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A Standardized Approach to Performing and Interpreting Functional Lumen Imaging Probe Panometry for Esophageal Motility Disorders: The Dallas Consensus

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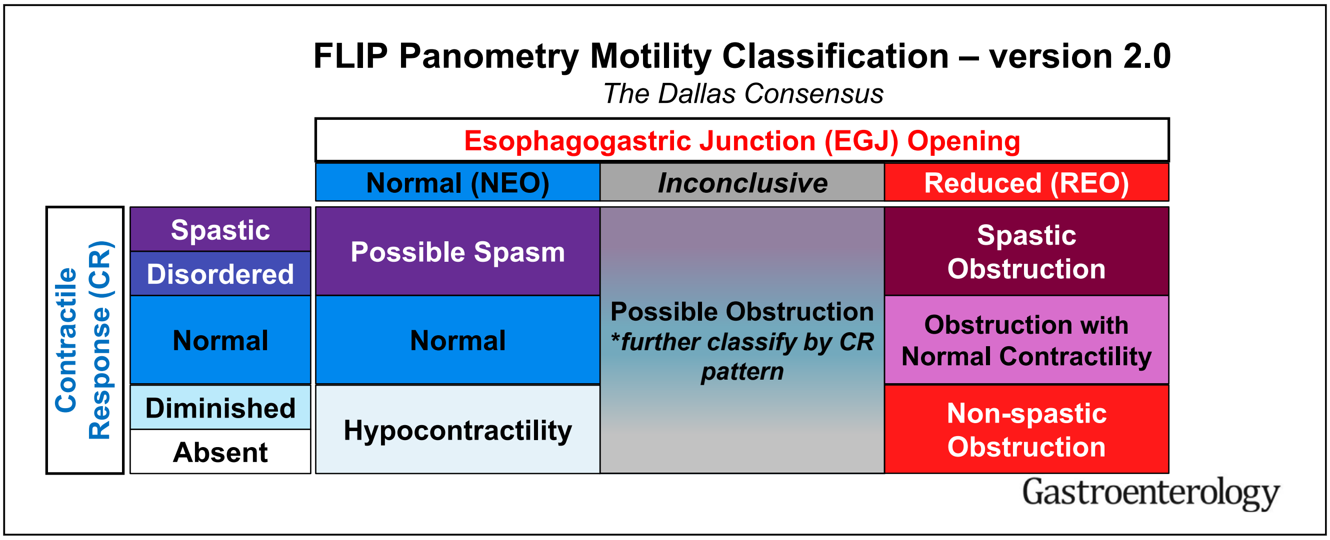

BACKGROUND & AIMS: Functional lumen imaging probe (FLIP) panometry provides assessment of the esophagogastric junction opening and esophageal body contractile activity during an endoscopic procedure and is increasingly being incorporated into comprehensive esophageal motility assessments. The aim of this study was to provide a standardized approach and vocabulary to the procedure and interpretation and update the motility classification scheme. **METHODS:** A working group of 19 FLIP panometry experts convened in a modified Delphi consensus process to produce and assess statements on the FLIP panometry procedure and interpretation. Three rounds of voting were conducted on an agreement scale of 1–9 for appropriateness, followed by face-to-face discussions and an opportunity for revisions of statements. The "percent agreement" was the proportion of votes with score ≥7 indicating level of agreement on appropriateness. **RESULTS:** A total of 40 statements were selected for final inclusion in the Dallas Consensus, including FLIP panometry protocol, interpretation of esophagogastric junction opening and contractile response, and motility classification scheme. Key statements included: "FLIP panometry should be interpreted in the context of the clinical presentation, the accompanying EGD [esophagogastroduodenoscopy] findings and other relevant complementary testing" (median response 9.0; 100% agreement). "A major motor disorder is unlikely in the setting of a 'normal' FLIP panometry classification" (median response 9.0; 94% agreement). "Diminished or absent contractile response with reduced esophageal opening (ie, nonspastic obstruction) supports the diagnosis of a disorder of EGJ [esophagogastric junction] outflow" (median response 8.5; 94% agreement). **CONCLUSIONS:** The standardized approach for performance and interpretation of the Dallas Consensus can facilitate use of FLIP panometry in broad clinical settings.

Keywords: Endoscopy; Achalasia; Impedance; Dysphagia.

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Functional lumen imaging probe (FLIP) panometry is performed on a sedated patient at the time of endoscopy and provides data for comprehensive assessments of esophageal motility.

NEW FINDINGS

A consensus-driven process provided a standardized approach to the performance of FLIP panometry and interpretation of findings and presents an updated classification scheme for FLIP panometry esophageal motility assessments.

LIMITATIONS

Clinically inconclusive categories and classifications are limitations to the current work and serve as potential targets of future investigations.

CLINICAL RESEARCH RELEVANCE

The Dallas Consensus provides a standardized approach that is amenable to a broad range of cases and providers. The updated motility classification scheme reflects the spectrum of esophageal motor disorders that can be applied to standardize the interpretation of FLIP panometry motility assessments used in clinical and research investigations.

BASIC RESEARCH RELEVANCE

The FLIP is a useful tool to measure esophageal physiology and mechanics in response to distention, which are important components of esophageal function. The Dallas Consensus provides a framework to facilitate investigations into esophageal motility pathophysiology, including unique and novel aspects of the esophageal response to sustained distention.

Functional lumen imaging probe (FLIP) panometry categorizes esophageal motility in response to a controlled volume distention protocol that is performed on a sedated patient, typically at the time of endoscopy. An initial classification scheme that incorporated the categorization of esophagogastric junction (EGJ) opening and contraction pattern was initially described in 2021 based on input from a FLIP panometry working group.[1] Over the past 3 years, clinical application and research investigation of FLIP panometry has expanded and prompted interest in refining the FLIP panometry motility classification to reflect these updates, as well as address limitations that were recognized in the initial scheme. A FLIP panometry working group with 19 members from the United States and Canada worked over the past year to formalize the standardized FLIP panometry approach for the protocol and interpretation and to develop the FLIP Panometry Classification, version 2.0, using a modified Delphi process. This effort sought to develop a common approach and vocabulary to describe FLIP panometry findings for application in clinical and research settings.

Methods

Working Group and Study Collaborators

The Impedance Planimetry Working Group included 19 members from the United States and Canada, who were selected based on reputation of esophageal motility expertise and experience in using FLIP panometry (all members with >100 FLIP studies performed; Supplementary Table 1), while also seeking diversity in gender and geographical distribution. Conflicts of interest were declared up front, with specific attention to relevant industry conflicts. The Impedance Planimetry Working Group was meeting periodically since 2020.[1,2] Dedicated iterative discussions to develop the FLIP Panometry Consensus, version 2.0, statements began with a meeting in Dallas, TX, in September 2023, and proceeded using a modified Delphi process over approximately 1 year. A methodological expert external to the working group was invited to participate (S.S.) and additional collaborators were invited to assist by performing an independent critical literature review for key statements (W.W.C., K.R.).

Study Design

A modified Delphi process was used to give panelists the opportunity to discuss their judgments in face-to-face meetings, both in person and virtual, between rating rounds (Supplementary Figure 1). Given that high-quality evidence (eg, randomized controlled trials) is not readily available in this field, this methodology was used, as it allowed the panelists to capture their expertise and the breadth of their experiences in

Abbreviations used in this paper: **DI, distensibility index; EGJ, esophagogastric junction; EGJOO, esophagogastric junction outflow obstruction; FLIP, functional lumen imaging probe; HRM, high-resolution manometry; LES, lower esophageal sphincter; NEO, normal esophagogastric opening; REO, reduced esophagogastric junction opening; RRC, repetitive retrograde contraction; SOC, sustained occluding contraction; TBE, timed barium esophagram.**

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everyday clinical practice.[3] Three members of this working group were responsible for developing the initial statements (J.E.P., D.A.C., V.J.A.K.). Voting among the other working group members was then conducted independently and anonymously off-line through 3 rounds of voting to assess appropriateness of each statement. Voters were instructed to rank each statement for perceived appropriateness on a scale of 1–9, where 1 is that the expected harms greatly outweigh the expected benefits and 9 is that the expected benefits greatly outweigh the expected harms. Voters also had the opportunity to provide written comments regarding each statement and suggest modifications. The instructions provided to voters are included in the Supplementary Material. After each of the survey rounds, data were analyzed and shared with the group before meetings (in person or virtual) for feedback and face-to-face discussion. Before meetings, the group members reviewed the existing literature, current clinical practice patterns, and areas of disagreement (determined by voting results). During meetings, decisions were made about which statements to highlight for voting based on clinical relevance and general agreement for protocol and working vocabulary. If wording or terminology was at question, there was an acknowledgment that there may be voting on a statement for that purpose. The meeting discussions were then incorporated to revise statements until there was stability of responses with respect to appropriateness for protocol and working vocabulary. In addition, during the meeting after the initial round of voting, decisions were made about which statements would require a formal literature review.

The initial proposal included 57 statements. After 2 rounds of voting and subsequent group meetings and statement revision (Supplementary Figure 1), the final version included 40 statements. The final sections and format agreed on by the group included: (1) Overview, (2) Protocol, (3) Interpretation (Obtaining Metrics and Findings, EGJ Opening, Contraction Assessment with Key Examples, Key Patterns, and Other, Contractile Response Categories), and (4) Classification. Revised statements were sent out for a final (round 3) of voting. Additional sentiments and discussion topics that were deprioritized for inclusion as dedicated statements were incorporated among written discussion of other statements or among future directions.

Literature Review and Summary

Two key statements related to clinical application of FLIP panometry classification were selected to be subjected to a literature review and summary: "A major motor disorder is unlikely in the setting of a 'normal' FLIP panometry classification" (normal contractile response with normal EGJ opening) and "Diminished or absent contractile response with reduced esophageal opening supports the diagnosis of a disorder of EGJ outflow." The other statements were assessed based on the group member's experience and knowledge of the existing literature, but were not subjected to systematic literature review.

Two authors (W.W.C.; K.R. [neither voting members of the working group]) independently performed unique searches in PubMed using the key terms: *functional lumen imaging probe*, *FLIP*, *impedance planimetry*, *panometry*, *FLIP panometry*, *esophagogastric junction outflow obstruction*, *EGJ outflow obstruction*, *EGJ outflow disorder*, *EGJOO*, and *contractile response*. Article titles and abstracts from the literature searches were reviewed to identify potential studies of interest. Studies that compared FLIP findings and/or diagnostic thresholds with esophageal manometry findings, barium esophagram emptying, dysphagia severity, and therapeutic response in patients and/or healthy controls were included for full review. Articles were also identified through citation searching and request for a literature search from a medical librarian. Study populations that included patients with prior foregut surgery, known mechanical obstruction, or upper gastrointestinal malignancy were excluded. Studies assessing intraoperative or intraprocedural FLIP were also excluded. Final determination of included studies was achieved after discussion between 2 authors (W.W.C., K.R.), with achievement of consensus after the conclusion of independent searches. After full literature screening and review, 22 studies were included as relevant to the statements (Supplementary Table 2).

Statistical Analysis

Analysis for each voting round included the median response and count (percentage) of each score for each statement. Scores of appropriateness were interpreted as 1, 2, or 3 as an inappropriate measure; 4, 5, or 6 as equivocal/uncertain appropriateness; and 7, 8, or 9 as an appropriate measure. The median response rating and group "agreement," defined as the percentage of raters who rated the statement with a $\geq$7 rank for appropriateness, from the final voting round are reported. Consensus was defined as group agreement $>$80%.

Results

Functional Lumen Imaging Probe Panometry Motility Evaluation: Overview

FLIP panometry should be interpreted in the context of the clinical presentation, the accompanying EGD [esophagogastroduodenoscopy] findings and other relevant complementary testing (*median response 9.0; 100% agreement*).

Endoscopy is integral to the performance of FLIP (*median response 9.0; 94% agreement*).

FLIP panometry is integral to help diagnose a motility disorder when endoscopy rules out a mechanical obstruction (*median response 7.0; 75% agreement; did not reach 80% acceptance threshold*).

The FLIP Panometry Dallas Consensus describes a standardized approach for FLIP protocol and interpretation of EGJ metrics and contractions that can be applied in broad clinical settings evaluating esophageal motility. These findings should be interpreted in the appropriate context both in terms of the patient characteristics and history and within the array of findings from other diagnostic testing, which may be completed before or after FLIP. Overall, no esophageal test (eg, high-resolution manometry [HRM], esophagram, or FLIP) should be applied in a vacuum when diagnosing an esophageal motility disorder, but instead should be applied within the global clinical context with other complementary clinical data.

There is an integral relationship between endoscopy and FLIP, which are performed in concert during the same sedated patient encounter. A high-quality endoscopic examination provides the essential clinical context within which to decide to perform FLIP and apply its interpretation, such as potentially diagnosing a primary motility disorder if mechanical obstruction is not observed on endoscopy. Furthermore, real-time FLIP results can prompt an immediate endoscopic re-evaluation that may facilitate detecting subtle mechanical obstructions that could direct use of endoscopic interventions, such as dilation. The potential for possible endoscopic intervention based on endoscopy and FLIP findings, as well as clinical presentation and other pre-existing data, should accompany the consent process before the endoscopic procedure.

The FLIP panometry esophageal motility classification is presented as a diagnostic tool to characterize esophageal motility to be applied in patients without previous foregut surgery and without mechanical obstruction or abnormal anatomy (eg, strictures or paraesophageal hernia), as these scenarios can alter esophageal motility, causing secondary motility abnormalities. Similar considerations apply to the diagnostic application of HRM, with these stipulations also described in the Chicago Classification, version 4.0.[4] Among patients with previous foregut surgery or mechanical obstruction, there should be recognition of the potential for secondary motility findings, and specific findings should be considered in the context of that specific anatomy and/or physiology.

Functional Lumen Imaging Probe Panometry Study Protocol

The working group sought to standardize the protocol for performing and interpreting the FLIP panometry study (Table 1). Setup of the FLIP catheter can be performed by a procedure nurse or technician while the initial endoscopic examination is being performed. Thereafter, the standard FLIP study protocol can typically be completed in approximately 4–5 minutes (Figure 1).

The protocol and interpretation recommendations are intended for use with the 16-cm FLIP (EF 322N; eg, FLIP positioning and fill volumes) for real-time (during endoscopy), post-endoscopy review or additional off-line analysis (eg, using research software). They are amenable to any of the FLIP systems (FLIP 1.0, 2.0, or 300), noting that FLIP 1.0 provides EGJ metrics without real-time topography (post-endoscopy processing required to generate topography), while FLIP panometry output is readily available during endoscopy with FLIP 2.0 or FLIP 300. Special consideration may be given for patients with short esophagi (eg, young pediatric patients), noting as well that although the majority of the data are in adult patients, this approach can generally be applied to pediatric patients as well. Studies can be reviewed later by recording studies with video or using the software or procedure unit display for archived FLIP 300 studies. Although there is not yet commercially available analysis software for FLIP, research software (http://www.wklytics.com/nmgi) can be applied to files that are “archived” from the FLIP system.

During the endoscopic examination, anatomic landmarks, including distance from incisors to crural impingement and EGJ should be noted. Placement of a piece of tape correlating to the distance to the crural impingement on the FLIP catheter may assist with initial positioning. Vertical placement may be confirmed by identifying the EGJ as the narrowed area (“waist” on FLIP display) above the gastric cavity at a fill volume of 40 mL and ideally should include 2 cm of the distal portion in the gastric cavity (Figure 1). Real-time performance of the FLIP study for optimal data acquisition requires some basic identification of anatomic and physiologic landmarks to place and maintain the positioning of the FLIP catheter relative to the EGJ or crural impingement (sometimes requiring advance or withdrawal of the FLIP or applied counter pressure on the FLIP throughout the FLIP study). Direct endoscopic visualization of FLIP positioning should be considered if there is uncertainty of FLIP positioning during the FLIP study.

The standard FLIP panometry study protocol was agreed on to involve sequential FLIP filling to 50 mL, 60 mL, and 70 mL, holding each fill volume for at least 30 seconds (Figure 1). Holding fill volumes for longer duration (eg, up to 60–90 seconds) can be considered at the discretion of the endoscopist if needed to obtain key metrics, especially if there are sustained and/or spastic contractions. The relevance of “high-pressure alarms” during the FLIP study was a point that garnered discussion among the working group and demonstrated a high degree of agreement (88% agreement) that, with the FLIP appropriately positioned, a high-pressure alarm (regardless of occurring at 60–100 mm Hg, depending on system settings) did not signify an increase in risk of the FLIP procedure. This related to the group members’ overall experience with FLIP as a safe procedure, with additional recognition for the relatively low pressure of the FLIP compared with therapeutic balloon dilations. For instance, esophageal balloon dilations are typically performed at a range of 3–8 ATMs; because 1 ATM = 760 mm Hg, this equates to 2280–6080 mm Hg. Furthermore, the gastric cavity provides a highly compliant area for pressure release, if necessary.[5,6] Thus, although high pressures may warrant limiting FLIP filling in certain scenarios (eg, a severe narrow-caliber esophagus with stricture), pressure alarms in a properly positioned FLIP should otherwise not unnecessarily prevent completion of an adequate FLIP study (eg, a target maximum fill volume of 70 mL) when being used to evaluate for esophageal motility disorders. Literature supporting the safety of FLIP also included studies of 722 subjects completing FLIP panometry without a FLIP-related adverse event, and a review of the MAUDE database without significant adverse events related to performance of the FLIP panometry motility evaluation.[1,5,6]

Functional Luminal Imaging Probe Panometry Approach for Acquisition of Key Metrics

The esophageal response can vary as the degree of esophageal distention increases during the volume-controlled filling of the FLIP study protocol. Furthermore, performance of the FLIP is also affected by the degree of filling, and is more prone to potential artifact at low fill volumes. Although multiple metrics are available at each fill

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Table 1. Statements regarding FLIP Panometry Approach: Protocol, Key Metrics, and Contraction Assessment

Statement	Median response	Percent agreement
FLIP panometry study protocol statement		
Use the 16-cm FLIP catheter for FLIP panometry.	9.0	94
Set filter settings to “off” for optimal intraprocedural FLIP panometry assessment.	8.5	100
The FLIP catheter is calibrated to atmospheric pressure before transoral placement.	9.0	100
Optimal FLIP positioning for FLIP panometry is with 2 sensors (2 cm) below the crural diaphragm and this positioning of the FLIP catheter should be maintained throughout the entire study.	9.0	100
Fill the FLIP catheter sequentially to 50 mL, 60 mL, and 70 mL and maintain each volume for at least 30 s.	9.0	94
The target maximum fill volume is 70 mL for a complete study when using FLIP panometry to evaluate for an esophageal motility disorder.	9.0	81
With the FLIP appropriately positioned, a high-pressure alarm does not increase the risk of the overall endoscopic procedure.	8.0	88
FLIP panometry acquisition of key EGJ metrics		
Key metrics of EGJ opening include the EGJ-DI at 60 mL and the maximum EGJ diameter at 70-mL fill volume	8.5	100
EGJ metrics should be measured >5 s after active FLIP filling to avoid filling-related effects.	8.5	88
Avoid obtaining EGJ metrics affected by “dry catheter artifact.”	9.0	100
Measure EGJ-DI and EGJ diameter at the time of greatest EGJ opening diameters.	9.0	100
Apply the median value of 3 EGJ-DI measurements taken during the 60-mL fill volume for EGJ opening classification.	8.0	81
EGJ-DI values are not reliable when associated FLIP pressure is <15 mm Hg.	9.0	88
Document if there is EGJ-crural diaphragm separation, which suggests a hiatal hernia.	9.0	94
Measures made during emptying of the FLIP should not be applied for clinical decision making.	8.5	94
FLIP panometry interpretation: Contraction assessments		
A “distinct antegrade contraction” can be defined when an antegrade contraction extends for ≥6 cm of axial length, with an associated pressure increase of ≥10 mm.	9.0	100
The repetitive antegrade contraction (RAC) pattern can be defined by the RAC “rule-of-6s”: ≥6 consecutive antegrade contractions of ≥6 cm in axial length occurring at 6 ± 3 contractions per minute at a regular cadence.	9.0	100
Sustained LES contraction (sLESCs) can be defined by the following criteria: a transient reduction in diameter at the LES, which lasts longer than 5 s, and is associated with an increase in FLIP pressure, and is independent of antegrade contractions or respiration or crural contraction.	8.0	100
SOC can be defined with the following criteria: a nonpropagating (ie, retrograde or horizontal), lumen-occluding (ie, achieving a diameter <6 mm) contraction of the esophageal body that persisted for >10 s with an associated FLIP pressure increase >35 mm Hg.	8.0	88
Contractile features and patterns other than those mentioned above can be observed during the FLIP panometry study and carry uncertain clinical significance.	9.0	94
The RRC pattern can be defined as ≥6 consecutive retrograde contractions of ≥6 cm in axial length occurring at a cadence of >9 contractions per minute.	9.0	88
The clinical relevance of RRCs is uncertain.	8.0	94
A “vigorous antegrade contraction” can be defined as an antegrade contraction with an appearance of consistent width in the body that correlates with ≥10 s and a pressure rise >35 mm Hg.[a]	8.0	75
The clinical relevance of vigorous antegrade contractions is uncertain.	8.0	94
Pressure at 60 mL (taken at the same time as when taking the EGJ-DI measurement) may help separate diminished vs disordered contractile response categories.	8.0	81
FLIP panometry interpretation: Contractile response categories		
Absent contractile response (ACR) is defined by no contractions in the body.	9.0	100
Spastic contractile response (SCR) is defined by SOCs or sustained LES contractions.	8.0	100

Table 1. Continued

Statement	Median response	Percent agreement
Normal contractile response (NCR) is defined by multiple (more than 1) distinct antegrade contractions.	8.0	100
Diminished contractile response is defined by contraction presence, not meeting ACR, NCR, or SCR criteria, with low FLIP pressure (<40 mm Hg).	7.0	94
Disordered contractile response is defined by contraction presence, not meeting ACR, NCR, or SCR criteria) with high FLIP pressure (≥40 mm Hg).	7.5	88

NOTE. Voting results for each statement shown with median response on scale of 1–9 and "percent agreement" as percentage of votes with score ≥7 indicating level of agreement on appropriateness.
[a]Statement did not reach 80% agreement threshold.

volume, the key metrics were determined to focus the FLIP panometry interpretation and standardize their application to classifying esophageal function. These include the contractile response category assessed as the aggregate, (ie, the entirety of the study over the duration of the 50-, 60-, and 70-mL fill volumes), the EGJ distensibility index (DI) during the 60-mL fill volume and the associated pressure, and the maximum EGJ diameter from the 70-mL fill volume (Table 1, Figure 1).

Furthermore, EGJ opening on FLIP is dynamic, occurring in response to esophageal contractility and FLIP filling. Thus, the EGJ-DI and maximum EGJ diameter should be measured at times of greatest EGJ opening diameters (Figure 1) and also omitting times and sensors that are affected by dry catheter artifact (ie, when lumen occlusion of the FLIP disrupts the electrical current used for the impedance planimetry technology, resulting in inaccurate diameter measures at affected measurement channels; Supplementary Figure 2). The EGJ-DI metric is calculated by the median of three 60-mL measures applied to classify EGJ opening. The pressures at time of EGJ-DI measurements should also be noted, both to recognize that the EGJ-DI can be unreliable when the pressure is low (eg, <15 mm Hg) and also as the FLIP pressure may carry value to predict spasm (see contractile response below).[7] Hiatal hernia can also be induced or enlarged during FLIP filling, and lower esophageal sphincter (LES)–crural signal separation can be measured (visualization of the crural contraction is facilitated by turning the FLIP filter to "off," as recommended (Table 1, Figure 1).

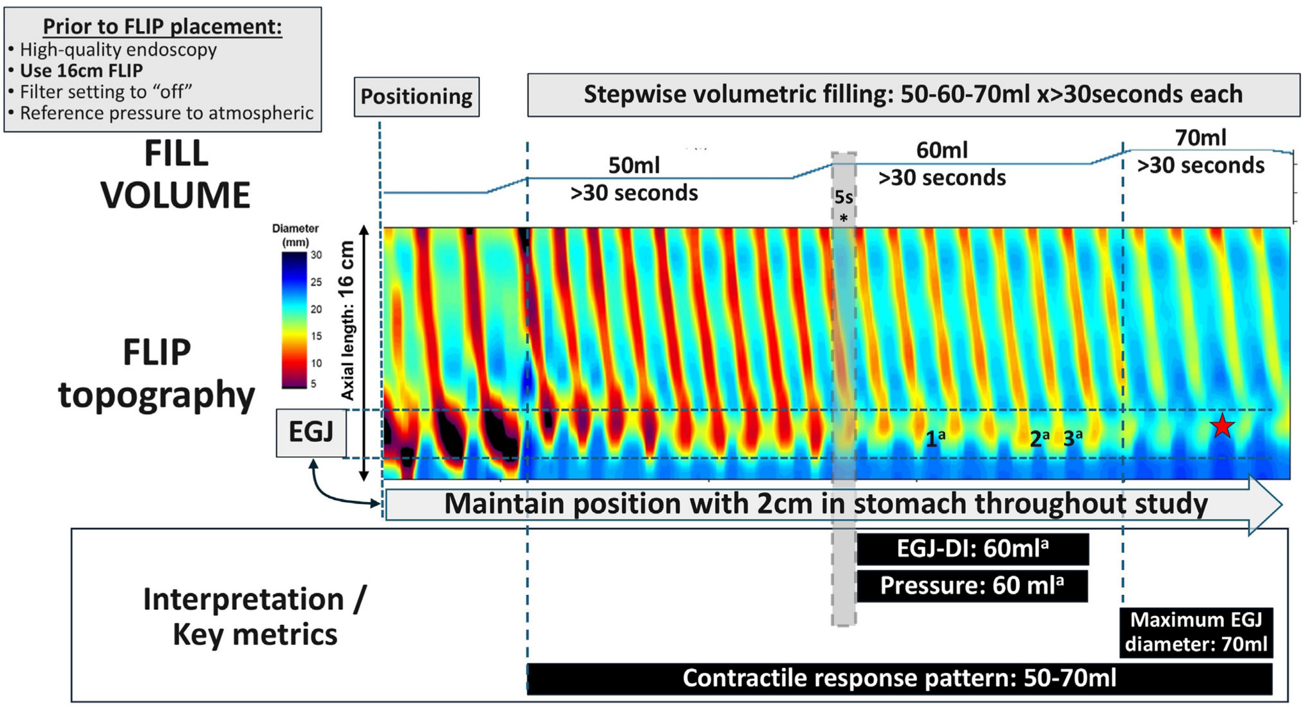

Figure 1. The FLIP panometry study protocol. Key components and steps of the FLIP panometry study protocol are illustrated. Key metrics are made relative to the FLIP fill volumes during the standardized filling protocol. *The first 5 seconds after filling to 60 mL should be omitted from the EGJ-DI measurement to avoid incorporating filling-associated effects in the metric. [a]Then, the EGJ-DI is measured at 3 points of greatest EGJ opening diameter (1[a]-2[a]-3[a]), applying the median value of the 3 measures to classify EGJ opening. The associated pressure at times of EGJ-DI measures should also be noted and median value applied. The maximum EGJ diameter is measured at the time of greatest EGJ opening during the 70-mL fill volume (*red star*). Reproduced with permission from the Esophageal Center of Northwestern Medicine. © Esophageal Center of Northwestern Medicine.

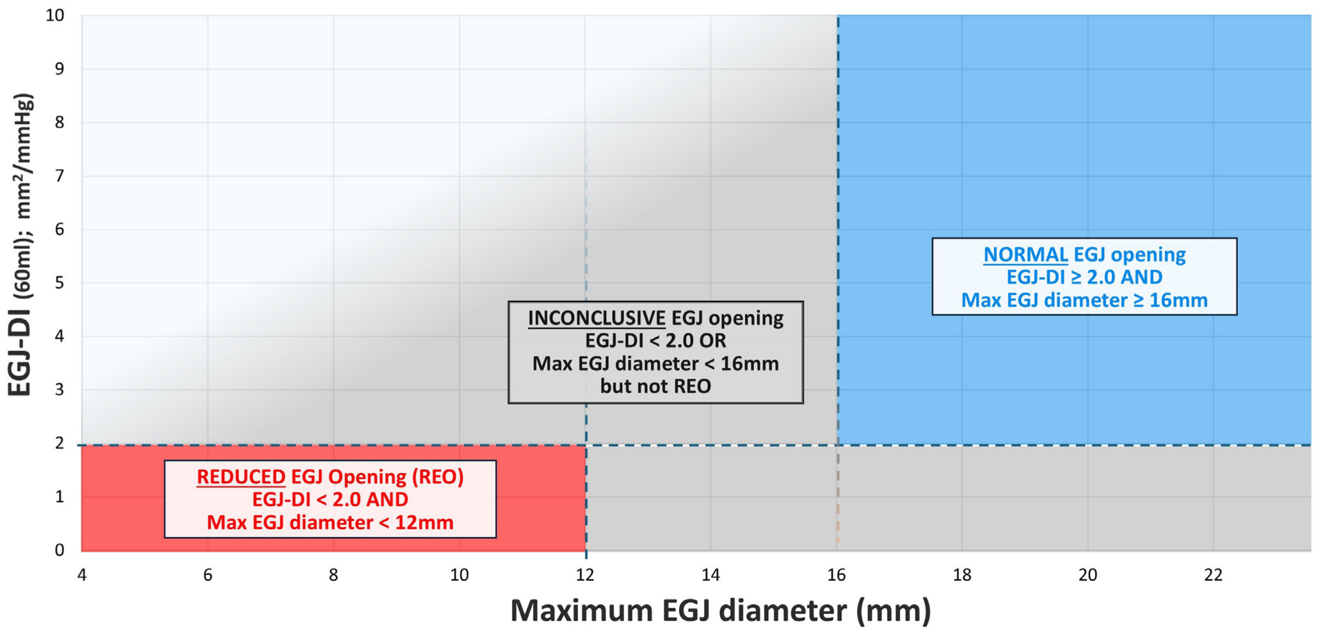

Figure 2. FLIP panometry EGJ opening classification. EGJ opening is classified by applying the following 2 metrics: the EGJ-DI at 60 mL and the maximum EGJ diameter at 70 mL. Reproduced with permission from the Esophageal Center of Northwestern Medicine. © Esophageal Center of Northwestern Medicine.

Functional Luminal Imaging Probe Panometry Interpretation: Esophagogastritic Junction Opening Categories

Reduced EGJ opening (REO) is defined by maximum EGJ diameter <12 mm and EGJ-DI at 60 mL <2.0 mm^2/mm Hg (*median response 9.0; 100% agreement*).

Normal EGJ opening (NEO) is defined by maximum EGJ diameter ≥16 mm and EGJ-DI at 60 mL ≥2.0 mm^2/mm Hg (*median response 9.0; 100% agreement*).

Inconclusive EGJ opening (formerly "borderline EGJ opening") can be considered all cases in between REO and NEO (*median response 8.0; 100% agreement*).

The EGJ opening thresholds based on the metrics of the EGJ-DI at 60 mL and the maximum EGJ diameter remained consistent with the previous classification scheme (Figure 2).[1,6] However, there was a change in terminology of 1 category from borderline EGJ opening to inconclusive EGJ opening. This terminology change mirrored the Chicago Classification[4] for HRM and was intended to reflect that EGJ opening parameters that were not REO or NEO could be considered as suggestive for possible EGJ obstruction, yet remained clinically inconclusive.

Functional Luminal Imaging Probe Panometry Interpretation: Contraction Assessment

Contraction assessment is based on observing features of the contraction morphology, cadence, and vigor in order to identify key contraction patterns and to determine the overall contractile response categories (Table 1). Esophageal contractile activity can be defined by a transient decrease in diameter, represented by the color variation on a scale of red being low diameter and blue being high diameter, and further defined by direction (antegrade or retrograde) or other morphologic appearance (Figure 3). Contraction features and patterns may be noted at specific volumes, whereas the contractile response category reflects an overall assessment of the aggregate of fill volumes 50, 60, and 70 mL (Figure 1, Table 1). Certain contraction examples may appear at one fill volume, but not be present at another, and it is reasonable to expect variability from one volume to another. For example, it is not uncommon for contractions to appear less distinct at higher fill volumes or not be generated at low volumes with inadequate pressure. A normal cadence includes a rate of 6 ± 3 contractions per minute at a regular rhythm, although abnormal cadence can be represented by rapid or slow rate and variations in rhythm from irregular to sporadic.[8] Pressure is a surrogate of the vigor of contraction and may be used as the change of pressure during a contraction or as a key metric accompanying the 60 mL EGJ-DI.[7]

Key Contraction Patterns and Contractile Response Categories

The key contraction patterns (Figure 3) and categories (Figure 4) reflect a nonlinear spectrum of function related to secondary peristalsis and the esophageal contractile response to distention. A hierarchal approach, informed by the presence of specific contraction features and patterns, can be applied to determine the contractile response categories (Figures 3–5, Table 1). Repetitive antegrade contractions or multiple (ie, more than 1) distinct antegrade contractions define a normal response.[1,9] On the other side of the spectrum is an absent contractile response or a spastic contractile response (Figure 4). Key spastic patterns, which are often irregular and associated with higher vigor, include sustained LES contractions and sustained occluding

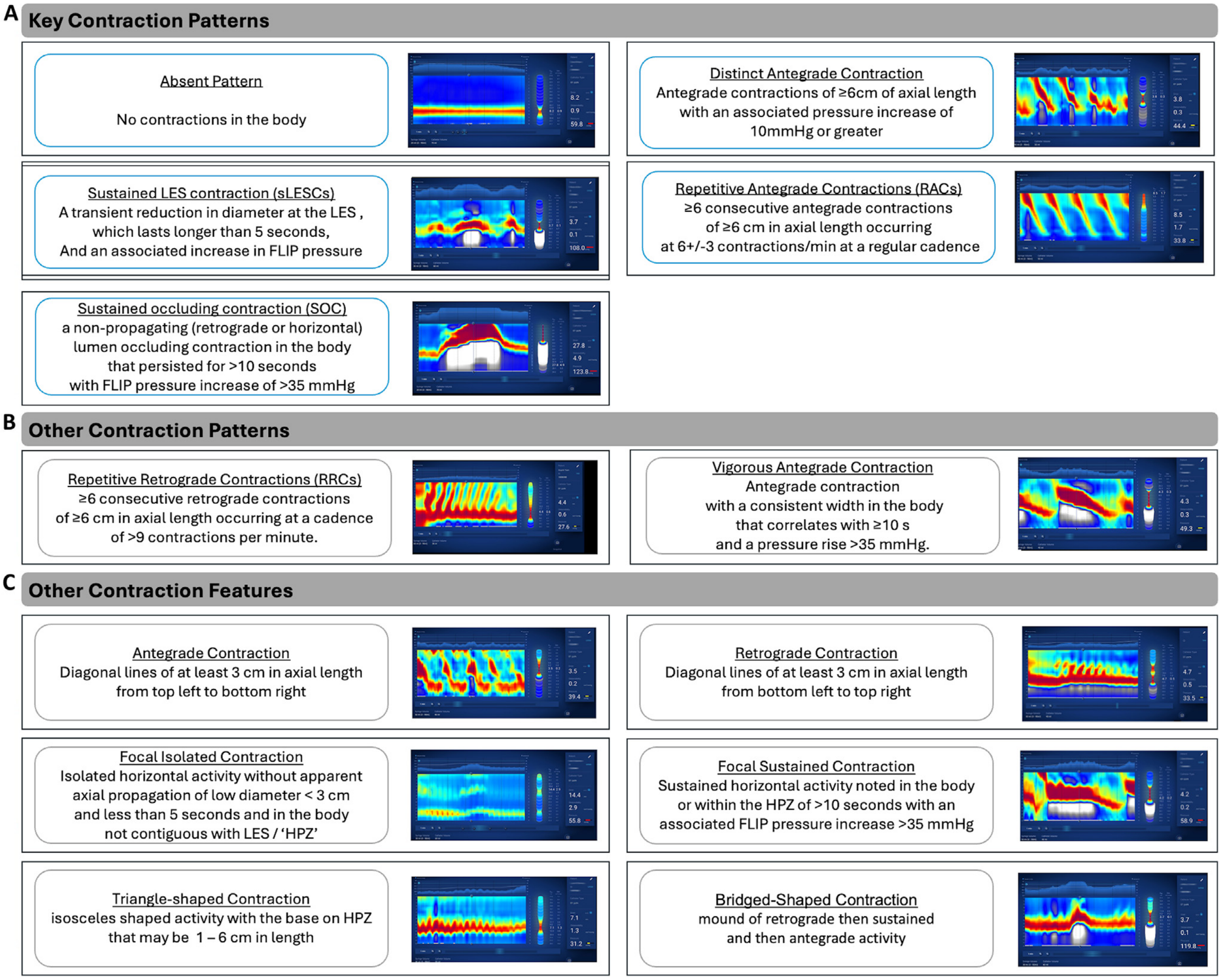

Figure 3. FLIP panometry key contraction patterns and additional common findings. (*A*) Key contraction patterns are listed below with criteria (outlined in *blue*) and representative example images. Additional findings are commonly seen during FLIP panometry and are also presented here to assist with a common vocabulary. (*B*) These include the contraction patterns of repetitive retrograde contractions and vigorous antegrade contractions, which have unclear clinical significance. (*C*) Other morphologic features that may be seen are listed with proposed definitions and examples. These may be used for teaching purposes, to describe nonclassic cases, and/or be a source of further investigation. Reproduced with permission from the Baylor University Medical Center, Dallas, TX. © Baylor Scott & White Center for Esophageal Diseases.

contractions (SOCs) (Figure 3), and are associated with spastic motility disorders, such as type III achalasia.[1,10] These may occur with or without an LES lift, a dynamic event when LES-EGJ complex migrates proximally in the setting of a spastic contraction. The vertical extent of "spastic feature," for example, vertical span of SOCs, should also be noted. Furthermore, spastic contractile response (or disordered contractile response, see below) may be reactive (secondary) processes to subtle mechanical obstruction and may prompt endoscopic reinspection and consideration for dilation. Presence or absence of distinct antegrade contractions should also be noted in spastic contractile response and then described as spastic contractile response with presence of distinct antegrade contractions.

For cases not meeting clear spastic, normal, or absent contractile response criteria, pressure can separate cases into "diminished" contractile response (low pressure), which may fall on the hypomotile spectrum, or "disordered" contractile response (high pressure), which may fall on the spectrum between normal and spastic.[7] A pressure threshold of 40 mm Hg was proposed (pressure at 60 mL associated with the EGJ-DI measurement), recognizing the potential limitation of applying a dichotomous threshold (ie, tradeoff of sensitivity and specificity) and that greater extremes from this threshold may also reflect higher probability for hypomotility (eg, pressure <30 mm Hg) or spasm (eg, pressure >55 mm Hg).[7]

Other Contraction Patterns and Features

Another key discussion topic among the working group related to other contraction patterns and examples beyond repetitive antegrade contractions, SOCs, or sustained LES

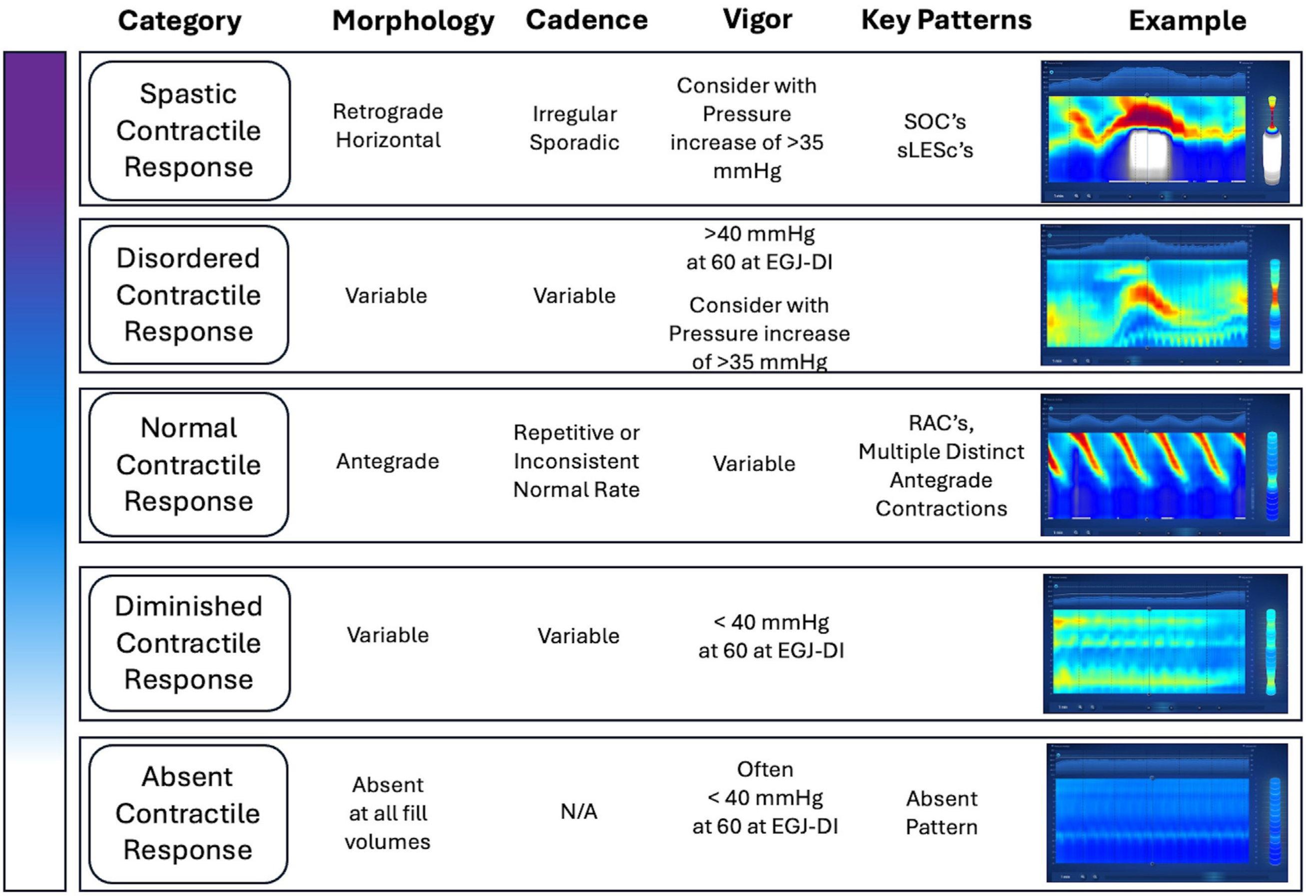

Figure 4. Contractile response categories. Each contractile response category is demonstrated with an example representative image, features based on morphology, cadence and vigor, and the associated key pattern. Reproduced with permission from the Baylor University Medical Center, Dallas, TX. © Baylor Scott & White Center for Esophageal Diseases.

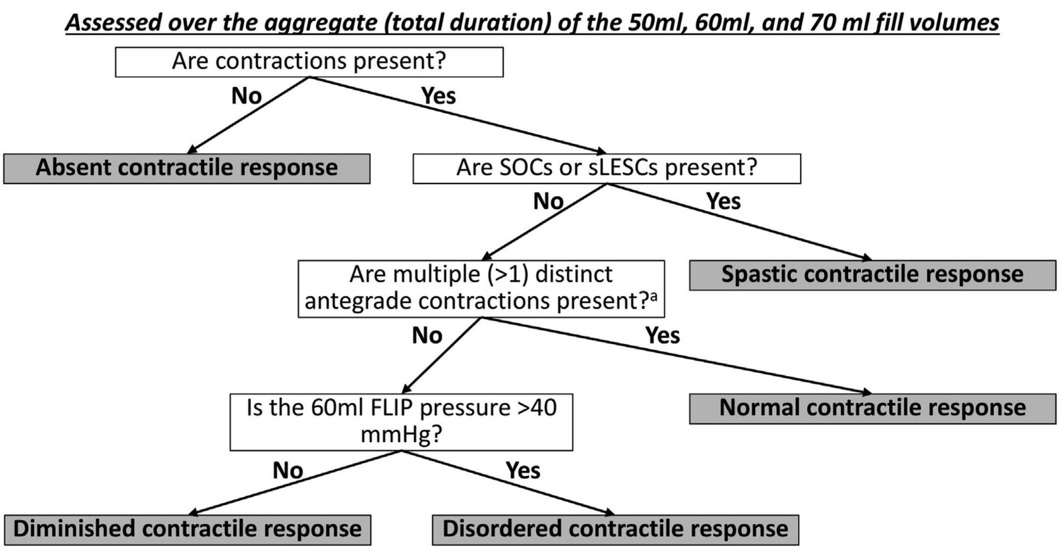

Figure 5. A hierarchical approach to classifying the FLIP panometry contractile response category. Presence (or absence) or key contractile features (in addition to the pressure taken with the EGJ-DI during the 60-mL fill volume) can be applied to classify the contractile response. [a]Presence of more than 1 distinct antegrade contraction defined the normal contractile response, which did not require that distinct antegrade contractions occur in the repetitive antegrade contraction (RAC) pattern.

contractions that may be observed during the FLIP panometry study. However, due to uncertainty with regard to the clinical significance of these other contractile features, the group consensus was to not incorporate them in the motility classification criteria as this time. However, appreciating the evolving nature of classification systems, standardized definitions were proposed to advance a common vocabulary for atypical or incomplete cases and to facilitate future studies (Figure 3). In particular, the repetitive retrograde contraction (RRC) pattern, while still recognized as an abnormal finding, was removed as a criterion of the spastic contractile response, given its potential as a nonspecific finding (Table 1, Figure 3). RRCs, particularly when occurring at a rapid (>9/min) rate, were initially associated with spastic achalasia.[11,12] With additional experience, RRCs were recognized as also occurring in other esophageal diseases states (eg, mechanical esophageal obstruction) and considered that RRCs seen at low volumes (ie, 30 and 40 mL) may represent passive propagation from a respiratory trigger. RRCs seen at higher fill volumes (ie, ≥50 mL) or associated with a higher pressure at 60 mL may be more indicative of an abnormal state. Additionally, exaggerated or prolonged antegrade contractions ("vigorous antegrade contractions"), which were possibly categorized among "borderline contractile response" in the previous classification categories, can be observed.[1,13] "Vigorous antegrade contractions" (Table 1, noting the definition did not meet the 80% acceptance threshold; Figure 3) may be reactive in nature in most cases, such as in the setting of an esophagus slowly propagating against a subtle mechanical obstruction, for example, stricture or hiatal hernia. Other overlapping features with key contraction patterns or categories, such as contractions associated with a pressure increase of >35 mm Hg that do not clearly meet criteria for SOC or sustained LES contractions, were also considered to possibly suggest variants of disordered spastic contractions. Other contraction patterns of unknown clinical significance, such as isolated focal, sustained focal, triangle-shaped, and bridge-shaped contractions may also be observed (Figure 3). Although there is not a clear association with RRCs, vigorous antegrade contractions, or these other features with a specific disease state, their presence may be appropriate to prompt endoscopic reinspection for subtle rings or strictures and take those findings in an appropriate context and determine the need for further investigation (eg, with HRM).

Functional Luminal Imaging Probe Panometry Motility Classification, Version 2.0

The FLIP panometry classification scheme incorporates the contractile response and EGJ opening to inform a motility impression (*median response 9.0; 88% agreement*).

Ultimately, the EGJ opening classification (Figure 2), and the contractile response categories (Figures 3–5) were jointly applied to designate a FLIP panometry motility classification (Figure 6). There was also recognition that esophageal dysmotility occurs along a spectrum (albeit one that is not linear), hence, designations or metrics falling with a certain category should also be interpreted with consideration for the probability of normal vs abnormal motility. For example, a FLIP panometry with a "disordered contractile response" may carry a lower probability for a spastic motor disorder than a "spastic contractile response" and FLIP panometry with a "diminished contractile response" would carry a lower probability for clinically relevant hypocontractility than an "absent contractile response."

At the figurative ends of the motility spectrum, there was considerable agreement about the clinical application of a "normal" FLIP panometry (ie, a normal contractile response with normal EGJ opening) and "nonspastic obstruction" (ie, an absent or diminished contractile response with reduced EGJ opening). These statements were subjected to independent literature review and summary:

A major motor disorder is unlikely in the setting of a "normal" FLIP panometry classification (ie, normal contractile response with NEO) (*median response 9.0; 94% agreement*).

The evidence supporting the clinical significance of FLIP panometry with both normal contractile response and NEO is primarily based on a series of cohort studies that consistently showed a major motor disorder on HRM is uncommon when FLIP panometry is normal.[1,9,14] In the largest cohort of the series (722 subjects), normal motility on FLIP (normal contractile response and NEO; n = 86 patients) was associated with 92% normal motility and 6% absent contractility/ineffective esophageal motility, with only 2% distal esophageal spasm or hypercontractile esophagus, and no achalasia or EGJ outflow obstruction (EGJOO) on HRM.[1]

Multiple studies have provided evidence to support this criteria of either NEO or a normal contractile response as diagnostic for the absence of achalasia or a major motility disorder on HRM independently (Supplementary Table 2). Of note, the definition and threshold for "normal EGJ opening" has varied between studies and some only apply EGJ-DI or EGJ diameter in isolation (instead of applying both to define NEO), which somewhat limits assessment of the current classification. A meta-analysis of 15 studies involving 154 healthy subjects found that the 5th–95th percentile EGJ-DI values at 60 mL was 3.1–8.1 mm^2/mm Hg and no healthy subjected had an EGJ-DI < 2.0 mm^2/mm Hg.[15] In a study of 687 total patients, 99% of 203 patients with NEO defined by an EGJ-DI ≥2.0 mm^2/mm Hg and maximum EGJ-diameter ≥16 mm had normal EGJ outflow per HRM/Chicago Classification, version 4.0.[4,6] Another study of 184 patients demonstrated that 0 of 23 patients with achalasia had "NEO" with an EGJ-DI ≥2.0 mm^2/mm Hg and maximum EGJ-diameter ≥16 mm.[16] Furthermore, among patients with NEO on FLIP and inconclusive EGJOO on HRM who received conservative, non-achalasia–type therapy, 90% reported good symptomatic outcomes.[17] Among earlier studies applying only EGJ-DI to define normal EGJ distensibility, a threshold of 2.8–3 mm^2/mm Hg showed reduced EGJ distensibility in only 0%–10% of patients with achalasia, conclusive EGJOO, or other major motility disorders on HRM[1,6,9,16,18,19] or abnormal timed barium esophagram (TBE)[17,20–22] (Supplementary Table 2).

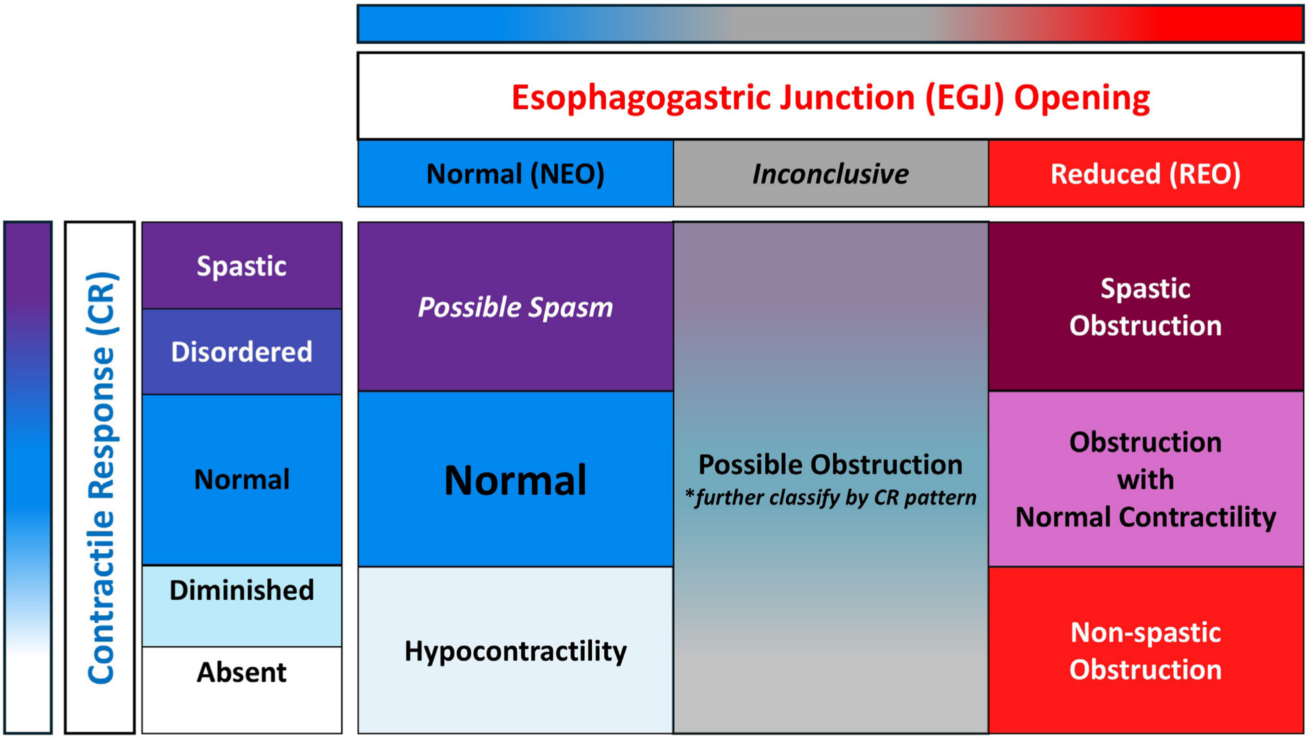

Figure 6. The FLIP Panometry Motility Classification, version 2.0. The Dallas consensus incorporated the contractile response (CR) and EGJ opening categories to classify esophageal motility with FLIP panometry. *With inconclusive EGJ opening, which suggests "possible obstruction," the motility classification should be further described with the contractile response category. These esophageal motility classifications should be applied in the context of the patient's history and endoscopy findings to help guide clinical management. *With inconclusive EGJ opening, which suggests "possible obstruction," the motility classification should be further described with the contractile response category.

Similarly, normal contractile response has been determined to be evidence against clinically significant major motility disorder, as repetitive antegrade contractions were rarely found among patients with achalasia or absent contractility[9,12,13,16,23] or patients with abnormal TBE.[9,24] Specifically, in a large cohort of 706 patients and 35 asymptomatic controls, no patient with normal contractile response (n = 108) had achalasia or absent contractility, although no patient with 100% failed peristalsis on HRM (n = 218) showed normal contractile response.[13]

Therefore, a normal FLIP panometry carries a high negative predictive value for a major, actionable esophageal motility disorder (including in the context of an inconclusive HRM, such as EGJOO), and the clinical management can likely be directed toward possible gastroesophageal reflux disorder or a functional syndrome.

Diminished or absent contractile response with reduced esophageal opening supports the diagnosis of a disorder of EGJ outflow (*median response 8.5; 94% agreement*).

Few studies have directly assessed the predictive value of a diminished or absent contractile response with REO on FLIP (ie, "nonspastic obstruction," Figure 6) for a disorder of EGJ outflow (Supplementary Table 2). A large cohort study of 722 subjects found that among 202 patients with diminished or absent contractile response and REO on FLIP, 92% had manometric findings consistent with achalasia or EGJOO with abnormal emptying on TBE in 77%.[1] In addition, a retrospective study of 139 patients meeting manometric criteria for EGJOO found that 72% with conclusive FLIP findings for a disorder of EGJ outflow had a diminished or absent contractile response, with these patients overall more likely to have abnormal emptying on TBE and high rates of clinical success with sphincter-directed therapy.[17]

Multiple studies have provided evidence for the diagnostic accuracy of either REO or a diminished or absent contractile response on FLIP for a disorder of EGJ outflow independently (Supplementary Table 2). Although the EGJ-DI threshold of REO on FLIP has changed over time, a series of studies from a large cohort have consistently demonstrated positive predictive values $>75\%$ for a manometric diagnosis of EGJ outflow disorder with EGJ DI <2 mm^2/mm Hg and EGJ diameter <12 mm along with negative predictive value $> 90\%$ when these criteria are not met.[1,6,18] Further REO was associated with abnormal emptying on TBE,[17,19,25,26] with 1 study reporting a positive predictive value of 75% for a DI <2 mm^2/mm Hg with a 100% negative predictive value with a DI ≥ 2 mm^2/mm Hg.[20] Another study found that a DI <2 mm^2/mm Hg had a sensitivity of 80% and a diameter <12 mm a specificity of 90% for an abnormal TBE.[21] Patients with REO on FLIP also have greater symptom burden, reflected by higher Eckardt scores compared with those with normal EGJ opening.[19,21,26,27] Clinical response to lower esophageal sphincter–directed therapy has also been associated with REO on FLIP.[16,17,20,25,27–30] Diminished or absent contractile response on FLIP further supports a clinically relevant disorder of EGJ outflow, representing the most common contractile response in patients with achalasia.[13,14,16,19,20,31] In addition, 1 prospective study demonstrated an odds ratio of 22.5 (95% CI, 2.5–206.7) for symptomatic response to botulinum toxin injection to the LES for patients with a diminished or absent contractile response on FLIP.[32]

Hence, with FLIP panometry of "nonspastic obstruction," a conclusive disorder of EGJ outflow, such as achalasia, is suspected. This finding may be sufficient to reach a definitive diagnosis in the context of supportive clinical data, including whether HRM is inconclusive in isolation (eg, HRM of EGJOO). However, if there is clinical uncertainty or discordant results, such as an endoscopy or other testing (eg, HRM or esophagram) that is not consistent with achalasia/EGJOO, additional testing is warranted to apply in a complementary manner.

A spastic or inconclusive FLIP panometry classification should prompt further workup, such as with HRM and/or TBE with tablet (*median response 9.0; 81% agreement*).

Furthermore, although group consensus of clinical relevance of criteria was generally applied in designating the EGJ opening, contractile response, and esophageal motility classifications, there was also recognition that some FLIP panometry categories would require additional evaluation to further characterize esophageal motility and better define clinical relevance. Thus, FLIP studies with "inconclusive EGJ opening" may indicate a "possible obstruction" (Figure 6), but typically requiring complementary application of results from other testing with TBE with tablet or HRM to further define. In addition, FLIP panometry classifications suggesting spasm, that is, "possible spasm," "spastic obstruction," or possible obstruction with spastic or disordered contractile response, may support pursuit of HRM to further characterize the type and extent of spastic motor activity. "Obstruction with normal contractility" (REO with normal contractile response) suggests mechanical obstruction and should prompt endoscopic reinspection for subtle stricture or ring and consideration of dilation. There was also consideration that other contractile features (eg, RRCs or vigorous antegrade contractions) may prompt additional workup in the appropriate clinical context. Ultimately, clinical application of these FLIP findings should be performed in a complementary nature with other clinical data to reach a global clinical impression. If diagnostic uncertainty persists, seeking additional testing or clinical monitoring during conservative management should be considered.

Future Directions

There is considerable excitement regarding use of FLIP panometry to help diagnosis esophageal motility disorders. Not only does it provide a patient-centered method (ie, well-tolerated and convenient), it also improves the diagnostic yield of the endoscopic encounter, leading to direction of immediate endoscopic intervention (eg, dilation) and/or need for additional evaluation. The present work represents efforts to advance the FLIP panometry approach, seeking to standardize the procedure and interpretation, as well as to refine the classification of esophageal motility using FLIP panometry. An accessible and standardized approach for use and interpretation for FLIP panometry hopes to facilitate a broader group of users and scenarios to streamline and advance care in esophageal dysmotility. Continued advancement and evolution of the FLIP approach is anticipated, similar to the process of serial updates for the Chicago Classification of HRM motility diagnosis.[4] There are limitations of the proposed approach, such as clinically inconclusive FLIP categories or findings (eg, inconclusive EGJ opening or RRCs) and knowledge gaps that will be targets of future investigation and evolution of the FLIP panometry approach. These include development and incorporation of novel metrics, such as contractile work or power; further application of machine learning (possibly to assist integration of other diagnostic test results); improved phenotyping of esophageal dysmotility; and studies to assess prediction of treatment outcomes. Future work will also seek to advance FLIP panometry utilization in other clinical scenarios beyond esophageal motility disorders, such as eosinophilic esophagitis.[33–35] Furthermore, the esophageal response to distention represents an important aspect of esophageal function and the advent of FLIP panometry offers opportunities to reinvigorate investigations into the related pathophysiology.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2025.01.234.

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Marcelo F. Vela, MD, MS (Investigation: Supporting; Writing – review & editing: Supporting)
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Conflicts of interest
These authors disclose the following: Dustin A. Carlson: Medtronic (speaking, consulting, license); Diversatek (consulting); Braintree (consulting); Medpace (consulting); Phathom Pharmaceuticals (speaking; advisory board); Regeneron/Sanofi (speaking). John E. Pandolfino: Medtronic (speaking, consulting, patent, license); Diversatek (grant), Phathom Pharmaceuticals (consulting); EndoGastric Solutions (speaking; consulting); Ethicon (speaking; consulting). Rena Yadlapati: Medtronic, Inc (institutional agreement: consulting; speaking; research); Phathom Pharmaceuticals (consulting; advisory board); StatLink MD (consulting); Braintree (consulting; advisory board); Reckitt Benckiser Healthcare Ltd (consulting); RJS Mediagnostix (advisory board). Marcelo F. Vela: Medtronic, Inc (consulting). Stuart J. Spechler: Phathom Pharmaceuticals (consulting); Castle Biosciences (consulting). Felice H. Schnoll-Sussman: Braintree Sebela (consulting); Ethicon (consulting); Implantica (consulting). Kristle Lynch: Medtronic, Inc (consulting; speaking); Regeneron (speaking); Sanofi (speaking); Phathom Pharmaceuticals (advisor); Takeda (advisor); Lucid (advisor). Adriana Lazarescu: Sanofi (speaking); Bausch (speaking; advisory board); Pfizer (speaking). Abraham Khan: Medtronic, Inc (consulting; speaking); Sanofi (speaking); Regeneron (speaking), Phathom Pharmaceuticals (speaking). Philip Katz: Phathom Pharmaceuticals (consulting); Sebella (consulting). Anand S. Jain: Medtronic, Inc (teaching observership agreement). C. Prakash Gyawali: Medtronic, Inc (consulting); Diversatek (consulting); Braintree/Sabela (consulting); Carnot (speaking). Milli Gupta: Medtronic, Inc (consulting; speaking); Sanofi (consulting; speaking; advisory); AVIR Pharma (consulting; speaking; advisory); Takeda (speaking); Astra Zeneca (speaking), Bausch Health (speaking). Jose M. Garza: Medtronic, Inc (consulting; speaking). Ronnie Fass: Medtronic (advisor); Diversatek (research); Phathom Pharmaceuticals (advisor); Dexcal (advisor); Syneos (advisor); GIE Medical (advisor); BrainTree Labs/Sebela (advisor); Renexxion (advisor); Daewoong (advisor); Takeda (speaker); Eisai Pharmaceuticals (speaker); Carnot (speaker); Daewoong (speaker). John O. Clarke: Medtronic (consulting); Alnylam (consulting); Sanofi (consulting). Reena V. Chokshi: Medtronic, Inc (consulting; speaking); Enterra (consulting; speaking). Joan Chen: Phathom Pharmaceuticals (consulting). Karthik Ravi: Sanofi (advisory board). Walter W. Chan: Regeneron (advisory board). Vani J. A. Konda: Medtronic (consulting); Exact Sciences (advisory board); Lucid (research), Braintree (consulting), Pentax (consulting), Olympus (consulting). The remaining author discloses no conflicts.

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Data Availability
The data that support the findings of this study are available from the corresponding author on reasonable request and completion of necessary privacy and ethical approvals.

Supplemental Materials and Methods

Instructions to Panelists for Each Round of Voting

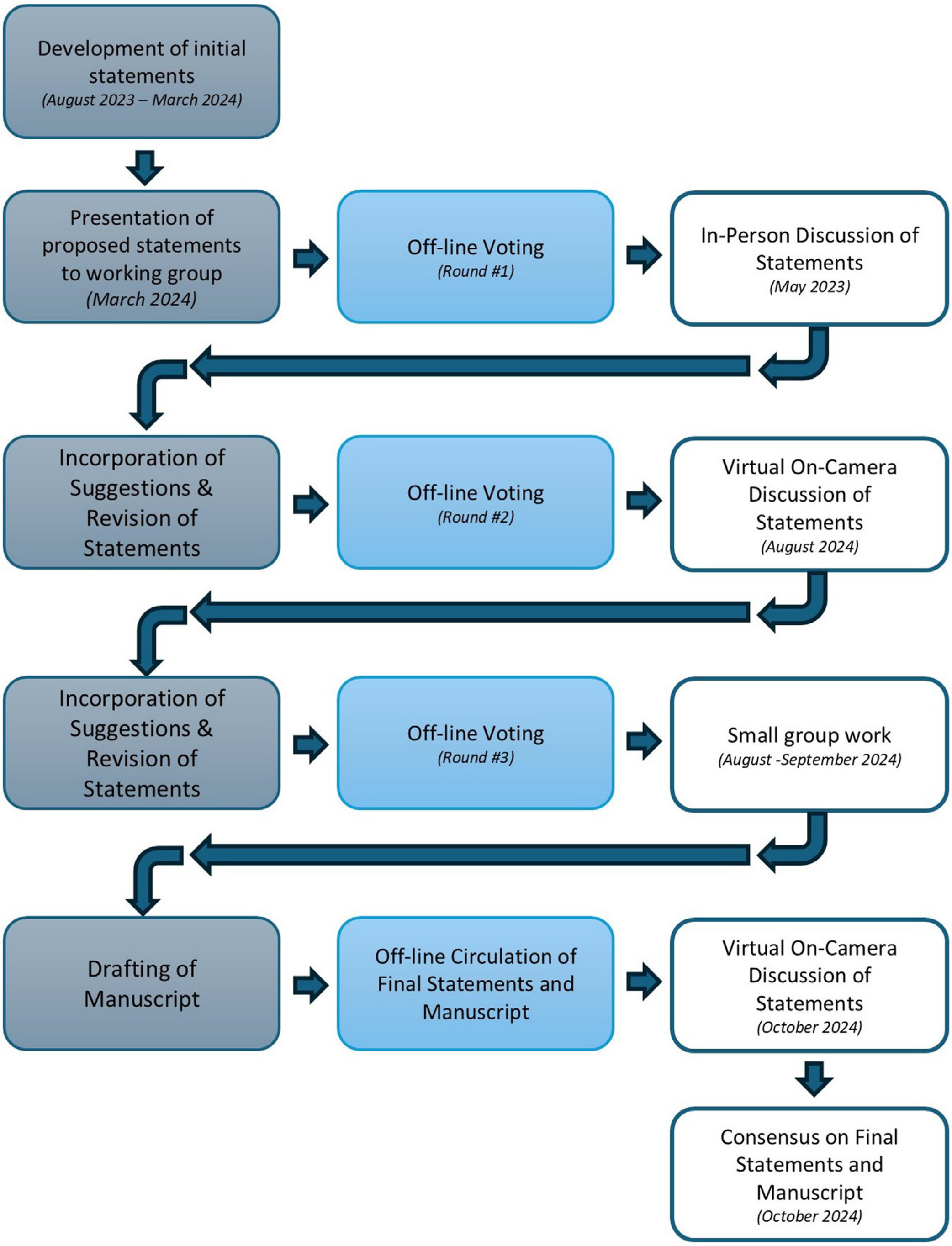
This round will assess the group's agreement for which statements regarding the FLIP panometry protocol and interpretation approach should be recommended, should be recommended against, or are not appropriate for a recommendation. Of note, we are not trying to force consensus, but rather to understand where there are high levels of agreement (or disagreement) among this group.

You will rank each statement for your perceived appropriateness. Ranking is on a scale of 1–9, where 1 means that the expected harms greatly outweigh the expected benefits and 9 means that the expected benefits greatly outweigh the expected harms.

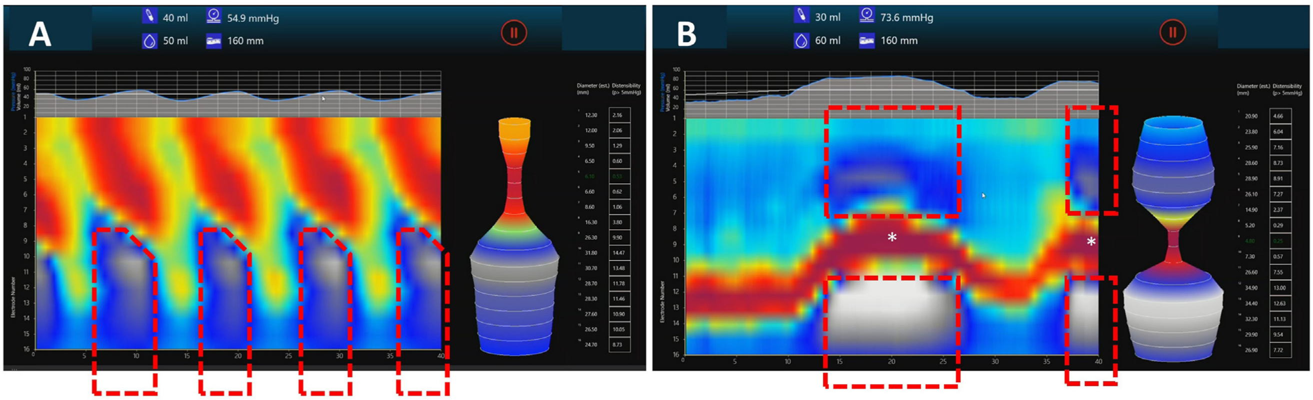
Generally, scores of: 1, 2, or 3 = inappropriate measure; 4, 5, or 6 = equivocal/uncertain appropriateness; and 7, 8, or 9 = appropriate measure.

Please use the following instructions when ranking the appropriateness of these statements:

1. The statements do not necessarily have to apply to any one specific patient, but rather, they may pertain to the overall care of patients.
2. A statement/measure (when applicable) is considered "valid" if adherence with this measure is critical to provide quality care to patients, exclusive of costs or feasibility.
3. Base your rankings on your own personal judgment, and not what you believe other experts or the panel might say.
4. Consider these measures for the average patient presenting to the average physician at an average hospital.



Supplementary Figure 1. Process for methodology for development of consensus statements.



Supplementary Figure 2. Dry catheter artifact. FLIP panometry output from 2 cases with example of the "dry catheter artifact" are displayed (*A, B*). Lumen occlusion (ie, luminal diameter approximately <6–7 mm) of the FLIP can disrupt the electrical current used by the impedance planimetry technology, causing a "dry catheter artifact" that results in falsely elevated diameter measures at FLIP sensors outside of the area of lumen occlusion. Areas affected by dry catheter artifact (which are represented in *red dashed boxes* on the FLIP topography plots) can occur distal (*A*) and proximal (*B*) to area of lumen occlusion and should be omitted from analysis. Achieving these actual diameters (>30 mm) on FLIP would likely rupture the bag. Reproduced with permission from the Esophageal Center of Northwestern Medicine. © Esophageal Center of Northwestern Medicine.

Supplementary Table 1. Working Group Characteristics

Characteristic	Data
Age, n (%)	
30–40 y	3 (19)
41–50 y	6 (38)
51–60 y	3 (19)
>60 y	4 (25)
Female, n (%)	7 (44)
Years in practice, mean (SD)	18 (11)

Clinical esophageal motility experience	FLIP	HRM	EGD
No. of procedures interpreted/ performed over career, n (%)			
25–100	0	0	0
101–500	7 (44)	1 (6)	0
501–1000	6 (38)	0	0
>1000	3 (19)	15 (94)	16 (100)
No. of procedures interpreted/ performed per month (average over the past year), n (%)			
1–10	5 (31)	1 (6)	0
11–20	7 (44)	3 (19)	0
21–30	2 (13)	5 (31)	5 (31)
>30	2 (13)	7 (44)	11 (69)

Supplementary Table 2. Summary of Key Citations of Formal Literature Review

Study, first author	Year	Study location	Study design	n	EGJ-DI threshold (*mm²/mm Hg*)	EGJ diameter threshold (*mm*)	Main findings
Triggs[20]	2020	Chicago, IL	Retrospective cohort	34	<2	NA	PPV of 75% for a DI <2 and NPV of 100% for DI ≥2 for abnormal TBE among 18 patients with HRM consistent with EGJOO, with 7 of 9 responding to sphincter-directed therapy. Of 7 patients with NEO on FLIP, all had normal TBE.
Carlson[1]	2021	Chicago, IL	Retrospective cohort	722	<2	<12	Among 202 patients with absent or diminished CR with REO on FLIP, 92% had HRM findings consistent with an EGJ outflow disorder and 77% had abnormal TBE. Among 86 patients with NEO and normal CR, 92% had normal HRM and 1% had findings consistent with an EGJ outflow disorder.
Rooney[18]	2021	Chicago, IL	Retrospective cohort	240	≤2	<12	Compared with 0% of healthy controls, 91% of patients with achalasia had a DI ≤2. Compared with 2% of healthy controls, 100% of achalasia patients had a diameter < 12 mm.
Carlson[21]	2021	Chicago, IL	Retrospective cohort	329	<2	<12	FLIP was superior to HRM to predict TBE (odds ratio, 30.7 vs 1.8)
Carlson[13]	2022	Chicago, IL	Retrospective cohort	741	<2	NA	Compared with healthy volunteers who all had normal or borderline CR, 91% of patients with achalasia or absent contractility on HRM had diminished or absent CR on FLIP. Patients with diminished or absent CR had a lower DI and diameter compared with those with normal CR.
Jain[26]	2022	Atlanta, GA	Prospective observational	79	<2.8	NA	Among a cohort with achalasia or barium tablet retention on esophagram, DI <1.25 had a sensitivity of 87% and specificity of 52% for significant dysphagia (Eckardt ≥2).
Carlson[6]	2022	Chicago, IL	Retrospective cohort	722	<2	<12	Patients with REO and higher symptom burden and 86% had a conclusive EGJ outflow disorder, with AUC of 0.897 for DI <2 and AUC of 0.963 for diameter <12 mm to discriminate conclusive EGJ outflow disorders of EGJ from normal EGJ outflow. Among 203 patients with NEO, 99% had normal EGJ outflow per Chicago Classification, version 4.0

Supplementary Table 2. Continued

Study, first author	Year	Study location	Study design	n	EGJ-DI threshold (*mm²/mm Hg*)	EGJ diameter threshold (*mm*)	Main findings
Carlson[17]	2023	Chicago, IL	Retrospective cohort	139	<2	<12	Of patients with conclusive FLIP findings for an EGJ outflow disorder, 72% diminished or absent CR with REO. Patients with conclusive FLIP for EGJ outflow disorder were more likely to have abnormal TBE compared with those with NEO (43% vs 0%) and 77% responded to achalasia-type sphincter-directed therapy. Among 13 patients with NEO, 1 of 3 (33%) treated with achalasia-type therapy had good outcomes compared with 9 of 10 (90%) treated with non-achalasia–type therapy.
Koop[24]	2023	Chicago, IL	Retrospective cohort	89	<2	<12	In this study of patients who underwent HRM, FLIP, and TBE, 31 patients had NCR (34.8%) and 34 had BCR (38.2%). 90% of NCR had normal TBE (and none had >5 cm at 5 min), while 82.3% of BCR had normal TBE (1 patient [2.9%] had >5 cm at 5 min).
Biermann[32]	2024	Atlanta, GA	Prospective observational	69	<2	<12	Among patients with REO, diminished or absent CR compared with normal or borderline CR was associated with symptomatic response to botulinum toxin injection to LES (odds ratio, 22.5)
Miller[22]	2024	Winston-Salem, NC	Retrospective cohort	413	<2	NA	Overall agreement between FLIP diagnoses and TBE was 49%, with a sensitivity of 98.1% and specificity of 36.5%. The sensitivity of DI <2 for diagnosing abnormal TBE was 45.1%, with specificity of 61.9%.

NOTE. The formal literature review assessed the following 2 key statements: “A major motor disorder is unlikely in the setting of a ‘normal’ FLIP panometry classification” and “Diminished or absent contractile response with reduced esophageal opening supports the diagnosis of a disorder of EGJ outflow.” Key findings of included supportive studies specifically assessing the diagnostic accuracy of applying these statements to both exclude a major motility disorder and identify a disorder of EGJ outflow are briefly described.
AUC, area under the curve; BCR, borderline contractile response; CR, contractile response; NA, not applied; NCR, normal contractile response; NPV, negative predictive value; PPV, positive predictive value.