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Diagnostic methods to measure spastic segment and guide tailored myotomy length in type 3 achalasia

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Abstract

Background: Myotomy length in type 3 achalasia is generally tailored based on segment of spasticity on high-resolution manometry (HRM). Potential of length of tertiary contractions on barium esophagram (BE) or length of thickened circular muscle on endoscopic ultrasound (EUS) to guide tailored myotomy is less understood. This study aimed to assess agreement between spastic segments lengths on HRM, BE, and EUS among patients with type 3 achalasia.

Methods: This retrospective study included adults with type 3 achalasia on HRM between November 2019 and August 2022 who underwent evaluation with EUS and/or BE. Spastic segments were defined as HRM—distance between proximal borders of lower esophageal sphincter and high-pressure area (isobaric contour ≥70 mmHg); EUS—length of thickened circular muscle (≥1.2 mm) from proximal border of esophagogastric junction (EGJ) to the transition to a non-thickened circular muscle; BE—distance between EGJ to proximal border of tertiary contractions. Pairwise comparisons assessed for correlation (Pearson's) and intraclass correlation classification (ICC) agreement.

Key Results: Twenty-six patients were included: mean age 66.9 years (SD 13.8), 15 (57.7%) male. Spastic segments were positively correlated on HRM and BE with good agreement (ICC 0.751, [95% CI 0.51, 0.88]). Spastic segments were negatively correlated with poor agreement on HRM and EUS (ICC −0.04, [−0.45, 0.39]) as well as BE and EUS (ICC −0.03, [−0.47, 0.42]).

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AUTHOR CONTRIBUTIONS

Eric E Low involved in study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and statistical analysis. Aws Hasan MD, Wilson Kwong MD, Mary L Krinsky DO, Gobind Anand MD, and Michael A. Chang MD involved in acquisition of data and approval of final manuscript. Syed Abbas Fehmi MD involved in acquisition of data, critical revision of the manuscript for important intellectual content, and approval of final manuscript. Madeline Greytak involved in critical revision of the manuscript for important intellectual content and administrative, technical, or material support. Alexander Kaizer involved in critical revision of the manuscript for important intellectual content, statistical analysis, and approval of final manuscript. Rena Yadlapati involved in study concept and design, acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, approval of final manuscript, and study supervision

CONFLICT OF INTEREST STATEMENT

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Conclusions & Inferences: Length of spastic segment was positively correlated on HRM and BE while negatively correlated when compared to EUS, supporting the common use of HRM and highlighting the uncertain role for EUS in tailoring myotomy length for type 3 achalasia.

Keywords

dilation; dysphagia; Heller Myotomy; per-oral endoscopic myotomy; swallowing

1 | INTRODUCTION

Achalasia is a well characterized esophageal motility disorder defined globally by impaired lower esophageal sphincter (LES) relaxation and failed peristalsis on high-resolution manometry (HRM).[1] The Chicago Classification describes three manometric subtypes of achalasia—type 1, type 2, and type 3—with distinct implications for treatment recommendations and clinical outcomes.[2–4] In type 1 and type 2 achalasia, there is impaired LES relaxation and complete absence of peristalsis in the esophageal body,[1] and thus, treatment is directed at disrupting the LES to permit bolus transit from the esophagus into the stomach. Current first-line therapies for type 1 and type 2 achalasia include laparoscopic Heller myotomy, per-oral endoscopic myotomy (POEM), or pneumatic dilation.[2–4]

Type 3 achalasia, however, is characterized by obstructive contractility at the distal esophagus and LES, and thus, treatment is directed at the LES and extension in the distal esophagus to treat the obstructive/spastic segment of esophageal muscle. The spastic segment in type 3 achalasia varies in length from person-to-person, and POEM is the first-line therapy for type 3 achalasia to enable proximal extension of the myotomy, which can be tailored to the spastic length.[3–7]

There is a knowledge gap in terms of how to best measure the involved esophageal muscle segment. While measurement of the spastic segment is generally based on HRM,[5] this clinical practice has not been fully studied or validated. Further, the diagnostic potential of other radiographic/physiologic measurements such as the length of tertiary contractions on barium esophagram (BE) or the length of thickened esophageal circular muscle layer on endoscopic ultrasound (EUS) to guide myotomy length is not well characterized. As a field, there is a need to inform and standardize methods to guide myotomy length in type 3 achalasia. Thus, this study aimed to assess agreement between measurements of spastic segment length on HRM, BE, and EUS in patients with type 3 achalasia.

2 | METHODS

2.1 | Study design and subject selection

We performed a retrospective single-center study of adult patients meeting diagnostic criteria for type 3 achalasia per CCv4.0 on HRM[1] over 44 months (January 2019 to August 2022). Patients with type 3 achalasia were included if they had undergone at least one of the following evaluations prior to achalasia directed therapy: EUS of the esophageal circular muscle or BE. Patients on chronic opiate use or who had a prior history of LES intervention/foregut surgery were excluded. The Institutional Review Board approved this study.

2.2 | HRM evaluation of spastic segment length

All HRM evaluations utilized a catheter (4.2-mm diameter; Medtronic Inc.) equipped with 36 pressure transducers spaced 1 cm apart and 18 impedance electrodes spaced 2 cm apart. Once the catheter was placed and a baseline period was recorded confirming catheter placement, a minimum of ten 5 mL wet swallows in the supine position were performed. If patient tolerated, additional swallows were performed including five wet swallows in the seated position, up to three multiple rapid swallows, and a rapid drink challenge.

CCv4.0 definition for type 3 achalasia was used for this study: an abnormal integrated relaxation pressure (IRP) and evidence of spasm (i.e., 20% or more swallows with premature contraction) with no evidence of peristalsis.[1] The length of spastic esophageal muscle segment on HRM was measured as the axial distance between the proximal border of LES to the proximal border of the high-pressure area—defined as an area with an isobaric contour ≥70 mmHg (Figure 1 and Figure S1). Given that standard HRM protocols require multiple swallows in the primary position, the average of the axial distances measured was used as the final measurement to best standardize measurements among patients. Spastic segment lengths were measured independently by two reviewers (EEL and RY), and those with disagreement were re-reviewed together. Reviewers were blinded other diagnostic study measurements and lengths.

2.3 | BE evaluation of spastic segment length

Data from BE were collected for patients that underwent BE prior to definitive LES therapy. Barium swallows were evaluated for the presence of tertiary contractions, which represent non-peristaltic esophageal muscle contractions.[8,9] Tertiary contractions were classified as contractions resulting in a significant narrowing, curling, corkscrewing, or beading appearance of the esophagus.[9]

The length of spastic muscle segment on BE was measured as the axial distance between the proximal border of esophagogastric junction (EGJ) to the proximal border of the tertiary contractions (Figure 1). Given that BE is a dynamic test, the average of the axial distance measurements was used as the final measurement to best standardize measurements among patients. Spastic segment lengths were measured independently by two reviewers (EEL and RY), and those with disagreement were re-reviewed together. Reviewers were blinded other diagnostic study measurements and lengths.

2.4 | EUS evaluation of spastic segment length

EUS was routinely performed by an advanced endoscopist for patients with achalasia in accordance with an adopted, standardized protocol to evaluate for pseudo-achalasia and measure esophageal muscle thickness to assist with myotomy length planning for definitive LES therapy (i.e., POEM). A radial EUS endoscope was utilized, and measurements of the circular muscle thickness were measured at the EGJ and then in 1 cm increments proximally until the muscle thickness reached 1 mm or less, which defined a normal circular muscle thickness.[10–14] Prior studies have demonstrated an average circular muscle thickness in the distal esophagus ranging from 0.6 to 1.1 mm among healthy control subjects, with normal manometry.[10–14] Therefore, for the purpose of this study and based on the available literature, we defined a thickened circular muscle layer in the distal esophagus equal to 1.2 mm or greater.

The length of spastic muscle segment on EUS was measured as the length of thickened circular muscle from the proximal border of LES (loss of gastric folds on EUS with no balloon insufflation) to the proximal transition point of thickened (muscle thickness of ≥1.2 mm) to a non-thickened (<1.2 mm) circular muscle (Figure 1). Endoscopists performing EUS were blinded to HRM and BE measurements.

2.5 | Data management and statistical analysis

Patient data were securely maintained in REDCap and deidentified prior to performing statistical analyses. Summary statistics of demographic and radiographic/physiologic measurements were described as mean values with standard deviation (SD) for continuous variables or as frequencies for categorical variables (Table 1). For this study, spastic segment length measurements which differed by >3 cm were considered to be outside of random measurement variability and therefore were clinically significantly different.

Primary analyses for our study consisted of pairwise comparisons between modalities using Pearson's correlation and intraclass correlation classification (ICC) for absolute agreement (i.e., the modalities arrive at the same exact estimate) and consistency (i.e., the modalities may be different but are consistently so). ICCs were estimated using a two-way model with a single measurement from each approach. ICC results are interpreted as <0.5 = poor agreement/consistency, 0.50–0 .750 = moderate agreement/consistency, 0.751–0.90 = good agreement/consistency, and >0.90 = excellent agreement/consistency.[15] For the primary analyses, measurements for all subjects were included in the analyses ($n = 26$).

Secondary analyses for our study were conducted, which included the same pairwise comparisons described above but only included patients who underwent all three diagnostic tests ($n = 20$).

3 | RESULTS

3.1 | Baseline characteristics

Overall 26 patients with type 3 achalasia on HRM met criteria for this study and are included. Mean age of the cohort was 66.9 years (SD 13.8), and 15 (57.7%) were male (Table 1). Mean body mass index was 27.5 kg/m^2 (SD 4.4), and mean Eckardt score at initial evaluation was 6.7 (SD 2.6). On HRM, the average median IRP was 31.4 mmHg (SD 12). Tertiary contractions were present in all (100%) patients who underwent BE. Of the 26 patients included in the study, 24 (92%) underwent BE, 22 (85%) underwent EUS, and 20 (77%) of subjects underwent all three diagnostic studies. Mean spastic segment length was 11.4 cm (SD 3.5) on HRM, 11.7 cm (SD 3.2) on BE, and 10.4 cm (SD 5.6) on EUS.

3.2 | Primary analyses of spastic segment length agreement assessments

Among the 24 patients that underwent HRM and BE, spastic segments were positively correlated (Pearson's 0.753, $p < 0.0001$; Figure 2) with good agreement (ICC agreement: 0.751 [95% CI 0.509, 0.883]) and moderate consistency (ICC consistency: 0.750 [95% CI

0.504, 0.884]; Table 2). The average absolute difference in spastic segment measurement for each patient between HRM and BE was 1.9 cm (SD 1.5), and the length differed by >3 cm for three of 24 patients (12.5% of cases). When compared to HRM, BE demonstrated a longer spastic segment by >3 cm in one case and a shorter spastic segment by >3 cm in two cases.

Among the 22 patients that underwent HRM and EUS, spastic segments were negatively correlated (Pearson's −0.040, $p = 0.859$) with poor agreement (ICC agreement: −0.036 [95% CI −0.449, 0.386]) and poor consistency (ICC consistency: −0.036 [95% CI −0.442, 0.383]; Table 2). The average absolute difference in spastic segment measurement for each patient between HRM and EUS was 5.5 cm (SD 3.9), and the length differed by >3 cm for 13 patients (59.1% of cases). When compared to HRM, EUS demonstrated a longer spastic segment by >3 cm in 36.4% of cases and a shorter spastic segment by >3 cm in 22.7% of cases.

Among the 20 patients that underwent BE and EUS, spastic segments were negatively correlated (Pearson's −0.030, $p = 0.902$) with poor agreement (ICC agreement: −0.025 [95% CI −0.446, 0.418]) and poor consistency (ICC consistency: −0.025 [95% CI −0.453, 0.413]; Table 2). The average absolute difference in spastic segment measurement for each patient between BE and EUS was 4.7 cm (SD 3.6), and the length differed by >3 cm for 12 patients (60% of cases). When compared to BE, EUS demonstrated a shorter spastic segment by >3 cm in 35% of cases and a longer spastic segment by >3 cm in 25% of cases.

3.3 | Secondary sub-group analyses of spastic segment length agreement assessments

In a sub-analysis of the 20 patients who underwent all three diagnostic studies, the spastic segments on HRM and BE were positively correlated (Pearson's 0.820, $p < 0.0001$) with good agreement (ICC agreement: 0.786 [95% CI 0.537, 0.909]) and good consistency (ICC consistency: 0.800 [95% CI 0.561, 0.916]). Spastic segment on HRM and EUS was positively correlated (Pearson's 0.023, $p = 0.923$) with poor agreement (ICC agreement: 0.022 [95% CI −0.445, 0.462]) and poor consistency (ICC consistency: 0.021 [95% CI −0.451, 0.450]). Spastic segment on BE and EUS was negatively correlated (Pearson's −0.030, $p = 0.902$) with poor agreement (ICC agreement: −0.025 [95% CI −0.466, 0.418]) and poor consistency (ICC consistency: −0.025 [95% CI −0.453, 0.413]).

3.4 | HRM spastic segment measurements and myotomy length

POEM with proximal extension in the esophagus was performed with an average myotomy beginning 1.3 cm (SD 1.2) proximal to the proximal margin of the spastic segment measured on HRM. Eckardt scores were less than 3 at 1-year follow-up for those undergoing POEM.

4 | DISCUSSION

Type 3 achalasia is increasingly diagnosed, and the first-line therapy is POEM with extended and tailored myotomy. However, there remains a knowledge gap in how to measure and tailor myotomy length. In this study of 26 patients with type 3 achalasia, we assessed the agreement between measurements of esophageal spastic segment length on three esophageal diagnostic tools—esophageal HRM, BE, and EUS. Spastic segment lengths on HRM and

BE were positively correlated with good measurement agreement and moderate consistency. On the contrary, spastic segment length measurement on EUS was negatively correlated with both HRM and BE, with poor measurement agreement and consistency. POEM was performed at our institution with an average myotomy beginning 1.3 cm proximal to the proximal margin of the spastic segment measured on HRM, which resulted in Eckardt scores less than 3 at 1-year follow-up. These findings support the use of HRM to measure the spastic segment length for those with type 3 achalasia and highlight the uncertain role for EUS in tailoring myotomy length.

In normal esophageal physiology, a peristaltic wave after swallowing is formed as a result of coordinated, antegrade esophageal circular muscle contractions in conjunction with longitudinal muscle shortening acts which acts to propel liquid and/or solid content toward the stomach.[16–18] In type 3 achalasia, circular muscle contraction is non-peristaltic, resulting in circular muscle spasticity and luminal obstruction after swallowing.[3–5] POEM is the ideal treatment for type 3 achalasia as the circular muscle myotomy can be extended proximally along the entire length of the spastic muscle segment.[3–5,7] However, there is a lack of data to support the optimal method to measure the spastic length in type 3 achalasia. Typically, in clinical practice, HRM findings are used to estimate the spastic length and guide the tailored myotomy; this practice is based on anecdotal experience and expert opinion.[5]

Evaluation for pseudo-achalasia is commonly performed with EUS. EUS also offers the potential to measure esophageal muscle thickness. Prior studies of esophageal muscle thickness in achalasia have identified greater esophageal muscle thickness, particularly the circular muscle, among those with type 3 achalasia compared to type 2 and type 1 achalasia.[10,11,19] Therefore, it has been hypothesized that identifying the thickened circular muscle segment on EUS may be a complementary diagnostic test to HRM for myotomy planning and/or during the POEM procedure, and some centers utilize EUS to guide myotomy length; however, there is a lack of research in the area to support this practice, and we do not recommend this in routine clinical practice.

Prior studies have demonstrated an average circular muscle thickness in the distal esophagus ranging from 0.6 to 1.1 mm among healthy control subjects, with normal manometry.[10–14] For our study, based on the available literature, we defined a thickened circular muscle layer in the distal esophagus equal to 1.2 mm or greater. Muscle segment lengths using this thickness definition did not agree with measurements obtained from HRM or from tertiary contraction lengths seen on BE. Our findings suggest that, although the spastic circular muscle may thicken or hypertrophy in type 3 achalasia, thickness of the muscle may not correlate with spasticity of the muscle itself. In many instances, EUS measurement of the thickened muscle segment both overestimated and underestimated the length when compared to either HRM or BE, suggesting that measurement of the muscle thickness is not a reliable determinate of muscle spasticity and therefore should not contribute to myotomy planning.

Serrano et al.[20] performed one of the first studies to measure agreement between the high-pressure zone on HRM and spastic segments on esophagography and esophagoscopy. They determined significant discordance of segment lengths between study modalities, cautioning the use of esophagography or esophagoscopy for the use of tailoring myotomy.[20] Our study, which contains a larger cohort of patients with well characterized type 3 achalasia, showed, conversely, that the length of high-pressure segment on HRM correlated well with the length of tertiary contractions seen on BE. Only three patients had a length discrepancy between HRM and BE greater than 3 cm in length (12.5% of the study cohort). Although not conclusive, as HRM and BE are not performed at the same time, the tertiary contractions on BE resulting in transient luminal narrowing likely correlate with the high-pressure segments seen on HRM and, moreover, demonstrate a physiologic representation of the classic manometric patterns in type 3 achalasia. We suggest that HRM and BE may be complementary in determining tailored myotomy planning prior to POEM; however, more research is needed to understand whether and how BE can be used in POEM planning. Based on our findings and available literature, we support the routine use of HRM to guide myotomy planning.

There are several strengths to our study. This is the first study to our knowledge to directly examine and compare the role of these three diagnostic modalities to measure spastic segment length in type 3 achalasia. Importantly, the manometric criteria for type 3 achalasia have evolved and become more stringent; this study utilized the latest contemporary CCv4.0 definitions to categorize HRM tracings as type 3 achalasia.[1] Additionally, given the low incidence and prevalence of type 3 achalasia, our study includes a robust cohort of patients with type 3 achalasia. For our study, subjects with a history of chronic opioid use and prior LES intervention/foregut surgery were excluded. All spastic segment measurements on HRM and BE were independently measured by two gastroenterologists. Lastly, our study utilized a standardized EUS protocol to measure the circular muscle thickness in patients being evaluated for POEM.

There are also important limitations to consider. First, there is no gold standard method to define spastic segment length in type 3 achalasia. HRM was used as the reference standard in our study as this is the method most used in clinical practice. Moreover, the definition of spastic segment on HRM is not well characterized; however, defining a spastic segment as a high-pressure area on HRM where the isobaric contour is ≥70 mmHg is in line with recent studies which suggest that this isobaric contour measurement represents physiologic luminal narrowing.[21] Given that HRM segment lengths correlated well with tertiary contractions on BE also support the hypothesis that an isobaric contour ≥70 mmHg represents physiologic luminal narrowing. It is important to note that HRM and BE were not performed simultaneously, and that HRM measurements were performed in the supine position whereas BE measurements were performed in the upright position. It is unclear how these position changes may affect the measurements of spastic segment lengths; however, we attempted to best standardize these measurements by taking the mean lengths over several dynamic swallows. An important next step would be to perform the studies simultaneously and then measure the segment lengths. Another limitation is that our HRM protocol does not routinely utilize provocative maneuvers such as a solid food challenge, which may enhance the identification of a spastic segment on HRM. This is an important area of future research. Additionally, technical issues could have potentially affected EUS measurements during the procedure, such as from varying circular muscle thickness during muscle contractions or from wall compression of an insufflated balloon. However, for our study, all endoscopists used a radial scope without balloon insufflation to standardize factors as much as possible. It is notable that not all participants underwent all three diagnostic studies. We performed a sub-analysis of only those who underwent all three studies to mitigate this limitation which demonstrated similar trends.

5 | CONCLUSION

Current guidelines for the management of achalasia recommend tailored POEM as the treatment of choice for patients with type 3 achalasia. A large clinical gap remains regarding how to best measure the spastic esophageal muscle segment and guide myotomy length. In this study of 26 patients with type 3 achalasia, we identified good agreement and correlation for the length of the high-pressure segment on HRM to the length of tertiary contractions on BE. Conversely, we identified poor agreement and correlation between the length of thickened circular muscle on EUS and measurements on HRM or BE. These findings have important clinical implications, supporting the common use of HRM and highlighting the uncertain role for EUS in tailoring myotomy length for type 3 achalasia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Key Points

- High-resolution manometry should be routinely used to guide tailored myotomy length in type 3 achalasia.
- Circular muscle thickness measured on endoscopic ultrasound does not correlate with the high-pressure area on high-resolution manometry, highlighting the uncertain role for endoscopic ultrasound in guiding tailored myotomy in type 3 achalasia.

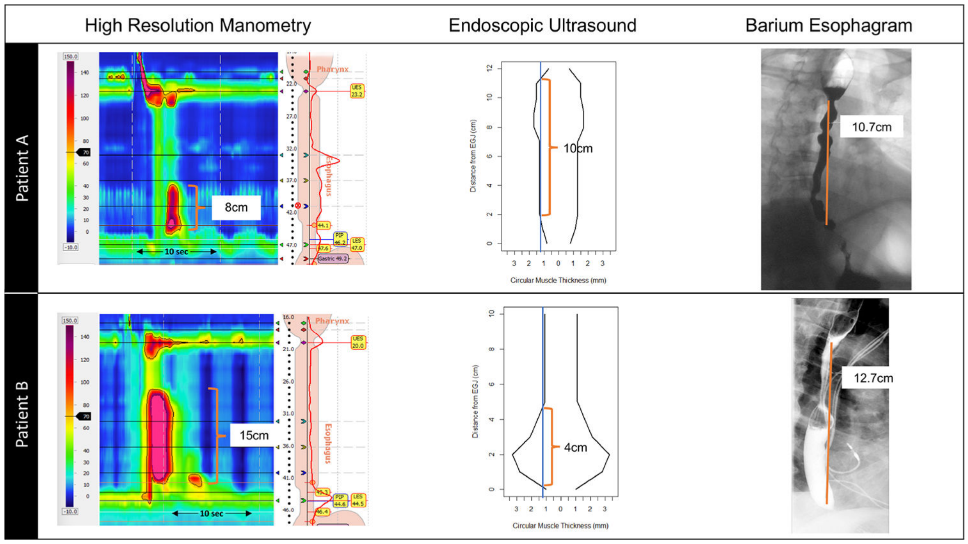

FIGURE 1.

Comparison of spastic segment measurements on HRM, EUS, and BE. Figure displays measured spastic segment lengths using HRM, EUS, and BE for two different patients (A) and (B). Patient (A) is an example where the measured spastic segment lengths are similar among the diagnostic tests. HRM demonstrates an isobaric contour segment ≥70 mmHg measuring 8 cm (orange bracket). EUS demonstrates a segment measuring 10 cm where the circular muscle thickness is ≥1.2 mm (the blue line marks 1.2 mm, and the orange bracket outlines the thickened segment). BE demonstrates a beading spastic segment measuring 10.7 cm (orange line). Patient (B) is an example where the measured spastic segment lengths differ among the diagnostic tests. HRM demonstrates an isobaric contour segment ≥70 mmHg measuring 15 cm (orange bracket). EUS demonstrates a segment measuring 4 cm where the circular muscle thickness is ≥1.2 mm (the blue line marks 1.2 mm, and the orange bracket outlines the thickened segment). BE demonstrates a corkscrew spastic segment measuring 12.7 cm (orange line).

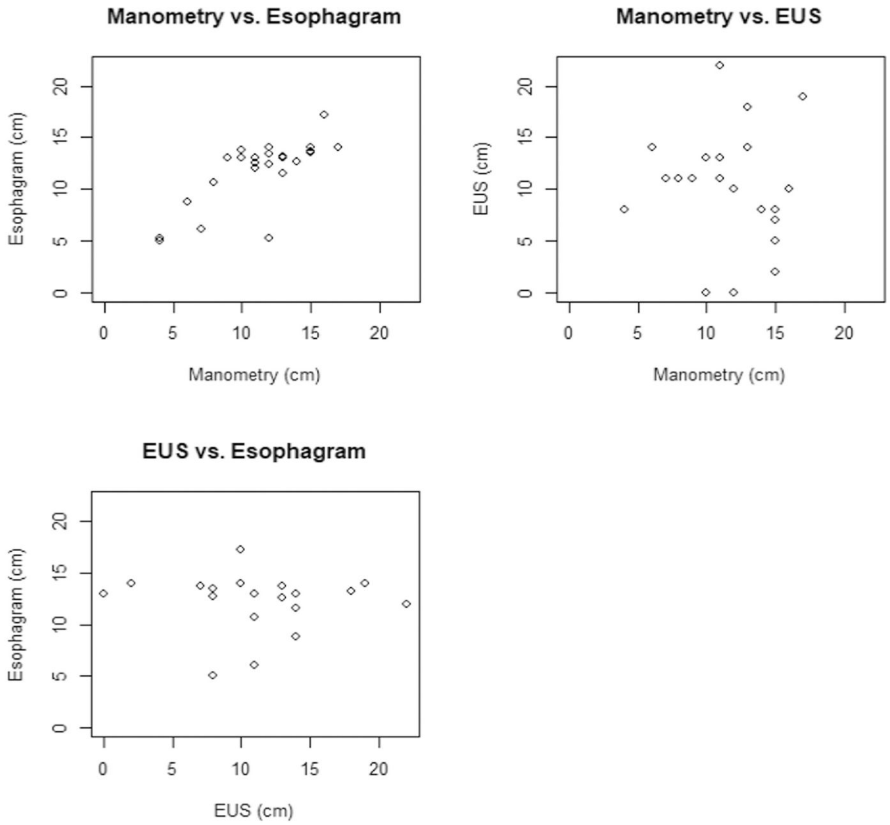

FIGURE 2.

Scatterplot of pairwise comparisons of modalities (primary analysis).

TABLE 1

Cohort characteristics.

Age (years), mean (SD)	66.9 (13.8)
Male gender, *n* (%)	15 (15.7)
Hispanic ethnicity, *n* (%)	5 (19.2)
Race, *n* (%)	
White	16 (61.5)
Black	1 (3.8)
Asian	1 (3.8)
Native Hawaiian or Other Pacific Islander	1 (3.8)
Other	7 (26.9)
Body mass index (kg/m^2), mean (SD)	27.5 (4.4)
Eckardt Score, mean (SD)	6.7 (2.6)
Median LES IRP on HRM (mmHg), mean (SD)	31.4 (12)
Spastic segment length in cm, mean (SD)	
High-resolution manometry	11.4 (3.5)
Barium esophagram	11.7 (3.2)
Endoscopic ultrasound	10.4 (5.6)

TABLE 2

Agreement/Association for pairwise comparisons of modalities.

Comparison	Pearson's correlation (*p*-value)	ICC agreement (95% CI)	ICC consistency (95% CI)
HRM versus BE	0.753 (<0.0001)	0.751 (0.509, 0.883)	0.750 (0.504, 0.884)
HRM versus EUS	−0.040 (0.859)	−0.036 (−0.449, 0.386)	−0.036 (−0.442, 0.383)
BE versus EUS	−0.030 (0.902)	−0.025 (−0.466, 0.418)	−0.025 (−0.453, 0.413)

Note: Green shading highlights a positive correlation and good agreement between study measurements. Grey shading highlights a negative correlation and poor agreement between study measurements.