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Improving the Diagnostic Yield of High-Resolution Esophageal Manometry for GERD: The "Straight Leg-Raise" International Study

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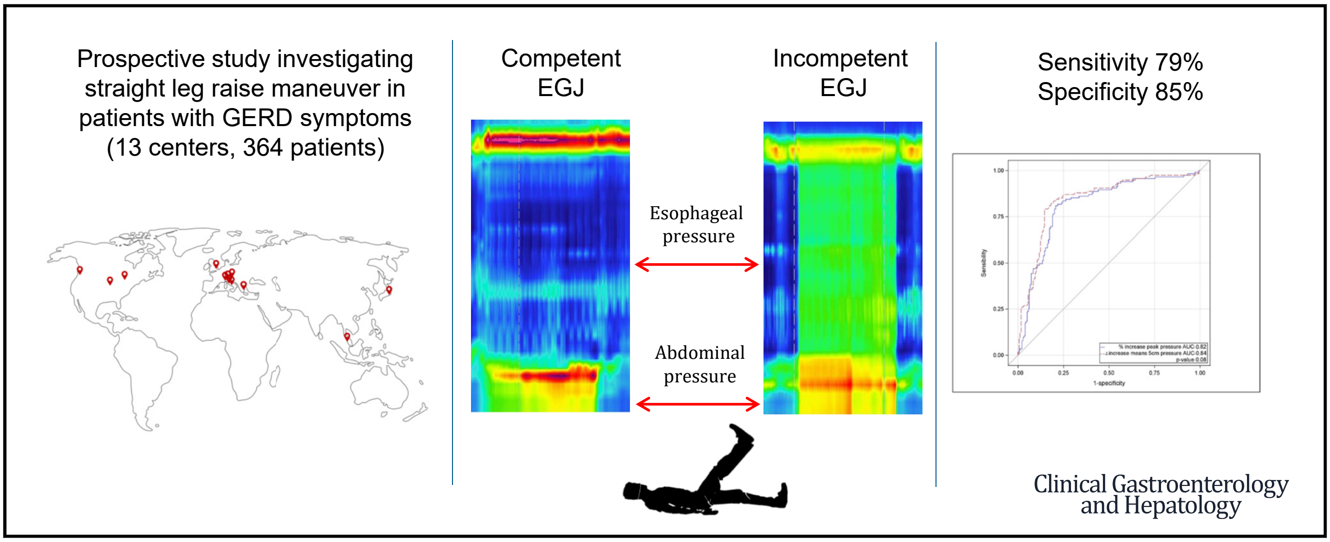

BACKGROUND & AIMS: The straight leg raise (SLR) maneuver during high-resolution manometry (HRM) can assess esophagogastric junction (EGJ) barrier function by measuring changes in intraesophageal

Abbreviations used in this paper: AET, acid exposure time; AUC, area under the receiver operating characteristic curve; BMI, body mass index; DCI, distal contractile integral; EGJ, esophagogastric junction; EGJ-CI, esophagogastric contractile integral; GERD, gastroesophageal reflux disease; HRM, high-resolution manometry; IAP, intra-abdominal pressure; IEP, intraesophageal pressure; LES, lower esophageal sphincter; OR, odds ratio; PPI, proton pump inhibitor; ROC, receiver operating characteristic curve; SLR, straight leg raise.

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pressure (IEP) when intra-abdominal pressure is increased. We aimed to determine whether increased esophageal pressure during SLR predicts pathologic esophageal acid exposure time (AET).

METHODS: **Adult patients with persistent gastroesophageal reflux disease (GERD) symptoms undergoing HRM and pH-impedance or wireless pH study off proton pump inhibitor were prospectively studied between July 2021 and March 2022. After the HRM Chicago 4.0 protocol, patients were requested to elevate 1 leg at 45o for 5 seconds while supine. The SLR maneuver was considered effective when intra-abdominal pressure increased by 50%. IEPs were recorded 5 cm above the lower esophageal sphincter at baseline and during SLR. GERD was defined as AET greater than 6%.**

RESULTS: **The SLR was effective in 295 patients (81%), 115 (39%) of whom had an AET greater than 6%. Hiatal hernia (EGJ type 2 or 3) was seen in 135 (46%) patients. Compared with patients with an AET less than 6%, peak IEP during SLR was significantly higher in the GERD group (29.7 vs 13.9 mm Hg; *P* < .001). Using receiver operating characteristic analysis, an increase of 11 mm Hg of peak IEP from baseline during SLR was the optimal cut-off value to predict an AET greater than 6% (area under the receiver operating characteristic curve, 0.84; sensitivity, 79%; and specificity, 85%), regardless of the presence of hiatal hernia. On multivariable analysis, an IEP pressure increase during the SLR maneuver, EGJ contractile integral, EGJ subtype 2, and EGJ subtype 3, were found to be significant predictors of AET greater than 6%**

CONCLUSIONS: **The SLR maneuver can predict abnormal an AET, thereby increasing the diagnostic value of HRM when GERD is suspected. ClinicalTrials.gov ID: NCT04813029.**

Keywords: Gastroesophageal Reflux Disease (GERD); High-Resolution Manometry; Esophagogastric Junction; Intra-abdominal Pressure; Intraesophageal Pressure; Straight Leg Raise Maneuver.

In patients with symptoms suspicious for gastroesophageal reflux disease (GERD), high-resolution manometry (HRM) generally is performed to exclude conditions that mimic reflux symptoms (ie, achalasia, rumination syndrome, supragastric belching), and to localize the lower esophageal sphincter (LES) for correct positioning of reflux monitoring probes.[1] Furthermore, the Lyon Consensus has indicated that HRM assesses esophagogastric junction (EGJ) barrier function, esophageal body motor function, and peristaltic reserve in patients with proton pump inhibitor (PPI)-refractory GERD, which facilitates selection of appropriate antireflux surgical procedures when these are indicated.[2] However, the sensitivity and specificity of HRM for GERD are low (53.6% and 72.5%, respectively), with significant overlap between GERD patients and controls in the majority of HRM parameters.[3] Therefore, the Porto consensus update has stated that the definitive diagnosis of GERD should follow endoscopic or pH study criteria.[4]

The effort to increase the diagnostic yield of esophageal manometry for GERD stems from the dawn of esophageal function testing. In 1982, Butterfield et al[5] proposed the "common cavity test," in which an increase in intra-abdominal pressure (IAP) caused an increase in intraesophageal pressure (IEP) in symptomatic GERD patients with a possibly defective EGJ. Masuda et al[6] attempted to improve HRM accuracy using a comprehensive index and new parameters, such as the backflow preventive and promotive pressure through the LES. Although a significant correlation between reflux burden and the new index was found, the sensitivity and specificity of HRM for GERD remained unchanged.

Recently, Rogers et al[7] translated the principle of the common cavity test into the HRM setting, introducing the straight leg raise (SLR) maneuver and proposing reference parameters for this technique. Increasing the IAP during HRM may help to better characterize GERD phenotypes in clinical practice.[8] Still, thresholds that predict pathologic acid exposure time (AET) and proof of real-life generalizability of SLR are lacking owing to the limited number of patients enrolled in preliminary studies.

We hypothesized that the SLR maneuver could increase the diagnostic yield of HRM by predicting abnormal esophageal AET at levels that define GERD. The primary study aim was to determine the optimal threshold of IEP augmentation during the SLR maneuver that would predict pathologic esophageal AET. The secondary study aim was to assess the diagnostic performance of HRM combined with the SLR maneuver.

Methods

A prospective multicenter study involving 13 high-volume esophageal function laboratories across Europe, North America, and Asia was performed. Patients were enrolled between July 2021 and March 2022. Inclusion criteria consisted of age between 18 and 75 years, esophageal function tests performed for persistent GERD symptoms, HRM and wireless pH-study or catheter pH-impedance study performed off PPI within 2 weeks of each other, and the ability to perform the SLR maneuver at the end of HRM. Patients with prior foregut surgery, body mass index (BMI) greater than 35 kg/m^2, paraesophageal hiatal hernia, scleroderma, eosinophilic esophagitis, and esophageal achalasia were excluded. GERD was defined as an AET greater than 6%, as recommended by the Lyon Consensus.[2] The study protocol, a detailed explanation of the performance, interpretation of the SLR maneuver including a demonstrative video, and electronic case-report forms were sent to the satellite centers. The study protocol was approved by the proposing center's ethic committee (identifier: HSR 94/int2021) and followed the Declaration of Helsinki principles. The study was published on ClinicalTrials.gov (identifier: NCT04813029).[9] All authors had access to the study data and reviewed and approved the final manuscript.

Clinical Evaluation

Clinical and demographic data collected for each patient included age, BMI, symptom onset, smoking, primary symptom, upper-gastrointestinal endoscopy findings (hiatal hernia, Barrett's esophagus, esophagitis), swallow study findings (hiatal hernia and reflux), and PPI dose, duration, and efficacy. Symptoms were assessed using validated questionnaires: Gastro Esophageal Reflux Disease; Q stands for Questionnaire (GERDQ),[10] GERD Health-Related Quality of Life,[11] and Reflux Symptom Index.[12]

High-Resolution Esophageal Manometry

High-resolution manometry was performed using each institution's preferred HRM system, using a solid-state catheter with 36 circumferentially incorporated sensors spaced at 1-cm intervals, and following the standardized protocol defined by the Chicago Classification 4.0 (CCv4.0).[13] HRM catheters were introduced by experienced physicians or nurses after an overnight fast. Ten swallows of 5 mL ambient temperature water were performed in the primary position (upright or recumbent), followed by 5 swallows in the secondary position. Each swallow was categorized as intact, weak, or failed based on the distal contractile integral (DCI) ($\geq$450 mm Hg/cm per second, 100–450 mm Hg/cm per second, and $\leq$100 mm Hg/cm per second, respectively). Ineffective esophageal motility (IEM) was defined as more than 70% weak swallows or 50% or more failed swallows. LES characteristics including total and intra-abdominal length, basal pressure, esophagogastric contractile integral (EGJ-CI), and EGJ morphology (presence or absence of hiatus hernia) were collected. The EGJ-CI was calculated during quiet rest by including the EGJ in the DCI tool box for 3 respiratory cycles using the isobaric contour of the gastric pressure and dividing the resultant value by duration.[14] Multiple rapid swallows, consisting of 5 swallows of 2 mL water administered at shorter than 3-second intervals also were performed. Contraction reserve was defined as a ratio between multiple rapid swallow DCI and the mean single swallow DCI greater than 1.

> **What You Need to Know**
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> **Background**
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> High-resolution manometry has low sensitivity and specificity for gastroesophageal reflux disease (GERD). The increase of intra-abdominal pressure with the straight leg raise (SLR) maneuver may function as a stress test of the esophagogastric junction to identify GERD patients.
>
> **Findings**
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> Mean and peak intraesophageal pressures during SLR were higher in GERD patients. An increase in intraesophageal pressure of 11 mm Hg provides 79% sensitivity and 85% specificity in identifying GERD patients.
>
> **Implications for patient care**
>
> The SLR is a simple provocative test to predict abnormal acid esophageal exposure time, thereby increasing the diagnostic value of high-resolution manometry when GERD is suspected.

Straight Leg Raise Maneuver

Upon completion of the standard Chicago Classification 4.0 protocol, patients were asked to perform the SLR maneuver. With the patient in the supine position, 1 leg was raised at an angle of 45o for at least 5 seconds. The maneuver was repeated after 20 to 30 seconds, and the first adequate maneuver was included in the analysis. IEP and IAP were analyzed both during baseline and during the SLR maneuver. IEP was measured as the peak and mean pressure over 5 seconds, 1 cm and 5 cm above the proximal margin of the LES. IAP was measured as the peak and mean over 5 seconds 1 cm below the distal margin of the diaphragmatic crural impression. Based on previous studies,[7] the SLR maneuver was considered effective if the IAP increased by 50% during SLR. To further investigate the relationships between esophageal and abdominal pressures, the ratio between IEP and IAP during SLR, the percentage increase of IEP during SLR, and the pressure increase between IEP at baseline and during SLR (delta increase) were determined.

Esophageal pH and pH-Impedance Study

All patients were asked to discontinue acid-suppressive drugs for at least 2 weeks before reflux monitoring studies. Wireless 48- or 96-hour pH-study and catheter 24-hour pH-impedance study were allowed. The wireless pH-study capsule (BRAVO) was placed 6 cm above the LES under endoscopic guidance. The multichannel intraluminal impedance-pH studies were performed using standard systems from various manufacturers based on each institution's preference; each catheter used had 8 impedance and 1 or 2 pH electrodes. The catheter was calibrated using buffer solutions at pH of 4.0 and 7.0 and then inserted transnasally with the pH electrode 5 cm above the proximal margin of the LES. The patients were asked to avoid acidic food and drinks and to record symptoms, duration of meal, and time spent in the recumbent position either on a diary or on the recorder itself.

Total, upright, and recumbent AET; DeMeester score; bolus exposure; number of acid, weakly acid, and weakly alkaline reflux episodes; symptom index; and symptom association probability were collected. Moreover, the mean nocturnal basal impedance and the postreflux swallow-induced peristaltic wave index were recorded when pH-impedance studies were usd.[15]

Data Collection and Statistical Analysis

De-identified data were uploaded and stored in the Research Electronic Data Capture platform. The Research Electronic Data Capture platform is an online, secure software designed to collect and manage data from different institutions.

Categoric variables are presented as frequency and percentages while continuous variables are presented as means ± SD for normal distributions or median and interquartile range for non-normal distributions. The study compared GERD vs no-GERD patients. Categoric variables were compared using the chi-squared test or the Fisher exact test as appropriate. The normality of continuous variables was assessed with the Shapiro–Wilk test. Normal variables were compared with the *t* test and nonparametric variables using the Kruskal–Wallis test. The performances of receiver operating characteristic (ROC) curves were evaluated with a univariate logistic regression model and the operating characteristic curves. The comparison of ROC curves was analyzed using the chi-squared test. The accuracy of the parameter was determined by the area under the ROC curve (AUC), which is a measure of the model's ability to discriminate subjects who experience the outcome vs those who do not. Typical value ranges of the AUC were from 0.5 (no discrimination beyond chance) to 1.0 (perfect discrimination). The ROC curve, which illustrates sensitivity against a false-positive rate, has been used to obtain optimal cut-off values. All optimal cut-off values were described by sensitivity and specificity. Multivariable logistic regression exploratory models were used to identify predictors of outcome, defined as an AET greater than 6%. The selection of variables included in the multivariable logistic regression model was based on clinical judgment. Odds ratios (ORs) were used to determine the strength of the association between an AET greater than 6% outcome and receiver operating and patient characteristics. All statistical tests were 2-sided. $P < .05$ was considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute, Inc, Cary, NC) and R software version 3.6.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Over the study period, 364 patients (median age, 50.0 [interquartile range, 23] y; median BMI, 24.8 [interquartile range, 5.6] kg/m^2) were enrolled. The median symptom duration was 36.0 [interquartile range, 48.0] months. Among patients with effective SLR, endoscopic variables, manometric variables, and pH impedance metrics associated with GERD were observed at a higher rate when the AET was greater than 6% compared with an AET less than 6% (Table 1). Of the included patients, 295 (81.0%) had an increased IAP during the SLR maneuver, with no clinically significant differences between patients with effective and noneffective SLR, including BMI (Supplementary Table 1). In the remaining 19% of patients, the IAP did not increase by 50% despite correct performance of the SLR maneuver. Therefore, we considered these maneuvers as noneffective, and these patients were excluded from the analysis. Of patients with IEM, 27% were in the GERD group and 15.1% were in the non-GERD group ($P = .010$), while absent peristalsis was identified in 0.9% and 1.1% of patients, respectively ($P = .661$). No patients with manometric features of distal esophageal spasm, hypercontractile esophagus, EGJ outflow obstruction, or esophageal achalasia were observed in the study cohort. Intra-abdominal LES length was significantly higher in EGJ types 2 and 3 than type 1 (0.9 vs 0.0 cm; $P < .001$) in the GERD group.

Mean and peak IEP during SLR, IAP during rest and SLR, as well as ratios, percentage increase, and delta values between these pressures were significantly higher among patients with an abnormal AET (Table 2). Furthermore, there was modest correlation between increased AET and IEP during SLR (correlation coefficient, 0.375; $P < .001$). Weak correlations were found between IEP and LES basal pressure as well as EGJ-CI (correlation coefficient, -0.136 and -0.112, respectively). The best parameter that discriminated GERD patients was the delta increase of peak IEP measured 5 cm above the LES (Table 3). ROC analysis showed that an increase of 11 mm Hg peak IEP predicted AET greater than 6% with a sensitivity of 79% and a specificity of 85% (AUC, 0.84; 95% CI, 0.79–0.89) (Figure 1). Only a weak correlation between a delta increase of IEP and AET was noted ($r = 0.31$).

The threshold of 11 mm Hg was used to investigate the possible effect of a hiatal hernia. When the study

Table 1. Demographic, Clinical, HRM, and pH Characteristics of the Overall Patient Population According to AET

	Total (n = 364)	AET, <6% (n = 227)	AET, >6% (n = 137)	*P* value
Male, n (%)	156 (42.9)	92 (40.5)	64 (46.7)	.155
Age, *y*	50.0 [23.0]	49.0 [26.0]	50.0 [18.0]	.455
BMI, *kg/m²*	24.8 [5.6]	24.2 [5.4]	26.1 [5.7]	<.001
Symptom duration, *mo*	36.0 [48]	24.0 [48.0]	36.0 [56.0]	.057
Primary typical symptoms, n (%)	270 (74.2)	153 (67.4)	117 (85.4)	.001
Primary extraesophageal symptoms, n (%)	94 (25.8)	74 (32.6)	20 (14.6)	.001
PPI use, n (%)	273 (81.5)	159 (76.1)	113 (90.4)	.001
Response to PPI				.010
No response, n (%)	72 (26.1)	53 (32.9)	19 (16.6)	
Partial response, n (%)	154 (55.8)	81 (50.3)	72 (63.2)	
Full benefit, n (%)	50 (18.1)	27 (16.8)	23 (20.2)	
Endoscopic findings				
Hiatal hernia, n (%)	189 (59.6)	95 (48.7)	94 (77.0)	<.001
Esophagitis, n (%)	93 (29.6)	41 (21.2)	52 (43.0)	<.001
Radiologic findings				
Reflux, n (%)	27 (50.9)	8 (32.0)	19 (67.9)	.013
Hiatal hernia, n (%)	25 (46.3)	7 (28.0)	18 (62.1)	.016
Questionnaires				
GERD-Q A	9.0 [5.0]	9.0 [5.0]	10.0 [4.0]	.003
GERD-Q B	2.0 [4.0]	2.0 [3.0]	3.0 [3.0]	.002
HRQL	17.0 [14.0]	15.0 [14.0]	18.0 [14.2]	.007
RSI	13.0 [15.0]	13.0 [15.0]	15.0 [16.3]	.279

HRM and pH data (effective SLR only)	Total (n = 295)	AET <6% (n = 180)	AET >6% (n = 115)	
EGJ type				<.001
1, n (%)	158 (53.9)	118 (66.3)	40 (34.8)	
2, n (%)	94 (32.1)	50 (28.1)	44 (38.3)	
3, n (%)	41 (14.0)	10 (5.6)	31 (27.0)	
Hiatal hernia, n (%)	136 (46.6)	61 (34.5)	75 (65.2)	<.001
LES total length, *cm*	2.1 [0.8]	2.1 [0.8]	1.9 [0.8]	.007
LES intra-abdominal length, *cm*	0.2 [1.0]	0.5 [1.2]	0.0 [0.5]	<.001
EGJ contractile integral, *mm Hg*cm*	35.2 [42.5]	46.0 [41.8]	22.6 [26.5]	<.001
Patients with IEM, n (%)	58 (19.7)	27.0 (15.1)	31 (27.0)	.010
AET, (%)	4.1 [8.7]	1.5 [3.0]	11.3 [11.6]	<.001
DeMeester score	16.2 [32.8]	6.5 [12.0]	45.7 [40.3]	<.001
Patients with SI >50%, n (%)	105 (36.3)	54 (30.9)	51 (44.7)	.018
Patients with SAP >95%, n (%)	98 (33.9)	47 (26.9)	50 (43.9)	.002
Total reflux episodes, n (%)	42.0 (37.5)	34.0 (34.0)	52.5 (49.3)	<.001
MNBI	1947.0 [1787.8]	2749.0 [1915.6]	1265.5 [1141.3]	<.001
PSPW index, %	44.0 [36.0]	65.0 [27.0]	29.5 [16.7]	<.001

NOTE. Continuous values are expressed as median [interquartile range].
AET, acid exposure time; BMI, body mass index; EGJ, esophagogastric junction; GERD, gastroesophageal reflux disease; HRQL, Health-Related Quality of Life; IEM, ineffective esophageal motility; LES, lower esophageal sphincter; MNBI, mean nocturnal basal impedance; PPI, proton pump inhibitor; PSPW, postreflux swallow-induced peristaltic wave; RSI, Reflux Symptom Index; SAP, symptom association probability; SI, Symptom Index; SLR, straight leg raise.

population was categorized by EGJ subtype, the AUC was similar between the 3 subtypes (AUC: EGJ-1, 0.84; 95% CI, 0.77–0.91; EGJ-2, 0.82; 95% CI, 0.73–0.91; and EGJ-3, 0.85; 95% CI, 0.72–0.98), despite significant differences in AET based on EGJ subtype (Supplementary Figure 1).

Table 2. Esophageal Pressure Measurements After Effective SLR Maneuver in Patients With and Without GERD

	AET, <6% (n = 180)	AET, >6% (n = 115)	*P* value
Esophageal peak pressure 5 cm above LES during rest, *mm Hg*	11.5 [10.8]	10.3 [6.8]	.05
Esophageal peak pressure 5 cm above LES during SLR, *mm Hg*	13.9 [12.0]	29.7 [18.2]	<.001
Mean esophageal pressure 5 cm above LES during rest, *mm Hg*	6.3 [7.9]	4.2 [6.2]	.058
Mean esophageal pressure 5 cm above LES during SLR, *mm Hg*	8.4 [10.0]	19.5 [14.2]	<.001
Abdominal pressure during SLR, *mm Hg*	28.5 [19]	38.7 [28.9]	<.001
Abdominal pressure during rest, *mm Hg*	8.2 [7.2]	10.3 [6.5]	.02
Ratio peak pressure, %	46 [52]	78 [51]	<.001
Ratio mean pressure, %	25 [41]	51 [43]	<.001
Increase peak pressure, %	11 [79]	205 [261]	<.001
Increase mean pressure, %	11 [140]	256 [558]	<.001
Δ increase peak pressure 5 cm, *mm Hg*	1.5 [8.3]	18.2 [17.2]	<.001
Δ increase mean pressure 5 cm, *mm Hg*	1.0 [6.3]	13.9 [12.8]	<.001
Δ increase peak pressure 1 cm, *mm Hg*	2.8 [12.2]	18.1 [20.5]	<.001
Δ increase mean pressure 1 cm, *mm Hg*	2.0 [11.7]	13.0 [19.1]	<.001

NOTE. Continuous values are expressed as median [interquartile range].
AET, acid exposure time; GERD, gastroesophageal reflux disease; LES, lower esophageal sphincter; SLR, straight leg raise.

On multivariable analysis, an IEP pressure increase during SLR (OR, 1.62 [95% CI,1.42–1.86]), EGJ-CI (OR, 0.87 [95% CI,0.78–0.98]), EGJ subtype 2 (OR, 2.00 [95% CI,1.04–3.84]), and EGJ subtype 3 (OR, 4.26 [95% CI,1.60–11.30]) were found to be significant predictors of AET greater than 6% (Table 4).

Discussion

In this multicenter study evaluating the clinical value of the SLR maneuver in symptomatic patients being evaluated for the presence or absence of conclusive GERD, we show that a positive SLR maneuver can predict pathologic AET.

Among patients who were able to perform an effective SLR maneuver, IEP was augmented in those with GERD, defined as an AET greater than 6% on reflux monitoring performed off PPI therapy. We show that in most patients without pathologic AET, LES-crural diaphragm pressure increases to prevent the backflow of gastric refluxate into the esophagus during the SLR maneuver, while in patients with GERD this protective mechanism is lost, and IAP spills into the esophageal body, thereby promoting abnormal reflux burden (Figure 2).

Table 3. Receiver Operating Characteristics Analysis of SLR Parameters in Predicting AET >6

	AUC (95% CI)	Cut-off	Sensitivity	Specificity
Esophageal peak pressure SLR	0.81 (0.80–0.89)	20.4	0.74	0.77
Mean esophageal pressure SLR	0.79 (0.73–0.84)	12.4	0.74	0.73
Ratio peak pressure	0.69 (0.63–0.75)	0.49	0.78	0.54
Ratio mean pressure	0.69 (0.63–0.75)	0.35	0.71	0.61
% increase peak pressure	0.82 (0.77–0.87)	77.8	0.81	0.79
% increase mean pressure	0.77 (0.71–0.83)	100	0.75	0.78
Δ increase peak 5-cm pressure	0.84 (0.79–0.89)	11	0.79	0.85
Δ increase mean 5-cm pressure	0.81 (0.76–0.87)	6.6	0.77	0.80
Δ increase peak 1-cm pressure	0.74 (0.68–0.80)	7.7	0.76	0.67
Δ increase mean 1-cm pressure	0.76 (0.70–0.81)	7.8	0.69	0.71

AET, acid exposure time; AUC, area under the receiver operating characteristic curve; 95% CI, 95% confidence interval; SLR, straight leg raise.

Table 4. Multivariable Analysis of Possible Predictors of AET >6%.

	Odds ratio (95% CI)	*P* value
IEM	1.55 (0.73–3.28)	.26
Δ 5-cm peak (units, 5)	1.62 (1.42–1.86)	<.001
EGJ-CI (units, 10)	0.87 (0.78–0.98)	.02
EGJ type 2	2.00 (1.04–3.84)	.04
EGJ type 3	4.26 (1.60–11.30)	.004

AET, acid exposure time; 95% CI, 95% confidence interval; EGJ, esophagogastric junction; IEM, ineffective esophageal motility.

Contrary to previous reports,[7] we show that the SLR maneuver has the capacity to identify pathologic GERD regardless of EGJ subtype. Our findings show the augmented value of interpreting HRM performed in the context of reflux monitoring, particularly if the SLR maneuver is performed as part of the protocol, because abnormal findings can provide further confidence in the clinical or pH impression of GERD.

Among all the analyzed interactions, we found that the increase in esophageal peak pressure between SLR and the resting phase had the best performance in identifying patients with AET greater than 6%. On ROC analysis, the optimal threshold of this pressure differential was 11 mm Hg, with impressive performance characteristics (AUC, 0.84; sensitivity, 79%; specificity, 85%). In their preliminary report, Rogers et al[7] also used the esophageal peak pressure gradient between baseline and SLR 5 cm above the LES, but the optimal cut-off value was set as 100% of the IEP gradient. The greater number of patients enrolled and the multicenter design of our study might explain the observed differences. Moreover, the delta increase of the IEP is easier to calculate, thus facilitating the implementation of this simple maneuver in the clinical setting. The threshold of 11 mm Hg might be used as a real-time tool to identify patients who may benefit from second-level pH or pH-impedance testing.

We noted significant differences in IAP during SLR between patients with pathologic and nonpathologic AET, and the higher IAP in GERD partly can be explained by the higher BMI in these patients. On the other hand, this association is consistent with the hypothesis that increased IAP is a risk factor for GERD. Baseline IGP may have influenced our results, so we measured delta IAP and IEP values to eliminate this potential bias. Intra-abdominal pressure did not augment in approximately 20% of patients who successfully performed the SLR maneuver, but no associations could be found for IAP augmentation or nonaugmentation during SLR. We speculate that raising both legs off the bed may raise the IAP more consistently, but this would make the SLR maneuver more difficult to perform; furthermore, a different threshold of IEP augmentation might apply.

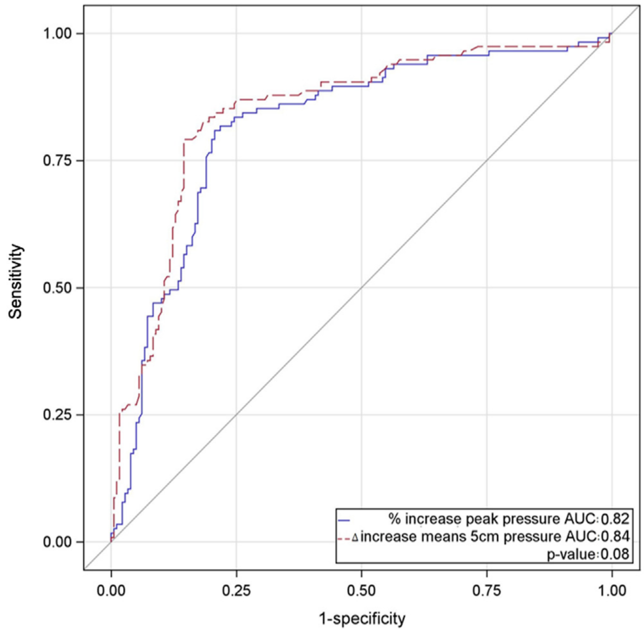

Figure 1. Receiver operating characteristic curve of the percentage increase in peak pressure and delta increase between esophageal pressure during straight leg raise and reference identification. AUC, area under the receiver operating characteristic curve.

Esophageal motility testing has been recommended in patients with symptomatic GERD to rule out major motility disorders, to complement the endoscopic and radiologic assessment of hiatal hernia, and to select the most appropriate ARS procedure based on the motility pattern, but HRM alone remains insufficient to diagnose GERD.[16,17] Although an abnormal AET is a predictor of treatment outcome, the quality of evidence is suboptimal, and increasing confidence in the presence of pathologic GERD will help with personalized patient care.[18] Because patients with persistent GERD symptoms undergo HRM as part of reflux monitoring for appropriate placement of pH and pH impedance probes, the HRM study is available for analysis in most of these instances. The inclusion of a simple provocative maneuver in the form of SLR could help to increase the diagnostic value of HRM by providing additional evidence for or against the presence of pressure metrics conducive to retrograde movement of gastric content. The combination of this parameter with low baseline impedance[19–21] measured at high-resolution impedance manometry or pH impedance monitoring may help refine the identification of patients with reflux and impaired mucosal integrity who could benefit from antireflux measures, including ARS.[22–24]

The major strengths of this study were the prospective design and the enrollment of patients from 12 different high-volume centers for esophageal disease. The fact that physiological variables known to be associated with pathologic AET (EGJ subtype, basal LES metrics, EGJ-CI, and IEM) also were shown in our study, provides further support that our patient cohort is representative of the symptomatic GERD population. Our study findings have to be tempered by a few limitations.

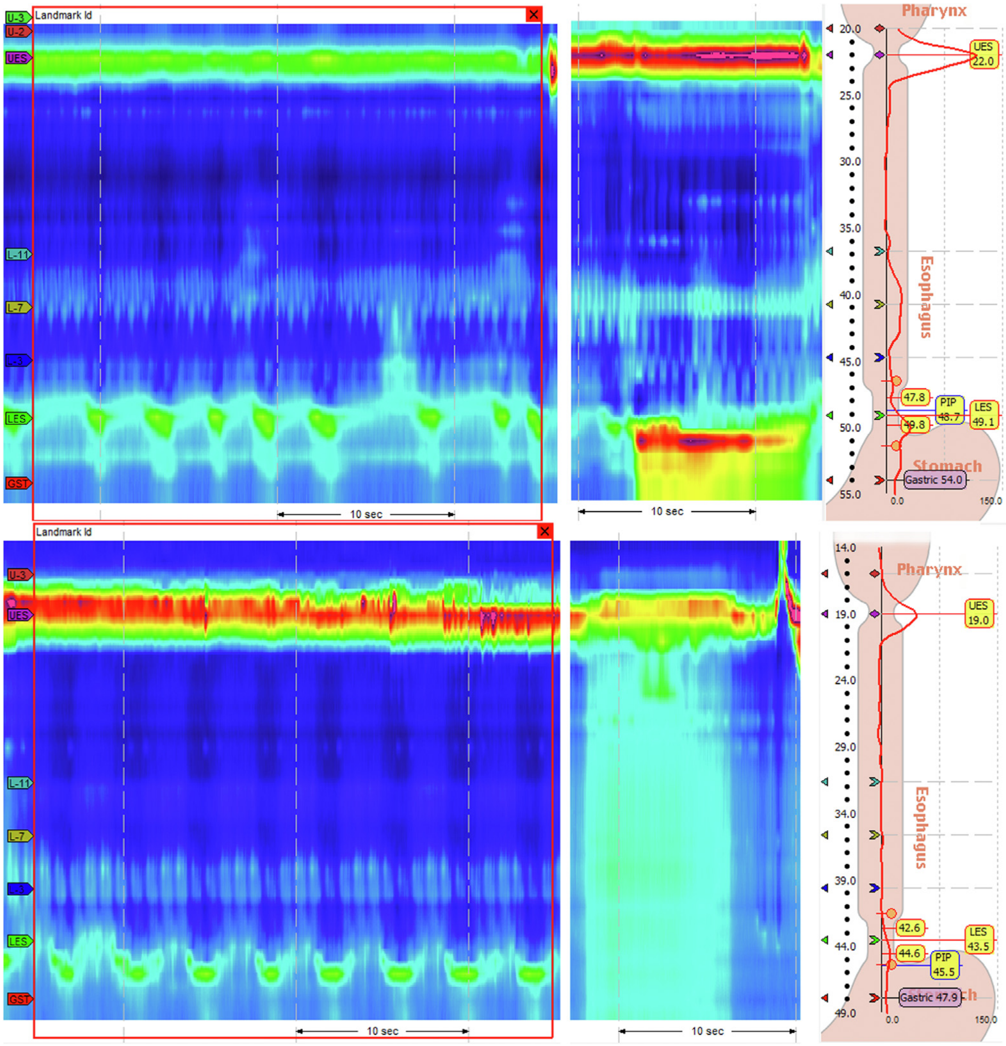

Figure 2. Lower esophageal sphincter (LES)/CD augmented pressure in a patient with a negative straight leg raise (SLR) maneuver (*upper plot*); the common cavity phenomenon is shown in a patient with a positive SLR maneuver (*lower plot*). Delta intraesophageal pressure and intra-abdominal pressure were calculated between the SLR maneuver and baseline reference identification. CD, crural diaphragm; GST, gastric; PIP, pressure inversion point; UES, upper esophageal sphincter.

First, 19% of our patients had a noneffective SLR maneuver, and further efforts to increase IAP (such as double leg raise) could have increased the number of patients with effective SLR. Second, we allowed various HRM and pH-impedance systems to be used depending on each institution's preference, which could have impacted some of the metrics, but available data indicate that AET, linear measurements, and pressure metrics (other than integrated relaxation pressure) generally are equivalent between manufacturers. Third, patients in the GERD group had a higher IAP increase during SLR, possibly owing to a higher median BMI. Fourth, we did not have a control group of asymptomatic volunteers, which could have added value to the study by determining normative SLR data. Finally, all centers participating in the study were tertiary care academic institutions, which could impact the generalizability of our findings to nonacademic environments.

Conclusions

A key concept emerging from the present study is that a simple HRM provocative test, the SLR maneuver, can increase the value of HRM performed in the context of symptomatic GERD.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2022.10.008.

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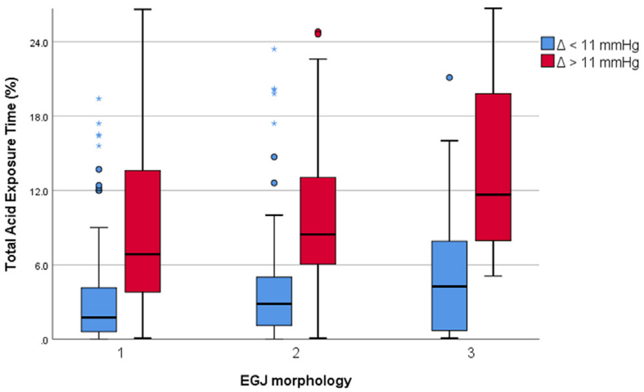
Conflicts of interest
The authors disclose no conflicts.

Data Sharing Statement
Individual participant data will not be shared.



Supplementary Figure 1. Efficacy of delta intraesophageal peak pressure cut-off value (11 mm Hg) in discriminating patients with gastroesophageal reflux disease based on esophagogastric junction (EGJ) morphology.

Supplementary Table 1. Comparison of Patient Characteristics Based on the Effectiveness of the SLR Maneuver

	Noneffective SLR- (n = 69)	Effective SLR+ (n = 295)	*P* value
Male, n (%)	22 (31.8)	134 (45.4)	.041
Age, *y*	51.0 [25.0]	49.5 [23.0]	.616
BMI, *kg/m*^{2}	24.7 [5.9]	24.8 [5.5]	.778
Symptom duration, *mo*	30.0 [72.0]	36.0 [48.0]	.943
Endoscopic findings			
Hiatal hernia, n (%)	38 (56.7)	150 (60.2)	.694
Barrett's esophagus, n (%)	3 (4.5)	8 (3.2)	.707
Esophagitis, n (%)	19 (28.4)	74 (30.1)	.747
EGJ type			.257
1, n (%)	44 (64.7)	158 (53.9)	
2, n (%)	16 (23.5)	94 (32.1)	
3, n (%)	8 (11.8)	41 (14.0)	
Hiatal hernia, n (%)	38 (54.4)	136 (46.6)	.195
EGJ contractile integral, *mm Hg*cm*	31.6 [41.0]	35.2 [42.5]	.115
Acid exposure total, %	3.8 [6.0]	4.1 [8.7]	.382
DeMeester score	12.1 [20.1]	16.2 [32.8]	.120

NOTE. Continuous values are expressed as median [interquartile range].
BMI, body mass index; EGJ, esophagogastric junction; SLR, straight leg raise.