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Manometric identikit of a functioning and effective fundoplication for gastroesophageal reflux disease in the high-resolution manometry ERA

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Abstract

Background: The pathophysiological and clinical value of performing High-Resolution Manometry (HRM) after laparoscopic fundoplication (LF) for gastroesophageal reflux disease (GERD) is still unclear and debated.

Objective: We sought to establish the HRM parameters indicative of functioning fundoplications, and whether HRM could distinguish them from tight or defective ones.

Methods: The study involved patients with GERD who underwent laparoscopic Nissen (LN) or Toupet (LT) fundoplication between 2010 and 2022. HRM and 24-h pH monitoring were performed before and 6 months after surgery. The study population was divided into 5 groups: LN and LT patients with normal 24h-pH findings (LNpH- and LTpH-, respectively); LN and LT patients with pathological 24h-pH findings (LNpH+ and LTpH + groups, respectively); and patients with a postoperative dysphagia intensity score >2 (Dysphagia group). The novel Hiatal Morphology (HM) classification was applied, envisaging 3 different subtypes: HM1 (normal), HM2 (intrathoracic fundoplication), and HM3 (slipped fundoplication).

Results: Among the 132 patients recruited during the study period, 46 were in the LNpH- group, 51 in the LTpH- group, 15 in the LNpH + group, 7 in the LTpH + group, and 5 in the Dysphagia group. In multivariate analysis, postoperative abdominal lower esophageal sphincter length ($p = 0.001$) and HM2 ($p < 0.001$) were both independently associated with surgical failure. Integrated relaxation pressure was significantly higher in the Dysphagia group than in the LNpH- group.

Renato Salvador and Giovanni Capovilla contributed equally to this study and therefore share the first authorship.

Conclusion: This study generated reference HRM values for an effective LF, and confirms that using HRM to assess the neo-sphincter and HM improves the clinical assessment in cases of symptom recurrence.

KEYWORDS
gastroesophageal reflux disease, laparoscopic fundoplication, manometry

INTRODUCTION

The introduction of laparoscopic fundoplication (LF) to treat gastroesophageal reflux disease (GERD) in 1991 gave patients a safe and effective alternative to medical treatment.[1–4] Several studies have demonstrated the effectiveness of LF in providing short- and long-term symptom relief not only for patients with typical reflux symptoms responding to proton pump inhibitors (PPI), but also in cases refractory to medical treatment or involving atypical symptoms.[5–9]

LF has been associated with various side effects, however, including dysphagia and dumping syndrome, which may reduce the effectiveness of surgery and patients' willingness to choose this treatment.[10–12] In a minority of cases, LF may also fail to achieve symptom relief or mucosal healing, so that patients have to continue medical treatment or undergo surgery again.[13,14] Understanding the reasons behind surgical failures and identifying predictors of a positive outcome after surgery have been the object of research for some time. Assessing patients following LF can be challenging. Endoscopy and barium swallowing can reveal anatomical abnormalities, but the functional information provided by pathophysiological testing—which can shed light on the cause of recurrent symptoms—could be key to clinical decision making. In the absence of evidence of pathological postoperative conditions, High-Resolution Manometry (HRM) might be appropriate for assessing and characterizing patients with a failed LF. The pathophysiological and clinical value of HRM performed after anti-reflux surgery remains unclear, however, and whether it could identify the causes of failure after LF is still debated.

The aims of this study were to establish an HRM manometric identikit for assessing how a fundoplication is functioning and to determine whether HRM can discriminate between well-functioning and tight or defective fundoplications.

MATERIAL AND METHODS

Patient population

We analyzed prospectively collected data on all patients who underwent LF for GERD at our Department between 2010 and 2022. The study included patients assessed with HRM before and after LF, and who underwent surgery according to SAGES and GISMAD guidelines.[15,16]

Key summary

- High-Resolution Manometry (HRM) is widely used in the pre-operative assessment of gastroesophageal reflux disease (GERD) patients; however, the pathophysiological and clinical value of performing HRM after laparoscopic fundoplication (LF) is still unclear and debated.
- This study generated reference HRM values for an effective LF.
- It confirms that using HRM to assess the abdominal portion of the neo-sphincter and an abnormal hiatal morphology (HM2—Intrathoracic fundoplication) improves the clinical assessment of recurrent symptoms and can distinguish patients with a well-functioning wrap from those developing recurrent GERD due to an ineffective wrap.

The exclusion criteria were:

- patients assessed with conventional manometry before and/or after surgery;
- patients who had previously been treated surgically or endoscopically for GERD;
- patients who had previously undergone upper GI surgery for other diseases;
- patients with a hiatal hernia >3 cm or a paraesophageal hernia prior to surgery;
- patients needing a mesh to reinforce the hiatoplasty during the surgical procedure;
- patients with connective tissue disease, diabetes, or other pathological conditions known to affect esophageal peristalsis (e.g., eosinophilic esophagitis).

This study has been performed in accordance with the Declaration of Helsinki and has been approved by the institutional board of our department. All patients gave informed consent for the work. The work has been reported in line with the STROCSS criteria.[17] The study is registered in researchregistry.com, where the research protocol can be accessed (unique identifying number: researchregistry9481).[18]

Preoperative assessment

Patients' clinical characteristics were recorded, including their response to previous medical treatment. GERD symptoms were recorded using the GerdQ questionnaire.[19] Postoperative dysphagia was assessed separately by combining the severity (0 = none, 2 = mild, 4 = moderate, 6 = severe) with its frequency (0 = never, 1 = occasionally, 2 = once a month, 3 = every week, 4 = twice a week, 5 = daily).

All patients were assessed preoperatively using endoscopy, barium swallow, HRM and 24-h pH monitoring.

High-Resolution Manometry and 24-h pH monitoring

HRM was performed before and 6 months after surgery using a catheter 4.2 mm in diameter with 36 solid-state circumferential sensors spaced at 1-cm intervals and spanning the entire esophagus (Medtronic). The manometric data were analyzed using ManoViewTM software (Medtronic). The HRM protocol has been described elsewhere.[16] Lower esophageal sphincter (LES) parameters (resting pressure, integrated relaxation pressure [IRP], total and abdominal length), and esophageal body function were reviewed by two experts (RS, GC) blinded to patients' surgical outcomes. A structurally defective LES was identified on the grounds of the HRM Rochester normal values for total and abdominal lengths and basal pressure.[20] The esophageal body findings were analyzed following the Chicago Classification v4.0.[21] Differences in postoperative HRM metrics between the groups were analyzed using the same blinded investigators and irrespective of any preoperative differences.

The novel HM classification was then applied. We considered 3 different subtypes following a previous publication by Hoshino[22]:

- **HM1 (Normal)**: a single distal esophageal High Pressure Zone (HPZ). The wrap, the native LES and the crura are in the same position as the Pressure Inversion Point (PIP) (Figure 1a);
- **HM2 (Intrathoracic fundoplication)**: the presence of a distinct double-hump configuration. The distal HPZ represents the crus and the proximal HPZ is the wrap around the native LES (Figure 1b). In this HM subtype, the distal HPZ does not relax during swallowing and respiratory variations are evident, while in the proximal HPZ, the relaxation of the sphincter is well-represented. In these cases, the PIP coincided with the distal HPZ.
- **HM3 (Slipped fundoplication)**: the presence of a distinct double-hump configuration. The native LES (proximal HPZ) migrates above the wrap (distal HPZ) (Figure 1c). In this type of HM, the fundoplication is slipped at the gastric body level and is represented by the distal HPZ. The distal HPZ does not relax and does not change according to respiratory variations, whereas the proximal HPZ relaxes during swallowing. The PIP is located above the distal HPZ.

Esophageal acid exposure was assessed using 24-h pH monitoring (Digitrapper, Medtronics). The procedure was performed in all patients at least 15 days after suspending any PPI, H2-blockers, or promotility agents. The test was used to identify any abnormal acid exposure by positioning an electrode 5 cm above the upper border of the LES according to the standard procedure adopted at our laboratory described elsewhere.[16,23,24]

Laparoscopic fundoplication technique

The surgical technique is described in detail elsewhere.[25] It involved reducing any hernia, primary closure of the crura with one or two stitches calibrated over a 40 French bougie, and a 360° fundoplication (Nissen, laparoscopic Nissen (LN)) sutured with three non-absorbable stitches, including the esophageal wall in the two distal sutures. Short gastric vessels were routinely divided to mobilize the gastric fundus and obtain a floppy, well-shaped fundoplication. A 270° partial fundoplication (Toupet, LT) was performed using three interrupted non-absorbable stitches for any gastric segment. The proximal sutures were used to anchor the stomach to the esophagus anteriorly and to the diaphragmatic crus laterally. The type of fundoplication (Nissen and Toupet) performed was not randomly chosen; a partial fundoplication was mainly performed in patients with an abnormal esophageal peristalsis.

Postoperative assessment

All consecutive patients were asked to submit to a post-LF assessment according to a standardized protocol adopted at our center for more than 30 years. The postoperative follow-up, routinely used at our Center, consisted of a barium swallow at one month after surgery and HRM and 24-h pH monitoring at 6 months after LF. At each visit, patients' GerdQ scores and any resumption of PPI therapy were recorded.

The study population was divided into 5 groups:

- LN patients with normal 24h-pH findings (LN pH−);
- LT patients with normal 24h-pH findings (LT pH−);
- LN patients with pathological 24h-pH findings (LN pH+);
- LT patients with pathological 24h-pH findings (LT pH+);
- patients with postoperative dysphagia scores >2 (Dysphagia group).

LF failure was defined as recurrent GERD symptoms (i.e., a GerdQ score ≥8)[21] with abnormal 24-h pH findings or just an abnormal 24-h pH monitoring.

Statistical analysis

Numerical data were summarized as medians and interquartile ranges, and categorical data as absolute frequencies (*n*) and relative frequencies (%). Continuous variables were compared with Student's

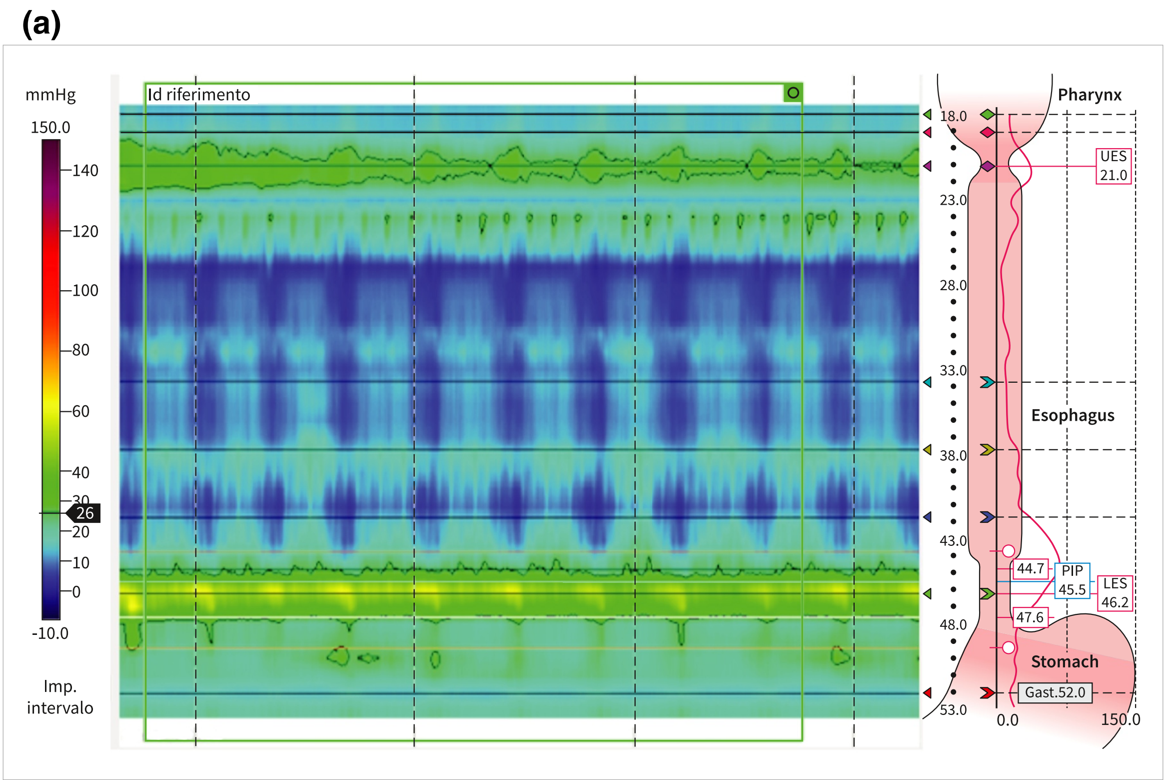

FIGURE 1 (a) HM1 (Normal): a single distal esophageal HPZ is evident, with the wrap, the native LES and the crura in the same position; (b) HM2 (Intrathoracic fundoplication): a distinct double-hump configuration is shown with the distal HPZ representing the crus and the proximal HPZ the wrap around the native LES; (c) HM3 (Slipped fundoplication): a distinct double-hump configuration is present with the native LES (proximal HPZ) which is migrated above the wrap (distal HPZ). HPZ, High-Pressure Zone; HM, Hiatal Morphology; LES, Lower esophageal sphincter.

t-test or the Mann–Whitney test, and categorical variables with the χ^2 or Fisher's exact test, as appropriate. A *p*-value lower than 0.05 was considered significant. All independent variables with associations of $p < 0.05$ at univariate analysis underwent multivariate analysis: logistic regression models were used to identify independent predictors of LF failure. Odds ratios with 95% confidence intervals were calculated. A probability of 5% was assumed to be statistically significant ($p = 0.05$). The statistical analysis was conducted using R 4.1 software (R Foundation for Statistical Computing).

RESULTS

Among the 525 patients who underwent LF in the study period, there were 132 patients treated with LF for GERD meeting the inclusion criteria (Figure 2): 93 males (70.5%), and 39 females (29.5%), with a median age of 49 (IQR: 42–60) years. The study population's demographic and preoperative clinical data are shown in Table 1. All patients had pathological 24-h pH findings before LF.

Fundoplication was completed laparoscopically in all cases and the 90-day postoperative mortality was nil. No major complications were detected (Clavier-Dindo grade 3 or 4).

During the follow-up, 115 patients had a GerdQ score <8 and 17 patients a GerdQ score ≥8. Five of the latter patients (5/132, 3%) had pathological symptom scores for dysphagia (Dysphagia group), and all of them had undergone a LN. Eight patients with recurrent GERD symptoms (GerdQ score ≥8) but normal 24h-pH findings were referred for gastroenterological evaluation and targeted treatments. Patients with a GerdQ score <8 and a normal postoperative pH monitoring were 97 (46 LN pH− patients and 51 LT pH− patients), while patients with abnormal postoperative pH monitoring, unregarding of the GerdQ score, were 22 (15 LN pH+ patients and 7 LT pH+ patients).

Nissen group (LN)

Table 2 summarizes the postoperative HRM findings in patients in the LN group. No significant associations emerged between the esophageal body HRM parameters and postoperative acid exposure. On the other hand, both total ($p = 0.03$) and intra-abdominal ($p < 0.001$) LES length, and LES resting pressure ($p = 0.03$) were significantly lower among patients with pathological postoperative acid exposure. EGJ morphology also differed among LN pH+ patients, with a significantly

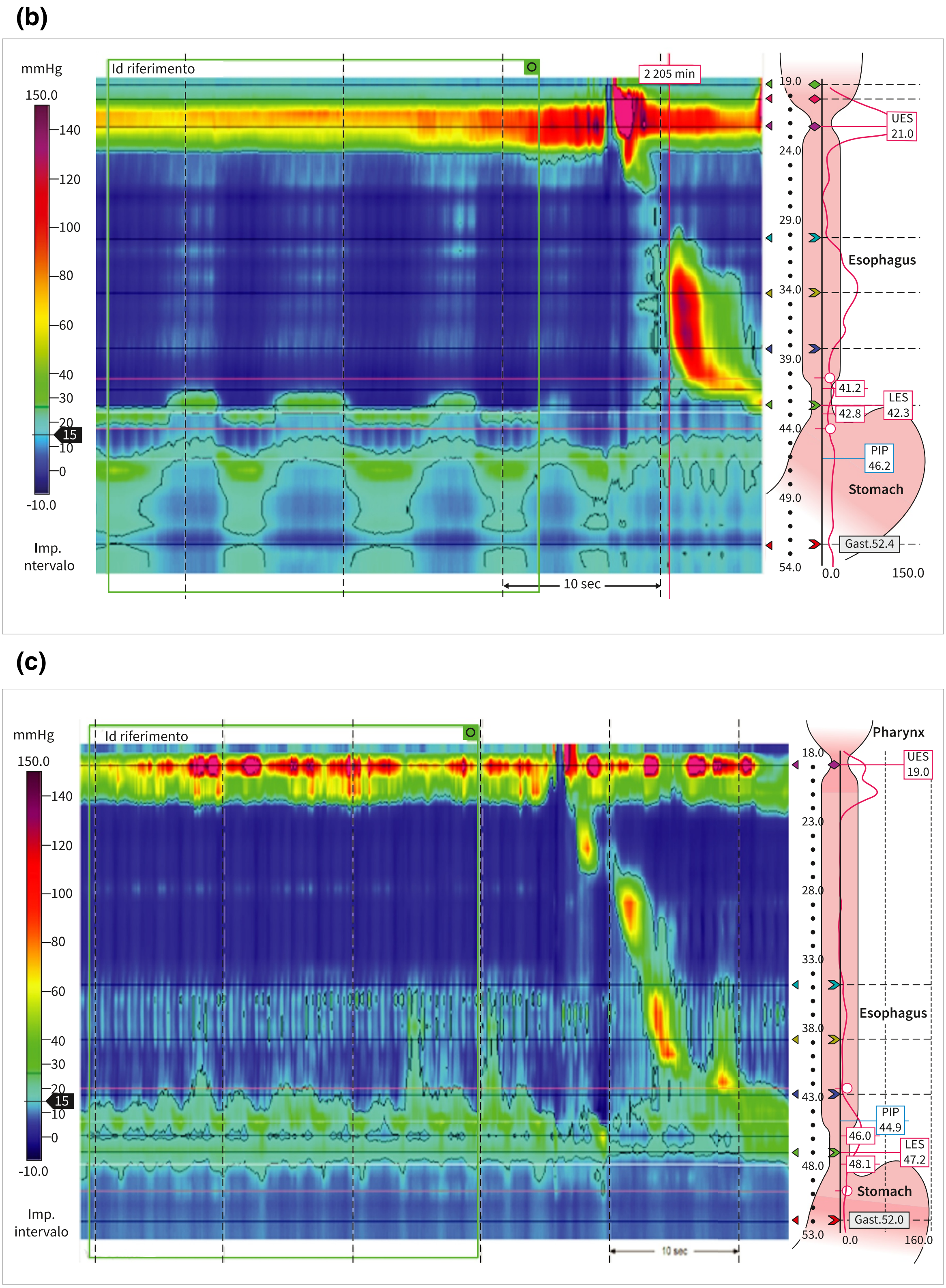

FIGURE 1 (Continued)

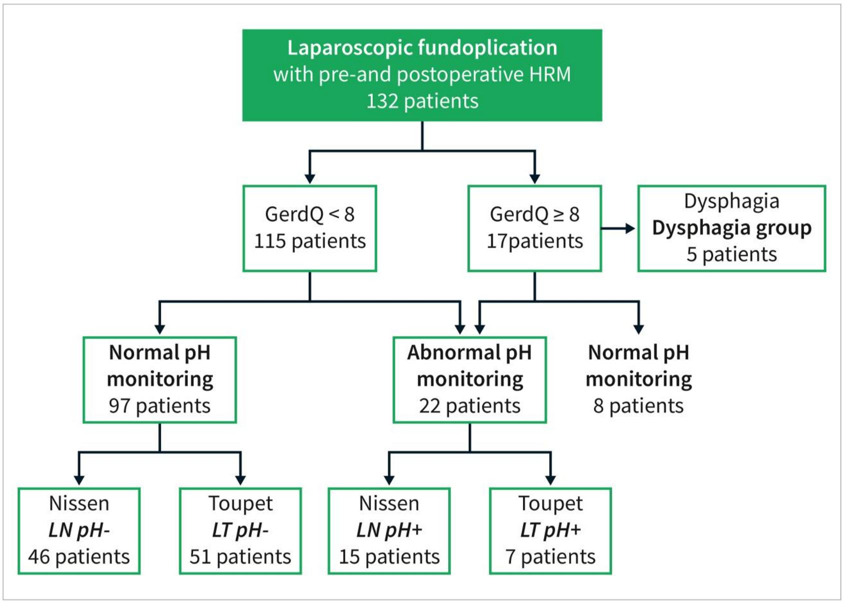

FIGURE 2 The flowchart of the patients' population.

TABLE 1 Preoperative demographic and clinical characteristics of patients.

Features	Nissen ($n = 71$)	Toupet ($n = 61$)	*p-value*
Sex (M/F)	52/19	41/20	0.57
Age*	48 (43–60)	53 (42–60)	0.72
BMI*	26.4 (23.7–28.2)	26.8 (24.6–28.5)	0.37
GerdQ score*	10 (8–14)	12 (9–15)	0.45
Coexistence of atypical symptoms	42 (59.2)	40 (65.6)	0.48
Esophagitis	49 (69)	45 (73.7)	0.57
Barrett's esophagus	14 (19.7)	7 (11.5)	0.24
PPI treatment:			
Clinical responder	46 (66.7)	36 (59)	0.71
Clinical non-responder/partial-responder	23 (33.3)	22 (41)	
Hiatal hernia	46 (64.8)	39 (64)	0.99
Pathological 24-h pH testing	71 (100)	61 (100)	1.00
DM score*	36.0 (28.4–64.1)	30.4 (21.4–54.4)	0.76
Esophageal motility:			
Normal	59 (83.1)	39 (64)	**0.03**
IEM	11 (15.5)	18 (29.5)	
DES	1 (1.4)	4 (6.5)	

Note: Data expressed as *n* (%) or as a *median (IQR). Significant *p*-values are shown in bold.
Abbreviations: BMI, body mass index; DES, distal esophageal spasm; DM, DeMeester; IEM, ineffective esophageal motility; PPI, proton pump inhibitor.

higher proportion of them showing manometric signs of intrathoracically displaced (HM2) or slipped (HM3) fundoplications ($p = 0.001$) (Table 3). All patients who showed an abnormal EGJ morphology underwent endoscopy and barium swallow that confirmed the manometric finding (HM2/HM3). Only three of these patients required revisional surgery.

Toupet group (LT)

The postoperative HRM findings in the LT group are shown in Table 2. Patients with a pathological postoperative acid exposure tended to have a weaker esophageal body motility, as shown by a lower distal contractile integral (DCI) ($p = 0.06$) and a higher

TABLE 2 The postoperative HRM parameters in all groups.

Postoperative HRM parameters	LN pH− (n = 46)	LN pH+ (n = 15)	*p-value* LN pH− versus LN pH+	LT pH− (n = 51)	LT pH+ (n = 7)	*p-value* LT pH− versus LT pH+	*p-value* LN pH− versus LT pH−	Dysphagia (n = 5)	*p-value* LN pH− versus dysphagia
Lower esophageal neo-sphincter									
LES resting pressure (mmHg)	25.8 (8–47.8)	17.4 (5.2–36.3)	0.03	18.9 (9.8–37.6)	12.9 (1.7–24)	0.06	0.02	34.5 (26.4–60.5)	0.06
LES total length (mm)	32 (17–49)	23 (17–41.9)	**0.03**	29 (18–45.9)	21 (15.5–46.2)	0.06	0.16	48 (18–49)	0.49
LES abdominal length (mm)	17 (8–35)	0 (0–14.8)	**<0.001**	17 (3–30.6)	0 (0–8.5)	**<0.001**	0.99	16 (6–18)	0.53
IRP (mmHg)	11.2 (2.5–19)	10.6 (2.8–26)	0.60	8.4 (1.9–17.3)	5.4 (0.9–12.8)	0.11	**0.004**	19,3 (17.5–26.4)	**0.001**
Esophageal body									
% Normal contraction	90 (30–100)	100 (0–100)	0.73	90 (35–100)	35 (0–100)	0.10	0.30	100 (100–100)	0.42
% Premature swallows	0 (0–20)	0 (0–32)	0.62	0 (0–26.5)	15 (0–85)	0.78	0.88	0 (0–0)	0.90
% Failed swallows	0 (0–50)	0 (0–34.5)	0.45	0 (0–40)	10 (5–30)	0.08	0.91	0 (0–0)	0.11
% Ineffective swallows	0 (0–20)	0 (0–86)	0.58	0 (0–66.5)	0 (0–80)	0.53	0.49	0 (0–0)	0.62
DCI (mmHg*cm*s)	1014.1 (252.6–2552.1)	708.5 (115–2552.4)	0.10	718.6 (189.7–3462.8)	263.7 (140.9–852.0)	0.06	**0.04**	2042.5 (1973–2818.6)	0.06

Note: Data are expressed as median (5th percentile—95th percentile). Significant p-values are shown in bold.

Abbreviations: DCI, distal contractile integral; HRM, high-resolution manometry; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; LN, laparoscopic Nissen; LT, laparoscopic Toupet.

TABLE 3 Analysis of the postoperative hiatal morphology in patients who underwent LF in all groups.

Hiatal morphology	LN pH− ($n = 46$)	LN pH+ ($n = 15$)	*p-value* LN pH− versus LN pH+	LT pH− ($n = 51$)	LT pH+ ($n = 7$)	*p-value* LT pH− versus LT pH+
HM1	40	6	**0.001**	50	3	**<0.001**
Normal fundoplication	(86.9)	(40)		(98)	(42.9)	
HM2	5	8		1	4	
Intrathoracic fundoplication	(10.9)	(53.3)		(2)	(57.1)	
HM3	1	1		0	0	
Slipped fundoplication	(2.2)	(6.7)		(0)	(0)	

Note: Data are expressed as *n* (%). Significant *p*-values are shown in bold.

Abbreviations: HM, hiatal morphology; LN, laparoscopic Nissen; LT, laparoscopic Toupet.

percentage of failed swallows ($p = 0.08$). Total LES length and resting pressure were also reduced among LT pH+ patients, though not significantly so ($p = 0.06$), while abdominal LES length was significantly shorter ($p < 0.001$). A postoperative manometric EGJ pattern showing intrathoracic fundoplication (HM2) was significantly associated with postoperative reflux ($p < 0.01$) (Table 3). All patients who showed a manometric HM2 morphology underwent endoscopy and barium swallow that confirmed the finding. Revisional surgery was deemed necessary only in 1 patient for recurrent esophagitis.

Nissen versus toupet (LN vs. LT)

Normal postoperative HRM findings after complete and partial fundoplication are compared in Table 2. The DCI was significantly higher after LN ($p = 0.04$). No other differences emerged for the esophageal body motility parameters. LES resting pressure ($p = 0.02$) and residual pressure ($p = 0.004$) were also significantly higher in the LN group.

Dysphagia group

The postoperative HRM parameters for the five patients with clinically significant dysphagia at follow-up are shown in Table 2 and compared with those of patients in the LN pH− group. The postoperative IRP was significantly higher in this group ($p = 0.001$), while the LES basal pressure was also increased, but not to a significant degree ($p = 0.06$).

Predictors of surgical failure

At univariate analysis (Table 4), the only preoperative manometric variables showing an association with the failure of antireflux surgery were the percentages of normal contractions ($p = 0.011$) and ineffective swallows ($p < 0.001$). No independent association emerged between preoperative manometric measurements and LF failure in multivariate analysis.

After LF, the LES basal pressure ($p = 0.011$), the total and abdominal LES length ($p = 0.014$, $p < 0.001$), and the percentages of normal contractions and ineffective swallows ($p = 0.019$, $p = 0.001$) all correlated with LF failure at univariate analysis. The manometric configuration according to the new HM classification also correlated with the surgical outcome. There was a significantly higher proportion of patients classified as HM2 in the failed LF group (54.5% vs. 6.2%, $p < 0.001$). At multivariate analysis (Table 5), abdominal LES length ($p = 0.001$) and the HM2 configuration ($p < 0.001$) were both independently associated with surgical failure.

DISCUSSION

The clinical role of HRM after antireflux procedures is a matter of debate. HRM is widely used to identify the LES when positioning catheters for 24-h pH monitoring to assess patients with persistent or recurrent symptoms after surgery. However, whether it can shed light on the causes of LF failure, and thereby contribute to clinical decision making is still unclear. Hence, our aim was to determine if HRM can reveal a HM and other parameters to adopt as a manometric identikit of a functioning LF and to discriminate between effective and defective or tight fundoplications.

This study describes one of the largest cohorts, offering a reference set of postoperative manometric data obtained in patients who underwent complete or partial fundoplication (Table 6). In addition, our findings uniquely identify the manometric parameters and HM associated with recurrent GERD after LN and LT fundoplication.

There is a paucity of reference parameters for the postoperative status of the esophageal body and EGJ, which limits the diagnostic potential of HRM in this setting. In a recent retrospective chart review of postoperative HRM studies on patients who underwent LN or LT, Müller et al.[26] produced a set of normal values derived from 33 post-Nissen and 17 post-Toupet patients with no clinical or functional signs of wrap failure. The authors reported no differences in LES parameters (total length, resting pressure and IRP) between partial and complete fundoplications, but the limited size of the LT group probably influenced their results. Our study included 46 LN and 51 LT patients with clinically and functionally effective

TABLE 4 The univariate analysis of patients who had a good outcome versus the failures.

HRM parameters	Good outcome	Failure	*p*-value
Preoperative			
LES resting pressure (mmHg)	16.70 (10.6–22.6)	14.60 (4.95–19.8)	0.210
LES total length (mm)	24.00 (18–31)	22.00 (21–24.5)	0.384
LES abdominal length (mm)	2 (0–15)	0 (0–9)	0.298
IRP (mmHg)	4.9 (2.6–7)	3.5 (2.3–6.1)	0.364
% Normal contraction	90 (55–100)	60 (7.5–92.5)	0.011
% Premature swallows	0 (0–0)	0 (0–0)	0.597
% Failed swallows	0 (0–0)	0 (0–0)	0.663
% Ineffective swallows	0 (0–0)	25 (0–72.5)	<0.001
DCI (mmHg*cm*s)	666.3 (433.4–1169.4)	426.9 (232.6–805.3)	0.174
Postoperative			
Type of fundoplication (Nissen/Toupet)	46/51	15/7	0.08
LES resting pressure (mmHg)	22.4 (18–29)	17 (12.1–21.1)	0.011
LES total length (mm)	31 (24–37)	21 (18–31.5)	0.014
LES abdominal length (mm)	17 (10–23)	0 (0–6.5)	<0.001
IRP (mmHg)	9.6 (5.9–12.7)	9.6 (4.9–12.5)	0.687
% Normal contraction	90 (80–100)	90 (10–100)	0.019
% Premature swallows	0 (0–0)	0 (0–0)	0.990
% Failed swallows	0 (0–10)	0 (0–17.5)	0.799
% Ineffective swallows	0 (0–0)	0 (0–42.5)	0.001
DCI (mmHg*cm*s)	899.9 (574.2–1551.7)	800.5 (159.1–927.9)	0.106
Hiatal morphology			
HM1	90 (92.8)	9 (40.9)	<0.001
HM2	6 (6.2)	12 (54.5)	
HM3	1 (1)	1 (4.5)	

Note: Data expressed as median (IQR).

Abbreviations: DCI, distal contractile integral; HM, hiatal morphology; HRM, high-resolution manometry; IRP, integrated relaxation pressure; LES, lower esophageal sphincter.

fundoplications, providing a representative set of postoperative HRM findings for both surgical procedures (Table 6). We detected significantly greater increases in LES resting pressure and IRP after complete fundoplications than after partial ones, with a comparable length of the HPZ. Our data are consistent with the long-term results of a Nissen versus Toupet randomized controlled trial published by Strate et al.,[27] in which the postoperative LES pressure was significantly higher after LN than after LT, while the intra-abdominal LES length was similar. More recently, Weijenborg et al.[28] published a set of normal postoperative HRM values derived from 20 LT to 20 LN patients, all asymptomatic, assessed using HRM. The authors reported post-Toupet parameters similar to those obtained in the healthy individuals used for the Chicago classification. As in our study, they found that the IRP and LES resting pressure were significantly higher after LN, while the total and abdominal LES lengths were similar after the two procedures.

Two main mechanisms can impair the functioning of the "new EGJ" after LF: (i) an inadequate wrap may be an inefficient barrier to reflux, resulting in recurrent GERD; or (ii) a tight fundoplication might result in postoperative dysphagia.

In our study, the length of the abdominal portion of the new LES and manometric signs of an intrathoracically displaced fundoplication (HM2) seemed to have the strongest association with recurrent GERD after LF.

In a landmark study from 2010, Tatum et al.[29] characterized the postoperative manometric elements associated with failure of LF in 23 patients with GERD symptoms and/or abnormal 24h-pH monitoring findings after a Nissen fundoplication. The authors also reported that the mean LES pressure tended to be lower in patients whose surgery failed. While they found no significant differences in the length of the HPZ, they did report an association between the postoperative finding of a dual HPZ and surgical failure. In a

TABLE 5 Multivariate analysis of risk factors for failure after laparoscopic fundoplication (LF).

Postoperative HRM parameters	ODDS-RATIO	95% CI	*p-value*
LES resting pressure	1.017	0.93–1.10	0.68
LES total length	1.013	0.92–1.01	0.78
LES abdominal length	***1.211***	***1.05–1.35***	***0.001***
% Normal contraction	0.993	0.97–1.02	0.58
% Ineffective swallows	1.013	0.97–1.05	0.54
HRM hiatal morphology:			
HM2 versus *HM1*	***17.021***	***3.19–90.96***	***<0.001***
HM3 versus HM1	0.049	0.05–27.61	0.93

Note: Significant values are shown in bold.
Abbreviaitons: HM, hiatal morphology; HRM, high-resolution manometry; LES, lower esophageal sphincter.

TABLE 6 Postoperative high-resolution manometry reference values for a functioning and effective fundoplication.

Postoperative HRM parameters	LN pH− (*n* = 46)	LT pH− (*n* = 51)
Lower esophageal neo-sphincter		
LES resting pressure (mmHg)	25.8 (8–47.8)	18.9 (9.8–37.6)
LES total length (mm)	32 (17–49)	29 (18–45.9)
LES abdominal length (mm)	17 (8–35)	17 (3–30.6)
IRP (mmHg)	11.2 (2.5–19)	8.4 (1.9–17.3)
Esophageal body		
% peristaltic swallows	90 (30–100)	90 (35–100)
% premature swallows	0 (0–20)	0 (0–26.5)
% failed swallows	0 (0–50)	0 (0–40)
% ineffective swallows	0 (0–20)	0 (0–66.5)
DCI (mmHg*cm*s)	1014.1 (252.6–2552.1)	718.6 (189.7–3462.8)

Note: Data are expressed as median (5th percentile—95th percentile).
Abbreviations: DCI, distal contractile integral; HRM, high-resolution manometry; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; LN, laparoscopic Nissen; LT, laparoscopic Toupet.

subsequent study by Hoshino et al.,[22] a double HPZ configuration was confirmed to correlate with endoscopic evidence of a slipped or intrathoracic fundoplication. In a more recent study by the same group,[30] only symptomatic post-Nissen patients with no endoscopic signs of anatomical failure (slippage, intrathoracic fundoplication, etc.) were considered; they found no association between the HRM parameters and any recurrence of GERD symptoms. Taken together, our data confirm that a shorter abdominal length of the new HPZ and a dual HPZ configuration of the EGJ are the two strongest post-operative predictors of an ineffective fundoplication. Therefore, the main mechanism related to recurrent GERD after LF is probably not a loss of function of the wrap per se but anatomical failure in the form of a slippage or intrathoracic displacement of the fundoplication.

Our cohort included a group of patients with dysphagia after LF. Since they had all undergone a complete fundoplication, the LN pH-group was chosen as a control. The IRP was the only variable significantly correlating with postoperative dysphagia, a finding in line with the report from Myers et al.[31] of a significant association between post-fundoplication dysphagia and a higher residual EGJ pressure, as measured by conventional water-perfused sleeve manometry. The same results were replicated using HRM (a Mano-view system) by Marjoux et al.[32], who compared the postoperative manometric findings in 8 dysphagic and 12 asymptomatic patients after LN-Rossetti and found that IRP was the only variable significantly correlating with the onset of dysphagia.

In our study, the LES resting pressure was higher among dysphagic patients compared to the LN pH− controls, even if we did not reach statistical significance. This may be due to the small sample size of the Dysphagia group.

A higher LES resting pressure in post-fundoplication patients with dysphagia was also recorded by the Rochester group[33] and by Yamamoto et al. with the Sandhill device.[30] Even in these studies, the difference was not statistically significant, but this was probably due to the small number of patients with post-surgical dysphagia in all cohorts. Moreover, the same groups also found the IRP and the Intrabolus pressure,[33] and the IRP and the length of the HPZ[27] to be significantly associated with dysphagia.

Taken together, these findings confirm that hiatal flow resistance secondary to a tight fundoplication or crura closure could be the main mechanism associated with the postoperative onset of dysphagia.

Some limitations of our study should be acknowledged. First, there is a rather limited sample size, especially in the Dysphagia group. Further studies, possibly with a prospective multicentric design, are needed to assess the role of HRM in the diagnosis of failed LF. Second, the choice of the type of fundoplication (Toupet vs. Nissen) was not random or well codified, but left to the judgment of the surgeon based on the presence of abnormal peristalsis or not at HRM. Finally, our follow-up protocol did not include endoscopy or barium swallow at the same time as HRM, so no correlations could be drawn between patients' manometric and anatomical findings.

CONCLUSION

In conclusion, this is one of the first studies providing a set of reference values for HRM in a functioning Nissen and Toupet fundoplication. Moreover, different from previous investigations, our study identified the intra-abdominal LES length and the postoperative hiatal morphology (HM2—Intrathoracic fundoplication) to be independent predictors of the effectiveness of the wrap. The reported data are clinically applicable and can guide the clinical decision making in these challenging clinical scenarios. Postoperative IRP also correlated significantly with the onset of dysphagia after the procedure.

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CONFLICT OF INTEREST STATEMENT

RS, GC, MS, AV, FF, LP, LN, AC, LM, MV, MC: none. Edoardo Vincenzo Savarino has served: as a speaker for Abbvie, Agave, AGPharma, Alfasigma, Aurora Pharma, CaDiGroup, Celltrion, Dr Falk, EG Stada Group, Fenix Pharma, Fresenius Kabi, Galapagos, Janssen, JB Pharmaceuticals, Innovamedica/Adacyte, Malesci, Mayoly Biohealth, Omega Pharma, Pfizer, Reckitt Benckiser, Sandoz, SILA, Sofar, Takeda, Tillots, Unifarco; as a consultant for Abbvie, Agave, Alfasigma, Biogen, Bristol-Myers Squibb, Celltrion, Diadema Farmaceutici, Dr. Falk, Fenix Pharma, Fresenius Kabi, Janssen, JB Pharmaceuticals, Merck & Co, Nestlè, Reckitt Benckiser, Regeneron, Sanofi, SILA, Sofar, Synformulas GmbH, Takeda, Unifarco; and he received research support from Pfizer, Reckitt Benckiser, SILA, Sofar, Unifarco, and Zeta Farmaceutici.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not applicable.

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