Management of Gastric Reflux Following Per-Oral Endoscopic Myotomy

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Introduction

The current most effective treatments for achalasia aim at relieving the obstruction at the lower esophageal sphincter by destruction. The fact that the normal physiological functions of the lower esophageal sphincter and the esophagus are not restored sometimes shifts the problem from "no flow" to "backflow." In some patients, the reflux symptoms can be as debilitating as the achalasia itself, and in those without symptoms, there would still be a concern of transformation into Barrett's esophagus or beyond if left untreated.

Heller myotomy was considered the gold standard treatment for years. It achieves good efficacy without the need of repeated procedures, and laparoscopic approach soon took over the thoracoscopic approach after it was introduced for its superiority in many outcome parameters [1]. For decades, surgeons struggled to balance between the treatment of dysphagia and the consequence of gastroesophageal reflux disease (GERD). Coexisting fundoplication was found to decrease the chance of reflux [2], although not completely. After further studies, we now come closest to the equilibrium between dysphagia and reflux with the concurrent use of laparoscopic Heller myotomy and partial fundoplication.

Per-oral endoscopic myotomy (POEM) utilizes an endoscopic submucosal approach to cut the circular fibers of the lower esophageal sphincter, while leaving the longitudinal fibers and peritoneal attachments intact. Given the minimal disruption of surrounding components of the anti-reflux mechanism within the esophagogastric complex, POEM is commonly performed without a concomitant anti-reflux procedure.

Gastroesophageal reflux is one of the more common challenges physicians encounter in the long-term follow-up of POEM procedures. While we are seeing a

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comparable therapeutic efficacy between POEM and the traditional Heller myotomy with partial fundoplication, it is important to understand how POEM manifests in terms of gastric regurgitation without fundoplication. This chapter outlines the current updates on what is known about gastroesophageal reflux after per-oral endoscopic myotomy.

Reflux After POEM: How Common Is It?

The report of initial experience by Inoue et al. [3] described a very low rate of reflux symptoms after POEM (1 out of 17 patients) with great treatment efficacy. This has drawn much attention to investigate the actual incidence of reflux for comparison with the other treatment modalities, although a conclusive prevalence is not well-defined yet.

Multi-year follow-up with patients undergoing POEM is now being reported since clinical application of this technique began in Japan in 2008. Initial reports of longer-term follow-up by Inoue et al. [4] (105 patients in a single-center with follow-up periods of 36 months), Werner et al. [5] (a multi-center report of 80 cases with at least 2 years of follow-up), and Chen et al. [6] (45 patients in a single-center with follow-up periods of 24 months) have included that.

Reported incidence of GERD after POEM differs, depending on whether one defines it by symptom, endoscopic finding, or objective pH study. In many different reported series, symptom assessments were noted, along with reporting of esophagitis upon surveillance endoscopy. Formal pH study was performed in several centers, revealing the occurrence of reflux in the asymptomatic patients as well.

Reflux Symptoms

Presence of reflux symptoms can be defined by the presence of an isolated symptom, or more standardized using structured questionnaires. A common questionnaire used among the literature when reporting post-POEM reflux is GerdQ score [7], which is a screening test with scoring based on the presence and frequency of symptoms within the period of 7 days. It sets a cut-off score to predict whether the subject has any gastroesophageal reflux. Those with frequent and only heartburn and regurgitation without symptoms of nausea or epigastric pain would score the highest. Incidence of GERD symptoms ranges from 0 to 42% (Table 13.1), with most reports from 14 to 22%, including that of a 500-patient series [4]. In general, the rates of complete symptom assessment were quite good, with a majority of the reports having had assessed symptoms in more than 85% of their patients. Of those who used GerdQ score equal to or greater than seven as their criteria for positive reflux symptoms, the incidence lies at around 15% [8, 9]. The frequency of reflux symptoms was stratified in some reports, and 1.5–8.2% of them reported reflux symptoms on a daily basis [5, 10, 11]. For the longer-term reports, Inoue reported that 21.3% of the interviewed patients had reflux symptoms at 36 months after

Table 13.1 Reported incidence of reflux symptoms

Author	Year of publication	Location	Number of cases reported	Time point after POEM in months	Percentage of patients with symptoms assessed	Percentage of those assessed with GERD symptom	Definition of having GERD symptom
Familiari	2016	Rome, Italy	149	Mean of 7.6 ± 3.6	69%	18.4%	/
Shiwaku	2016	Fukuoka, Japan	100	3	100%	9.0%	FSSG
Chen	2015	Shanghai, China	26	Mean of 24.6	100%	14.8%	/
Inoue	2015	Yokohama, Japan	500	2 (n = 500)	85%	16.8%	/
			370	12–24 (n = 370)	78%	19.4%	
			105	36 (n = 105)	58%	21.3%	
Ramchandani	2015	Hyderabad, India	102	12	100%	21.6%	/
Werner	2015	International multicenter	85	3–6	93%	24.1%	Presence of heartburn
				12–18	89%	31.6%	
				>24 (mean 29)	86%	37.0%	
Ling	2014	Nanjing, China	87	3	100%	10.3%	/
Stavropoulos	2014	Mineola, New York, US		Mean of 13.3		32% (daily 3%, few times per week 13%, few times per months 16%)	/
Teitelbaum	2014	Chicago, Illinois, US	41	12	95%	14.6%	GERDQ score > 7
Li	2013	Shanghai, China	234	12	94%	16.7%	GERDQ score > =7

(continued)

Table 13.1 (continued)

Author	Year of publication	Location	Number of cases reported	Time point after POEM in months	Percentage of patients with symptoms assessed	Percentage of those assessed with GERD symptom	Definition of having GERD symptom
von Renteln	2013	European MCT	70	3	100%	32.8% (daily 1.5%, occasionally 31.3%)	/
			61	6		30% (daily 6.6% daily, occasionally 23.4%)	
			51	12		37.2% (daily 7.8%, occasionally 29.4%)	
Chiu	2013	Hong Kong, China	16	3	100%	6.3%	/
Minami	2013	Nagasaki, Japan	28	Median of 16	100%	21.4%	/
Verlaan	2013	Amsterdam, Netherlands	10	3	100%	30.0%	/
Swanstrom	2012	Portland, Oregon, US	18	6	100%	44% (daily 11.1%, occasionally 16.7%, rarely 16.7%)	/
von Renteln	2012	Hamburg, Frankfurt	16	3	100%	0.0%	/

POEM [4], while 37.0% of those in the centers reported by Werner at 24 months or beyond (8.2% with daily symptoms) [5].

Endoscopic Evidence of Reflux

Esophagitis found upon endoscopy is an objective indication of the likely presence of reflux, but endoscopy is not routinely performed in all centers that have reported their series. Stratification of severity in esophagitis is mostly reported using the Los Angeles classification of esophagitis [12].

Rate of esophagitis seen upon endoscopy had a larger variation compared with rate of symptoms, ranging from 6.3 to 64.7% (Table 13.2). The proportion of studied patients who received an endoscopy also varies quite significantly from 10 to 100%. Series with a lower endoscopy surveillance rate often report a higher incidence of esophagitis, likely due to selection bias. Studies with less than 60% of the studied patients having had endoscopy all reported an incidence of over 50% [4, 8, 13]. The incidence in the remaining reports still varies significantly, but most reports lie within 20–42%.

As in primary GERD, discordance between the rates of reflux symptoms and endoscopic evidence of reflux disease exists. Presence of symptoms has low sensitivity in predicting the presence of mucosal damage. As many as 88.9% of patients with esophagitis of Los Angeles Classification grade A or above can be asymptomatic, as reported by Shiwaku et al. [14] Some groups also reported a rate of 10% to almost 70% of asymptomatic patients having esophagitis (Table 13.2). Since longstanding esophagitis left untreated may lead to severe consequences, many authors advocate regular endoscopic surveillance to facilitate timely intervention.

Objective Studies on Reflux

Gastroesophageal reflux disease can also be objectively diagnosed using pH studies. Overall, the rate of an abnormal pH study generally ranges from 20.2% [15] to 57.7% [16], excluding one series in which pH testing was only provided for a single patient who had reflux symptoms registering 13.4% total time with esophageal acid exposure [17]. Assessing reflux with pH testing provides reliable objective data; however, diagnosing GERD with such a singular test may also lack standardization with the presence of different measurement methods and parameters.

In the literature, both 24-h probe-based monitoring and more prolonged monitoring using wireless capsules are used in different centers, some even within the same center (Table 13.3). Prolonged pH studies with wireless capsules are shown to be more sensitive in detecting pathological esophageal acid exposure and positive symptom association [18, 19]. Different normative values of percentage of total time of abnormal esophageal acid exposure for the wireless capsule system, ranging from 4.4 to 5.3%, have been reported [19, 20], which are slightly higher than the most referenced 4.2% for probe-based monitoring [21].

Table 13.2 Reported incidence of esophagitis

Author	Year of publication	Location	Number of cases reported	Time point after POEM in months	Percentage of studied patients that received endoscopy	Percentage of endoscopy done having esophagitis	LA Grade A	LA Grade B	LA Grade C	LA Grade D	Percentage of patients with esophagitis having symptoms
Familiari	2016	Rome, Italy	149	Mean of 7.6 ± 3.6 months	69%	20.4%	8.7%	5.8%	4.9%	1.0%	42.8%
Chen	2015	Shanghai, China	26	Mean of 24.6	100%	11.5%	0.0%	11.5%		0.0%	66.7%
Inoue	2015	Yokohama, Japan	500	2 (n = 500)	83%	64.7%	33.8%	25.8%	4.8%	0.2%	–
			370	12–24 (n = 370)	52%	59.2%	35.6%	13.1%	7.9%	2.6%	
			105	36 (n = 105)	15%	56.3%	43.8%	6.3%	6.3%	0.0%	
Ramchandani	2015	Hyderabad, India	102	12	82%	16.6%	12.0%	4.8%	0.0%	0.0%	–
Sharata	2015	Portland, Oregon, US	100	Mean of 21.5	73%	27.4%	20.5%	4.1%	2.7%	0.0%	–
Shiwaku	2015	Fukuoka, Japan	70	3	100%	64.0%	48.6%	5.7%	10.0%	0.0%	11.1%
Werner	2015	International MCT	85	3–6	80%	36.8%	20.6%	16.2%	0.0%	0.0%	–
				12–18	85%	37.5%	20.8%	12.5%	2.8%	0.0%	
Ling	2014	Nanjing, China	87	3	10%	55.6%	33.3%	22.2%	0.0%	0.0%	Only symptomatic patients had endoscopy

Stavropoulos	2014	Mineola, New York, US		Mean of 13.3	53%	32.1%	–	–	–	–	–
Teitelbaum	2014	Chicago, Illinois, US	41	12	54%	59.0%	50.0%	0.0%	0.0%	9.0%	30.8%
Li	2013	Shanghai, China	234	12	100%	8.5%	–	–	–	–	90.0%
Minami	2013	Nagasaki, Japan	28	Median of 16	100%	39.3%	25.0%	3.6%	3.6%	0.0%	–
Verlaan	2013	Amsterdam, Netherlands	10	3	100%	60.0%	30.0%	30.0%	0.0%	0.0%	50.0%
von Renteln	2013	European MCT	70	3	–	42.0%	29.2%	12.3%	0.0%	0.0%	–
von Renteln	2012	Hamburg, Frankfurt	16	3	100%	6.3%	6.3%	0.0%	0.0%	0.0%	–

Table 13.3 Reported incidence of esophageal pH studies

Author	Year of publication	Location	Number of cases reported	Time point after POEM in months	Percentage of patients with pH study done	Percentage of pH studies done with positive result	pH monitoring method	Definition of positive pH study
Familiari	2016	Rome, Italy	149	6–12	69%	50.5%	24 h pH probe at 5 cm from OGJ	>5% of total time with pH < 4
Jones	2015	Columbus, Ohio, USA	42	6	62%	57.7%	48 h Bravo capsule	DeMeester score > 14.72
Sharata	2015	Portland, Oregon, US	100	6	68%	38.2%	24 h pH probe	DeMeester score > 14.7
Stavropoulos	2014	Mineola, New York, US	100	–	52%	32.7%	48 h Bravo capsule	–
Teitelbaum	2014	Chicago, Illinois, US	41	12	32%	30.8%	24 h pH impedence/96 h Bravo capsule at 6 cm from SC junction	>4.5% of the 24-h period of highest acid exposure with pH < 4
Chiu	2013	Hong Kong, China	16	3	94%	20.0%	24 h pH probe at 4 cm above OGJ	>4.5% of total time with pH < 4
Verlaan	2013	Amsterdam, Netherlands	10	3	10% (one symptomatic case)	100.0%	24 h pH impedence	–

Table 13.4 Reported DeMeester scores

Author	Year of publication	Location	Time point after POEM in months	Number of patients with pH study done	Number of patients with DeMeester score > 14.7	Number of patients with DeMeester score > 30
Familiari	2016	Rome, Italy	6–12	102	52	N/A (mean 39.7 ± 43.2)
Jones	2015	Columbus, Ohio, USA	6	26	15	7 (26.9%)
Sharata	2015	Portland, Oregon, US	6	68	26	21 (30.9%)
Shiwaku	2015	Fukuoka, Japan	3	67	N/A	10 (14.9%)
Teitelbaum	2014	Chicago, Illinois, US	12	13	4	0

Some centers also performed pH impendence studies, but did not address the issue of non-acid reflux in their results. Whether symptomatic patients with normal time of esophageal exposure to acid are having non-acid refluxes remains unknown.

Parameters adopted to define a positive test also varied between centers, namely using a cut-off of DeMeester score of greater than 14.7 or percentage of total time with esophageal pH less than 4 of greater than 4.5 or 5 (Table 13.3). The parameter chosen does not always correlate with the device chosen to perform the test. The reported incidence defined by either DeMeester score (57.7% [16] and 38.2% [22]) or percentage of total time of esophageal acid exposure (50.5% [23], 30.8% [8], and 20.0% [15]) between the different centers did not seem to differ, but there was no report of both figures from one center. Reports that showed the distribution of DeMeester scores [16, 22, 24] suggested that around 15–30% of patients would have DeMeester score of over 30 (Table 13.4).

The benefit of a routine pH study as a management guide is not yet evident, although it is still suggested to be done as part of the protocol for patients receiving POEM. Firstly, a low pH detected within the esophagus may not be solely due to gastroesophageal reflux. Due to persistent aperistalsis of the esophagus, food stasis and hence fermentation may still occur after treatment. Crookes et al. [25] have shown in vitro that bland food with saliva would ferment and result in a gradual drop of pH down to not below 3, and that the acid resulted would not be injurious to the esophageal mucosa in the absence of pepsin. Various studies also showed a similar pattern clinically in achalasia patients after treatment [26]. The drop in pH is slow over the span of hours, usually occurs at night, and does not drop below 3. A careful recognition of this pattern against the true gastroesophageal reflux pattern (an abrupt drop of pH down to 1 or 2 with recovery) would avoid overdiagnosing reflux.

On the other hand, an abnormal pH study may not be clinically significant: the Oregon Clinic has demonstrated that almost half of the patients with an abnormal pH study result are asymptomatic [22], and in the series by Teitelbaum et al., only

23.1% of them would have esophagitis (and only 37.5% of those with esophagitis would register a positive pH study) [8]. In fact, clinically relevant reflux disease (with the presence of concurrent reflux symptoms or esophagitis) may be present in as low as 29.1% of those with an abnormal pH study [23]. Yet of course, these are short-term results and it is too soon to conclude on the effect of the silent acid regurgitation. For this reason, we still see the value of a routine pH study in our current patients who received POEM.

POEM Compared to Other Treatment Modalities

Heller Myotomy

A common discussion surrounds POEM without fundoplication and if it results in more reflux than the standard Heller myotomy with partial fundoplication. Current data available for the two approaches reveal comparable figures. Reported direct comparisons between Heller myotomy (HM) with Dor or Toupet fundoplication and POEM are retrospective at the moment, and we also see no difference between the two relating to reflux. Bhayani et al. (The Oregon Clinic) looked into 101 patients treated with either Heller myotomy with Dor or Toupet fundoplication (37 with Dor, 27 with Toupet), or POEM (37 patients). At 6 months, symptoms of heartburn, reflux, and chest pain were similar between the two groups. Part of these patients received a 24-h pH study, and the percent of patients with a DeMeester score greater than 14.7 was similar (32.3% after HM and 39.1% after POEM, $p = 0.4$) [27]. A Hong Kong series of 33 cases with POEM and 23 Heller myotomy with Dor fundoplication performed also showed no difference in terms of GERD symptoms (26% in HM group versus 15.2% in POEM group) and need of proton-pump inhibitor treatment (13% versus 9%) [28]. Prospective randomized trials would provide a better comparison, and there are a few currently in progress.

Diminished reflux was demonstrated using limited hiatal dissection in surgical myotomy in a recent study [29], where the phrenoesophageal ligament was not completely dissected during the operation. This may support the postulation of why POEM seems to result in modest reflux, despite its lack of concomitant anti-reflux procedure. The phrenoesophageal ligament contributes to the anti-reflux mechanism by maintaining the angle of His and is disrupted during Heller myotomy. In POEM, the myotomy is carried out without impacting the ligament, and the anatomical architecture remains largely intact.

Pneumodilatation

No direct comparison of pneumodilatation and POEM has been published at the moment. There are at least two randomized controlled trials ongoing, for some of which the recruitment phase is completed and we anticipate those results in the near future.

There are some recent prospective studies evaluating pneumodilatation and surgical myotomy, which may shed some light on how pneumodilatation compares to POEM. Randomized controlled trials showed either no significant difference in terms of percentage of time of pH lower than 4 (15% had acid exposure more than 4.5% of total time) and esophagitis at 1 year (19%) [30], or that pneumodilatation has a much higher reflux rate posttreatment as measured by percentage of time of pH less than 4 (31%) [26]. A meta-analysis of the two studies showed no significant difference [31]. Based on the finite controlled nature of the POEM technique compared to Pneumodilatation, we can anticipate that POEM will result in similar or less incidence of pathologic reflux.

Treatment for Reflux

In many publications on the subject, medical management of reflux following POEM is not documented in detail, but in general the use of proton-pump inhibitors (PPI) appears to be a common approach. Many authors reported that the use of PPI gives satisfactory control to any reflux symptom that occurred after POEM. Some authors have described the rate of PPI use, which ranged from 4 to 37% [4–6, 10, 13, 15, 32, 33], and some reported further on the frequency of use. Overall, 5.1–24.6% of patients were reported to take daily PPI [5, 10]. It is now generally accepted that around 15% of patients will require some use of medical treatment for gastric reflux after POEM.

Operative management of reflux following POEM is not widely present in the medical literature. There are few accounts of animal trials and a case report of treating refractory reflux endoscopically [34–36], but among the over 4000 cases published so far, there is no series in which a case of reflux after POEM was treated with a surgical fundoplication.

Indeed, endoscopic solutions to the problem of post-POEM reflux are emerging. Transoral incisionless fundoplication [37], radiofrequency therapy [38] and, more recently, the anti-reflux mucosectomy [39] are some of the current endoscopic approaches to treat index gastroesophageal reflux. Transoral incisionless fundoplication (TIF) with EsophyX™ was shown in 2010 to be feasible after POEM in animal models in a stepwise approach, where the TIF was performed 4 weeks after POEM [36]. The technique of TIF involves insertion of an endoscopic device that anchors the wall of the gastric fundus to the abdominal part of the esophagus to create a 2–3 cm wrap of 270° [40]. Clinical application of the technique on one patient suffering from refractory reflux after POEM was then described with a good clinical outcome [35].

Before endoscopic treatment for reflux disease becomes more established, surgical fundoplication is the standard therapy to consider for reflux after POEM. Fortunately, POEM appears to result in minimal submucosal and intraperitoneal adhesions, facilitating revisional procedures if necessary. In a report of two cases of laparoscopic Heller myotomy performed for recurrent symptom after POEM, only minimal adhesion was encountered upon establishing the submucosal plane, and no mediastinal inflammation was encountered [41].

Prevention of Reflux

The main objective of the POEM procedure is to achieve adequate dysphagia relief, while maximally preserving the anti-reflux mechanism. The site of the myotomy, its depth, and length are all being investigated; however, there is currently no consensus to what consists of the "optimal cut."

The initial location for the mucosotomy and entry into the submucosal space is currently under debate. Many practitioners report starting the mucosotomy at the 2 o'clock position (antegrade view) on the esophagus above the anterior lesser curvature of the stomach or, posteriorly, at 4 o'clock above the posterior lesser curvature [42]. Approaches can be classified as anterior and posterior, or along the lesser and greater curvature. Both anterior (10 or 2 o'clock) and posterior (4 or 8 o'clock) approaches can access the lesser or greater gastric curvature. The consequence of cutting at different sites becomes apparent as the myotomy engages the stomach, where the anatomic layers become less organized. Each approach varies in terms of ease of procedure [43], feasibility for those with previous Heller myotomy, and the ability to better identify the esophagogastric junction [44]. In terms of minimizing the incidence of reflux, it is conventionally believed that cutting along the lesser curvature would better preserve the Angle of His, which serves as a key component in the anti-reflux barrier complex. Inoue et al. looked at 21 cases of myotomy along the greater curve in their series of over 500 patients and reported 52% of esophagitis rate at 3 months; however, many were asymptomatic with a rate of symptomatic reflux rate of 9.5% [44]. The authors commented that the rate in their study may be higher than the rate of reflux reported commonly in the literature. Following subgroup analysis, it was determined that both rates of esophagitis and symptoms in the overall group of 500 patients [4] were higher than that seen in the greater curvature subgroup. As a result, there is a line of thought that myotomy along the lesser curvature, particularly at the 2 o'clock region, may be more predisposed to the development of symptomatic reflux. Currently, a multicenter study is in progress to further investigate this issue.

Thickness of myotomy and inclusion of the circular versus circular and longitudinal muscle layers have also been investigated. A randomized trial that involved 234 patients who underwent POEM either with full-thickness or circular muscle myotomy showed a trend in favor of selective circular muscle myotomy; however, this was not statistically significant [9]. The overall clinical reflux rates, defined as the rate of patients who had symptomatic reflux or endoscopic evidence of esophagitis, were 21.2% and 16.5% for the full-thickness myotomy group and circular muscle myotomy group, respectively ($p = 0.38$).

Length of myotomy has been a source of rich debate for decades. General consensus following quality comparisons involves a generous esophageal myotomy terminating a couple of centimeters below the esophagogastric junction, which includes myotomy of a portion of the gastric clasp fibers [4]. To minimize the risk of reflux, the length is ideally long enough to just obliterate the lower sphincter obstruction, while preserving some of the anti-reflux complex. In a recent study of 103 patients, no significant association is found between total, esophageal, or

gastric myotomy length with reflux, whether measured in terms of symptoms, esophagitis, pH study parameters, or clinical relevancy [23]. Shiwaku et al. considered esophagitis of Los Angeles class B or above as significant reflux and found no significant correlation with the total length of myotomy as well [24].

Rather than a "one size fits all" approach, it is now being proposed that a different length may be optimal for each patient, and that myotomies should be tailor-made. The development and clinical introduction of a compliance and distensibility measurement device has propelled the concept of "tailor-made myotomy." Measuring the distensibility, or the resistance of the sphincter against pressure, is different from measuring its tonic contraction as seen in manometry [45]. In the context of achalasia, it may be a better parameter for assessment of the lower esophageal sphincter. A functional lumen imaging tool (Endoflip; Crospon Ltd, Galway, Ireland) assesses real-time distensibility of the lower esophageal sphincter to help determine the adequacy of myotomy during an esophageal procedure, using the technology of impendance planimetry. Pandolfino et al. have demonstrated the significant difference in the distensibility index between treated and untreated patients with achalasia, and also between treated patients with good clinical outcome [46]. If an optimal distensibility of the sphincter to achieve can be determined, tailored myotomies for achalasia can be calculated in each patient to achieve best relief of dysphagia with the least amount of collateral tissue destruction.

Studying the change in distensibility following POEM is helpful in characterizing how each step of the procedure affects the efficacy for future studies. Distensibility measurements in pig models showed that the diameter and distensibility of the esophagogastric junction improves remarkably after clasp circular fibers of the Laimer bracket were cut, and further proximal extension of the myotomy through higher levels of the esophagus provided only marginal additional benefit [47]. Although studies in healthy animals cannot match those of a diseased esophagus, they do provide some perspective on how much proximal esophageal extension of the myotomy above the lower esophageal sphincter is actually necessary for optimal results.

Distensibility of the lower esophageal sphincter is derived from relative changes in the diameter and cross-sectional area before and following POEM. Which of these dimensions is predictive of an optimal outcome is currently a source of intrigue. Teitelbaum et al. suggested that the distensibility index, defined as the minimum cross-sectional area at the esophagogastric junction divided by distensive pressure, could predict the clinical outcome of a myotomy [48]. They reported that the difference in distensibility index measured after induction and after the completion of operation correlates with postoperative Eckardt score for patients with Heller myotomy. The absolute value of the final index after both Heller myotomy with partial fundoplication and POEM also can predict postoperative symptoms: a small final distensibility index results in higher chance of persistent dysphagia, while a large value predicts the likelihood of iatrogenic reflux symptoms. In the study group, the range of final distensibility index of 4.5–8.5 mm^2/mmHg best predicted optimal symptomatic results (Eckardt scores $\leq$1 and GerdQ scores $\leq$7) with a sensitivity of 68% and a specificity of 80%. Ngamruengphong et al. reported a

retrospective multicenter study, which showed a difference in the post-myotomy diameter and cross-sectional area between patients with and without post-POEM reflux esophagitis at 30 mL filling. Distensibility was not significantly different between the groups [49]. Familiari et al. then reported the contrary, showing no significant difference in post-myotomy diameter measured by EndoFLIP for those with and without esophagitis, reflux in pH monitoring, or heartburn symptom. Further studies, evaluating the relative change in these parameters instead of an absolute value, may reveal a predictive reference range.

Conclusion

POEM is a promising novel technique for treatment of achalasia, giving very good initial treatment outcomes. In terms of the development of gastric reflux, we now see that POEM compares well with standard surgical myotomy coupled with partial fundoplication. Although objective studies show a prevalence of abnormal esophageal acid exposure from 30 to 40%, only a portion of patients (15%) are symptomatic and thus in need of antacid medication for symptom control. Esophagitis is found to be present in some of those who are otherwise asymptomatic, possibly due to a lack of sensory innervation to the area of concern. Surveillance endoscopy, particularly in this patient subset, is appropriate to monitor potential neoplastic changes.

Several factors contribute to the development of reflux after POEM, including the inherent components of myotomy sans reconstruction, extent of dissection and myotomy as well as the procedural learning curve. Pending long-term results as well as ongoing prospective studies will allow us to determine the long-term incidence of gastroesophageal reflux after POEM.

In conjunction with the development of POEM, endoscopic anti-reflux procedures will likely contribute substantially to the durable success of the treatment of achalasia and related obstructive conditions.

To coalesce each of the advancements thus far, the development of imaging modalities that allow us to perform intraoperative real-time assessment of changes within the esophagogastric junction is ushering in the era of tailored myotomy.

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