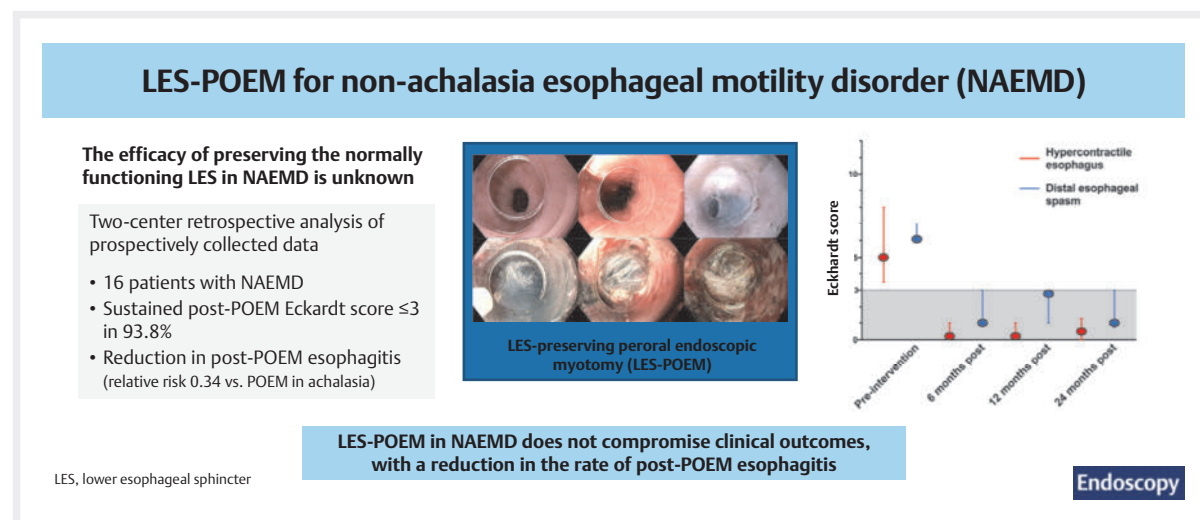




When less is more: lower esophageal sphincter-preserving peroral endoscopic myotomy is effective for non-achalasia esophageal motility disorders ▶

GRAPHICAL ABSTRACT



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ABSTRACT

Background Non-achalasia esophageal motility disorders (NAEMDs), encompassing distal esophageal spasm (DES) and hypercontractile esophagus (HCE), are rare conditions. Peroral endoscopic myotomy (POEM) is a promising treatment option. In NAEMDs, unlike with achalasia, the lower esophageal sphincter (LES) functions normally, suggesting the potential of LES preservation during POEM.

Methods This retrospective two-center observational study focused on patients undergoing LES-preserving POEM (LES-POEM) for NAEMD. Eckardt scores were assessed pre-POEM and at 6, 12, and 24 months post-POEM, with follow-up endoscopy at 6 months to evaluate for reflux

esophagitis. Clinical success, defined as an Eckardt score ≤ 3 , served as the primary outcome.

Results 227 patients were recruited over 84 months until May 2021. Of these, 16 underwent LES-POEM for an NAEMD (9 with HCE and 7 with DES). The median pre-POEM Eckardt score was 6.0 (interquartile range [IQR] 5.0–7.0), which decreased to 1.0 (IQR 0.0–1.8; $P < 0.001$) 6 months post-POEM. This was sustained at 24 months, with an Eckardt score of 1.0 (IQR 0.0–1.8; $P < 0.001$). Two patients (12.5%) developed Los Angeles grade A or B esophagitis.

Conclusions LES-POEM for NAEMD demonstrates favorable clinical outcomes, with infrequent esophagitis and re-intervention for LES dysfunction rarely required.

Introduction

Non-achalasia esophageal motility disorders (NAEMDs), including hypercontractile esophagus (HCE), distal esophageal spasm (DES), and esophagogastric junction outflow obstruction (EJGOO), are rare conditions, with a prevalence lower than that of achalasia [1]. Hypercontractile esophageal disorders account for 1.5%–3% of manometric diagnoses for patients with dysphagia [2,3]. Common symptoms include chest pain and dysphagia, leading to significant healthcare costs and compromised quality of life [4].

Pharmacological treatments, including calcium channel blockers, phosphodiesterase type 5 inhibitors, and nitrates, have failure rates of 74% and notable side effects [5,6]. Alternative approaches like botulinum toxin injection and pneumatic balloon dilation offer only transient relief.

Peroral endoscopic myotomy (POEM) has emerged as a promising treatment option with pooled data reporting efficacy in 72% of patients with HCE and in 88% with DES [7]. Unlike achalasia, the lower esophageal sphincter (LES) functions normally in DES and HCE [8,9,10], and therefore it could theoretically be preserved during POEM. This may also protect against gastroesophageal reflux disease (GERD), which is the most frequent and significant adverse event (AE) following POEM for achalasia, being proven in 44% of patients with 24-hour pH monitoring [11,12]. The clinical efficacy of LES-preserving POEM (LES-POEM), defined as an Eckardt score ≤ 3 , in NAEMD without the need for reintervention at 6 months is unknown.

Methods

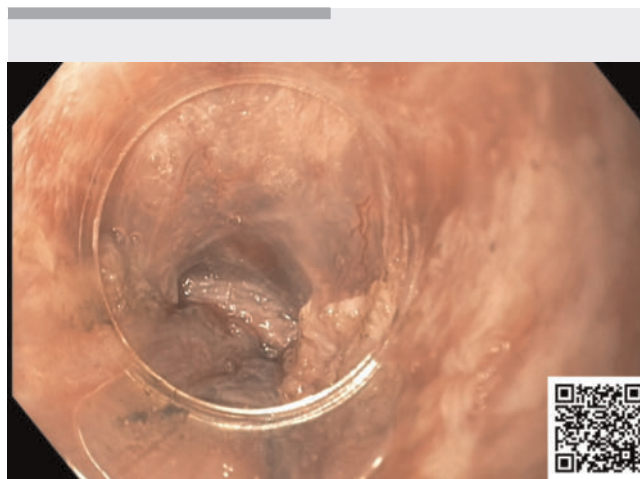
Study design and patient selection

We performed a retrospective analysis of data collected prospectively over 84 months until May 2021 in two Australian tertiary referral centers that followed the same protocol. All consecutive patients undergoing LES-POEM provided written consent. All had assessment with upper gastrointestinal endoscopy, barium swallow, and esophageal high resolution manometry (HRM) prior to undergoing LES-POEM. All pharmacological therapies that might have impacted HRM were ceased prior

to the test. The diagnosis of an esophageal motility disorder and its subtype were based on the Chicago classification version 3 (version 4 was not available during our study period). Exclusion criteria included age < 18 years, inability to tolerate anesthetic sedation, and previous Heller's myotomy or pneumatic dilation. Previous botulinum toxin was not an exclusion. Our centers were not referred patients with EJGOO, most likely owing to the heterogeneity of the condition and the limited data on the efficacy of POEM in this subset of NAEMD.

Eckardt scores were calculated pre-POEM and at 6, 12, and 24 months post-POEM. The primary outcome measure was achievement of an Eckardt score ≤ 3 without the need for reintervention [13]. Secondary outcomes were AEs and endoscopic evidence of post-POEM esophagitis at 6 months, assessed by follow-up gastroscopy.

Outcomes were compared with a contemporaneous group of consecutive patients undergoing POEM for achalasia at the same institutions. The study was approved by the Human Re-



Video 1 Performance of a lower esophageal sphincter-preserving peroral endoscopic myotomy (LES-POEM).

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search Ethics Committee at Westmead Hospital, Sydney (reference: [4274] AURED LNR/15/WMEAD/152).

LES-POEM procedure

LES-POEM (► **Video 1**), which was performed by an experienced interventionalist or a closely supervised fellow, is initiated with the identification of the gastroesophageal junction (GEJ) and measuring of its distance from the incisors. Cold water (<18°C) is instilled to assess the esophageal lumen for spasm, corroborating with the HRM. A submucosal injection of succinylated gelatin (Gelofusine; B. Braun, Bella Vista, Australia) with 0.4% indigo carmine is placed 2 cm proximal to the hypercontractile area. A triangular-tip knife (Olympus, Tokyo, Japan) with a microprocessor-controlled generator (ERBE VIO 300 D or VIO3; ERBE, Tübingen, Germany) is used to create a submucosal tunnel anteriorly (2 o'clock) with swift coagulation (50W, effect 2, VIO 300D; or preciseSECT, effect 4, VIO 3, ERBE).

After the findings of the HRM have been corroborated, the LES is identified within the submucosal tunnel by the characteristic narrowing, sudden widening, and presence of palisading vessels within the submucosa (► **Fig. 1**). The distance from the incisors is noted and corroborated with the previous measurement, again noting the characteristic pinch seen within the esophageal lumen at the same level, the superior aspect of the gastric folds in deflation, and the palisading vessels. The tunnel is extended slightly, no further than 1 cm beyond the LES. During this process, the LES is repeatedly and sequentially identified by the characteristic features described above and the tun-

nel extent is corroborated frequently with the esophageal luminal features.

A selective myotomy of the inner circular muscle fibers is performed with dry cut current (80W, effect 3, VIO 300D; or preciseSect, effect 4, VIO 3), preserving the longitudinal muscle fibers. As the LES is slowly approached, frequent tunnel and luminal corroboration of the myotomy extent, based on the standard landmarks described, is performed. Finally, the extent of the tunnel myotomy and its luminal coordinate is confirmed. Bleeding is treated with soft coagulation (80W, effect 4, ERBE), avoiding large vessels. The mucosal defect is then closed with clips.

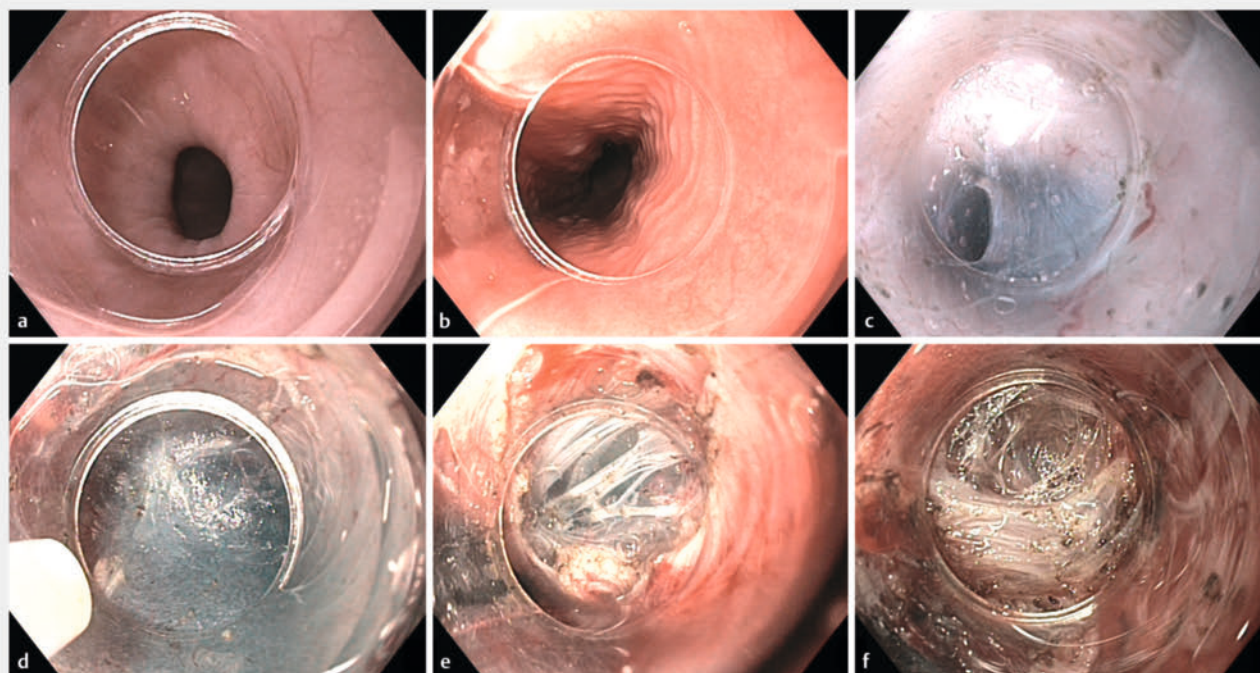
All of the study patients underwent general anesthesia for the procedure and were given a single dose of intraprocedural ceftriaxone and metronidazole.

Post-POEM management

After the POEM procedure, the patients were fasted and observed overnight. If they were well, they were commenced on clear fluids and discharged if they were stable, afebrile, pain free, and tolerating liquids. On discharge, patients were prescribed proton pump inhibitors twice daily for 3 months, which were then stepped down as needed. Clinical review occurred at 6 weeks and at 6, 12, and 24 months post-POEM.

Statistical analysis

Data analysis was performed using R Studio (Vienna, Austria) and Prism 9 (GraphPad Software, San Diego, California, USA).



► **Fig. 1** Endoscopic images of the pertinent steps in performing lower esophageal sphincter-preserving peroral endoscopic myotomy (LES-POEM) showing: **a,b** the patterns of spasm and hypercontractility are identified; **c** identification of the narrowing of the submucosal tunnel at the LES; **d** identification of the sudden widening of the submucosal tunnel beyond the LES; **e** myotomy with preservation of the longitudinal muscle; **f** identification and preservation of the LES.

Continuous variables are reported as median with interquartile range (IQR) and categorical variables are reported as frequencies and percentages. Comparisons were made between time using the non-parametric Wilcoxon signed rank test for Eckardt scores calculated pre-POEM and 6, 12, and 24 months post-POEM. The risk of post-POEM esophagitis in NAEMD was compared relative to achalasia.

Results

Patient and procedure characteristics

A total of 227 patients underwent POEM in two Australian tertiary centers over 84 months until May 2021. Of these, 211 had achalasia and 16 had NAEMD (9 with HCE and 7 with DES). There were 10 procedures performed at Westmead Hospital and six at Sir Charles Gairdner Hospital. All patients had their diagnosis confirmed on HRM, and the integrated relaxation pressure (IRP) was confirmed as being normal in all NAEMD patients prior to LES-POEM (► **Table 1**).

Within the NAEMD cohort, the median age was 66.0 years (IQR 58.0–81.0) and 43.8% were men (► **Table 2**). At the time of data analysis, all 16 patients had completed follow-up at 24 months. Pharmacological therapies trialed prior to LES-POEM included a calcium channel blocker (n=5; 31.3%) and nitrates (n=4; 25.0%). Previous therapeutic procedures included endoscopic balloon dilation (n=5; 31.3%) and previous botulinum toxin (n=2; 12.5%) (► **Table 3**).

The median procedure time was 72.0 minutes (IQR 55.5–97.8) and the submucosal tunnelling time was 33.0 minutes (IQR 25.5–48.5) (► **Table 2**). The median myotomy length was 10.0 cm (IQR 10.0–13.0), with no significant difference in the myotomy length between patients with DES (median 11.5 cm [IQR 9.3–13.5]) and HCE (median 10.0 cm [IQR 10.0–13.0]). A median of seven clips (IQR 6.0–7.0) were used to close the tunnel orifice. The median length of hospital stay was 2.0 days (IQR 1.0–3.0).

Clinical success

The median pre-POEM Eckardt score was 6.0 (IQR 5.0–7.0). Of the 16 patients, 15 patients (93.8%) experienced an excellent clinical result, with a sustained Eckardt score ≤ 3 over the follow-up period. The Eckardt score decreased to 1.0 (IQR 0.0–1.8; $P<0.001$) 6 months post-POEM, with results sustained at 12 months (Eckardt score 1.0 [IQR 0.0–2.8]; $P<0.001$) and 24 months (Eckardt score 1.0 [IQR 0.0–1.8]; $P<0.001$).

In the DES cohort, the median pre-POEM Eckardt score was 6.0 (IQR 6.0–7.0), which was reduced to 1.0 (IQR 0.8–3.0; $P=0.003$) at 24 months. In the HCE cohort, the median pre-POEM Eckardt score was 5.0 (IQR 3.5–8.0), which was reduced to 0.5 (IQR 0.0–1.25; $P=0.003$) at 24 months (► **Fig. 2**).

Reintervention

One patient (6.3%) with DES initially responded to LES-POEM, with their Eckardt score reducing from 7 pre-POEM to 4 at 6 months post-POEM, but they then progressed to type III achalasia. A subsequent LES myotomy was performed 12 months la-

► **Table 1** Manometric findings before lower esophageal sphincter-preserving POEM (all values are median [interquartile range]).

	Hypercontractile esophagus (n=9)	Distal esophageal spasm (n=7)
Residual IRP, mmHg	6 (4–11)	10 (3–11)
Distal contractile integral, mmHg s cm	9538 (5590–1431)	1091 (747–4647)
Distal latency, seconds	7 (6–8)	4 (4–5)
POEM, peroral endoscopic myotomy; IRP, integrated relaxation pressure.		

► **Table 2** Characteristics of the patients within the non-achalasia esophageal motility disorders cohort and the procedures they underwent (all values unless otherwise stated are median [interquartile range]).

	Hypercontractile esophagus (n=9)	Distal esophageal spasm (n=7)	All (n=16)
Age, years	68.5 (55.0–74.0)	64.0 (58.0–85.0)	66.0 (58.0–81.0)
Sex, male, n (%)	2 (22.2%)	6 (85.7%)	8 (50.0%)
LES-POEM duration, minutes	81.0 (53.3–101.5)	68.5 (61.3–93.0)	72.0 (55.5–97.8)
Tunnel duration, minutes	30.0 (25.0–50.0)	34.0 (33.0–35.0)	33.0 (25.5–48.5)
Incision distance, cm	26.0 (25.0–28.5)	25.0 (14.5–27.8)	26.0 (25.0–27.0)
Myotomy length, cm	10.0 (10.0–13.0)	11.5 (9.3–13.5)	10.0 (10.0–13.0)
Clips, n	7.0 (5.0–7.0)	7.0 (6.0–8.0)	7.0 (6.0–7.0)
Follow-up time, months	24.0 (18.0–24.0)	24.0 (18.0–24.0)	24.0 (18.0–24.0)
Length of stay, days	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)
LES-POEM, lower esophageal sphincter-preserving peroral endoscopic myotomy.			

ter, leading to sustained symptom remission, with an Eckardt score of 0 at 6, 12, and 24 months following this procedure.

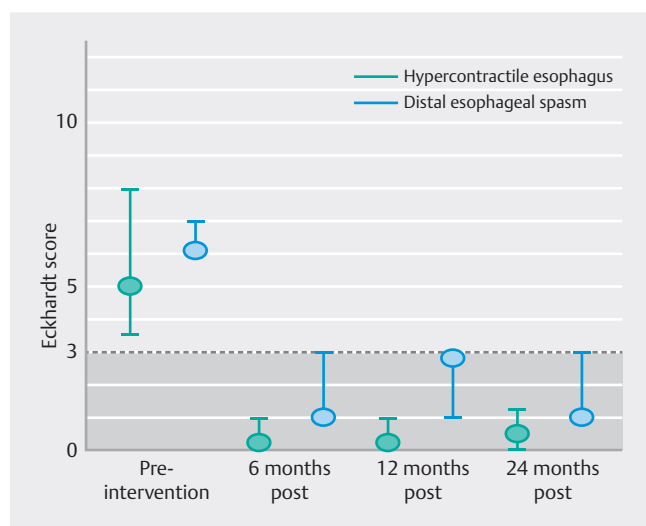
Adverse events

There was only one patient (6.3%) who had a serious AE, which was a transudative pleural effusion in the context of underlying cardiac failure. The patient recovered during their inpatient stay, with no long-term sequelae and no impact on the success of LES-POEM.

► **Table 3** Previous treatments before the lower esophageal sphincter-preserving POEM procedure (all values are n [%]).

	Hypercontractile esophagus (n=9)	Distal esophageal spasm (n=7)	All (n=16)
Proton pump inhibitor	4 (44.4%)	4 (57.1%)	8 (50.0%)
Calcium channel blocker	3 (33.3%)	2 (28.6%)	5 (31.3%)
Nitrates	1 (11.1%)	3 (42.9%)	4 (25.0%)
Endoscopic dilation*	3 (33.3%)	2 (28.6%)	5 (31.3%)
Pneumatic dilation	0 (0%)	0 (0%)	0 (0%)
Botulinum toxin	1 (11.1%)	1 (14.3%)	2 (12.5%)

*Endoscopic dilation refers to either through-the-scope (TTS) or Savary–Gilliard dilation.



► **Fig. 2** Graph showing the median (IQR) Eckardt scores before and after lower esophageal sphincter-preserving peroral endoscopic myotomy (LES-POEM) for patients with a non-achalasia esophageal motility disorder.

Post-POEM esophagitis

Two patients (12.5%) had post-POEM esophagitis, which was graded as Los Angeles grade A/B at their 6-month follow-up endoscopy. This rate was compared with the rate of post-POEM esophagitis in patients with achalasia, which was higher at 36.9% (41/111). The relative risk of post-POEM esophagitis in the NAEMD cohort was 0.34 (95%CI 0.09–1.02) when compared with the achalasia cohort.

Discussion

Although NAEMDs are relatively rare, they profoundly affect patients' quality of life, as was evident from our cohort's median Eckardt score of 6. LES-POEM demonstrated efficacy, with a sustained reduction in the Eckardt score to a median of 1 over 2 years. Furthermore, it exhibited a favorable safety profile and, although not adequately powered and not reaching statistical significance, there was a lower rate of reflux esophagitis compared with achalasia patients undergoing POEM. Notably, LES-POEM aligns well with principles of precision medicine, offering tailored treatments based on individual pathology [14]. The question arises as to whether division of the LES is justified when the pathophysiology does not involve this structure.

NAEMDs, characterized by a panesophageal pathophysiological basis, have shown suboptimal responses to pharmacological options [15]. Modified Heller's myotomy has been trialed in NAEMD and type III achalasia; however, the procedure is limited by a poor safety profile and its inability to facilitate a longer myotomy [15, 16]. POEM presents an advantage as it enables a long myotomy that can correspond to the abnormal segment determined by HRM.

Based on the Chicago classification, HCE and DES exhibit a normal IRP, indicating normal transit across the gastroesophageal junction [8, 9, 10]. Therefore, preserving the LES in patients with an NAEMD is a theoretical consideration. Our study demonstrated favorable outcomes in the majority of cases, with 15 patients (93.8%) achieving a clinical response with LES-POEM. Although one patient progressed to type III achalasia, necessitating a subsequent LES myotomy; such progression is uncommon, occurring in 8% of patients [17]. Therefore, a universal approach involving LES myotomy may not be warranted. Moreover, close follow-up, as demonstrated in our cohort, enables timely identification and management of disease progression.

Within the limitations of our small cohort, LES-POEM showed a nonstatistically significant reduction in reflux esophagitis, a significant side effect [18]. Only two patients (12.5%) experienced Los Angeles grade A/B esophagitis, a notably lower incidence compared with contemporary studies, which report rates as high as 44% on 24-hour pH monitoring and 57% at 3-month follow-up endoscopy [11]. Furthermore, in our cohort, the relative risk of reflux esophagitis in patients undergoing LES-POEM for an NAEMD was nearly three times lower (relative risk 0.34) compared with those undergoing POEM for achalasia; however, this did not reach statistical significance owing to lack of power.

Preservation of the LES in patients with an NAEMD may raise concerns about dysphagia owing to a potential imbalance between the propulsive strength of the dissected tubular esophagus and the normal pressure of the undissected LES; however, this concern was not observed in our patient cohort within the 2-year follow-up.

This study is not without limitations. The small cohort of 16 patients is consistent with the rarity of NAEMDs, which makes large randomized controlled trials challenging. Furthermore, despite the Eckardt score being validated specifically for achala-

sia, it has been widely used, owing to the lack of an alternative clinical score, in NAEMD [7]. Additionally, confirmatory testing of LES distensibility using EndoFlip is not routinely available in Australia, as it not funded by our healthcare system; we would advocate for its routine use if available. Furthermore, our cohort did not routinely undergo confirmatory physiological and 24-hour pH testing for post-POEM reflux, potentially resulting in under-reporting of this incidence; however, all of our patients underwent a 6-month follow-up endoscopy, which reflects real-world clinical practice.

In conclusion, our experience confirms that LES-POEM is an effective and safe treatment for NAEMDs. LES-POEM resulted in significantly improved Eckardt scores, which were sustained over a 2-year period, with minimal AEs and a low incidence of post-POEM esophagitis. We advocate for LES-POEM as the preferred endoscopic approach for DES and HCE when intervention is warranted; however, our findings require further validation with larger studies.

Conflict of Interest

S. Raftopoulos has received research support from Olympus. M.J. Bourke has received research support from Olympus, Cook Medical, and Boston Scientific. V. Peranathan, S. Gupta, A. Whitfield, A. Craciun, O. Cronin, T. O'Sullivan, K. Byth, M. Sidhu, L.F. Hourigan, and N. G. Burgess declare that they have no conflict of interest.

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CORRECTION

Correction: When less is more: lower esophageal sphincter-preserving peroral endoscopic myotomy is effective for non-achalasia esophageal motility disorders

Varan Peranathan, Sunil Gupta, Anthony Whitfield et al. When less is more: lower esophageal sphincter-preserving peroral endoscopic myotomy is effective for non-achalasia esophageal motility disorders *Endoscopy* 2024; doi: 10.1055/a-2239-7371.

In the above-mentioned article the title has been corrected. Correct is: When less is more: lower esophageal sphincter-preserving peroral endoscopic myotomy is effective for non-achalasia esophageal motility disorders. This was corrected in the online version on March 11, 2024.