

Routine esophagram to detect early esophageal leakage after peroral endoscopic myotomy



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ABSTRACT

Background and study aims Peroral endoscopic myotomy (POEM) is highly successful in treating patients with achalasia. The aim of this study was to evaluate the incidence of early adverse events (AEs) following POEM and to assess whether post-procedure imaging with routine esophagram prevents serious AEs due to early detection of esophageal leakage after POEM.

Patients and methods Patients who underwent POEM between August 2011 and December 2022 were included in this retrospective cohort study. Post-procedure AEs were graded according to the AGREE classification. Until July 2016, routine esophagram was routinely performed 1 day after POEM; after that time, the practice was abandoned. The number and severity of post-procedure AEs were compared between patients with and without routine esophagram after POEM.

Results In total, 352 patients were included (mean age 47 years, 48.3% female). Nineteen post-procedure AEs occurred, 10 of which were grade I (2.8%), three grade II (0.9%), five grade IIIa (1.4%), and one grade IVa (0.3%). No difference was found in the number and severity of post-procedure AEs between patients who did and did not undergo routine esophagram. In 129 patients, routine esophagram was performed 1 day after POEM. In two patients, esophageal leakage was seen, after which repeat endoscopy was performed to close the incision with additional clips. After abolishing routine esophagram from the protocol, no AEs led to severe complications related to esophageal leakage. **Conclusions** POEM is safe with a relatively low number of AEs. The benefit of routine esophagram 1 day after POEM is limited because it does not prevent serious complications resulting from esophageal leakage.

Introduction

Achalasia is a rare esophageal motility disorder that is characterized by absent or uncoordinated esophageal peristalsis and insufficient relaxation of the lower esophageal sphincter (LES), resulting in impaired propulsion of food through the esophagus. The most common symptoms include dysphagia, regurgitation of undigested food, chest pain, and weight loss [1]. Current treatment aims at reducing symptoms by lowering the pressure of the LES, therefore improving passage of food through the esophagus. Treatment options are pneumatic dilatation (PD), laparoscopic Heller myotomy (LHM) which is often combined with fundoplication, botulinum toxin injection, and peroral endoscopic myotomy (POEM) [2].

Since the first successful POEM was reported in 2010, this procedure is increasingly being performed worldwide and it is now a key element in achalasia treatment [3]. POEM is a minimally invasive procedure in which muscle fibers of the distal esophagus and LES are cut endoscopically by making a submucosal tunnel toward the stomach.

Previous studies have shown that POEM is non-inferior to LHM in controlling symptoms of achalasia [4, 5]. The long-term efficacy of POEM is higher than for PD with treatment success rates of 81% for POEM and 40% for PD after 5 years [6].

POEM appeared to be safe when performed by experienced endoscopists [4, 7, 8, 9, 10, 11, 12]. However, the definition and classification of adverse events (AEs) varies between studies, and therefore, the number of AEs are wide-ranging from 0% to 35.8% [9, 10, 12, 13, 14, 15, 16, 17, 18]. Initially, all types of mucosal injury and gas-related events such as pneumoperitoneum and pneumomediastinum were reported as AEs. These events are commonly encountered on routinely performed post-procedure imaging after POEM, are often asymptomatic and usually do not affect patient outcome, hospital stay, or clinical management [19]. Therefore, routine imaging after POEM is not always recommended [20, 21, 22, 23, 24]. However, a clinical practice guideline for POEM states that upper gastrointestinal endoscopy has to be carried out after POEM to check for mucosal damage or hemorrhage and that a routine esophagram has to be performed to exclude esophageal leakage [25]. Another study concluded that routine postoperative computed tomography (CT) might be helpful in early detection of potential significant AEs, although most CT findings did not result in a need for additional treatment [26].

Currently, there is no consensus about postoperative care after POEM and it is unknown to what extent performing routine postoperative imaging will result in early detection and better treatment of AEs [23, 25, 26, 27]. The aim of this study was to evaluate the incidence of early AEs following POEM and to assess whether post-procedure imaging by routine esophagram prevents serious AEs due to early detection of esophageal leakage after POEM.

Patients and methods

Study design

This retrospective cohort study was performed at the Amsterdam University Medical Center. Data were extracted from medical records of all consecutive patients who underwent POEM between August 2011 and December 2022. Diagnosis of achalasia, hypercontractile esophagus, or diffuse esophageal spasm had to be confirmed by manometry in order to be included in this study. Other inclusion criteria were a technical successful POEM procedure, at least 1 month of follow-up and aged ≥ 18 years. The first 25 procedures after introduction of POEM in our center were excluded, taking into account the learning curve for the procedure [28]. Patients undergoing gastric-POEM were also excluded from this study.

POEM procedure

All POEM procedures were performed by two experienced interventional endoscopists (BB, PF) according to our protocol under general anesthesia and all patients received perioperative intravenous antibiotics. Carbon dioxide insufflation was routinely used in all patients. POEM started with submucosal injection of saline and indigo carmine halfway into the esophageal body followed by a 2-cm mucosal incision to enter the submucosal space. A submucosal tunnel toward the LES was created and colored saline was used to increase demarcation and to enlarge the submucosal working space. The submucosal tunnel was continued to approximately 3 cm beyond the LES. Afterward, myotomy of the circular muscle layer and part of the longitudinal muscle layer was performed. Once the myotomy was completed, the mucosal incision was closed with multiple endoclips.

Post-procedure care

According to the protocol, standard observation after POEM was 1-night admission. Until July 2016, routine esophagram was performed 1 day after POEM in all patients to assess for signs of esophageal leakage. Patients had to drink ≥ 100 mL of liquid iodized contrast (Ultravist 300) in upright position. Radiographs of the esophagus were made to rule out leakage of contrast in the submucosal tunnel and/or in the mediastinum. Patients were discharged when no significant esophageal leakage was identified on routine esophagram and liquids were well tolerated. After July 2016, routine esophagram or chest CT in the first days post-POEM was only performed in case of symptoms suggestive for post-procedure AEs (e.g. uncontrolled retrosternal pain or fever) and patients were discharged when they were able to tolerate liquids 1 day post-POEM. After discharge, all patients followed a liquid diet for 1 week and a ground diet for another week. Standard endoscopy in the first postoperative days after POEM to assess mucosal damage, the location of the clips, and hemorrhage was not performed routinely. Repeat upper gastrointestinal endoscopy was only performed on indication.

Outcome measures

The primary outcome was the number of early post-procedure AEs after POEM. Early post-procedure AEs were defined as any unfavorable event within 30 days after POEM and were graded according to the Adverse events Gastrointestinal Endoscopy (AGREE) classification [29]. The occurrence of early post-procedure AEs was routinely assessed shortly after the procedure, before discharge, after 2 weeks, and 1 to 3 months after POEM. This was documented in the medical record during follow-up. The number and grade of post-procedure AEs was compared between two cohorts of patients, with a focus on the AEs resulting from esophageal leakage. The first group included patients undergoing POEM before July 2016 with routine esophagram 1 day post-POEM. In the other group of patients, POEM was carried out after July 2016 and routine esophagram was not routinely performed in any of these patients. Secondary outcomes included hospital stay, signs of esophageal leakage on routine esophagram, and repeat endoscopy after POEM. Intraprocedure AEs were documented in the report of the POEM procedure. Pneumoperitoneum was reported as an intraprocedure AE when abdominal needle drainage was necessary or when the procedure was temporarily stopped because of a change in ventilation pressure. Bleeding was indicated as major in case of hemodynamic instability, blood transfusion, or prolonged hospitalization. Mucosal injury that occurred during POEM for which extra clips were needed was also considered to be an intraprocedure AE. All AEs were discussed by the adjudication committee, which consisted of the two experienced interventional endoscopists who performed the POEM procedures (BB, PF), to determine if the AEs could have been prevented or could have been less severe with early detection of esophageal leakage on routine esophagram.

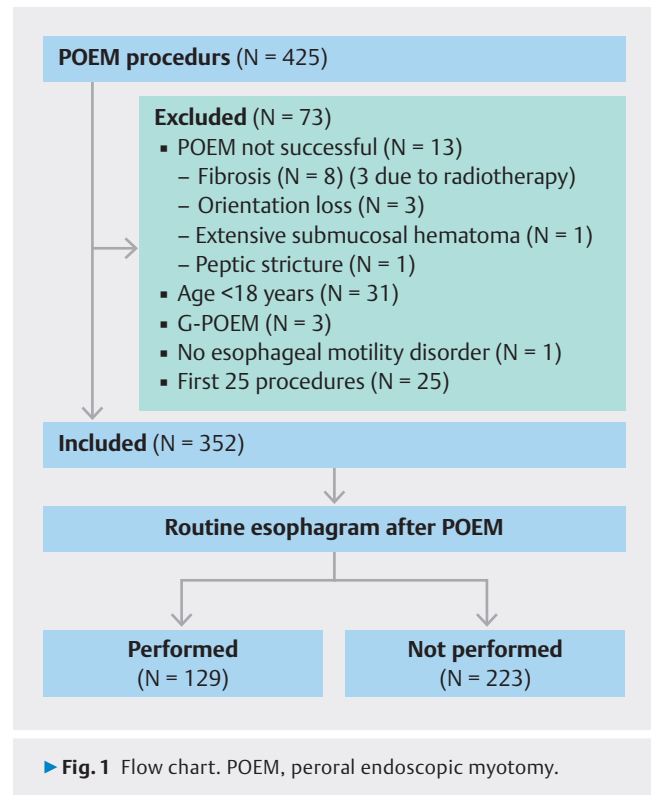
Statistical analysis

SPSS statistics version 28.0 was used for statistical analysis. Comparisons were made using Chi-square test, Fisher's exact test or non-parametric testing (Mann-Whitney U test) where appropriate. Two-sided $P < 0.05$ was considered to be statistically significant.

Results

Patient characteristics

In total 425 patients underwent POEM between August 2011 and December 2022. Thirteen procedures were not successful due to submucosal fibrosis in the distal esophagus or around the LES, orientation loss, extensive submucosal hematoma, or peptic stricture. Of the remaining 412 patients, 31 patients were aged < 18 years, three patients underwent gastric-POEM, and one patient had no esophageal motility disorder. The first 25 POEM procedures were excluded taking into account the POEM learning curve of the endoscopists. Hence, 352 patients were included in this study of whom 129 underwent POEM before July 2016 and 223 after July 2016 (► Fig. 1). All patients were routinely followed for at least 1 month and no patients



were lost to follow-up. Patient characteristics are specified in ► Table 1 and procedure-related outcomes in ► Table 2.

Post-procedure adverse events

Post-procedure AEs within 30 days after POEM occurred in 19 patients (5.4%) of which 10 AEs were grade I (2.8%), three were grade II (0.9%), five were grade IIIa (1.4%) and one was grade IVa (0.3%) according to the AGREE classification [29].

Supplementary Table 1 provides an overview of all post-procedure AEs. One patient had symptomatic pneumothorax, pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema after POEM (► Fig. 2). In this patient, the procedure was inadvertently started with room air insufflation instead of carbon dioxide. This was noticed 30 minutes after introduction of the endoscope and insufflation was at that point switched to carbon dioxide. After the procedure, no chest or abdominal drainage or other intervention was necessary and the patient was hemodynamically stable and received extra oxygen for 3 days. Pain was controlled with opioids for 4 days and the patient was discharged after 7 days. Five patients underwent repeat endoscopy after POEM (grade III). In two of these patients, POEM was performed before July 2016 and those patients underwent repeat endoscopy because submucosal esophageal leakage was seen on routine esophagram and was closed with extra clips (► Fig. 3). One of these patients had deep submucosal leakage that extended through the submucosal tunnel up to the stomach but did not enter the mediastinum. The other patient had superficial esophageal leakage that was limited to the level of the mucosal incision (► Fig. 3). Because of persistent esophageal leakage on the esophagram

► **Table 1** Patient characteristics.

	Total (N = 352)	Routine esophagram (N = 129)	No routine esophagram (N = 223)
Age, years, mean (SD)	47 (17)	47 (16)	47 (17)
Sex			
▪ Female	170 (48.3)	61 (47.3)	109 (48.9)
▪ Male	182 (51.7)	68 (52.7)	114 (51.1)
BMI, kg/m ² , median (IQR)	24.0 (5.3)	23.6 (5.3)	24.2 (5.3)
ASA score			
▪ I	126 (35.8)	65 (50.4)	61 (27.4)
▪ II	193 (54.8)	56 (43.4)	137 (61.4)
▪ III	33 (9.4)	8 (6.2)	25 (11.2)
Comorbidities			
▪ Diabetes mellitus type II	23 (6.5)	6 (4.7)	17 (7.6)
▪ Hypertension	54 (15.3)	20 (15.5)	34 (15.2)
▪ OSAS	10 (2.8)	1 (0.8)	9 (4.0)
▪ COPD or asthma	28 (8.0)	9 (7.0)	19 (8.5)
▪ Thyroid disease	22 (6.3)	9 (7.0)	13 (5.8)
▪ Malignancy (past or current)	14 (4.0)	3 (2.3)	11 (4.9)
▪ Chronic inflammatory disease	16 (4.5)	5 (4.9)	11 (4.9)
▪ Chronic renal failure	3 (0.9)	0 (0.0)	3 (1.3)
▪ Barrett esophagus	1 (0.3)	1 (0.8)	0 (0.0)
▪ Other cardiac or vascular disease	33 (9.4)	23 (10.3)	10 (7.8)
▪ Other hematological disease	5 (1.4)	1 (0.8)	4 (1.8)
▪ Other neurological disease	25 (7.1)	6 (4.7)	19 (8.5)
Previous surgery			
▪ Abdominal surgery*	67 (19.0)	22 (17.1)	45 (20.2)
▪ Thoracic surgery	4 (1.1)	1 (0.8)	3 (1.3)
Esophageal motility disorder†			
▪ Achalasia	344 (97.7)	125 (96.9)	219 (98.2)
– Type I	69 (19.6)	34 (26.4)	35 (15.7)
– Type II	190 (54.0)	56 (43.4)	134 (60.1)
– Type III	34 (9.7)	19 (14.7)	15 (6.7)
– Non-specified	51 (14.5)	16 (12.4)	35 (15.7)
▪ Jackhammer esophagus	3 (0.9)	0 (0.0)	3 (1.3)
▪ DES	5 (1.4)	4 (3.1)	1 (0.4)
Previous treatment	259 (73.6)	83 (64.3)	176 (78.9)
▪ PD	228 (64.8)	70 (54.3)	158 (70.9)
▪ BTI	41 (11.6)	17 (13.2)	24 (10.8)
▪ LHM	85 (24.1)	28 (21.7)	57 (25.6)
▪ POEM	9 (2.6)	0 (0.0)	9 (4.0)

► **Table 1** (Continuation)

	Total (N = 352)	Routine esophagram (N = 129)	No routine esophagram (N = 223)
TBE before POEM			
▪ Column height, cm, median (IQR)			
– 0 min	8.0 (6.1)	9.0 (7.2)	7.7 (5.4)
– 1 min	6.4 (5.3)	7.4 (5.2)	6.0 (4.8)
– 2 min	5.8 (4.7)	6.0 (5.7)	5.7 (4.3)
– 5 min	4.9 (4.8)	5.0 (5.0)	4.9 (4.6)
▪ Max diameter, cm, mean (SD)	3.2 (1.2)	3.2 (1.2)	3.2 (1.2)
▪ Sigmoid esophagus	10 (2.9)	2 (1.6)	8 (3.7)
▪ Time between diagnosis and POEM, months, median (IQR)	14.0 (45.0)	9.0 (43.5)	15.0 (45.0)

Results are presented as n (%) unless otherwise stated.

*Laparoscopic Heller myotomy not included.

†Based on Chicago classification version 3.0.

ASA, American Society of Anesthesiologists; BMI, body mass index; BTI, botulinum toxin injection; COPD, chronic obstructive pulmonary disease; DES, diffuse esophageal spasm; HIV, human immunodeficiency virus; IQR, interquartile range; LHM, laparoscopic Heller myotomy; OSAS, obstructive sleep apnea syndrome; PD, pneumatic dilatation; POEM, peroral endoscopic myotomy; SD, standard deviation; TBE, timed barium esophagram.

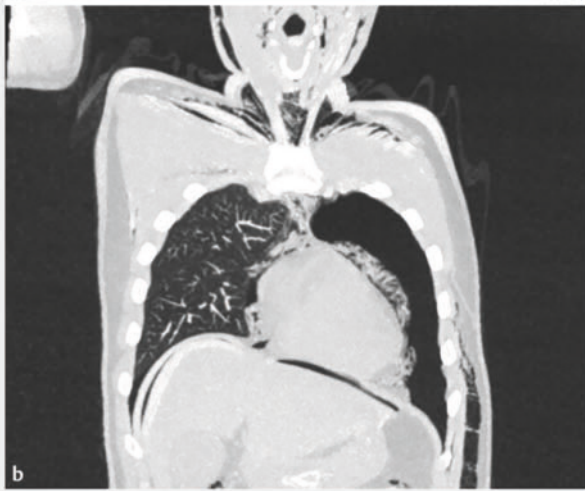
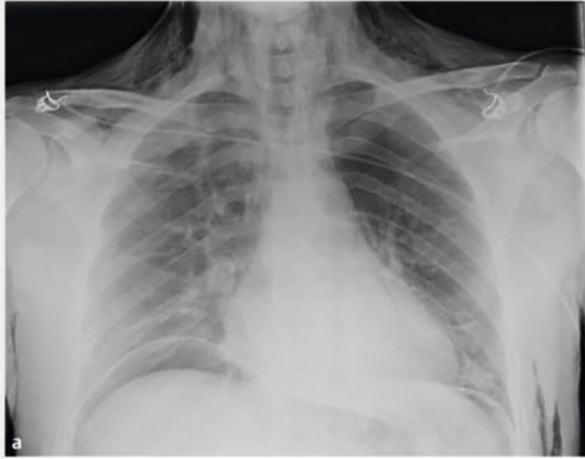
► **Table 2** Procedure-related outcomes.

	Total (N = 352)	Routine esophagram (N = 129)	No routine esophagram (N = 223)
Procedure time, minutes, median (IQR)	73 (39)	90 (37)	60 (32)
Length of myotomy, cm, median (IQR)	11 (3)	13 (4)	11 (3)
▪ Selective circular	3 (3)	4 (4)	3 (3)
▪ Full-thickness	9 (4)	9 (4)	8 (4)
Intraprocedure adverse events, number	41*	23	18
▪ Pneumoperitoneum requiring abdominal needle drainage	18	15	3
▪ Mucosal injury closed with clips	13	6	7
▪ Second submucosal tunnel	4	0	4
▪ Bleeding	6	2	4
– Minor	4	1	3
– Major	2	1	1
Number of days in hospital, days, median (IQR)	2 (0)	2 (0)	2 (0)
Routine esophagram post-POEM			
▪ No esophageal leakage		124 (96.1)	
▪ Signs of esophageal leakage		5 (3.9)	
Post-procedure adverse events†	19 (5.4)	5 (3.9)	14 (6.3)
▪ Grade I	10 (2.8)	2 (1.6)	8 (3.6)
▪ Grade II	3 (0.9)	1 (0.9)	2 (0.9)
▪ Grade IIIa	5 (1.4)	2 (1.6)	3 (1.3)
▪ Grade IVa	1 (0.3)	0 (0.0)	1 (0.4)

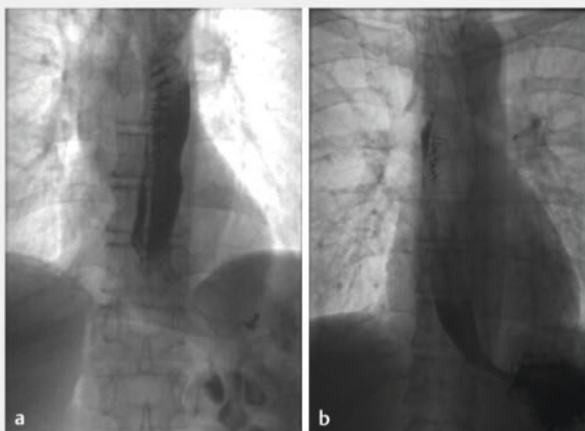
Results are presented as n (%) unless otherwise stated.

*In total, 41 intraprocedure adverse events occurred in 38 patients (10.8%).

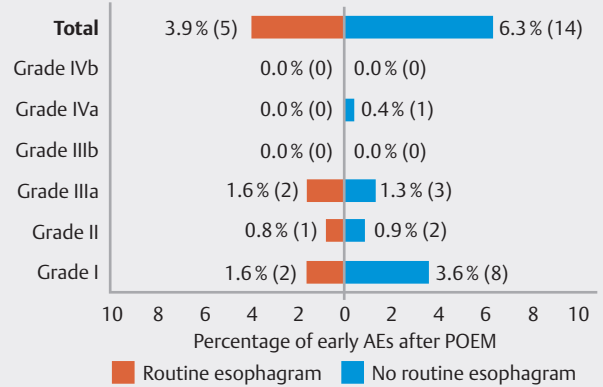
†Based on Classification for Adverse events Gastrointestinal Endoscopy (AGREE) [29]. IQR, interquartile range; POEM, peroral endoscopic myotomy.



► **Fig. 2** Pneumothorax, pneumoperitoneum, pneumomediastinum and subcutaneous emphysema after POEM. **a** Chest X-ray. **b** Chest CT. POEM, peroral endoscopic myotomy; CT, computed tomography.



► **Fig. 3** Submucosal esophageal leakage on routine esophagram. **a** Deep leakage into the submucosal tunnel toward the stomach. **b** Superficial leakage limited to the mucosal incision.



► **Fig. 4** Percentage (number) of patients with an early AE after POEM. There was no difference in the number and severity of AEs among patients with and without routine esophagram. AE, adverse event. POEM, peroral endoscopic myotomy.

the day after repeat endoscopy in both patients, another repeat endoscopy was carried out in which two extra clips were used to close the incision and a duodenal feeding tube was placed. Both patients were asymptomatic before repeat endoscopy and no opioids were necessary for retrosternal pain. One of these patients received antibiotics for 2 weeks because of fever measured once after repeat endoscopy. The patients were discharged after 5 and 7 days.

One patient was readmitted to the intensive care unit (ICU) because of respiratory insufficiency 3 days after POEM and required ICU observation with oxygen support (grade IVa). CT showed significant pleural effusion and debris in the right main bronchus without signs of esophageal leakage. Upper endoscopy was performed and did not show leakage or perforation and all clips were in place. The pleural effusion was punctured, but no bacteria were identified on culture. The patient was stable with high flow oxygen and antibiotics and able to be discharged from the hospital after 9 days, 6 of which were in the ICU. Further recovery was unremarkable. No AEs resulted in death.

Routine esophagram

Routine esophagram was standard performed 1 day after POEM in 129 patients of whom five had post-procedure AEs (n = 5/129, 3.9%). Two were classified as grade I (n = 2/129, 1.6%), one as grade II (n = 1/129, 0.8%), and two as grade IIIa (n = 2/129, 1.6%). Fourteen post-procedure AEs (n = 14/223, 6.3%) occurred in the other group in which routine esophagram was not standard performed (► **Fig. 4**). Of these AEs, eight were grade I (n = 8/223, 3.6%), two were grade II (n = 2/223, 0.9%), three were grade IIIa (n = 3/223, 1.3%), and one was grade IVa (n = 1/223, 0.4%). Overall, the number and severity of the AEs was not different between patients with and without routine esophagram. Most importantly, no severe complications due to esophageal leakage (e.g. sepsis or mediastinitis) were observed.

In five patients, possible signs of esophageal leakage were reported ($n = 5/129$, 3.9%) of whom two patients underwent a subsequent endoscopy to close the potential leakage with additional clips. The esophageal leakage on routine esophagram of the other three asymptomatic patients was questionable because it was very minimal and limited to the level of the mucosal incision. These patients were treated conservatively without repeat endoscopy; therefore, this was not classified as an AE.

If routine esophagram had been performed after July 2016, esophageal leakage may have been seen in one patient with retrosternal pain in whom partial dehiscence of the mucosal incision was observed during repeat endoscopy 5 days after POEM. However, no endoscopic intervention was needed and the patient recovered with conservative treatment. The adjudication committee decided that a routine esophagram would only have detected the esophageal leakage earlier, but management would not have changed because the esophageal leakage was limited to the mucosal incision and no endoscopic intervention was needed. Adjudication concluded that none of the other AEs could have been detected earlier by routine esophagram because no other AE was associated with esophageal leakage.

Discussion

This study demonstrated that POEM is safe and that the number and severity of AEs is not different whether or not an esophagram is performed routinely 1 day after POEM. Even more importantly, after abolishing routine esophagram from the protocol, no AEs associated with esophageal leakage led to severe complications that necessitated additional or more comprehensive interventions. Therefore, routine esophagram after POEM could not have prevented the occurrence of any AEs and would not have impacted management to a significant extent.

Post-procedure AEs within 30 days after POEM occurred in 19 of 352 patients (5.4%). Intraprocedure AEs occurred more frequently than post-procedure AEs. In total 41 intraprocedure AEs occurred in 38 patients (11.6%). These procedure-related events were already managed during POEM and did not influence patient outcome or hospital stay. Pneumoperitoneum for which abdominal needle drainage was necessary occurred primarily before July 2016. A possible explanation for this might be that it became common practice to increasingly widen the submucosal tunnel, allowing carbon dioxide to escape more easily.

The number of AEs in this study was slightly lower compared with the study of Haito-Chavez (2017), who reported that AEs after POEM occurred in 7.5% of the 1826 included patients. However, that percentage comprised intraprocedure AEs as well as post-procedure AEs. In total, 156 AEs occurred, of which 89 were during the procedure and 67 post-POEM [7]. The difference in AE rates might also be explained by the different classification that was used. For example, post-procedure medical consultation without presentation in the hospital and without intervention is seen as mild AE according to the ASGE lexicon's severity grading system and as no AE when using the AGREE classification [29, 30]. In a study comparing POEM and

LHM in 221 patients, serious AEs occurred in 2.7% and 7.3% of patients undergoing POEM and LHM, respectively. The number of non-serious AEs was 12 (11%) after both procedures. Intraprocedure AEs were also included in this number [4]. Another randomized controlled trial by Ponds et al. (2019) reported two serious AEs after PD and absence of serious AEs after POEM. Non-serious AEs occurred in 67% and 22% of the patients after POEM and PD, respectively. However, 37 of 42 non-serious AEs after POEM were ascribed to the presence of reflux esophagitis and reflux symptoms after follow-up of more than 30 days [8].

Currently, post-procedure care varies per hospital and routine esophagram 1 day post-POEM still is often performed [27, 31]. Five of 154 patients had signs of esophageal leakage on routine esophagram, of which two were indicated as clinically relevant and repeat endoscopy was performed to close the leakage with additional clips. After July 2016, routine esophagram was no longer performed and no serious complication occurred due to esophageal leakage, such as mediastinitis or an abscess, which could have been prevented by performing routine esophagram 1 day after POEM. After July 2016, more patients were observed 1 day longer because of symptoms suggestive for esophageal leakage, but this did not influence hospital stay. In these patients, CT was performed, which did not show esophageal leakage, and symptoms improved the next day in all patients. Repeat endoscopy was carried out three times after July 2016 because of retrosternal pain 4 and 5 days after POEM in two patients and melena 3 weeks after POEM in one patient. For these patients, extra clips or other additional endoscopic intervention were not needed during repeat endoscopy. These patients fully recovered with conservative management. Although severe complications resulting from esophageal leakage did not occur in any of the patients in our study, these complications can be life-threatening. Therefore, we recommend performing CT or upper endoscopy as a valid surrogate for routine esophagram after POEM when symptoms suggest that esophageal leakage is present.

A previous study with 78 patients evaluating the need for routine esophagram 1 day after POEM reported a high sensitivity of 100% and a low specificity of 45%. Abnormal findings on routine esophagram were present in 72% of the patients and usually had no clinical significance [21]. Another study in which routine esophagram after POEM was performed in 170 patients found abnormalities with limited clinical significance in most patients. Routine esophagram correctly identified esophageal leakage in two patients, but the findings were false-negative in two other patients and false-positive in one patient. The authors concluded that routine esophagram alone was not reliable enough to identify AEs [23]. Some studies are in favor of performing CT to detect AEs and to initiate prompt intervention [26, 32], but others do not recommend routine postoperative CT because of limited clinical significance [20, 22]. Abnormal findings, such as pneumoperitoneum and subcutaneous emphysema, are often seen on radiographic imaging after POEM and do not influence clinical management or patient outcome [19, 20, 21, 23, 26, 32, 33]. Therefore, findings for which intervention is not necessary should not be regarded as AEs

[19,33]. Performing routine esophagram 1 day post-POEM to assess delay in passage of contrast does not predict long-term efficacy of POEM, and thus, is not useful for that purpose either [34, 35].

This is the first study comparing AEs after POEM in patients with and without routine esophagram 1 day post-POEM. The year in which POEM was carried out differed between the two groups in our study, but other factors remained the same and a difference in post-procedure care would probably not have influenced the number or severity of post-procedure AEs. No changes have been made to the antibiotics prophylaxis and the post-procedure fasting protocol. It is plausible that the level of experience of the endoscopist was higher after July 2016, which might also explain the shorter procedure time after July 2016. A systematic review concluded that proficiency in performing POEM is obtained after 25 procedures. Although no post-procedure AEs occurred in the first 25 procedures, they were excluded for the above-mentioned reason from further analysis. A limitation of the study is that we do not know whether the two patients in which esophageal leakage was seen on routine esophagram and subsequent repeat endoscopy was carried out would have become symptomatic when repeat endoscopy with additional clip placement was not performed, and thus, whether potentially more serious AEs may have been prevented. This study is also limited by the absence of esophageal perforations in patients undergoing POEM after July 2016. However, this illustrates that esophageal perforation after POEM is uncommon and that POEM is safe. Finally, this was a retrospective cohort study performed in one center and the best study design to assess the need for routine esophagram after POEM would be a randomized controlled trial, but that would require very large numbers of patients, which does not seem feasible for this rare disease. The prospective collected data in this study and the accurate registration of AEs resulted in a high-quality database with limited missing data and would seem a good alternative to the above. A relatively large number of patients were included in this study and no patients were lost to follow-up. Nevertheless, due to the small number of AEs, we could not perform multivariate logistic regression analysis to assess possible predictors of AEs occurrence.

Conclusions

In conclusion, the results of this study show that POEM is safe and routine esophagram 1 day after POEM is unlikely to be of additional value in preventing serious AEs resulting from esophageal leakage. AEs occurring after July 2016 could not have been prevented by performing routine esophagram 1 day after POEM, therefore, we recommend performing postoperative imaging only in patients who have symptoms suggestive of post-procedure AEs. This approach will reduce costs and radiation exposure and allow for more rapid discharge of patients after POEM.

Acknowledgement

Authorship Statement: SN, EMW, GMCM and AJB designed the study. AJB supervised the project. SN and EMW collected the data and were responsible for project administration. EMW performed the data and statistical analysis. All authors contributed to the interpretation of the results. EMW wrote the manuscript with input from all authors. All authors had full access to the data and approved the final manuscript.

Conflict of Interest

EMW has nothing to declare. SN received consultancy fees from Ipsen and Truvion. GMCM has nothing to declare. BAJB has nothing to declare. PF received consultancy from Cook Medical and Olympus. AJB received research funding from Norgine, DrFalkPharma, Thelial, Sanofi/Regeneron and SST and received speaker and/or consulting fees from Laborie, Medtronic, BMS, Dr. Falk Pharma, Reckitt, Aqilion, Eupraxia, Alimentiv, Sanofi/Regeneron and AstraZeneca.

References

- [1] Pandolfino JE, Gawron AJ. Achalasia: a systematic review. *JAMA* 2015; 313: 1841–1852
- [2] Costantini M, Salvador R, Costantini A. Esophageal achalasia: Pros and cons of the treatment options. *World J Surg* 2022; 46: 1554–1560
- [3] Inoue H, Minami H, Kobayashi Y et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. *Endoscopy* 2010; 42: 265–271
- [4] Werner YB, Hakanson B, Martinek J et al. Endoscopic or surgical myotomy in patients with idiopathic achalasia. *N Engl J Med* 2019; 381: 2219–2229
- [5] Mundre P, Black CJ, Mohammed N et al. Efficacy of surgical or endoscopic treatment of idiopathic achalasia: a systematic review and network meta-analysis. *Lancet Gastroenterol Hepatol* 2021; 6: 30–38
- [6] Kuipers T, Ponds FA, Fockens P et al. Peroral endoscopic myotomy versus pneumatic dilation in treatment-naïve patients with achalasia: 5-year follow-up of a randomised controlled trial. *Lancet Gastroenterol Hepatol* 2022; 7: 1103–1111
- [7] Haito-Chavez Y, Inoue H, Beard KW et al. Comprehensive analysis of adverse events associated with per oral endoscopic myotomy in 1826 patients: An international multicenter study. *Am J Gastroenterol* 2017; 112: 1267–1276
- [8] Ponds FA, Fockens P, Lei A et al. Effect of peroral endoscopic myotomy vs pneumatic dilation on symptom severity and treatment outcomes among treatment-naïve patients with achalasia: A randomized clinical trial. *JAMA* 2019; 322: 134–144
- [9] Brewer Gutierrez OI, Moran RA, Familiari P et al. Long-term outcomes of per-oral endoscopic myotomy in achalasia patients with a minimum follow-up of 4 years: a multicenter study. *Endosc Int Open* 2020; 8: E650–E655
- [10] Simkova D, Mares J, Vackova Z et al. Peri-procedural safety profile of peroral endoscopic myotomy (POEM) – a retrospective analysis of adverse events according to two different classifications. *Surg Endosc* 2023; 37: 1242–1251
- [11] Zhang XC, Li QL, Xu MD et al. Major perioperative adverse events of peroral endoscopic myotomy: a systematic 5-year analysis. *Endoscopy* 2016; 48: 967–978
- [12] Lee JY, Lim CH, Kim DH et al. Adverse events associated with peroral endoscopic myotomy affecting extended hospital stay: A multi-cent-

- ter retrospective study in South Korea. *J Neurogastroenterol Motil* 2022; 28: 247–254
- [13] Inoue H, Sato H, Ikeda H et al. Per-oral endoscopic myotomy: A series of 500 patients. *J Am Coll Surg* 2015; 221: 256–264
- [14] Werner YB, von Renteln D, Noder T et al. Early adverse events of peroral endoscopic myotomy. *Gastrointest Endosc* 2017; 85: 708–718 e2
- [15] Khashab MA, El Zein M, Kumbhari V et al. Comprehensive analysis of efficacy and safety of peroral endoscopic myotomy performed by a gastroenterologist in the endoscopy unit: a single-center experience. *Gastrointest Endosc* 2016; 83: 117–125
- [16] Shiwaku H, Inoue H, Yamashita K et al. Peroral endoscopic myotomy for esophageal achalasia: outcomes of the first over 100 patients with short-term follow-up. *Surg Endosc* 2016; 30: 4817–4826
- [17] Von Renteln D, Fuchs KH, Fockens P et al. Peroral endoscopic myotomy for the treatment of achalasia: an international prospective multicenter study. *Gastroenterology* 2013; 145: 309–11 e1
- [18] Familiari P, Gigante G, Marchese M et al. Peroral endoscopic myotomy for esophageal achalasia: Outcomes of the first 100 patients with short-term follow-up. *Ann Surg* 2016; 263: 82–87
- [19] Nabi Z, Reddy DN, Ramchandani M. Adverse events during and after per-oral endoscopic myotomy: prevention, diagnosis, and management. *Gastrointest Endosc* 2018; 87: 4–17
- [20] Cai MY, Zhou PH, Yao LQ et al. Thoracic CT after peroral endoscopic myotomy for the treatment of achalasia. *Gastrointest Endosc* 2014; 80: 1046–1055
- [21] El Khoury R, Teitelbaum EN, Sternbach JM et al. Evaluation of the need for routine esophagram after peroral endoscopic myotomy (POEM). *Surg Endosc* 2016; 30: 2969–2974
- [22] Chartier M, Barat M, Dohan A et al. Clinical impact of routine CT esophagogram after peroral endoscopic myotomy (POEM) for esophageal motility disorders. *Endosc Int Open* 2021; 9: E1355–E1360
- [23] Reddy CA, Tavakkoli A, Abdul-Hussein M et al. Clinical impact of routine esophagram after peroral endoscopic myotomy. *Gastrointest Endosc* 2021; 93: 102–106
- [24] Nast JF, Berliner C, Rosch T et al. Endoscopy versus radiology in post-procedural monitoring after peroral endoscopic myotomy (POEM). *Surg Endosc* 2018; 32: 3956–3963
- [25] Inoue H, Shiwaku H, Iwakiri K et al. Clinical practice guidelines for peroral endoscopic myotomy. *Dig Endosc* 2018; 30: 563–579
- [26] Pannu D, Yang D, Abbitt PL et al. Prospective evaluation of CT esophagram findings after peroral endoscopic myotomy. *Gastrointest Endosc* 2016; 84: 408–415
- [27] Stavropoulos SN, Modayil RJ, Friedel D et al. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. *Surg Endosc* 2013; 27: 3322–3338
- [28] Puli SR, Wagh MS, Forcione D et al. Learning curve for esophageal peroral endoscopic myotomy: a systematic review and meta-analysis. *Endoscopy* 2023; 55: 355–360
- [29] Nass KJ, Zwager LW, van der Vlugt M et al. Novel classification for adverse events in GI endoscopy: the AGREE classification. *Gastrointest Endosc* 2022; 95: 1078–85 e8
- [30] Cotton PB, Eisen GM, Aabakken L et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc* 2010; 71: 446–454
- [31] Petrov RV, Fajardo RA, Bakhos CT et al. Peroral endoscopic myotomy: techniques and outcomes. *Shanghai Chest* 2021; 5: 14
- [32] Pannu D, Draganov PV. CT esophagram findings after POEM procedure. *Gastrointest Endosc* 2015; 81: 1502
- [33] Yang S, Zeng MS, Zhang ZY et al. Pneumomediastinum and pneumoperitoneum on computed tomography after peroral endoscopic myotomy (POEM): postoperative changes or complications? *Acta Radiol* 2015; 56: 1216–1221
- [34] Sternbach JM, El Khoury R, Teitelbaum EN et al. Early esophagram in per-oral endoscopic myotomy (POEM) for achalasia does not predict long-term outcomes. *Surgery* 2015; 158: 1128–1135
- [35] DeWitt JM, Siwiec RM, Perkins A et al. Evaluation of timed barium esophagram after per-oral endoscopic myotomy to predict clinical response. *Endosc Int Open* 2021; 9: E1692–E1701