive behavioral therapy) could be appropriate if they offered a high chance of success.

PPI Nonresponder With Further Impedance-pH Testing

The next 16 patient scenarios mirrored the RAND Appropriateness Method published in 2018, which examined esophageal gastroenterologists expert opinion for management of PPI nonresponders based on further testing with impedance-pH monitoring (Table 6, Supplementary Tables).[11] The International GERD Working Group recommendation in the Lyon consensus is to test PPI nonresponders further with impedance-pH monitoring on PPI.[6,7] Although this was a controversial topic, the panelists still ranked twelve patient scenarios based on symptom (heartburn or regurgitation), presence of clinically significant hernia, and impedance-pH on PPI result (breakthrough distal esophageal acid exposure, reflux hypersensitivity, elevated nonacid reflux burden, or negative testing).

Ranked as Appropriate—LF and MSA were ranked as appropriate interventions for all PPI nonresponder patient scenarios based on impedance-pH testing with the exception of the patient with heartburn predominant symptoms and evidence of reflux hypersensitivity that does not have a clinically significant hernia, and the patient with a completely normal impedance-pH study that does not have a clinically significant hernia.

TIF without crural repair was ranked as appropriate for all PPI nonresponder patient scenarios without a clinically significant hernia regardless of impedance-pH testing results. TIF with crural repair was ranked highly for some scenarios, although did not meet criteria for agreement for any PPI nonresponder patient scenarios with a clinically significant hernia regardless of impedance-pH testing results.

Radiofrequency energy delivery was ranked highly although did not meet criteria for agreement for the PPI nonresponder patients without a clinically significant hernia and evidence of reflux hypersensitivity or elevated reflux burden on impedance-pH testing.

Ranked as Inappropriate—Similar to previous rankings, TIF without crural repair and radiofrequency energy delivery alone were ranked with agreement as inappropriate interventions for all PPI nonresponder patient scenarios with a clinically significant hiatal hernia, regardless of impedance-pH results.

DISCUSSION / CONCLUSIONS

This study used RAND methodology to evaluate multidisciplinary expert (foregut surgeons and interventional gastroenterologists) agreement on the treatment of 28 distinct GERD profiles. In summary, there was agreement that continuation of PPI therapy is appropriate in complete responders. Antireflux surgery with LF and MSA were ranked as appropriate for all complete and partial PPI responder scenarios in cases where PPI discontinuation is requested or necessary. TIF was ranked as being appropriate in complete and partial responders without a hiatal hernia. TIF with crural repair was ranked high but did not meet criteria for appropriateness for complete or partial responders, and this was mainly driven by specialty differences in rankings, due to lack of objective long-term data. Radiofrequency energy was not ranked as appropriate for complete or partial responders. For PPI nonresponders, LF was ranked as appropriate when a clinically significant hiatal hernia was present, MSA specifically for regurgitation predominant PPI nonresponse regardless of

hiatal hernia, and TIF when a clinically significant hiatal hernia was not present. Rankings for PPI nonresponders were generally similar when results from impedance-pH testing on PPI therapy were available, except that LF and MSA were not ranked as appropriate for PPI nonresponders if the impedance-pH study was negative.

In comparison with the prior study[11] evaluating agreement between expert diagnostic esophagologists there were both similarities and differences. Both studies focused on patients with baseline objective evidence of GERD with heartburn or regurgitation symptoms. The prior article focused solely on patients with PPI nonresponsive GERD as this population comprises a large referral population to esophageal experts, whereas this study distinguished between patients with partial but unsatisfactory response to PPIs and patients with complete nonresponse to PPIs. In addition, in the prior article all nine patient scenarios assumed patients underwent impedance-pH testing, in accordance with the Lyon consensus for guiding therapeutic decision making.[6,9] However in the current initiative, some panelists challenged the role of further testing with impedance-pH testing on PPI therapy for PPI nonresponders. The current panelists pointed to the paucity of evidence to support this practice, and that the literature does not show that negative impedance-pH monitoring on PPI is a negative predictive factor of outcome after antireflux intervention. The current panelists noted that the decision to offer an antireflux intervention based on impedance-pH results, as recommended in the Lyon consensus, may deprive candidates that would benefit from the antireflux intervention. Further, many of the foregut surgeons expressed that impedance-pH would not alter their decision to intervene if a patient with GERD and a clinically significant hernia has nonresponse to PPI. At the same time, some panelists valued the impedance-pH results to guide their understanding as to the source of the symptom and increase their confidence that the patient will be more likely to have a positive outcome after intervention, especially in patients without hernias.

In clinical practice, PPI nonresponders are often the most challenging to treat, and this was highlighted by the ranking process for scenarios with and without further impedance-pH testing. Without further testing, TIF without crural repair was ranked as the only appropriate intervention for the 2 PPI nonresponder patient scenarios (heartburn and regurgitation) without a clinically significant hernia. Without further testing, there was specialty specific disagreement on the appropriateness of surgical interventions (laparoscopic fundoplication, magnetic sphincter augmentation), and the discussion highlighted the lack of controlled trial data in this area. There was complete agreement that TIF without crural repair and radiofrequency energy delivery alone are inappropriate for patients with a clinically significant hiatal hernia, regardless of impedance-pH results. For patients without a hernia and a completely normal impedance-pH study, laparoscopic fundoplication and magnetic sphincter augmentation were not ranked as appropriate, indicating that further testing could play a role in avoiding a surgical intervention. Specialty specific differences in opinion (therapeutic gastroenterology vs surgery) on the role of further testing (impedance-pH) and impact on therapy choice resulted in surgical interventions (laparoscopic fundoplication and magnetic sphincter augmentation) as not meeting criteria for appropriateness based on agreement from the entire panel.

Strengths of this study include having a diverse and balanced group of both therapeutic gastroenterologists and foregut surgeons, from various practice settings.The RAND process has been widely used in prior studies and allows for a rigorous approach to revealing areas of agreement and disagreement in clinical care and present knowledge gaps for future generation of evidence. Patient scenarios were more comprehensive than the prior similar study[11] and included complete, partial, and non-PPI responders both with and without further testing.

There are several limitations to this work. Real world clinical practice and patient presentations are diverse and heterogeneous. Surgeons and therapeutic gastroenterologists have different training backgrounds and implicit biases that could impact what is judged as appropriate. We did not include patients with multiple symptoms, including extraesophageal, and we did not examine the potential role of high-resolution manometry in diagnosing motility disorders. During the discussions panelists also raised the fact that even if patients have some response to PPI therapy they may continue to experience a reduced quality of life on PPI. For this patient group, resumption of PPI therapy after an intervention should not be a sole indicator of procedure failure. In fact, transforming a partial PPI responder to a complete PPI responder with an antireflux intervention combined with continued PPI therapy could be considered a positive successful outcome. It was noted that BMI often plays a role in decision making and that some experts felt that patients with BMI >35 would be best served for reflux control with bariatric surgery.

In conclusion, these recommendations provide a framework for approaching patients with heartburn or regurgitation-predominant GERD based on symptom response to PPI. Patients with GERD symptoms are heterogenous and there are evidence gaps comparing therapeutic approaches, especially for PPI-non responders. We acknowledge that the outcomes of different therapeutic approaches may not be equivalent and choices are driven by multiple factors, including provider expertise, bias and patient preference. The results of this study should not be used for a strict approach to therapeutic decision making. Rather, our hope is that these findings in combination with the results incorporating diagnostic esophagologist perspectives[11] provide a foundation to balance “thinking fast and slow” in cases of complex decision making to avoid error prone emotionally driven decisions.[17] This work provides impetus for further interdisciplinary collaboration and trials to compare and generate novel and effective treatment approaches and care pathways. Future work should also focus on the diverse scenarios of extraesophageal symptoms and the utility of incorporating esophageal function testing into decision making. Individual physicians, whether surgeon, therapeutic or diagnostic gastroenterologist, should approach complex GERD patients in a collaborative, multidisciplinary fashion and try to understand their own and others personal biases that may be driving diagnostic and therapeutic preferences.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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RB: Receives consulting fees from Ethicon EndoSurgery, Diversatek, Intuitive

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SAE: Receives consulting fees from Medtronic; Has stock options in Endostim, freehold surgical

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Abbreviations

GERD	Gastroesophageal reflux disease
PPI	proton pump inhibitors
LF	laparoscopic fundoplication
MSA	magnetic sphincter augmentation
TIF	transoral incisionless fundoplication
EAE	esophageal acid exposure

BMI	body mass index

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Table 1.

Patient Scenarios Evaluated

PPI Response	Symptom	Hernia	Imp-pH testing results if performed
Complete PPI Responder	Heartburn	Significant	Not performed
		Not significant	Not performed
	Regurgitation	Significant	Not performed
		Not significant	Not performed
Partial PPI responder	Heartburn	Significant	Not performed
		Not significant	Not performed
	Regurgitation	Significant	Not performed
		Not significant	Not performed
PPI nonresponder	Heartburn	Significant	Not performed
		Not significant	Not performed
	Regurgitation	Significant	Not performed
		Not significant	Not performed
PPI nonresponder	Heartburn	Significant	breakthrough acid exposure
		Not significant	breakthrough acid exposure
	Regurgitation	Significant	breakthrough acid exposure
		Not significant	breakthrough acid exposure
PPI nonresponder	Heartburn	Significant	normal acid exposure, reflux hypersensitivity
		Not significant	normal acid exposure, reflux hypersensitivity
	Regurgitation	Significant	normal acid exposure, reflux hypersensitivity
		Not significant	normal acid exposure, reflux hypersensitivity
PPI nonresponder	Heartburn	Significant	normal acid exposure, negative symptom-reflux correlation, elevated reflux burdern
		Not significant	normal acid exposure, negative symptom-reflux correlation, elevated reflux burdern
	Regurgitation	Significant	normal acid exposure, negative symptom-reflux correlation, elevated reflux burdern
		Not significant	normal acid exposure, negative symptom-reflux correlation, elevated reflux burdern
PPI nonresponder	Heartburn	Significant	normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden
		Not significant	normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden
	Regurgitation	Significant	normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden

PPI Response	Symptom	Hernia	Imp-pH testing results if performed
		Not significant	normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden

Table 2:

Baseline characteristics of expert panel

Covariate	Overall (N=15)	Foregut surgeon (N=8)	Advanced therapeutic gastroenterologist (N=7)
Age range			
30 to 49 years	5 (33.3%)	3 (37.5%)	2 (28.6%)
50–69 years	10 (66.7%)	5 (62.5%)	5 (71.4%)
Female	2 (13.3%)	1 (12.5%)	1 (14.3%)
Practice Type:			
Academic	9 (60.0%)	4 (50.0%)	5 (71.4%)
Community	2 (13.3%)	2 (25.0%)	0 (0.0%)
Hybrid	4 (26.7%)	2 (25.0%)	2 (28.6%)
Do you personally perform:			
Laparoscopic fundoplication	8 (53.3%)	8 (100.0%)	0 (0.0%)
Magnetic sphincter augmentation	7 (46.7%)	7 (87.5%)	0 (0.0%)
Transoral incisionless fundoplication	9 (60.0%)	4 (50.0%)	5 (71.4%)
Radiofrequency energy delivery	10 (66.7%)	6 (75.0%)	4 (57.1%)
In the past year have your referred for and/or performed the following:			
Laparoscopic fundoplication	15 (100.0%)	8 (100.0%)	7 (100.0%)
Magnetic sphincter augmentation	12 (80.0%)	8 (100.0%)	4 (57.1%)
Transoral incisionless fundoplication	11 (73.3%)	4 (50.0%)	7 (100.0%)
Radiofrequency energy delivery	10 (66.7%)	6 (75.0%)	4 (57.1%)
Do you consider the following for surgical or endoluminal antireflux interventions:			
Central Obesity	12 (80.0%)	6 (75.0%)	6 (85.7%)
Axial Length of Hiatal Hernia	14 (93.3%)	7 (87.5%)	7 (100.0%)
Gastroesophageal Flap Valve Grade	12 (80.0%)	7 (87.5%)	5 (71.4%)
Esophageal Motility/Peristaltic Reserve	14 (93.3%)	7 (87.5%)	7 (100.0%)
Acid/Reflux Burden on pH testing off PPI	14 (93.3%)	7 (87.5%)	7 (100.0%)
Acid/Reflux Burden on pH Impedance on PPI	10 (66.7%)	4 (50.0%)	6 (85.7%)
Gastric Emptying	11 (73.3%)	7 (87.5%)	4 (57.1%)

Table 3

Complete responder scenarios.

Four patient scenarios, and six interventions per scenario considered for complete PPI responders. Rankings from the entire group, surgeon subset and therapeutic GI (iGI) subset are displayed. Each cell displays ranking for appropriateness [% agreement, median (min-max)]. Cells shaded green indicate agreement as an appropriate intervention, red indicate agreement as an inappropriate intervention, and white indicate lack of agreement and/or uncertain appropriateness.

	All Experts						Surgeons Subset						iGI Subset					
Scenario	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**
Heartburn, + Sig Hernia	60%, 7 (1-9)	100%, 9 (7-9)	100%, 9 (7-9)	0%, 1 (1-2)	60%, 7 (1-9)	0%, 1 (1-1)	50%, 6.5 (1-9)	100%, 9 (9-9)	100%, 9 (7-9)	0%, 1 (1-8)	38%, 5.5 (1-8)	0%, 1 (1-1)	71%, 7 (5-9)	100%, 9 (7-9)	100%, 8 (7-9)	0%, 1 (1-2)	86%, 7 (5-9)	0%, 1 (1-1)
Regurigtation, + Sig Hernia	40%, 5 (1-9)	100%, 9 (9-9)	100%, 9 (7-9)	0%, 1 (1-2)	60%, 7 (1-9)	0%, 1 (1-1)	25%, 5 (1-9)	100%, 9 (9-9)	100%, 9 (7-9)	0%, 1 (1-1)	38%, 5.5 (1-8)	0%, 1 (1-1)	57%, 7 (1-9)	100%, 9 (9-9)	100%, 9 (8-9)	0%, 1 (1-2)	86%, 7 (3-9)	0%, 1 (1-1)
Heartburn, No Sig Hernia	100%, 9 (7-9)	93%, 9 (6-9)	100%, 8 (7-9)	87%, 8 (6-9)	40%, 6 (1-9)	40%, 6 (2-9)	100%, 9 (8-9)	100%, 9 (7-9)	100%, 9 (7-9)	75%, 7.5 (6-9)	50%, 6.5 (1-8)	25%, 6 (3-9)	100%, 8 (7-9)	86%, 7 (6-9)	100%, 7 (7-9)	100%, 8 (7-9)	29%, 5 (1-9)	57%, 7 (2-9)
Regurgitations, No Sig Hernia	60%, 9 (2-9)	87%, 9 (6-9)	93%, 9 (6-9)	80%, 8 (6-9)	40%, 6 (1-8)	33%, 6 (1-8)	63%, 9 (4-9)	100%, 9 (7-9)	100%, 9 (7-9)	75%, 7.5 (6-9)	50%, 6.5 (1-8)	25%, 6 (1-8)	57%, 8 (2-9)	71%, 8 (6-9)	86%, 7 (6-9)	867%, 8 (6-9)	29%, 5 (1-8)	43%, 5 (1-8)

Optimization of medical therapy (OMT); Laparoscopic fundoplication (LF); Magnetic sphincter augmentation (MSA); Transoral incisionless fundoplication (TIF); TIF with crural repair (TIFCR); Radiofrequency energy delivery (RFED)

Table 4

Partial responder scenarios

Four patient scenarios, and six interventions per scenario considered for partial PPI responders. Rankings from the entire group, surgeon subset and therapeutic GI (iGI) subset are displayed. Each cell displays ranking for appropriateness [% agreement, median (min-max)]. Cells shaded green indicate agreement as an appropriate intervention, red indicate agreement as an inappropriate intervention, and white indicate lack of agreement and/or uncertain appropriateness.

	All Experts						Surgeons Subset						iGI Subset					
Scenario	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**
Heartburn, + Sig Hernia	33%, 5 (2-7)	100%, 9 (7-9)	100%, 9 (7-9)	7%, 1 (1-7)	53%, 7 (1-9)	0%, 1 (1-5)	25%, 5 (3-7)	100%, 9 (8-9)	100%, 9 (7-9)	0%, 1 (1-1)	38%, 6 (1-8)	0%, 1 (1-1)	43%, 6 (2-7)	100%, 8 (7-9)	100%, 8 (7-9)	14%, 2 (1-7)	71%, 7 (5-9)	0%, 1 (1-5)
Regurigtation, + Sig Hernia	20%, 3 (1-7)	100%, 9 (7-9)	100%, 9 (7-9)	7%, 1 (1-7)	53%, 7 (1-9)	0%, 1 (1-2)	0%, 3 (1-5)	100%, 9 (8-9)	100%, 9 (7-9)	0%, 1 (1-1)	38%, 6 (1-8)	0%, 1 (1-1)	43%, 5 (1-7)	100%, 9 (7-9)	100%, 8 (7-9)	14%, 1 (1-7)	71%, 7 (6-9)	0%, 1 (1-2)
Heartburn, No Sig Hernia	40%, 6 (3-9)	87%, 9 (6-9)	87%, 9 (6-9)	93%, 7 (6-9)	53%, 7 (1-9)	27%, 6 (2-9)	50%, 6.5 (5-9)	100%, 9 (8-9)	100%, 9 (9-9)	100%, 7 (7-8)	38%, 6 (1-8)	25%, 6 (4-9)	29%, 6 (3-7)	71%, 7 (6-9)	71%, 8 (6-9)	86%, 8 (6-9)	71%, 7 (1-9)	29%, 6 (2-9)
Regurgitations, No Sig Hernia	27%, 5 (1-7)	100%, 9 (7-9)	100%, 9 (7-9)	93%, 7 (6-9)	60%, 7 (1-9)	27%, 6 (1-8)	25%, 5.5 (1-7)	100%, 9 (8-9)	100%, 9 (9-9)	100%, 7 (7-9)	38%, 6 (1-8)	25%, 6 (4-8)	29%, 4 (1-7)	100%, 8 (7-9)	100%, 9 (7-9)	86%, 8 (6-9)	86%, 7 (1-9)	29%, 5 (1-8)

Optimization of medical therapy (OMT); Laparoscopic fundoplication (LF); Magnetic sphincter augmentation (MSA); Transoral incisionless fundoplication (TIF); TIF with crural repair (TIFCR); Radiofrequency energy delivery (RFED)

Table 5

Nonresponder scenarios

Four patient scenarios, and six interventions per scenario considered for PPI nonresponders (without data from pH impedance monitoring on PPI available). Rankings from the entire group, surgeon subset and therapeutic GI (iGI) subset are displayed. Each cell displays ranking for appropriateness [% agreement, median (min-max)]. Cells shaded green indicate agreement as an appropriate intervention, red indicate agreement as an inappropriate intervention, and white indicate lack of agreement and/or uncertain appropriateness.

	All Experts						Surgeons Subset						iGI Subset					
Scenario	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**
Heartburn, + Sig Hernia	13%, 2 (1-9)	80%, 8 (2-9)	73%, 8 (1-9)	0%, 1 (1-6)	47%, 6 (1-9)	0%, 1 (1-6)	13%, 3 (2-8)	100%, 8 (8-9)	100%, 8 (7-9)	0%, 1 (1-1)	50%, 6.5 (1-9)	0%, 1 (1-6)	14%, 2 (1-9)	57%, 7 (2-9)	43%, 6 (1-9)	0%, 1 (1-6)	43%, 6 (1-7)	0%, 1 (1-3)
Regurigtation, + Sig Hernia	13%, 2 (1-9)	80%, 9 (3-9)	80%, 8 (3-9)	7%, 1 (1-8)	60%, 7 (1-9)	0%, 1 (1-6)	13%, 2.5 (1-8)	100%, 9 (8-9)	100%, 8.5 (7-9)	13%, 1 (1-8)	50%, 6 (1-9)	0%, 1 (1-6)	14%, 2 (1-9)	57%, 7 (3-9)	57%, 7 (3-9)	0%, 1 (1-6)	71%, 7 (4-7)	0%, 1 (1-3)
Heartburn, No Sig Hernia	27%, 5 (2-9)	67%, 7 (1-9)	73%, 7 (2-9)	100%, 7 (7-9)	20%, 5 (1-7)	73%, 7 (4-9)	13%, 4.5 (2-8)	100%, 7.5 (7-9)	100%, 7 (7-9)	100%, 7 (7-9)	25%, 5.5 (1-7)	88%, 7 (6-9)	43%, 6 (2-9)	29%, 5 (1-9)	43%, 6 (2-9)	100%, 8 (7-9)	14%, 4 (1-7)	57%, 7 (4-9)
Regurgitations, No Sig Hernia	13%, 4 (2-9)	73%, 8 (1-9)	80%, 8 (3-9)	100%, 8 (7-9)	13%, 5 (1-7)	60%, 7 (4-9)	13%, 3 (2-8)	100%, 8 (7-9)	100%, 8 (7-9)	100%, 7 (7-9)	13%, 5.5 (1-7)	75%, 7 (4-9)	14%, 4 (2-9)	43%, 5 (1-9)	57%, 7 (3-9)	100%, 8 (7-9)	14%, 4 (1-7)	43%, 6 (5-8)

Optimization of medical therapy (OMT); Laparoscopic fundoplication (LF); Magnetic sphincter augmentation (MSA); Transoral incisionless fundoplication (TIF); TIF with crural repair (TIFCR); Radiofrequency energy delivery (RFED)

Table 6

All nonresponder with impedance-pH scenarios for all experts.

Sixteen patient scenarios, and six interventions per scenario considered. Rankings from the entire group are displayed. Each cell displays ranking for appropriateness [% agreement, median (min-max)]. Cells shaded green indicate agreement as an appropriate intervention, red indicate agreement as an inappropriate intervention, and white indicate lack of agreement and/or uncertain appropriateness.

NonResponders with pH-All Experts	**Ranking for appropriateness (% agreement, median, (min-max))**					
Hypothetical Patient Scenario	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**
PPI nonresponders with heartburn predominant GERD, breakthrough acid exposure, and large hiatal hernia	33%, 3 (1-8)	100%, 9 (7-9)	100%, 8 (7-9)	0%, 1 (1-6)	67%, 7 (1-9)	0%, 1 (1-3)
PPI nonresponders with regurgitation predominant GERD, breakthrough acid exposure, and large hiatal hernia	20%, 3 (1-8)	100%, 9 (7-9)	100%, 9 (7-9)	0%, 1 (1-6)	73%, 7 (1-9)	0%, 1 (1-3)
PPI nonresponders with heartburn predominant GERD, breakthrough acid exposure, and small or no hiatal hernia	60%, 7 (2-8)	100%, 9 (7-9)	100%, 8 (7-9)	87%, 7 (5-9)	40%, 6 (1-9)	40%, 6 (1-9)
PPI nonresponders with regurgitation predominant GERD, breakthrough acid exposure, and small or no hiatal hernia	33%, 5 (1-8)	93%, 9 (6-9)	100%, 9 (7-9)	87%, 8 (5-9)	40%, 6 (1-9)	47%, 6 (1-9)
PPI nonresponders with heartburn predominant GERD, normal acid exposure, reflux hypersensitivity and large hiatal hernia	47%, 6 (1-8)	80%, 8 (3-9)	80%, 8 (3-9)	0%, 1 (1-5)	60%, 7 (1-9)	0%, 1 (1-5)
PPI nonresponders with regurgitation predominant GERD, normal acid exposure, reflux hypersensitivity, and large hiatal hernia	20%, 5 (1-7)	87%, 9 (5-9)	87%, 8 (5-9)	0%, 1 (1-6)	60%, 7 (1-9)	0%, 1 (1-6)
PPI nonresponders with heartburn predominant GERD, normal acid exposure, reflux hypersensitivity, and small or no hiatal hernia	73%, 7 (3-8)	73%, 7 (1-9)	73%, 8 (1-9)	80%, 7 (4-9)	27%, 4 (1-7)	60%, 7 (1-9)
PPI nonresponders with regurgitation predominant GERD, normal acid exposure, reflux hypersensitivity, and small or no hiatal hernia	40%, 5 (1-8)	87%, 9 (3-9)	87%, 9 (3-9)	80%, 7 (5-9)	33%, 5 (1-8)	53%, 7 (1-9)
PPI nonresponders with heartburn predominant GERD, normal acid exposure, negative symptom-reflux correlation, elevated reflux burdern, and large hiatal hernia	27%, 3 (1-8)	93%, 8 (5-9)	93%, 8 (5-9)	7%, 1 (1-8)	73%, 7 (1-9)	7%, 1 (1-8)
PPI nonresponders with regurgitation predominant GERD, normal acid exposure, negative symptom-reflux correlation, elevated reflux burdern, and large hiatal hernia	20%, 2 (1-8)	93%, 9 (5-9)	93%, 8 (5-9)	7%, 1 (1-8)	73%, 7 (1-9)	7%, 1 (1-7)
PPI nonresponders with heartburn predominant GERD, normal acid exposure, negative symptom-reflux correlation, elevated reflux burden, and small or no hiatal hernia	27%, 3 (1-8)	87%, 8 (4-9)	87%, 8 (4-9)	93%, 7 (5-9)	33%, 5 (1-8)	53%, 7 (1-9)
PPI nonresponders with regurgitation predominant GERD, normal acid exposure, negative symptom-reflux correlation, elevated reflux burden, and small or no hiatal hernia	13%, 3 (1-8)	87%, 9 (5-9)	87%, 9 (4-9)	93%, 8 (5-9)	40%, 5 (1-9)	53%, 7 (1-9)
PPI nonresponders with heartburn predominant GERD, large hiatal hernia and negative pH impedance study (normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden)	33%, 5 (1-9)	80%, 8 (4-9)	80%, 8 (4-9)	0%, 1 (1-5)	53%, 7 (1-9)	0%, 1 (1-3)
PPI nonresponders with regurgitation predominant GERD, large hiatal hernia and negative pH impedance study (normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden)	27%, 4 (1-9)	80%, 9 (5-9)	80%, 8 (5-9)	0%, 1 (1-5)	67%, 7 (1-9)	7%, 1 (1-7)
PPI nonresponders with heartburn predominant GERD, small or no hiatal hernia and negative pH impedance study (normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden)	47%, 6 (1-9)	53%, 7 (1-9)	53%, 7 (1-9)	80%, 7 (3-9)	20%, 3 (1-8)	47%, 6 (1-9)

NonResponders with pH-All Experts	Ranking for appropriateness (% agreement, median, (min-max))					
Hypothetical Patient Scenario	**OMT**	**LF**	**MSA**	**TIF**	**TIFCR**	**RFED**
PPI nonresponders with regurgitation predominant GERD, small or no hiatal hernia and negative pH impedance study (normal acid exposure, negative symptom-reflux correlation, nonelevated reflux burden)	40%, 4 (1-9)	53%, 7 (1-9)	60%, 7 (1-9)	73%, 7 (4-9)	20%, 2 (1-8)	40%, 6 (1-9)

Optimization of medical therapy (OMT); Laparoscopic fundoplication (LF); Magnetic sphincter augmentation (MSA); Transoral incisionless fundoplication (TIF); TIF with crural repair (TIFCR); Radiofrequency energy delivery (RFED)