Single-session endoscopic fundoplication after peroral endoscopic myotomy (POEM+F) for prevention of post gastroesophageal reflux – 1-year follow-up study

Authors
Amol Bapaye, Parag Dashatwar, Siddharth Dharamsi, Rajendra Pujari, Harshal Gadhiorkar

Institution
Shivanand Desai Center for Digestive Disorders, Deenanath Mangeshkar Hospital and Research Center, Pune, India

Table 1,2, Figs 1,2 Supplementary material is available under https://doi.org/10.1055/a-1332-5911

Corresponding author
Amol Bapaye, MD, Shivanand Desai Center for Digestive Disorders, Deenanath Mangeshkar Hospital and Research Center, Erandwane, Pune 411004, Maharashtra, India
amolbapaye@gmail.com

ABSTRACT
Background Peroral endoscopic myotomy (POEM) is an established treatment for achalasia cardia; however, post-POEM gastroesophageal reflux (GER) remains a significant problem. Concomitant endoscopic fundoplication following POEM (POEM+F) was recently described to reduce post-POEM GER. This single-center study reports short-term outcomes of POEM+F.

Methods This was a retrospective analysis of a prospectively maintained database of patients undergoing POEM+F. Abstracted data included demographics, achalasia type, pre-POEM Eckardt score, prior therapy, follow-up. Follow-up assessment was 3-monthly for 1 year and included post-POEM Eckardt score, GerdQ score, wrap integrity and esophagitis on esophagogastroduodenoscopy, and pH studies. GER was defined according to Lyon Consensus.

Results 25 patients underwent POEM+F (mean age 40.1 years [standard deviation (SD) 13.7]; 12 females). POEM+F was technically successful in 23/25 (92.0 %). Significant dysphagia improvement was seen in all 25 patients (mean pre- and post-POEM Eckardt scores 8.21 [SD 1.08] and 0.1 [SD 0.3], respectively; \( P = 0.001 \)). Mean total procedure and fundoplication times were 115.6 (SD 27.2) minutes and 46.7 (SD 12.4) minutes, respectively; times reduced significantly after the initial five cases. Median follow-up was 12 months (interquartile range [IQR] 9–13). Intact wrap was seen in 19/23 (82.6 %). GER (abnormal esophageal acid exposure time [EAET]) was seen in 2/18 (11.1 %) and there was one reported GerdQ > 8. Borderline GER (asymptomatic grade A esophagitis, normal EAET) was identified in 4/22 (18.2 %). Three (12.0 %) minor delayed adverse events occurred but required no intervention.

Conclusions POEM+F was safe and reproducible. At 12 months' follow-up, incidence of post-POEM+F GER was low and acceptable.

Introduction
Peroral endoscopic myotomy (POEM) is an accepted treatment modality for achalasia cardia [1–4]. Results of POEM have demonstrated excellent medium- and long-term success rates [4–6]. The procedure is minimally invasive, has an excellent safety profile, and can be performed even in cases of prior treatment failure [7]. Results of POEM are superior to single-session endoscopic balloon dilation (EBD) and are comparable to laparoscopic Heller myotomy (LHM) [8,9]. However, in recent years, there has been increasing concern about post-POEM gastroesophageal reflux (GER) [10–13]. All treatment modalities for achalasia cardia induce loss of control of the lower esophageal sphincter, and are therefore prone to post-procedure GER. Conventional teaching recommends that LHM is always combined with partial or full 360° fundoplication (LHM+F), more often anterior (Dor fundoplication), to protect against postoperative GER; overall reported post-LHM+F GER rates have been acceptable [14–16].
To date, fundoplication has not been standard after POEM. Early results of POEM reported low GER rates (6%–21%) [5, 6, 17], possibly due to selection bias and limited follow-up data without objective evidence such as pH studies [4]. Recent studies have reported high incidence of post-POEM GER (15%–88%) [10–12, 18]. A recent meta-analysis reviewing POEM, LHM, and EBD demonstrated that POEM had the highest efficacy for relief of dysphagia but also the highest incidence of post-POEM GER [19]. A prospective randomized trial comparing POEM with LHM also demonstrated high incidence of post-POEM GER [10]. Although most post-POEM GER occurrences are mild (grade A or B), severe GER (grade C or D) or development of Barrett’s esophagus has also been reported [10, 12, 20, 21]. Currently, most POEM centers recommend long-term endoscopic surveillance to identify such changes [22, 23].

In an attempt to reduce post-POEM GER, Inoue et al. described a novel endoscopic fundoplication following anterior POEM, either as a single-stage concomitant procedure (POEM+F) or later as a separate subsequent procedure (POEF) [24, 25]. The procedure aimed to replicate surgical (laparoscopic) or later as a separate subsequent procedure (POEF) [24, 26]. A short description is presented here to ensure understanding in an evolving procedure (Fig. 1).

Standard anterior POEM is first performed with a 2–3 cm full-thickness gastric side myotomy. An ultrasonic transnasal endoscope is introduced and passed into the gastric fundus alongside the gastroscopy in the tunnel (Fig. 1a). Using double endoscope transillumination as a guide along with other anatomical landmarks (diaphragmatic crus, perigastric fat and serosa overlaying the gastric myotomy is dissected and opened to gain entry into the peritoneal cavity (Fig. 1b). The gastroscope is advanced through the peritoneal opening and angled upwards and leftwards to reach the gastric fundus. The fundus is grasped using a grasper and retracted into the tunnel to simulate the wrap. Wrap formation is continuously monitored using the transnasal endoscope retroflexed in the stomach. Once a satisfactory wrap is confirmed, the corresponding spot on the fundic serosa is marked using diathermy (Fig. 1c). The gastroscopy is withdrawn. A 3-cm nylon endoloop is clasped within a reconstrainable clip and the assembly, along with the gastroscopy, is reintroduced through the tunnel into the peritoneal cavity. The endoloop is fixed to the gastric fundus using four endoclips (Fig. 1d). The proximal end of the loop is fixed to the distal end of the myotomy using a further four clips (Fig. 1e). The endoloop is gradually tightened while monitoring the wrap formation by the ultrasound scope (Fig. 1f).

All patients were admitted to hospital for overnight observation. All patients were prescribed proton pump inhibitors (PPI) for 2 weeks post-procedure with subsequent instructions to consume PPI on demand if they experienced GER symptoms. First follow-up was between 4 and 6 weeks. At follow-up, patients were questioned about dysphagia and GER symptoms. Eckardt scores and Gastroesophageal Reflux Questionnaire (GerdQ) scores were calculated. PPI usage was documented including the drug, dosage, and frequency of administration. All patients were recommended EGD in order to document intactness of the wrap and presence of endoscopic evidence of esophagitis, and 24-hour ambulatory pH studies for objective

Methods

The study was a retrospective analysis of a prospectively maintained database of all patients with achalasia cardia who underwent POEM+F. Achalasia cardia was diagnosed by esophagogastroduodenoscopy (EGD) and high-resolution manometry. We previously reported short-term outcomes of POEM+F in four patients [26]; the current study includes these four patients. POEM+F was offered and performed for naïve achalasia cardia and for all post-EBD recurrences. The following patients were not offered POEM+F but were offered standard POEM without fundoplication: those with prior history of LHM; those with a high anesthesia risk (American Society of Anesthesiologists [ASA] Class III or higher); those with sigmoid achalasia and a grossly tortuous esophagus (on earlier EGD assessment) in whom POEM was anticipated to be technically difficult; and those who refused consent for fundoplication.

The detailed technique of POEM+F has been described previously [24, 26]. A short description is presented here to ensure understanding in an evolving procedure (Fig. 1).

Video 1 Step-by-step pororal endoscopic myotomy with fundoplication (POEM+F) procedure. After anterior full-thickness myotomy, the anterior peritoneum is opened. The wrap is simulated under guidance from a transnasal endoscope positioned in parallel in the stomach, and subsequently completed by fixing the fundus using endoloop and clips to the distal end of the myotomy.

Online content viewable at: https://doi.org/10.1055/a-1332-5911

Bapaye Amol et al. Single-session endoscopic fundoplication... Endoscopy 2021; 53: 1114–1121 | © 2020. Thieme. All rights reserved.
documentation of GER. Both EGD and pH studies were performed in patients following a minimum of 1 week off PPI medication.

Subsequent follow-up was by periodic telephone standardized questionnaire at 3, 6, 9, and 12 months post-procedure to assess Eckardt and GerdQ scores. Patients experiencing symptomatic GER and with evidence of erosive esophagitis or abnormal esophageal acid exposure time (EAET) were recommended long-term PPI therapy.

Outcome assessments and definitions

The primary outcome of the study was the incidence of significant post-POEM + F GER. Secondary outcomes were clinical resolution of dysphagia, development of inapprrocedural or delayed adverse events, and integrity of the wrap at follow-up.

Technical success was defined as successful completion of POEM + F. Clinical success was defined as resolution of dysphagia as determined by post-procedure Eckardt score ≤3 and absence of post-POEM + F GER. Post-POEM + F GER was defined according to the Lyon Consensus as EAET >6% on pH studies or endoscopic evidence of Grade C or D esophagitis. Presence of Grade A or B esophagitis and EAET 4%–6% was considered as borderline evidence [27]. Presence of significant GER symptoms (GerdQ score ≥8) was recorded [28]. Adverse events were defined according to the American Society for Gastrointestinal Endoscopy lexicon for endoscopic adverse events [29].

Statistical analysis

Continuous variables were recorded as mean and standard deviation (SD) or median and interquartile range (IQR), and categorical variables were recorded as counts and percentages. A P value of <0.05 was considered statistically significant. Wilcoxon sign rank test was used to calculate the P value. All statistical analyses were computed using SPSS software version 22 (IBM Corp, Armonk, New York, USA).

Results

During an 11-month period (March 2019 to January 2020), 25 of 36 patients with achalasia cardia underwent POEM + F. The patient recruitment, procedure, and follow-up algorithm is detailed in Fig. 1s in the online-only Supplementary material. A total of 11 patients were only offered standard POEM because they were unsuitable for POEM + F (5 patients had post-LHM recurrent achalasia, 4 patients were high risk for anesthesia [ASA Class III or higher], 1 patient refused consent, and another pa-
tient had severely tortuous sigmoid achalasia for which POEM was anticipated to be technically difficult and time consuming, and therefore POEM+F was considered unsuitable because it was likely to prolong the procedure time significantly.

Baseline demographics and clinical characteristics of patients are summarized in Table 1. Mean age was 40.1 (SD 13.7) years and there were 12 females. Mean duration of symptoms before POEM+F was 12.7 (SD 10.2) months. A total of 23 patients (92.0%) had type II achalasia cardia, whereas type I and type III achalasia cardia were only seen in one patient each. Two patients had recurrent achalasia cardia after prior failed EBD. All other 23 patients (92.0%) were naïve achalasia cardia. Mean pre-procedure Eckardt score was 8.21 (SD 1.08).

Perioperative characteristics and outcomes are detailed in Table 1. Although POEM was successful in all patients, POEM+F was successful in 23/25 patients (technical success 92.0%). In two patients, fundoplication could not be performed after POEM due to device failure in one patient (breaking of the endoloop after fixation while tightening) and unfavorable anatomy in the other (sliding hiatal hernia with thick perigastric pad of fat). Mean and median total procedure times for POEM+F were 115.6 (SD 27.2) minutes and 105 (IQR 90–270) minutes, respectively, of which mean 46.7 (SD 12.4) minutes and median 45 (IQR 35–90) minutes were additionally required for fundoplication. The moving average curve demonstrated significant improvement in total procedure time after the first five procedures (88 [SD 23.4] minutes for first five cases vs. 51.2 [SD 9.1] minutes for subsequent cases; P < 0.05) (Fig. 2s). No intra- or immediate post-procedure adverse events related to POEM+F were encountered. Mean post-procedure hospital stay was 2.1 (SD 0.5) days.

Clinical follow-up was available for all 25 patients. Median duration of follow-up was 12 months (IQR 9–13). Significant improvement in dysphagia was seen in all patients (mean post-procedure Eckardt score 0.1 [SD 0.3] vs. mean pre-procedure score 8.21 [SD 1.08]; P = 0.001) (Table 1).

GER was evaluated in 23 patients who underwent successful POEM+F (Table 2). Two patients who underwent only POEM were excluded from the GER evaluation. GERQ scores for all 23 patients were obtained at a median of 12 months (IQR 9–13) after POEM+F. Scores were < 8 in 22/23 patients (95.7%) signifying low probability of GER [28, 30]. Regular PPI use was not reported by any patients. Post POEM+F 24-hour pH studies were obtained in 18/23 patients (78.3%) at a median of 2 months (IQR 1.5–6.75). All pH studies were performed with patients after 1 week off PPI. DeMeester scores and EAET were positive for GER in 2 patients (11.1%) (EAET > 6%) whereas these values were normal in the remaining 16 patients (88.9%) (EAET < 6%). The symptom index demonstrated 100% and 80% correlation, respectively, in the two patients with positive scores. For the remaining 16 patients, mean EAET was 1.12 (SD 0.7). Meaningful symptom index calculation could not be performed in these patients due to the low values.

Follow-up EGD was performed in 22 patients (95.7%) at a mean of 2.78 (SD 3.54) months post-procedure (median interval 1.5 months, IQR 1–2). All EGDs were performed after patients had been off PPI for at least 1 week. One patient refused EGD because of lack of symptoms. EGD revealed an intact wrap in 19/22 patients (86.4%) (Fig. 2a). The wrap was not distinctly visible (indistinct) in two patients (Fig. 2b), whereas it appeared loose with an open lower esophageal sphincter in one patient (Fig. 2c). Overall, the wrap was found to be intact in 19/23 patients who underwent successful POEM-F (82.6%). Erosive esophagitis (Grade A) was seen in 4/22 patients (18.2%), two of whom had an indistinct wrap. Notably, all four patients had normal EAET and Demeester scores, and none reported GER symptoms.

Three delayed adverse events were reported (12.0%): EGD revealed that an endoclip (one patient) and the cut ends of the endoloop (two patients) had eroded through the mucosa overlying the submucosal tunnel in the distal esophagus or at the gastroesophageal junction. In all three patients, surrounding
esophageal mucosa had completely healed around the clip or loop without any residual visible mucosal breach. No patient reported any directly attributable symptoms to these findings.

Follow-up of the two patients with failed POEM + F revealed an elevated GerdQ score and Grade B esophagitis in one patient, whereas the other patient was asymptomatic and did not have erosive esophagitis on EGD. Both patients did not undergo pH studies. Long-term PPI was prescribed to the patient reporting GER.

Post-POEM + F GER as per the Lyon Consensus was identified in two patients (11.1%; 95% confidence interval 10.6–11.5%). One of these patients had a loose wrap on EGD and was also significantly symptomatic (GerdQ score 11). Neither patient demonstrated erosive esophagitis on EGD. Borderline evidence of GER as evidenced by Grade A esophagitis was additionally observed in four patients but pH studies and symptom scores were all normal (Table 2).

### Discussion

Although POEM is a well-established treatment modality for achalasia cardia [1–3], post-POEM GER has been a significant challenge in recent years [10–12, 18]. POEM has therefore been criticized by surgical experts and several other sources [10–13]. Post-POEM GER is often asymptomatic, may remain undiagnosed, and surveillance endoscopies and long-term PPI have been recommended for all post-POEM patients [23]. Long-term effects of such GER are largely unknown, but occasional reports of post-POEM Barrett’s esophagus and cancer have raised significant alarm [31].

In comparison, LHM – the surgical counterpart of POEM – has always incorporated a partial or complete 360° fundoplication as an integral part of the surgical procedure. The addition of fundoplication to LHM has demonstrated significant reduction in the incidence of post-operative GER [16, 32, 33]. GER in post-LHM + F patients is significantly less frequent compared with that after POEM [19, 21].

Based on the principle of LHM + F, Inoue et al. reported POEM + F and POEF as endoscopic antireflux procedures following POEM [24]. The fundoplication wrap in POEM + F closely mimics the Dor partial fundoplication – a standard recommended procedure following LHM. The initial series of Inoue et al. included 21 patients and reported safety, feasibility, and short-term outcomes following POEM + F; results demonstrated an intact wrap in 95% of patients at 1-month follow-up. The current study reports short-term outcomes following POEM + F. POEM was effective in all 25 patients as evidenced by significant improvement in dysphagia and pre- and post-POEM Eckardt scores, whereas POEM + F was successful in 23 patients (92.0%).

The primary aim of this study was to calculate the incidence of significant post-POEM + F GER. Our results demonstrate that significant GER (EAET > 6%) was documented in only 2/18 patients (11.1%) with excellent symptom index correlation. This is much lower than that documented in other POEM studies [10–12, 18]. These results are promising and suggest that POEM + F could protect against post-POEM GER, although additional studies are required to confirm these results.
Wrap integrity at follow-up was another parameter assessed during the current study. The wrap appeared to be intact in 19 patients (82.6%) at follow-up EGD at a median 1.5 months. POEM + F is based on surgical principles that depend on tissue healing, fibrosis, and adhesion formation to maintain wrap integrity. As tissue healing is usually completed by 6 weeks, it is likely that a wrap intact at 6 weeks will maintain integrity in the long term. The wrap was loose in one patient (abnormal EAET >6% and elevated GerdQ score confirming GER) and indistinct in two patients (both reported Grade A esophagitis). It is therefore important to note that all three patients with wrap failures had either conclusive or borderline evidence of GER on follow-up evaluation. On the other hand, the fact that all 19 patients with an intact wrap reported normal GerdQ scores at a median of 12 months’ follow-up suggests that the wrap could be an effective barrier against GER.

Grade A erosive esophagitis was found in four patients, two of whom had wrap failure whereas it was intact in the other two. However, as GerdQ scores and EAET were normal in all four patients, it is impossible to determine whether the esophagitis was due to GER or food stasis.

Diagnosis of post-POEM GER is challenging, and the guidelines presented by the Lyon Consensus are possibly most relevant in this regard [27]. The results of the present study demonstrate conclusive evidence of GER in 11.1% patients and if both conclusive and borderline evidence were to be considered = 26.1%. Of these, only one patient was symptomatic (1/23, 4.3%), four had endoscopic evidence (4/22, 18.2%), whereas EAET was abnormal in 2/18 (11.1%). In comparison, symptomatic post-POEM GER has been reported in 19%, by pH studies in 39%, and on endoscopy in 29.4% in a recent large meta-analysis [11]. It appears, therefore, that POEM + F could be protective against post-POEM GER.

Fundoplication has been a standard procedure for prevention of postoperative GER after LHM. In a large meta-analysis of 64 articles reporting outcomes of 4871 LHM + F procedures, Campos et al. reported a mean postoperative GER incidence of 8.8% (range 0–44) [16]. The current study demonstrated 11.1% post-POEM + F GER incidence, which is comparable to that reported for LHM + F. Further validation by larger randomized studies is necessary to confirm these findings.

Is POEM + F reproducible? We previously reported an initial series of four patients undergoing successful POEM + F [26]. Further to this, the current series reported 92.0% (23/25) technical success of POEM + F. No intra-procedural adverse events were encountered, although technical failures occurred in two patients. In the first patient, the endoloop snapped while tightening the wrap, possibly owing to friction from an endoclip. Although it was technically feasible to redo the fundoplication using a new endoloop and clips, we preferred not to pursue this in the interest of patient safety owing to the increased anesthetic time that would be required. The other patient had a sliding hiatal hernia with an angulated anatomy at the gastro-esophageal junction, and a thick pad of fat at the point of entry into the peritoneal cavity. Dissection and entry into the peritoneal cavity and subsequent visualization was considered difficult and could likely compromise procedural safety. Fundoplication was therefore aborted to avoid inadvertent intraoperative injury or adverse events. Both these patients were among our initial five patients when experience with this technique was limited. No technical challenges were encountered in the remaining 23 patients. Additional operative time was necessary to perform POEM + F; however, the learning curve was identified to be short (five cases). POEM + F can therefore be considered a safe procedure with acceptably low failure rates, and these may further reduce with increased experience.

Delayed adverse events were reported in our study, involving a clip or endoloop tail eroding through the mucosa in three patients (12.0%); no other adverse events were encountered. No endoscopically visible mucosal breach was identified in any of these patients and the mucosa had completely healed around these inclusions. Patients had no related symptoms and therefore these findings have doubtful clinical significance.

Currently no consensus exists regarding the optimal approach for the prevention of post-POEM GER. Most patients are maintained on PPI with good symptom control [34]. Endoscopic antireflux procedures have been reported to be used in conjunction with POEM in an attempt to reduce post-POEM GER. Tyberg et al. reported a series of five patients treated with second-session transoral incisionless fundoplication performed after POEM, which demonstrated impressive short-term results [35]. The same group then also reported a single-session approach in a solitary case report [36]. Toshimori et al. reported on POEF (POEM + F performed over two independent sessions) as a subsequent second procedure to control post-POEM GER [25]. The authors also demonstrated use of endoscopic suturing instead of endoloop and clips to create the wrap. It will be interesting to evaluate which of these techniques can provide a more robust and secure fundoplication in the long term.

Although the two-session approaches are plausible alternatives, they have the inherent drawback of requiring two separate procedures, thereby increasing procedure costs, invasiveness, and potential morbidity. They may therefore be less preferred to POEM + F or LHM + F in routine practice. In contrast, POEM + F offers the advantage of a single-session fundoplication akin to what is practiced and recommended for surgical myotomy. The procedure is also less device dependent, and therefore costs are likely to be lower. Although it may be argued that not all POEM patients develop GER and therefore an antireflux procedure may not be required in all, the reported high incidence of post-POEM GER (especially asymptomatic GER), along with the fact that fundoplication has been a standard procedure following LHM for several decades, surely justify the approach of single-session POEM + F. Laparoscopic fundoplication has also been described after POEM to treat post-POEM GER [34]. Although effective, this approach defeats the primary purpose of performing a less-invasive procedure such as POEM if a more invasive approach is later required to control its side-effects.

The current study has several limitations. First, it was a retrospective case series from a single center, and therefore these results need confirmation in larger multicenter trials. Second, nearly one-third of eligible patients (11/36, 30.6%) were not of...
ferred POEM+F, and therefore possible bias exists regarding pa-
ent selection. Third, although clinical follow-up was obtained
in all patients, follow-up EGD and pH studies could not be ob-
tained for all. It is possible that asymptomatic GER could have
been missed in these patients. Furthermore, we understand
that nonavailability of impedance pH may limit interpretation
of some of the results. Fourth, the study was a single-arm study
without a POEM-only comparator arm. Future comparative
studies will be required to address this issue. Finally, POEM+F
is an evolving procedure. It is therefore likely that with increas-
ing experience, the technique may be simplified, and that the
results and outcomes may demonstrate more solidarity in fu-
ture.

In conclusion, this single-center study demonstrated excel-
alent short-term outcomes of POEM+F for the control of post-
POEM GER. The procedure was reproducible and safe, and the
integrity of the wrap was well maintained at follow-up. Inci-
dence of post-POEM+F GER at a median 12-month follow-up
was low and acceptable. POEM+F offers the advantage of a sin-
gle-session endoscopic solution for achalasia cardia treat-
ment with possible control of GER. These findings require further va-
lidation in larger randomized studies with longer follow-up.

Competing interests

The authors declare that they have no conflict of interest.

References

[2] Khashab MA, Vela MF, Thosani N et al. ASGE guideline on the man-
agement of achalasia. Gastrointest Endosc 2020; 91: 213–227
achalasia cardia: expert consensus statements. J Gastroenterol Hepa-
tol 2018; 33: 1436–1444
sions learnt from a decade of submucosal endoscopy. J Clin Gastro-
enterol 2020; 54: 114–129
Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global
peroral endoscopic myotomy for treatment of achalasia after failed
vs pneumatic dilatation on symptom severity and treatment outcomes
among treatment-naive patients with achalasia: a randomized clinical
trial. JAMA 2019; 322: 134–144
versus peroral endoscopic myotomy (POEM) for achalasia: a systema-
381: 2219–2229
myotomy as compared with Heller’s myotomy with fundoplication: a
systematic review with meta-analysis. Gastrointest Endosc 2018; 87:
934–943
after peroral endoscopic myotomy: a multicenter case-control study.
Endoscopy 2017; 49: 634–642
2017; 49: 625–628
[14] Rebecchi F, Allaix ME, Schlootmann F et al. Laparoscopic Heller myot-
omy and fundoplication: what is the evidence? Am Surg 2018; 84:
481–488
fundoplication is necessary to control gastroesophageal reflux. J La-
therapies for achalasia: a systematic review and meta-analysis. Ann
Surg 2009; 249: 45–57
for the treatment of achalasia: a prospective single center study. Am J
Gastroenterol 2012; 107: 411–417
after peroral endoscopic myotomy: analysis of clinical, procedural
and functional factors, associated with gastroesophageal reflux dis-
ease and esophagitis. Dig Endosc 2016; 28: 33–41
[19] Aioffi A, Bona D, Riva CC et al. Systematic review and Bayesian net-
work meta-analysis comparing laparoscopic Heller myotomy, pneu-
matic dilatation, and peroral endoscopic myotomy for esophageal
[20] Shiwaku H, Inoue H, Onimaru M et al. Multicenter collaborative ret-
rospective evaluation of peroral endoscopic myotomy for esophageal
achalasia: analysis of data from more than 1300 patients at eight fa-
[21] Sanaka MR, Thota PN, Parikh MP et al. Peroral endoscopic myotomy
leads to higher rates of abnormal esophageal acid exposure than la-
paroscopic Heller myotomy in achalasia. Surg Endosc 2019; 33:
2284–2292
[22] Bechara R, Inoue H, Shimamura Y et al. Gastroesophageal reflux dis-
eease after peroral endoscopic myotomy: lest we forget what we al-
ready know. Dis Esophagus 2019; 32: doi:106
per-oral endoscopic myotomy in achalasia: expert review and best
practice advice from the AGA Institute. Gastroenterology 2017; 153:
1205–1211
[24] Inoue H, Ueno A, Shimamura Y et al. Peroral endoscopic myotomy and
fundoplication: a novel NOTES procedure. Endoscopy 2019; 51:
161–164
plication: a brand-new intervention for GERD. VideoGIE 2020; 5:
244–246
[26] Bapaye A, Dharamsi S, Jain R et al. Concomitant endoscopic fundopli-
cation – can it reduce the risk of gastroesophageal reflux following
peroral endoscopic myotomy? Endoscopy 2020; 52: E73–E74
[27] Gyawali CP, Kahrlas PJ, Savarino E et al. Modern diagnosis of GERD:
the Lyon Consensus. Gut 2018; 67: 1351–1362
for the diagnosis and management of gastro-oesophageal reflux dis-
[29] Cotton PB, Eisen GM, Aabakken L et al. A lexicon for endoscopic ad-
verse events: report of an ASGE workshop. Gastrointest Endosc 2010;
71: 446–454


[34] Inoue H, Shiwaku H, Kobayashi Y et al. Statement for gastroesophageal reflux disease after peroral endoscopic myotomy from an international multicenter experience. Esophagus 2020; 17: 3–10


[36] Brewer Gutierrez OI, Benias PC, Khashab MA. Same-session per-oral endoscopic myotomy followed by transoral incisionless fundoplication in achalasia: are we there yet? Am J Gastroenterol 2020; 115: 162