10 anni di POEM: quale bilancio

Francesco Azzolini

GI Endoscopy Unit

Gastroenterology and Gastrointestinal Endoscopy Division

San Raffaele Scientific Institute

Vita Salute San Raffaele University

MIOTOMIA ENDOSCOPICA PERORALE (POEM)

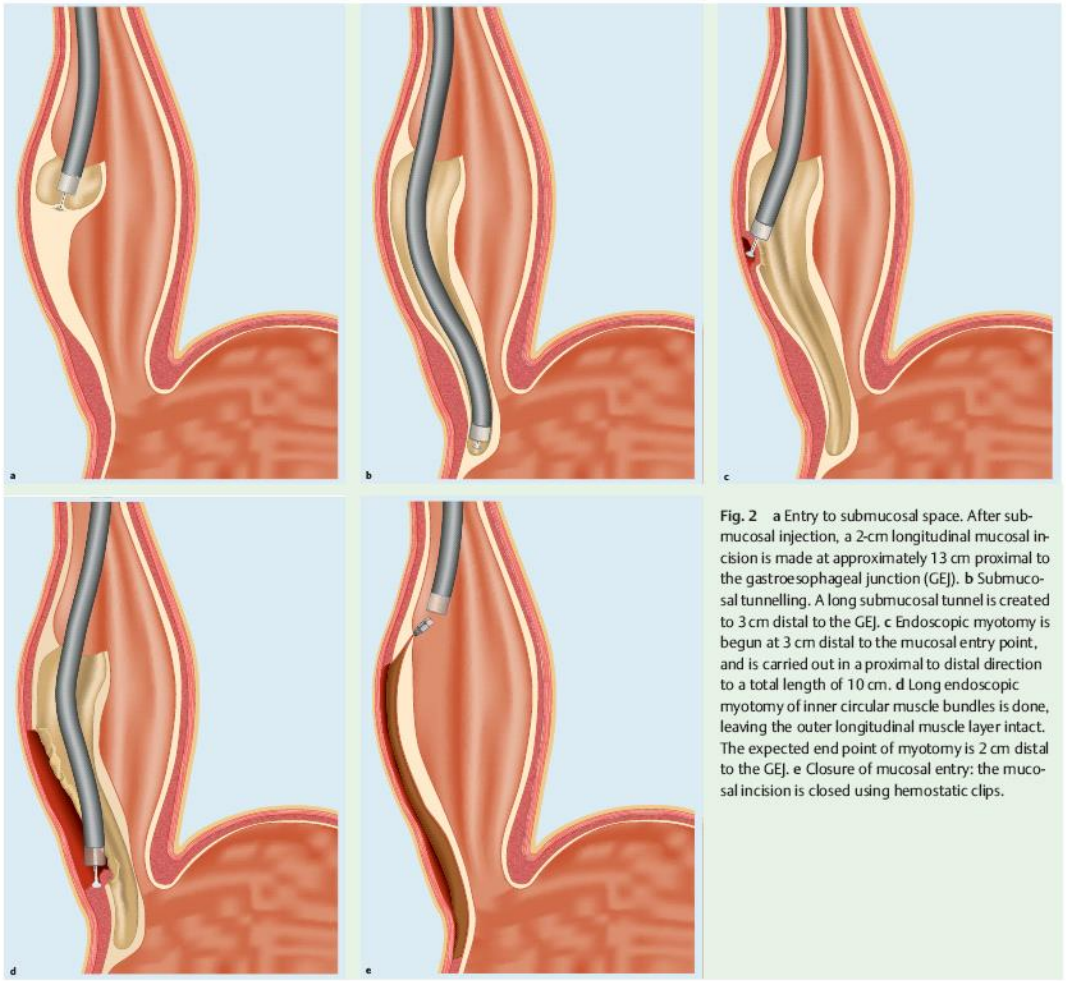


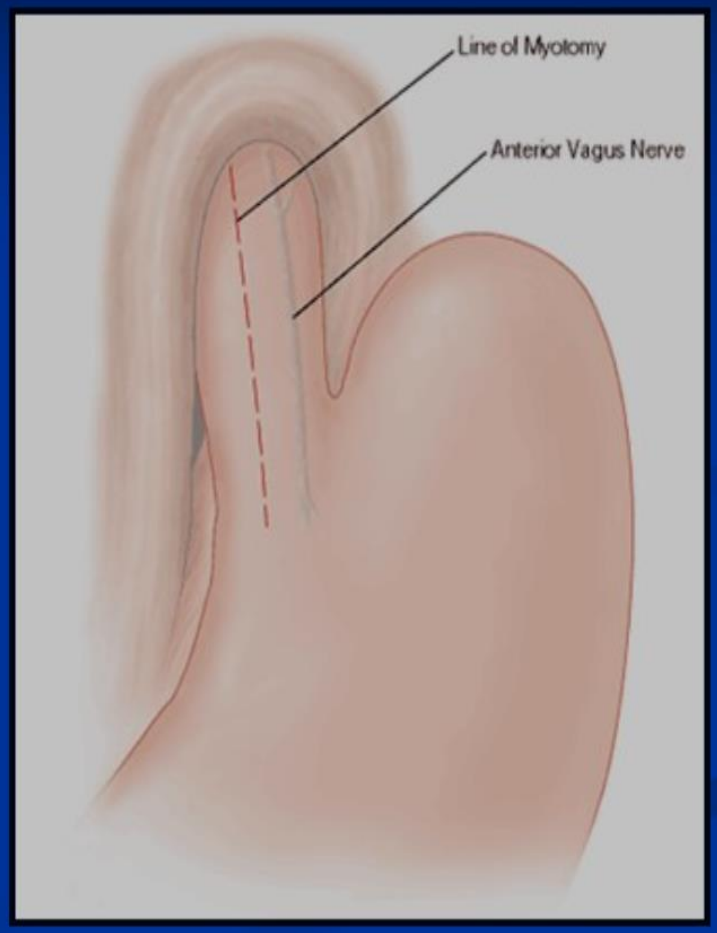
Fig. 2 **a** Entry to submucosal space. After submucosal injection, a 2-cm longitudinal mucosal incision is made at approximately 13 cm proximal to the gastroesophageal junction (GEJ). **b** Submucosal tunnelling. A long submucosal tunnel is created to 3 cm distal to the GEJ. **c** Endoscopic myotomy is begun at 3 cm distal to the mucosal entry point, and is carried out in a proximal to distal direction to a total length of 10 cm. **d** Long endoscopic myotomy of inner circular muscle bundles is done, leaving the outer longitudinal muscle layer intact. The expected end point of myotomy is 2 cm distal to the GEJ. **e** Closure of mucosal entry: the mucosal incision is closed using hemostatic clips.

La miotomia esofagea orale (POEM) è una procedura chirurgica endoscopica per il trattamento di acalasia che è stata eseguita prima dal Inoue nel 2008.

La POEM utilizza una gastroscopio flessibile standard per creare un miotomia chirurgica controllata attraverso la giunzione gastrico esofagea e nel parete dello stomaco.

Inoue H et al. POEM for esophageal achalasia… Endoscopy 2010; 42: 265–271

- The myotomy is performed at the 11 o'clock position.
- The myotomy is started about 3 cm above the esophagogastric junction. Before it is extended upward and downward.
- The proper submucosal plane should be reached at a single point; in this way, the likelihood of subsequent mucosal perforation can be reduced .
- The total length of the myotomy is typically about 8 cm.

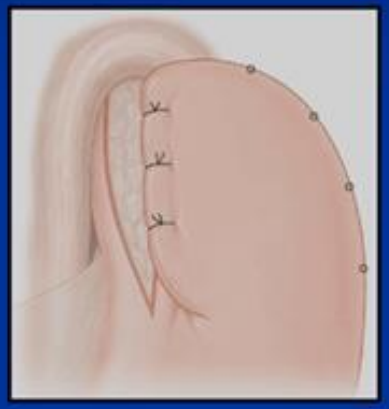


Dor Procedure - Anterior Partial Fundoplication

- anterior 180° wrap

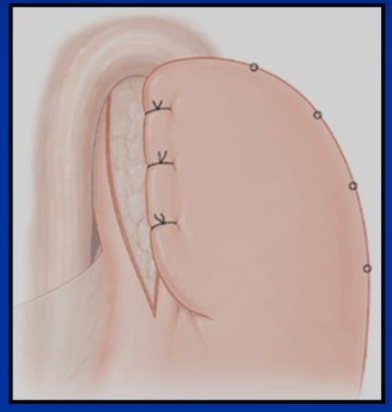
The uppermost stitch in the first row incorporates the fundus, the esophageal wall, and the left pillar of the crus.

Dor Procedure - Anterior Partial Fundoplication



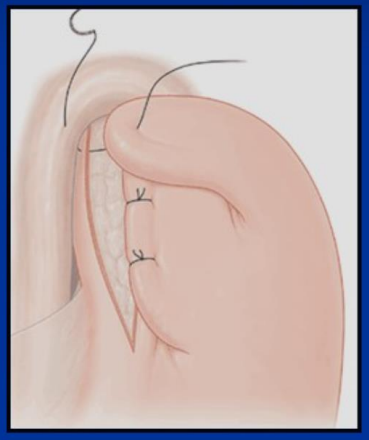
The second and third stitches in the first row incorporate only the fundus and the left side of the esophageal wall. .

Dor Procedure - Anterior Partial Fundoplication

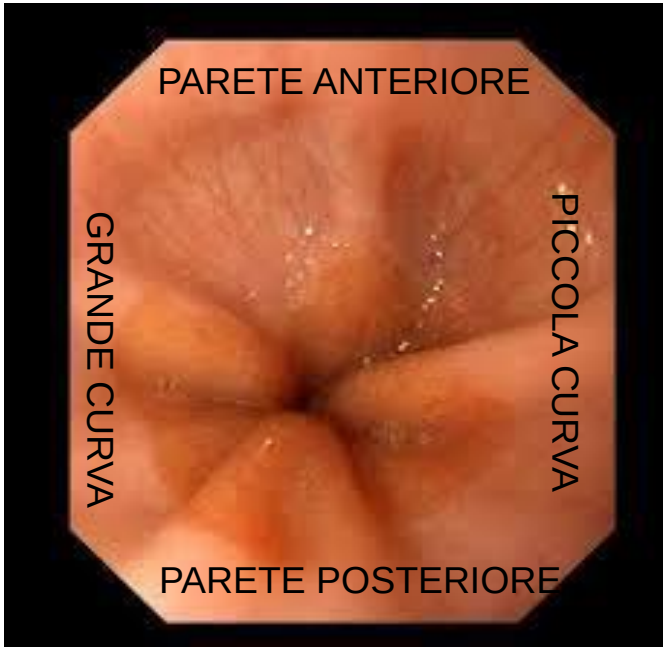


The second and third stitches in the first row incorporate only the fundus and the left side of the esophageal wall. .

Dor Procedure - Anterior Partial Fundoplication

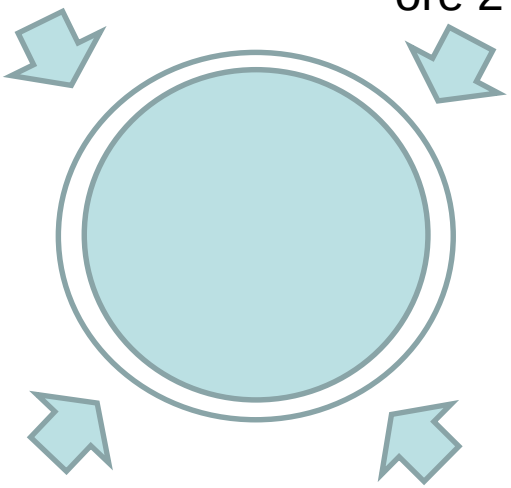


The uppermost stitch in the second row incorporates the fundus, the esophageal wall, and the right crus.



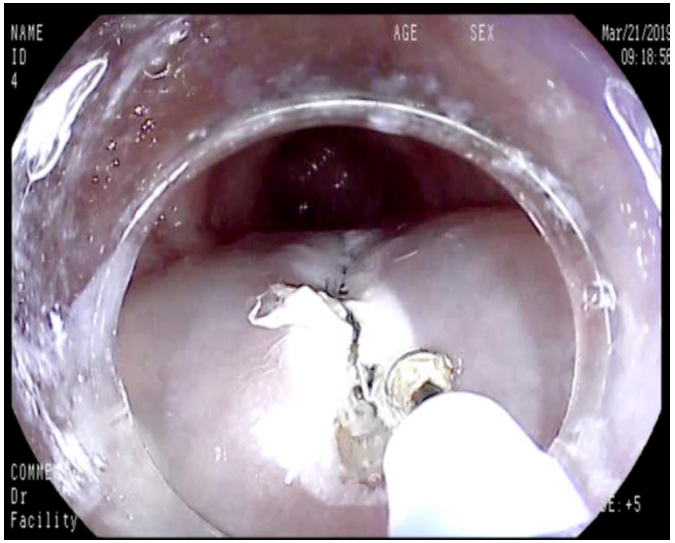
Heller ore 11

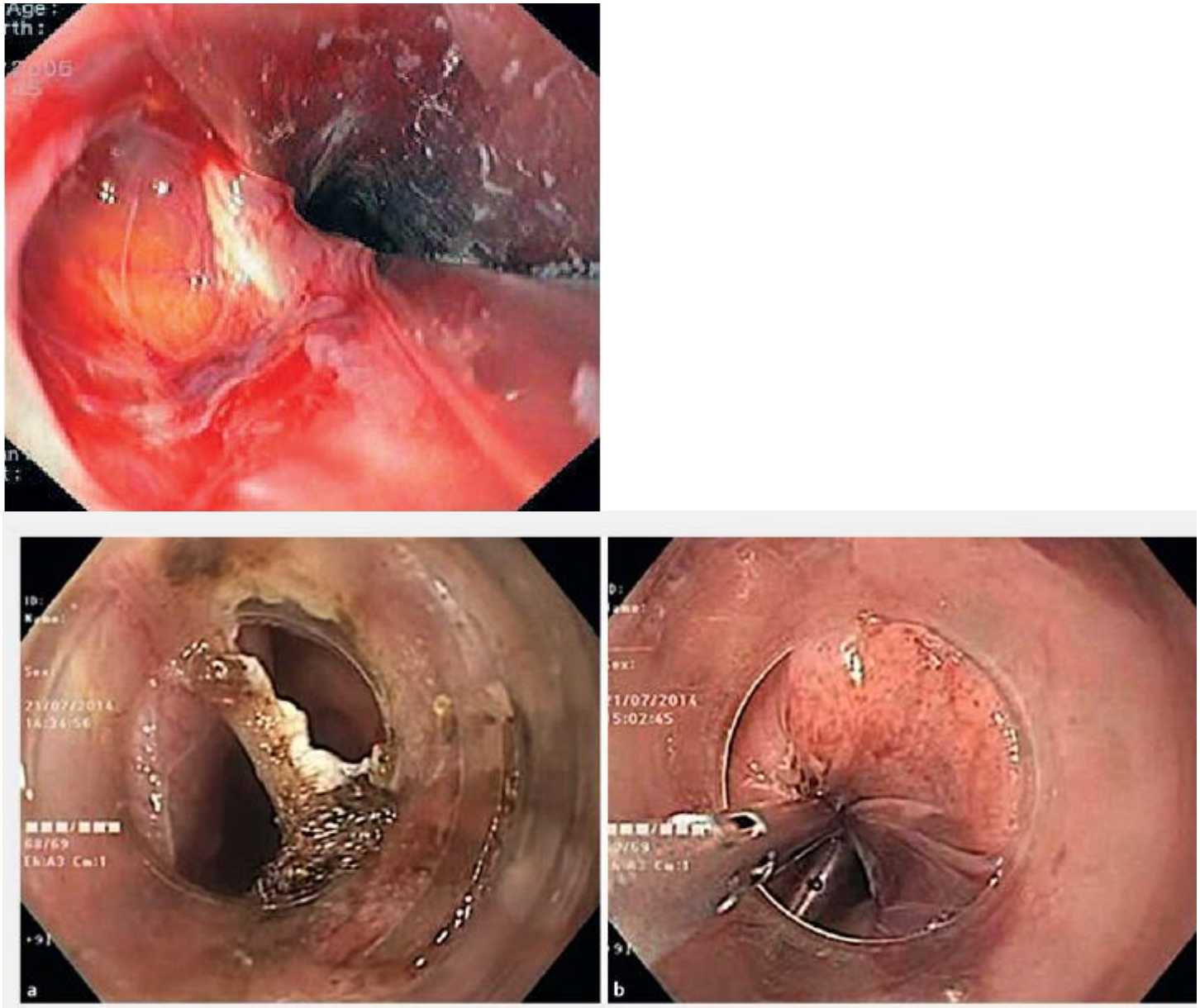
POEM Anteriore ore 2



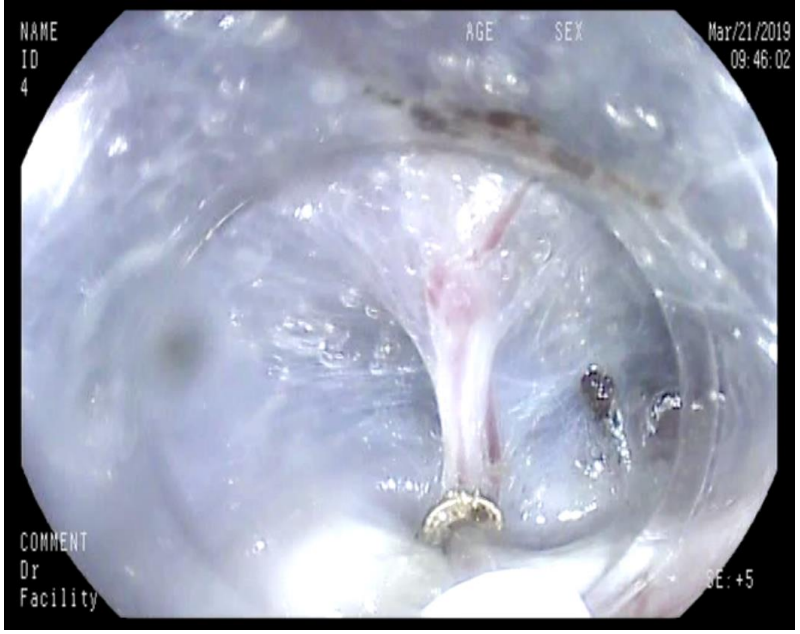
Grande curva ore 7

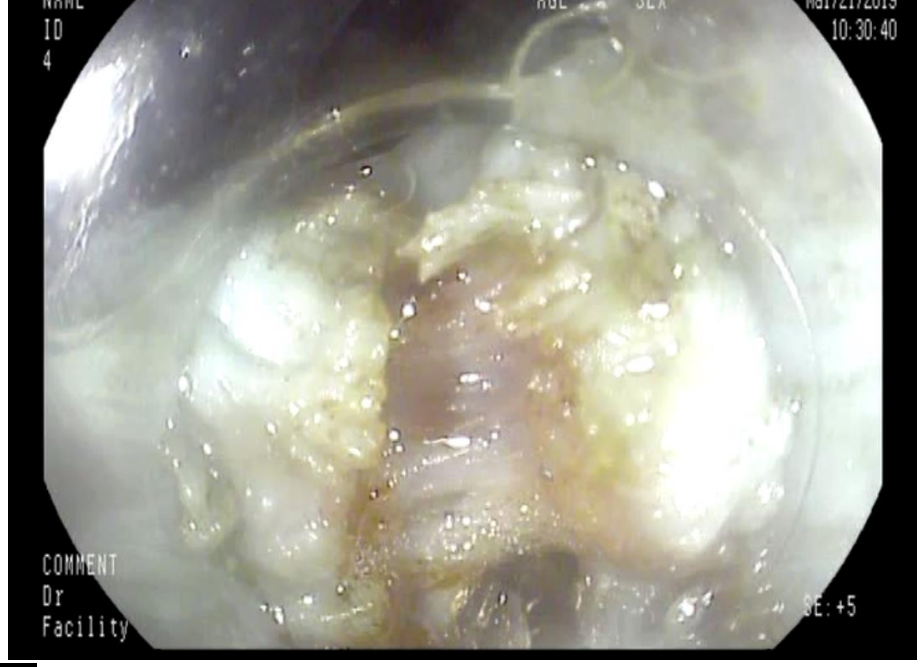
POEM Posteriore ore 5

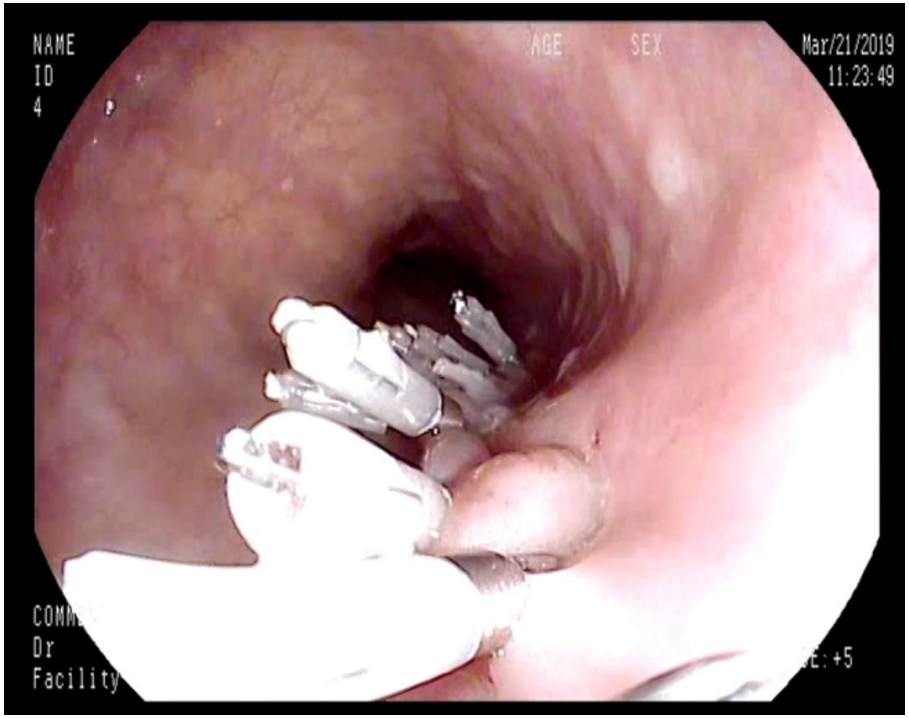




►**Fig. 5** Mucosal injury during peroral endoscopic myotomy. **a** Large mucosal perforation. **b** Successful closure of the mucosal injury with endoclips.


NAME
ID
4
AGE
SEX
Mar/21/2019
09:46:02
COMMENT
Dr
Facility


NAME
ID
4
AGE
SEX
10:30:40
COMMENT
Dr
Facility


NAME
ID
4
AGE
SEX
Mar/21/2019
11:23:49
Dr
Facility

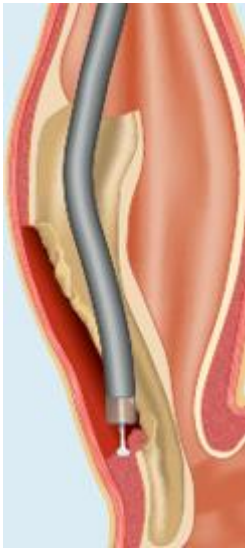
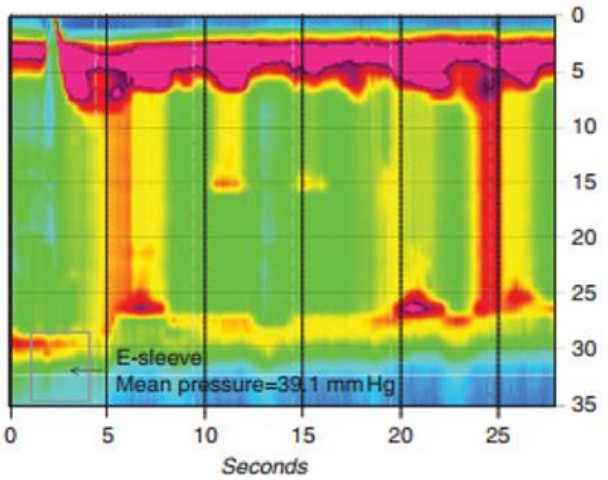


Table 2. Comparison of manometric abnormalities in conventional and high-resolution manometry

Manometric features of achalasia	Conventional manometry Line tracing format	High-resolution manometry Esophageal pressure topography
LES		
	Impaired LES relaxation[a] • Mean swallow induced fall in resting LES pressure to a nadir value of >8 mm Hg above gastric pressure • Complete relaxation to gastric baseline with a short duration (<6 s)[b] *Basal pressure*[b] • >45 mm Hg	*Impaired EGJ relaxation* • Mean 4 s IRP ≥10 mm Hg over test swallows[a]
Esophageal peristalsis		
	Aperistalsis in distal 2/3 of the esophagus • No apparent contractions • Simultaneous contractions with amplitudes <40 mm Hg	*Aperistalsis* • Absent peristalsis (type I) • Pan-esophageal pressurization (type II)
Atypical/variants		
	Vigorous • Preserved peristalsis with esophageal contractions >40 mm Hg • Simultaneous contractions >40 mm Hg -Isobaric -Nonisobaric	• Spastic achalasia (type III)

EGJ, esophagogastric junction; IRP, integrated relaxation pressure; LES, lower esophageal sphincter.
[a]Required for diagnosis.
[b]Supportive for the diagnosis.



Lunghezza della miotomia

	Esofago	Stomaco\LES
Acalasia tipo I,II	5-8 cm	3 cm
Acalasia tipo III	>15 cm	3 cm
Jackhammer, SED	>15 cm	0 cm
EG Outlet Obstruction	2 cm	3 cm

Tuason J, Inoue H J Gastroenterology 2017

Variable	Studies, n	Patients, n	Clinical success rate (95%CI), %	*P* value[1]
Female, %[2]				0.03
≤48	9	631	97 (95–99)	
49–55	8	721	97 (93–99)	
≥46	8	661	100 (99–100)	
Continent				0.05
Asia	16	1493	99 (98–100)	
Europe	3[3]	184	99 (97–100)	
North America	8	388	94 (91–97)	
Study design				0.09
Retrospective	10	879	97 (95–98)	
Prospective	13	1082	99 (97–100)	

Table 2 Sources of heterogeneity of clinical success (Eckardt score ≤3) among 27 studies of patients who underwent peroral endoscopic myotomy.

CI, confidence interval

[1] Potential sources of heterogeneity was assessed with metaregression. We considered $P<0.05$ to indicate that a variable significantly explains part of the between-study heterogeneity (i.e. an effect modifier). However, differences in continent and study design were marginally significant and may also be a potential source of heterogeneity.

[2] Percentage of females across studies was cut at tertiles in order to ensure comparability of number of studies between groups.

[3] One of the European studies was a multicenter study that involved three European countries.

Endoscopy. 2016 ;48:1059-1068

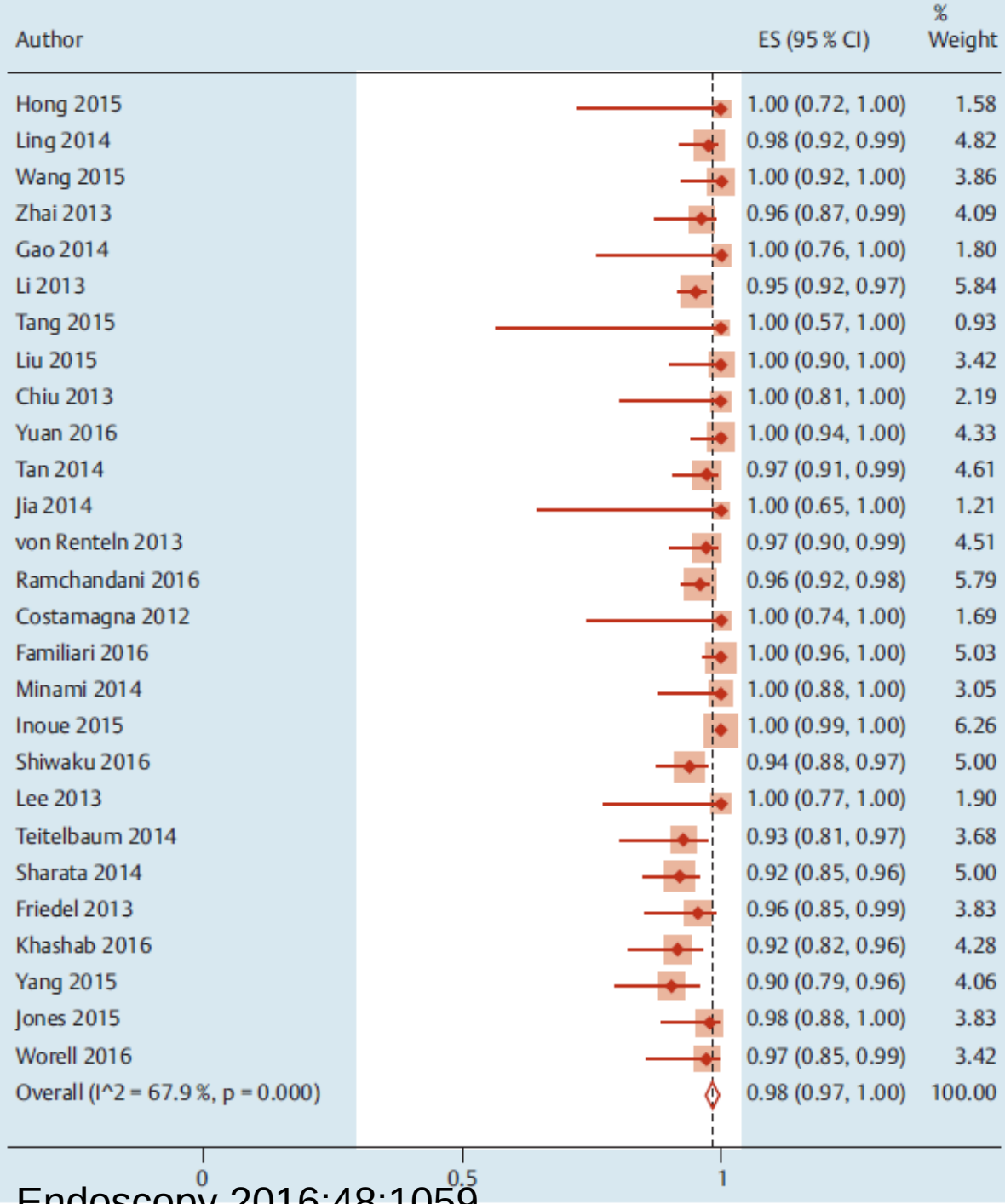


Fig. 3 Meta-analysis of proportion of patients with an Eckardt score ≤3 after peroral endoscopic myotomy procedure in 27 studies involving 2065 patients. The size, center, and horizontal line through each box correspond to the weight, point estimate, and confidence interval from each study, respectively, and the diamond corresponds to the pooled estimate. ES indicates estimate.

The Eckardt score

Symptom/sign	Score for each symptom/sign 0	1	2	3
Recent weight loss (kg)	None	< 5	5–10	> 10
Dysphagia	None	Occasional	Daily	Each meal
Chest pain	None	Occasional	Daily	Several times per day
Regurgitation	None	Occasional	Daily	Each meal

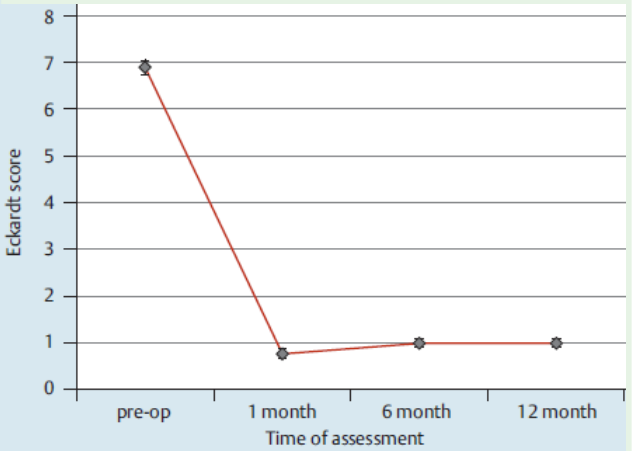


Fig. 6 Eckardt score in patients undergoing peroral endoscopic myotomy. The diamond corresponds to the mean, and the lines extending from them indicate standard error above and below the mean. Values are presented preoperatively, and at 1, 6, and 12 months postoperatively. 2223 patients in 31 studies, 648 patients in 11 studies, 1437 patients in 17 studies, and 1249 patients in 11 studies contributed to the preoperative, 1, 6, and 12 months postoperative values, respectively. Overall, compared with preoperative values, there were significant decreases ($P<0.05$) in postoperative Eckardt scores in each study.

			Subjective achalasia related outcome				
Author, Year of publication	Number of patients	Follow-up (months)	Pre-POEM Inoue dysphagia symptom score	Post-POEM Inoue dysphagia symptom score	Pre-POEM Eckardt score	Post-POEM Eckardt score	Pre-POEM TBE (column height at 5 min/% contrast clearance)
Inoue, 2010	17	5 (1–16)	10	1.3 (0–4)			
Von Renteln, 2012	16	3			8.8	1.4	
Costamagna, 2012	10	3			7.1 ± 1.6	1.1	
Swanstrom, 2012	18	11.4 (4–18)			6† (2–9)	0† (0–3)	48%† (4–100)
Ren, 2012	119						
Chiu, 2013	16	5.9 (3.3–7.7)			5.5† (0–8)	0† (0–3)	
Lee, 2013	13	6.9			6.4 ± 1.9	0.4 (0.7)	
Verlaan, 2013	10	3			8† (4–8)	1† (0–1)	10.1 cm† (5.7–10.8
Von Renteln, 2013	70	10.1 (3–12)			6.9‡ (6.4–7.4)	1.7‡ (24.2–31)	
Onimaru, 2013	10	3			6.5 ± 1.3	1.1 ± 1.3	
Li 201							
FTM	103	6.1 ± 4.3			7.6 ± 2	1.2 ± 1.5	
CMM	131	10.5 ± 3.8			8 ± 1.9	1.1 ± 1.3	
Minami, 2014	28	16† (3–28)	10	0.8 (0–3)	6.7 (3–12)	0.7 (0–3)	
Ling, 2014	87	14.4 (12–19.2)			7.1 ± 2.1	0.8 ± 0.9	9.1 ± 1.6 cm
Teitelbaum, 2014	41	15 (12–33)			7 ± 2	1 ± 2	22/41 16 ± 8 cm
Familiari, 2014	100	11 (3–24)			8.1 ± 1.9 (4–12)	1.1	
Chen, 2014							
Total	45	24			6.64 ± 1.08	2 ± 0.68	
AST 1	14				6.23 ± 1.06	2.08 ± 0.83	
AST 2	24				6.14 ± 0.90	2 ± 0.82	
AST 3	7						
Yang, 2014	108						
Hu, 2014	32	30 (24–44)			7.8 (4–12)	1.4 (0–5)	
Sharata, 2014	75	20.1			6 (2–9)	1	
Hungness, 2013	18	6 (1–18)			7† (5–12)	1† (0–9)	14 cm (0–31)
Bhayani, 2013	37	6.8 (5.7–10)			5.4 ± 2.2	0.8	
Ujiki, 2013	18	3.8 ± 0.8			6.4 ± 0.5	0.7 ± 0.5	
n	**1122**	**10.2 ± 7.4**	**10 ± 0**	**1.1 ± 0.4**	6.8 ± 1.0	1.2 ± 0.6	**12.3 ± 3.2**
Mean ± SD *n*/total number investigated (%)							

Cells not containing zeros/values did not report on the outcome. Values are mean ± SD/(range). †Median (IQR). ‡Mean (95% C
OGD, esophagogastric duodenoscopy; POEM, peroral endoscopic myotomy; TBE, timed barium esophagogram.

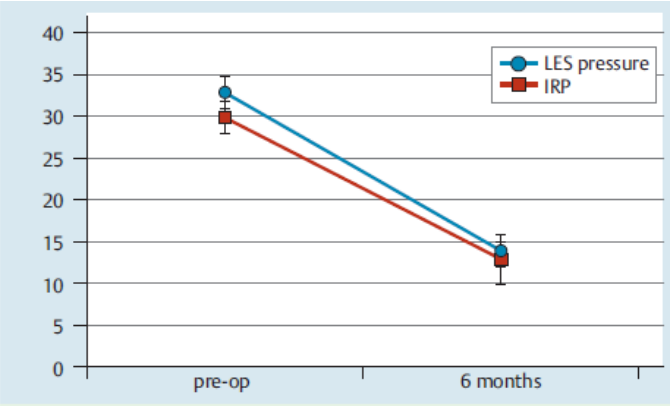


Fig. 7 Manometry findings in patients undergoing peroral endoscopic myotomy. Values are presented for the preoperative state and within 6 months after the procedure. The diamond and the box correspond to means of lower esophageal sphincter (LES) pressure and integrated relaxation pressure (IRP), respectively, and the lines extending from them indicate the standard error above and below the mean. 1976 patients in 24 studies and 1569 patients in 18 studies contributed to the preoperative and 6-month postoperative values of LES pressure, respectively; 470 patients in 11 studies and 456 patients in 10 studies contributed to the preoperative and postoperative values of IRP, respectively. Overall, compared with preoperative values, there were significant improvements ($P<0.05$) in the postoperative values of these markers in each study.

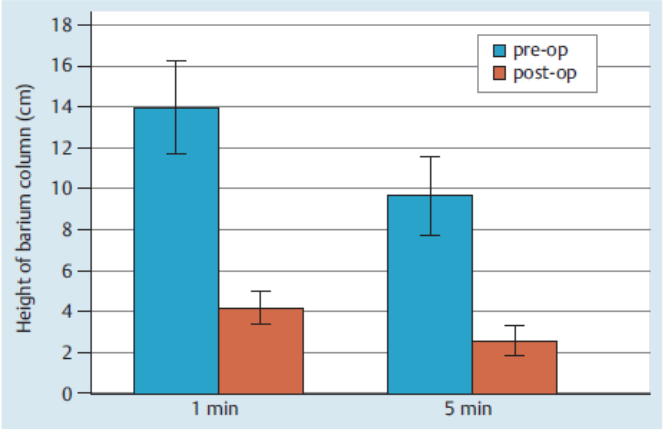


Fig. 8 Height of barium column after a timed barium esophagogram in patients undergoing peroral endoscopic myotomy. The heights of the barium column were assessed at 1 and 5 minutes before and after the procedure, and values are presented here as mean ± SE. 186 patients in 3 studies and 232 patients in 4 studies contributed to the values at 1 and 5 minutes, respectively. Overall, compared with preoperative values, there were significant decreases ($P<0.05$) in the postoperative heights of the barium column in each study

Endoscopy 2016;48:1059

Author, Year of publication	Number of patients	Objective achalasia related outcomes			GERD morbidity outcomes					
		Post-POEM TBE (column height at 5 mins/% contrast clearance)	Pre-POEM LES pressure (mmHg)	Post-POEM LES Pressure (mmHg)	Pre-POEM GERD symptoms (*n*)	Post-POEM GERD symptoms (*n*)	Pre-POEM excess acid exposure (*n*)	Post-POEM excess acid exposure (*n*)	Pre-POEM OGD esophagitis/ ulcer (*n*)	Post-POEM OGD esophagitis/ ulcer (*n*)
Inoue, 2010	17					1				1
Von Renteln, 2012	16		27.2	11.8	1	2			0	3
Costamagna, 2012	10					0				
Swanstrom, 2012	18	16/18 100%† (80–100)			5	8		6/13	0	4/14
Ren, 2012	119									
Chiu, 2013	16					1		3/15		
Lee, 2013	13					0			0	1
Verlaan, 2013	10	8) 2.3 cm† (0–3.2)				3		1		6
Von Renteln, 2013	70		27.6‡ (24.2–31)	8.9‡ (7.3–10.5)		19/51				29
Onimaru, 2013	10					1				
Li 201										
FTM	103		30.5 ± 14.5	12.4 ± 3.6		19				13
CMM	131		29.6 ± 11.5	12.2 ± 4.3		20				7
Minami, 2014	28		71.2 (35.8–119)	21 (6.7–41)		6				11
Ling, 2014	87	2.7 ± 1.1 cm	32.4 ± 15.3	7.2 ± 2.3		9				5
Teitelbaum, 2014	41	19/41 5 ± 3 cm				6/39		4/13		13/22
Familiari, 2014	100					17/73		39/73		20/92
Chen, 2014										
Total	45									
AST 1	14									
AST 2	24									
AST 3	7									
Yang, 2014	108									
Hu, 2014	32		37.9 (21.9–70.3)	12.9 (7.7–22.5)		7/30				6/30
Sharata, 2014	75					3/59				
Hungness, 2013	18	13/18 0 cm (0–9)				4				5/15
Bhayani, 2013	37				17/37	9/23				
Ujiki, 2013	18					3				
n	**1122**	**2.5 ± 2.0**	36.6 ± 15.7	12.3 ± 4.4	**23/71 (32)**	**19/57 (33)**		53/124 (43)	0/47 (0)	-8/43 (19)
Mean ± SD *n*/total number investigated (%)										

Adverse outcomes	Studies, n	Patients, n	Rate (95%CI), %	I^2, %
Perioperative				
Mucosal injury	20	1682	4.8 (2.0–8.5)	79
Esophageal perforation	25	1537	0.2 (0–1.1)	36
Major bleeding	28	1794	0.2 (0–1.4)	42
Subcutaneous emphysema	24	1286	7.5 (3.5–12)	85
Pneumothorax	19	1676	1.2 (0.1–4.3)	88
Pneumomediastinum	16	1012	1.1 (0.1–4.7)	81
Pneumoperitoneum	22	1760	6.8 (1.9–14)	94
Pleural effusion	16	1410	1.2 (0–8.3)	96
Gastroesophageal reflux				
Symptomatic	29	2142	8.5 (4.9–13)	87
Esophagitis on EGD	20	1762	13 (5.0–23)	96
Abnormal exposure on 24-hour pH study	5	336	47 (21–74)	96

EGD, esophagogastroduodenoscopy; I^2 indicates percentage of heterogeneity of outcome estimates between included studies.

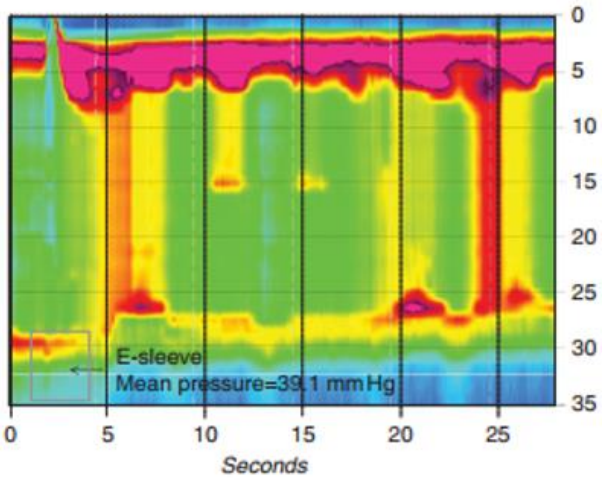
Table 3 Rates of adverse outcomes in patients undergoing peroral endoscopic myotomy between 2008 and 2014.

Endoscopy 2016;48:1059

Author, year of publication	Number of patients	Procedure time (minutes)	Length of stay (days)	Esophageal perforation/ mediastinal leak (*n*)	Gastric perforation/ peritoneal leak (*n*)	Capno/ Pneumo-peritoneum (*n*)	Capno/ Pneumo-peritoneum (*n*)	Capno/ Pneumo-peritoneum requiring decompression (*n*)	Capno/ Pneumo-thorax (*n*)	Capno/ Pneumo-thorax requiring decompression (*n*)	Subcutaneous Emphysema (*n*)	Postoperative bleeding (*n*)	Mortality (*n*)
Inoue, 2010	17	126 (100–180)	4.8 (3–8)	0	0	1	1	1			0	0	0
Von Renteln,2012	16	114 (65–188)		0	0	8	8	8			6	0	0
Costamagna,2012	10	100.7 (275-140)	4	0	0						2	0	0
Swanstrom, 2012	18	139† (90–260)	1† (1–2)	0	0	1	1	1	1	1			0
Ren, 2012	119	65.8 (21–193)		0	0	47	47	0	33	17	88	1	0
Chiu, 2013	16	117 ± 34.1	3 ± 1.18	0	0						2		0
Lee, 2013	13			0	0							0	0
Verlaan, 2013	10			0	0								0
Von Renteln,2013	70	105‡ (95–114)		0	0							2	0
Onimaru, 2013	10	118.2 (60–180)		0	0								0
Li 2013													
FTM	103	41.7 ± 18.9	2.7 ± 1.1	0	0	37	37	1	17	0	30	0	1
CMM	131	48.9 ± 28.6	3.6 ± 2.7	0	0	54	54	1	28	1	79	1	0
Minami, 2014	28	99.1 (61–160)	6.4 (5–19)	0	0	0	0	0	0	0		2	0
Ling 2014	87	42 ± 6.5	6.2 (6–8)	0	0	1	1	0	1	0	10	0	0
Teitelbaum, 2014	41	110 ± 35	1.4 ± 1.9	0	0	14	14	14			1		0
Familiari, 2014	94	83 ± 21.5 (49–140)	4 (2–6)	0	0	29	29	29	0	0	11		0
Chen, 2014													
Total	45	73.78 ± 24.22		0	0						2	1	0
AST 1	14	76.07 ± 29.23											
AST 2	24	75.63 ± 22.76											
AST 3	7	62.86 ± 17.29											
Yang, 2014	108		4.4 ± 3.3	1	0	47	47	0	1	0	32	1	0
Hu, 2014	32	63.7 (22–130)	3.9 (1–29)	0	0	7	7	2	1	1	4		0
Sharata, 2014	75			0	0								0
Hungness, 2013	18	113† (88–220)	1† (1–13)	1	0	7	7	7	0	0	3		0
Bhayani, 2013	37	120† (60–215)	1.1 ± 0.6	0	0							1	0
Ujiki, 2013	18	155.8 ± 12.8	3.4 ± 1.3	1	0	3	3	3			2		0
Mean ± SD *n*/total investigated (%)	**1122**	**99.3 ± 35.8**	**4.0 ± 1.9**	**3/1122 (0.3)**	**0/1122 (0)**	**256/836 (30.6)**	**256/836 (30.6)**	**67/836 (8.0)**	**82/744 (11.0)**	**20/744 (2.7)**	**272/861 (31.6)**	**9/790 (1.1)**	**1/1122 (0.09)**

- Le complicanze più frequenti sono lievi e gas related (pneumoperitoneo da detendere, pneumotorace, enfisema sottocutaneo)
- Mediastinal leak 0,3%
- Mortalità 0,09%

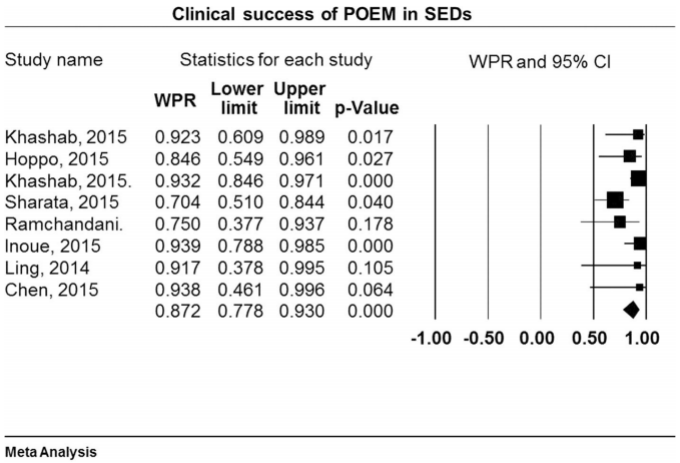
- **Type I, II, EGJOO:** All treatments (Pneumatic Dilation, Heller, POEM)
- **Type III:** Best response in case of POEM

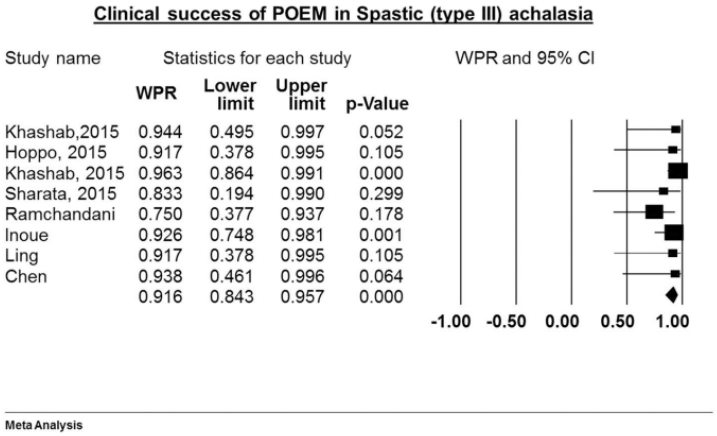


Kahrilas, Treatment of achalasia in 2017 Curr Opin Gastroenterol

Is POEM the Answer for Management of Spastic Esophageal Disorders? A Systematic Review and Meta-Analysis

- Spastic achalasia (type III)
- SEDs (diffuse esophageal spasm and nutcracker/jackhammer esophagus)





Dig Dis Sci (2017) 62:35–44

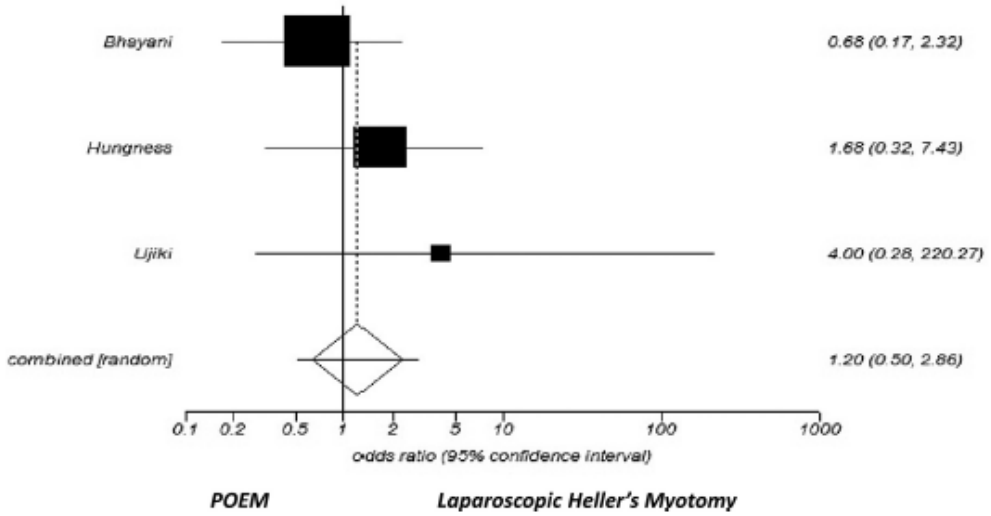


Fig. 2 Forrest plot showing no significant difference between the groups in the incidence of total adverse events.

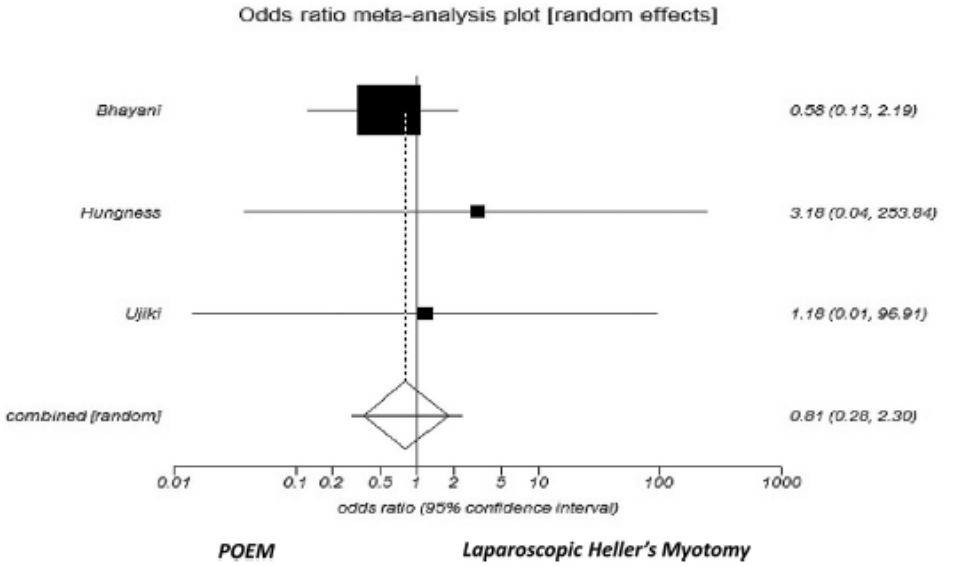


Fig. 3 Forrest plot showing no significant difference between the groups in the incidence of perforation.

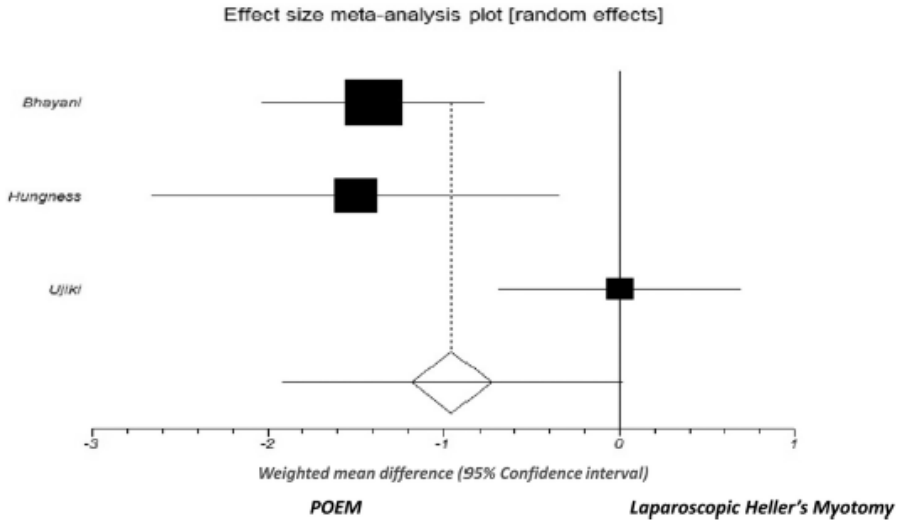


Fig. 5 Forrest plot demonstrating a nonsignificant trend toward reduced length of hospital stay in the peroral endoscopic myotomy (POEM) group.

Table 2 Procedure related parameters

	POEM (32)	SM (42)	p
Operation time, median minutes [range]	63.4 [32–114]	76.5 [54–192]	0.0005
Myotomy length,			
Total, median cm [range]	12 [10–13]	9 [7–10]	0.001
Esophageal side, median cm [range]	9 [6–11]	7 [5–8]	0.001
Gastric side, median cm [range]	3 [2–4]	2 [2–2]	0.001
Intraoperative major complications			
Pneumothorax	1 (3.1)	0	n.s.
Intraoperative minor complications			
Pneumoperitonuem decompression (%)	3 (9.3)	0	
Mucosal tear (%)	0	5 (11.9)	

Table 3 Follow-up: clinical and morphofunctional parameters

	POEM (32)	SM (42)	*p*
Eckardt score [range]	1 [0–10]	1 [0–3]	0.001*
GER symptoms, n° pts (%)	4 (12.5)	4 (9.5)	n.s.
High-resolution manometry, n° pts (%)	18 (56)	18 (43)	
LES basal pressure, median mmHg [range]	17.5 [3.9–26.2]	13.1 [3.5–25.4]	0.001*
Integrated relaxation pressure (IRP), median mmHg [range]	9.7 [15.7–60.5]	8 [3.5–14]	0.001*
24h MII pH-impedance, n° pts (%)	18 (56)	18 (43)	
Pathological DeMeester score, n° pts (%)	5 (28)	4 (22)	n.s.
Endoscopy, n° pts (%)	20 (62.5)	20 (47.6)	
Esophagitis, n° pts (%)	8 (40)	1 (5)	0.04

*p-value obtained from the comparison of preoperative and postoperative results.

Table 4 Review of comparative studies

		Sample size	POEM/SM	Eckardt score reduction*	pH test†	Morphological evaluation‡	HR Manometry**
Ujiki *et al.*[16]	Retrospective	39	18/21	$P < 0.001$	Data n.a.§	Data n.a	Data n.a.
Hungness *et al.*[17]	Prospective	73	18/55	$P < 0.001$	Data n.a.	15 (33%)/Data n.a	$P < 0.001$
Teitelbaum *et al.* [18]	Prospective	29	12/17	$P < 0.001$	Data n.a.	Data n.a	Data n.a
Bhayani *et al.* [19]	Retrospective	101	37/64	$P < 0.001$	23(39%)/31(32%)	Data n.a	$P < 0.001$
Kumagai *et al.* [20]	Prospective	83	42/41	Data n.a	Data n.a.	Data n.a	Data n.a
Schneider *et al.* [21]	Retrospective	50	25/25	$P < 0.001$	8 (50%)/7 (30%)	13 (53%)/19 (32%)	$P < 0.001$
Chan *et al.* [22]	Retrospective	56	23/33	Data n.a	Data n.a.	Data n.a	Data n.a
Present study	Retrospective	74	32/42	$P < 0.001$	18 (28%)/18 (22%)	20 (40%)/20 (5%)	$P < 0.001$

*Significant symptomatic regression: *P* value of POEM and SM. **Significant improvements in postmyotomy lower esophageal sphincter profiles: *P* value of POEM and SM. †Patients receiving postoperative pH tests (% of phatological responses) after POEM /SM. ‡Patients receiving postoperative endoscopic follow-up (% of phatological responses) after POEM/SM. §Data not available in the results of the studies.

Table 2. Reported Per-Oral Endoscopic Myotomy Treatment Data, Stratified By Quality of Evidence

First author, year	Comparison, n	Follow-up, *mo*	Post-treatment reflux, %	Efficacy, %
Randomized controlled trials				
Ponds,[33] 2017	POEM 67 PD 66	12	POEM esophagitis, 40 PD esophagitis, 13.1	POEM 92 PD 70
Nonrandomized comparisons, LHM vs POEM				
Bhayani,[34] 2014	POEM 37 LHM 64	6	POEM 39 LHM 32	POEM 100 LHM 92
Chan,[35] 2016	POEM 33 LHM 23	>6	POEM 15 LHM 26	POEM 100 LHM 87
Kumbhari,[36] 2015	POEM 49 LHM 26	9	POEM 39 LHM 46	POEM 98 LHM 81
Schneider,[37] 2016	POEM 42 LHM 84	12	Not reported	POEM 91 LHM 84
Teitelbaum,[38] 2013	POEM 17 LHM 12	Not reported	POEM 17 LHM 31	POEM 100 LHM 87
Author	Series, n	Mean follow-up, mo	Adverse events, %	Symptom improvement, %
Uncontrolled trials (>100 patients, ≥12 month follow-up)				
Cai,[39] 2014	100	11.5	0	97
Familiari,[40] 2016	100	11	0	95
Hungness,[41] 2016	115	19	3	92
Inoue,[30] 2015	500	>36	3	89
Kumbhari,[42] 2017	282	12	58 GER[a]	94
Ngamruengphong,[43] 2017	205	31	8	91
Ramchandani,[44] 2016	200	12	0	92

GER, gastroesophageal reflux.
[a]All patients were studied with pH-metry after POEM.

Gastroesophageal reflux disease after per-oral endoscopic myotomy as compared with Heller's myotomy with fundoplication: a systematic review with meta-analysis

Abnormal acid exposure at pH-monitoring:

- 39.0%(95% CI, 24.5%–55.8%) after POEM,
- 16.8% (95% CI, 10.2%–26.4%) after LHM, respectively

Rate of post-POEM esophagitis:

29.4% after POEM

According to LA classification, most of the esophagitis was classified as mild grade, accounting for 92.0% (54.3%, LAA and 37.6%, 169 in LA-B).
Considering moderate to severe grade (LA-C and LAD)the overall pooled rate of reflux disease was 4.47%

7.6% after LHM

According to LA classification, most of the esophagitis were classified as mild grade, accounting for 48.5% (39.4%, LA-A and 9.1%, in LA-B). Considering moderate to severe grade (LA-C and LA-D) as a clinically relevant disease, the overall pooled rate of reflux disease was 1.0%

LHM with fundoplication, the rate of reflux disease was from multivariate model
8.6% by symptoms evaluation
14.9% disease determined, esophageal pH test
8.3% for endoscopic findings, respectively.
The corresponding rates in POEM cohorts were
18.1% by symptoms evaluation
39.3% disease determined, esophageal pH test
30.7% for endoscopic findings, respectively.

Gastrointestinal Endoscopy 2017

Gastroesophageal reflux disease after per-oral endoscopic myotomy as compared with Heller's myotomy with fundoplication: a systematic review with meta-analysis

•POEM is associated with a 2 to 3 folds increased risk of postintervention reflux when compared with LHM with fundoplication, the result being consistent across the three main parameters assessed, namely reflux-symptoms, abnormal pH-monitoring or endoscopic diagnosis of esophagitis.

•However, the clinical implications of such higher incidence of reflux appeared to be somewhat less relevant. For instance, as many as **9 patients should be treated with LHM over POEM to prevent the incidence of symptomatic reflux disease**.

•In addition, despite the incidence of esophagitis was significantly more frequent after POEM than LHM, the gradient in severe esophagitis was quite low, so that approximately **30 patients should be treated with LHM over POEM to prevent one case of postprocedure severe esophagitis.** This appears to be indirectly confirmed by the low rate of prolonged PPI therapy shown in our analysis after POEM.

•This lower rate of post-POEM symptomatic GERD or severe esophagitis may be related with the preservation of all the anatomic structures that contribute to the gastroesophageal barrier, representing a main advantage on LHM,

Gastrointestinal Endoscopy 2017

Peroral endoscopic myotomy as salvation technique post-Heller: International experience

No. patients	51
Sex (M)	24 (47%)
Mean age (years)	54.2
Type of achalasia	
Type I	13
Type II	29
Type III	6
Other	3
Technical success	51 (100%)
Clinical success	
Eckardt ≤ 3	48 (94%)
Change in Eckardt score	6.25
Significant adverse events	6 mucosal defects 2 mediastinitis treated conservatively
Mean time between myotomies (months)	113.5 months
Average follow up (months)	24.4 months

HM, Heller myotomy; POEM, peroral endoscopic myotomy.

For patients with persistent symptoms after HM, POEM is a safe salvation technique with good short-term efficacy.

Dig Endosc. 2018 Jan;30:52-56

Peroral endoscopic myotomy in treatment-naïve achalasia patients versus prior treatment failure cases.

▶ **Table 2** Operative findings during peroral endoscopic myotomy procedure (n = 502).

	Treatment naïve (n = 260)	PTF (n = 242)	P value
Operative time, mean ± SD, minutes	67.0 ± 27.1	74.9 ± 30.6	0.002
Site of myotomy, n (%)			
▪ Anterior	210 (80.8)	186 (76.9)	0.32
▪ Posterior	50 (19.2)	56 (23.1)	0.32
Length of myotomy, mean ± SD, cm	12.1 ± 2.6	12.5 ± 2.5	0.08
▪ Esophageal	9.0 ± 2.5	9.4 ± 2.4	0.07
▪ Gastric	3.08 ± 0.5	3.1 ± 0.5	0.65
No. of clips, mean ± SD	5.71 ± 0.88	5.73 ± 0.76	0.78
Technical success, n (%) (overall 490/502 [97.6%])	255 (98.1)	235 (97.1)	0.56
Reason for technical failure, n			
▪ Submucosal fibrosis	4	5	0.74
▪ Mucosal incision enlargement	1	2	0.61
Hospital stay, mean (range), days	3 (2 – 5)	3 (2 – 5)	

PTF, prior treatment failure.

Endoscopy. 2018;50:358-370

▶ **Table 4** Predictors of operative time (multiple logistic regression analysis) (n = 502).

Factors	Coefficient	Odds ratio (95 %CI)	Probability of increased operative time, %	P value
Median disease duration, months	4.92	138.29 (27.74 – 689.46)	99.2	0.001
Type of achalasia	6.58	726.38 (101.23 – 5211.93)	99.8	0.001
Esophageal diameter	2.42	11.29 (1.53 – 82.99)	91.8	0.02
Adverse events	3.15	23.41 (1.11 – 494.72)	95.9	0.04
Prior treatment	1.12	3.08 (1.31 – 7.27)	75.5	0.01
Type of knife used	4.33	76.18 (1.63 – 355.71)	98.7	0.03

CI, confidence interval.

▶ **Table 5** Clinical outcomes including clinical success (intention to treat), clinical or technical failure, and lost to follow-up.

	6 months	1 year	2 years	3 years
Clinical success, n/N (%)	n = 424	n = 342	n = 229	69
▪ Treatment-naïve	206/223 (92.4)	166/183 (90.7)	112/128 (87.5)	27/31 (87.1)
▪ PTF	186/201 (92.5)	145/159 (91.2)	85/101 (84.2)	29/38 (76.3)
Technical failure and lost to follow-up, n/N (%)	14/424 (3.3)	16/311 (5.1)	17/229 (7.4)	7/69 (10.1)

PTF, prior treatment failure.

Endoscopy. 2018;50:358-370

	Treatment-naïve (n = 260)	PTF (n = 242)	*P* value
Adverse events, n (%)	93 (35.8)	80 (33.1)	0.57
Major adverse events, n (%)	5 (1.9)	3 (1.2)	
▪ Capnopericardium	2 (0.8)	0	0.50
▪ Capnothorax (requiring decompression)	1 (0.4)	1 (0.4)	>0.99
▪ Enlargement of mucosal incision	1 (0.4)	2 (0.8)	0.61
▪ 30-day readmission	1 (0.4)	0	>0.99
Minor adverse events, n (%)	90 (34.6)	79 (32.6)	0.70
▪ Mucosal injury	8 (3.1)	11 (4.5)	0.48
▪ Capnothorax (not requiring decompression)	1 (0.4)	2 (0.8)	0.61
▪ Capnoperitoneum	35 (13.5)	27 (11.1)	0.49
▪ Retroperitoneal air (requiring temporary stoppage of procedure)	45 (17.3)	39 (16.1)	0.81
▪ Capnomediastinum	1 (0.4)	0	>0.99
Other events, n (%)	53 (20.4)	54 (22.3)	
▪ Subcutaneous emphysema	52 (20.0)	54 (22.3)	0.58
▪ Pleural effusion	1 (0.4)	0	>0.99

PTF, prior treatment failure.

▶ **Table 9** Incidence of gastroesophageal reflux disease after peroral endoscopic myotomy procedure.

	Treatment-naïve	PTF	*P* value
Clinical symptoms at 1 year (280/342), n/N (%)	22/134 (16.4)	26/146 (17.8)	0.87
Esophagitis by EGD (247/342)	29/131 (22.1)	24/116 (20.7)	0.88
24-hour pH study (n = 97), DeMeester score > 14.7, n (%)	11/44 (25.0)	17/53 (32.0)	0.50

PTF, prior treatment failure; EGD, esophagogastroduodenoscopy.

Endoscopy. 2018;50:358-370

POEM e REFLUSSO

A total of 36 studies involving 2373 patients

- Abnormal Acid Exposure 47%
- Syntomatic GERD 8,5%
- Esophagitis 13%

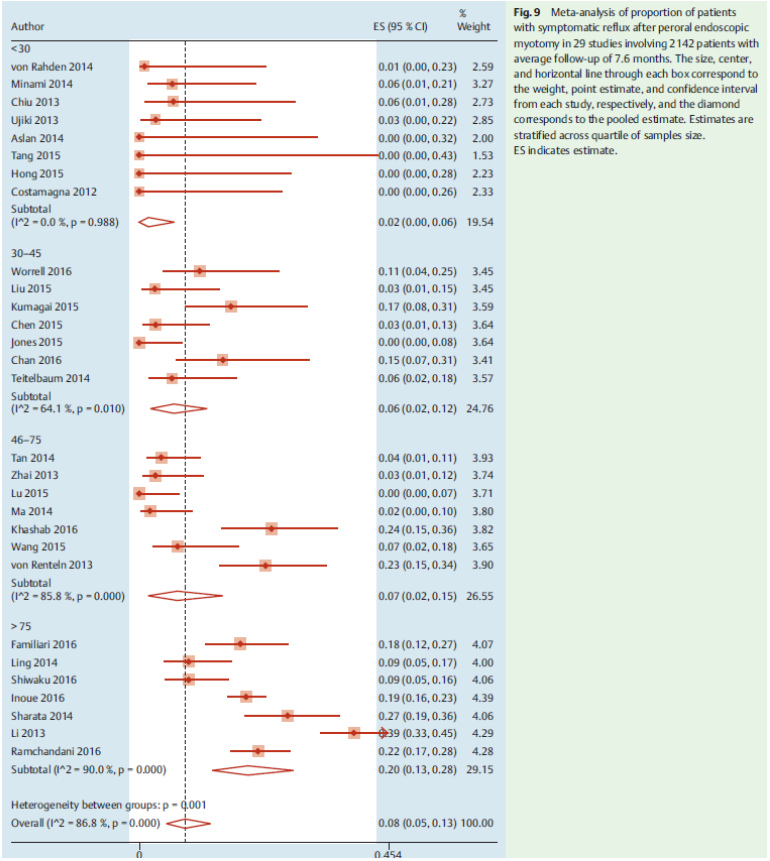


Fig. 9 Meta-analysis of proportion of patients with symptomatic reflux after peroral endoscopic myotomy in 29 studies involving 2142 patients with average follow-up of 7.6 months. The size, center, and horizontal line through each box correspond to the weight, point estimate, and confidence interval from each study, respectively, and the diamond corresponds to the pooled estimate. Estimates are stratified across quartile of samples size. ES indicates estimate.

Endoscopy 2016;48:1059

Gastroesophageal reflux after peroral endoscopic myotomy: a multicenter case-control study

▶**Table 2** Patient, intraprocedural and postprocedure characteristics comparing patients without vs. with gastroesophageal reflux (according to DeMeester score).

	Controls – No reflux[1] (n = 119)	Cases – Reflux[2] (n = 163)	*P* value
Patient characteristics			
Age, mean ± SD, years	47.1 ± 17	50.5 ± 17	0.11
Female, n (%)	49 (41)	87 (53)	0.04
Race, n (%)			0.61
▪ Caucasian	104 (87.4)	135 (82.8)	
▪ Black	6 (5.0)	9 (5.6)	
▪ Other	9 (7.6)	19 (11.6)	
BMI, mean ± SD, kg/m^2	24.0 ± 5.1	24.2 ± 5.6	0.73
Motility disease subtype, n (%)			0.42
▪ Achalasia type I	23 (19.3)	26 (16.0)	
▪ Achalasia type II	58 (48.7)	88 (54.0)	
▪ Achalasia type III	8 (6.7)	13 (8.0)	

- Prevalence of post-POEM GER in this large international multicenter study was 58 %. As the majority of patients were asymptomatic, it is probably necessary to perform objective postprocedure testing in all patients who undergo POEM.
- No intraprocedural variables were identified to allow for potential alteration in procedural technique

Endoscopy. 2017;49:634-642.

Very late results of esophagomyotomy for patients with achalasia: clinical, endoscopic, histologic, manometric, and acid reflux studies in 67 patients for a mean follow-up of 190 months

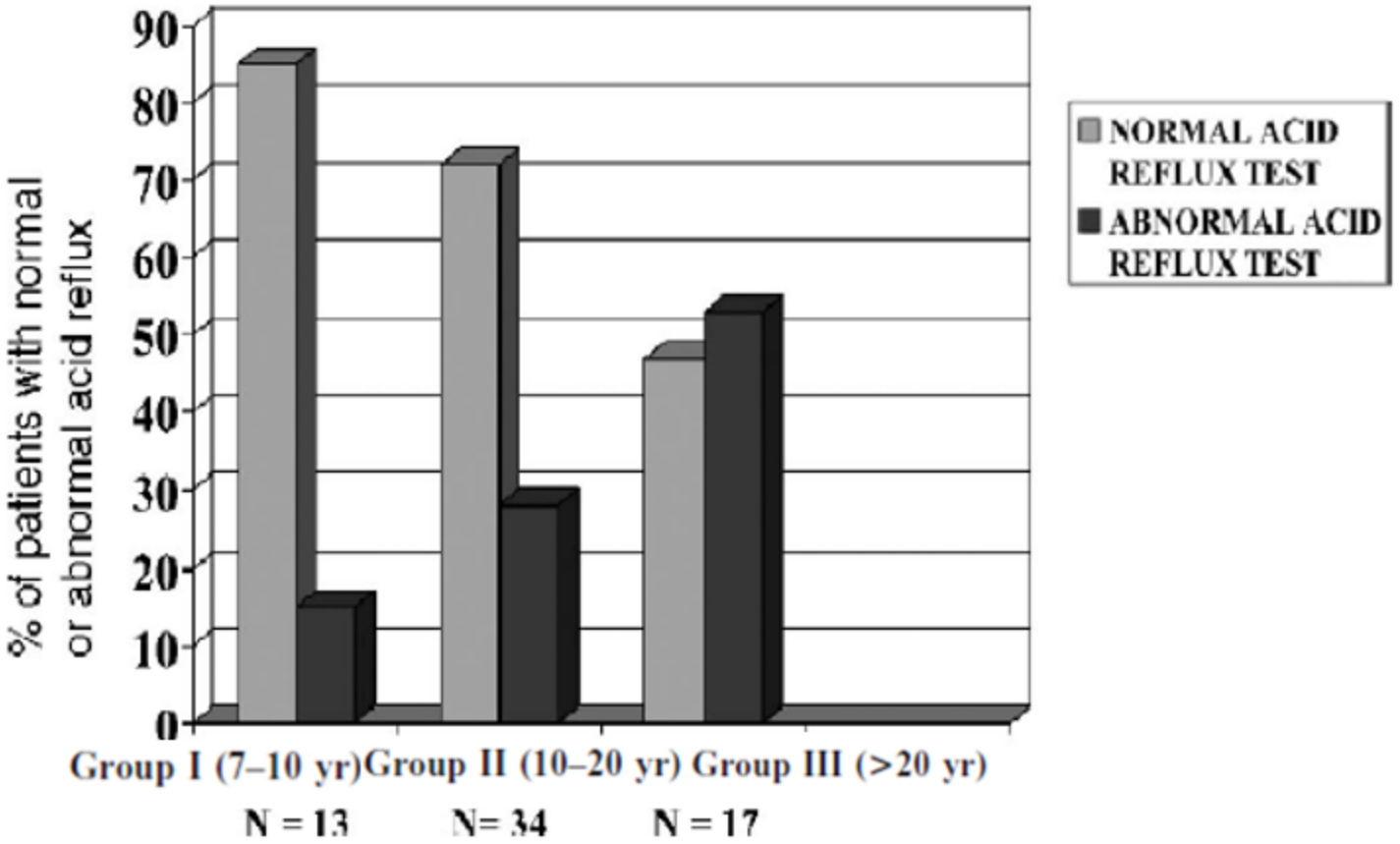
patients with achalasia submitted to esophagomyotomy and Dor's antireflux procedure, there is a progressive clinical deterioration of initially good results if a very long follow-up is performed mainly due to an increase in pathologic acid reflux disease and the development of short- or long-segment Barrett esophagus

TABLE 2. Radiologic and Endoscopic Results in Patients With Achalasia Submitted to Esophagomyotomy (n = 64)

	Group I (7–10 yr) (n = 13)	Group II (10–20 yr) (n = 34)	Group III (>20 yr) (n = 17)	*P*
Radiology				
Mean internal diameter GE junction (mm)				
Before operation	2.07 ± 0.5	2.52 ± 0.6	2.3 ± 0.5	<0.0001 (before and after operation in each group)
1 mo after operation	9.35 ± 1.1	10.6 ± 1.8	10.7 ± 1.7	
P	<0.001	<0.001	<0.001	
Mean internal diameter of middle third thoracic esophagus (mm)				
Before operation	55 ± 10.5	51.9 ± 12	56 ± 11.6	<0.0001 (before and after operation in each group)
1 mo after operation	25.3 ± 5.5	26.8 ± 5	26.7 ± 6.2	
P	<0.0001	<0.0001		
Endoscopy				
Time after surgery	88 mo	173 mo	281 mo	
Normal	11 (84.6%)	26 (76.5%)	9 (52.9%)	
Esophagitis	1 (7.7%)	2 (5.9%)	5 (29.4%)	NS
Peptic ulcer				
+Esophagitis	1 (7.7%)	6 (17.6%)	3 (17.6%)	

GE indicates gastroesophageal; NS, not significant.

Ann Surg. 2006 Feb;243:196-203.



Ann Surg. 2006 Feb;243:196-203.

TABLE 3. Histologic Findings Distal to Squamocolumnar Junction in Patients With Achalasia Submitted to Esophagomyotomy (Late After Surgery) (n = 64)

	Group I (7–10 yr) (n = 13)	Group II (10–20 yr) (n = 34)	Group III (>20 yr) (n = 17)	*P*
Type of mucosa				
Fundic	8 (61.5%)	11 (32.3%)	2 (11.8%)	<0.006
Cardiac	4 (30.8%)	17 (50%)	10 (58.8%)	NS
Intestinal metaplasia	1 (7.7%)	6 (17.6%)	5 (29.4%)	NS
H. pylori				
Juxtacardial	3 (23%)	7 (20.6%)	3 (17.6%)	NS
Antrum	6 (46.1%)	12 (35.3%)	6 (35.3%)	NS

NS indicates not significant.

Ann Surg. 2006 Feb;243:196-203.

Acalasia e Cancro

- Il rischio di tumore esofageo nella acalasia è legato principalmente alla malattia stessa e non reflusso. Infatti la stasi causare una sovracrescita batterica e l'aumento di produzione di nitrosamine che causano infiammazione cronica che può portare displasia e carcinoma squamoso.

- Alcuni autori riportano esofago di Barrett dopo Heller (in tutto 40 casi in letteratura) e 1 adenocarcinoma mucoso.

Endoscopy 1987;19:76-78
Dig Dis Sci 1990;35:1549
Ann Thorac Surg 1996;61:1106

Onset timing of delayed complications and criteria of follow-up after operation for esophageal achalasia.

METHODS:

129 patients submitted to Heller myotomy were clinically and objectively followed up. Mean follow-up was 97.4 months (range, 12 to 268 months).

RESULTS:

In 11 patients, **severe dysphagia due to insufficient myotomy** reappeared a mean of 12.4 months after the operation (range, 3 to 30 months).

In 7 patients with **periesophageal scarring**, dysphagia recurred a mean of 18.8 months (range, 6 to 28 months) after the operation.

Postoperative reflux esophagitis appeared in 22 patients a mean of 76.5 months (range 21 to 168 months) after the operation.

Columnar-lined esophagus was detected in 8 patients a mean of 143.1 months (range, 85 to 230 months) after the operation. **Mild to moderate dysplasia was found in 5 of 8 patients** with columnar-lined esophagus a mean of 191.6 months after the operation (range, 152 to 287 months), and intramucosal adenocarcinoma was found in 1 patient with columnar-lined esophagus after 8 years.

CONCLUSIONS:

Dysphagia secondary to insufficient myotomy and periesophageal scarring recurs early, not later than 3 years. Conversely, abnormal gastroesophageal reflux with related complications can appear more than 10 years postoperatively. Five years after the operation the follow-up should be primarily endoscopic and histologic. Results should withstand a follow-up of at least 10 years

Ann Thorac Surg 1996 Aug;62(2):632.

Transoral Incisionless fundoplication for reflux after peroral endoscopic myotomy: a crucial addition to our arsenal

▶ **Fig. 1 a, b** Esophyx device creating the wrap.

▶ **Fig. 2** Successful 270 degree fundoplication.

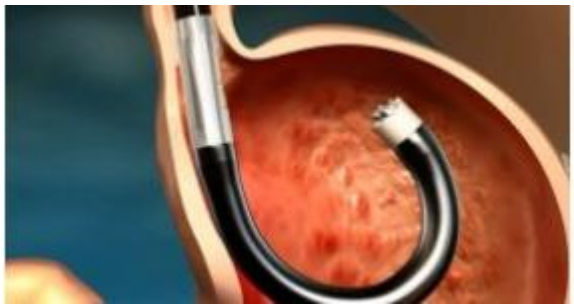
▶ **Table 2** TIF post-POEM results.

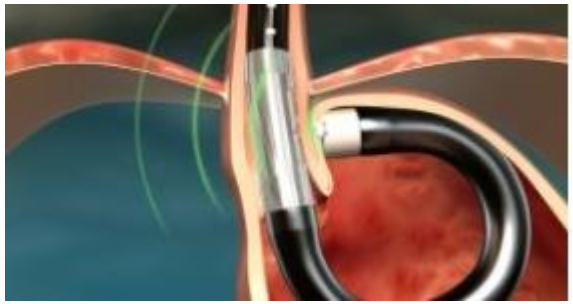
Technical success	100 % (n = 5)
Off of PPI	100 % (n = 5)
Healing of esophagitis	100 % (n = 2)
Adverse events	0
Mean follow-up time	27 months (range 5 – 34 months)

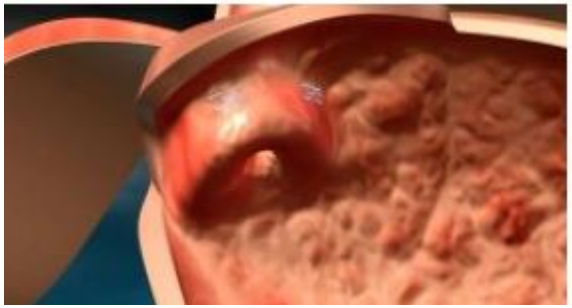
POEM, peroral endoscopic myotomy; PPI, proton-pump inhibitor; TIF, transoral fundoplication.

Endosc Int Open 2018;: E549-E552

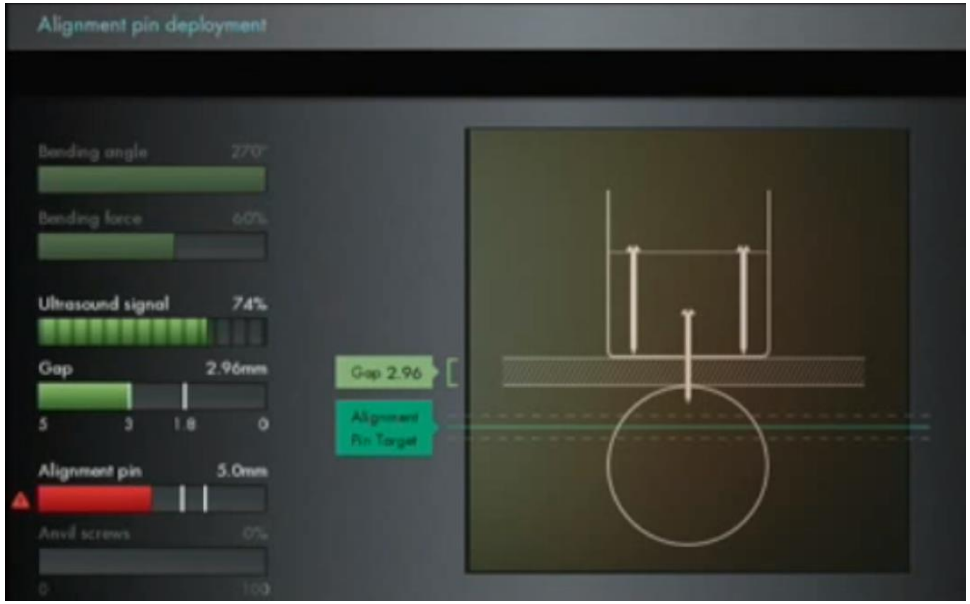

MUSE
SYSTEM







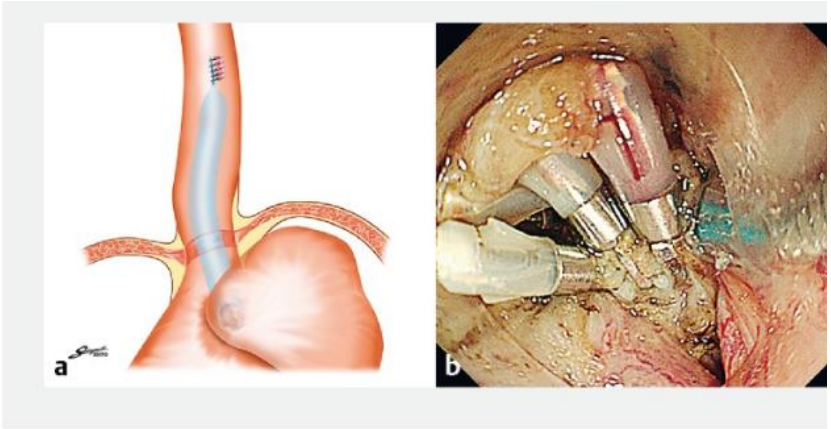

Medigus


Alignment pin deployment
Bending angle
270°
Bending force
60%
Ultrasound signal
74%
Gap
2.96mm
5
3
1 8
0
Alignment pin
5.0mm
Anvil screws
0%
0
100
Gap 2.96
Alignment Pin Target

| **Fig.1** Conventional peroral endoscopic myotomy (POEM) is completed at the anterior wall of the esophagus. Next, the peritoneal cavity is accessed through the submucosal tunnel. **a** Schematic drawing of POEM with fundoplication (POEM+F) procedure (Step 1). The endoscope is advanced into the peritoneal cavity, just after passing the diaphragmatic crus. **b** Entry into the peritoneal cavity. Distal to the diaphragm, a full-thickness myotomy is carried out along the anterior wall of the submucosal tunnel in a 12 o'clock orientation. This defect is enlarged using a combination of a Triangle Tip knife (Olympus, Tokyo, Japan) and coagulation forceps. **c** The endoscope is advanced into the peritoneal cavity. The left lobe of the liver and the anterior side of the stomach can be seen. Source for illustration: Kent Sakaguchi|

| **Fig.2** Anchoring the endoloop with endoclips to the anterior wall of the gastric fornix and the esophagogastric junction. **a** Schematic drawing of peroral endoscopic myotomy with fundoplication (POEM+F) procedure (Step 2). The endoloop is fixed to the anterior gastric wall and the distal end of the submucosal tunnel with clips. **b** The distal anchor at the gastric anterior wall. **c** Proximal anchor clips at the distal end of the submucosal tunnel. Source for illustration: Kent Sakaguchi|

Endoscopy 2019; 51(02): 161-164



| **Fig.3** Closure of the endoloop, creating fundoplication. **a** Schematic drawing of peroral endoscopic myotomy with fundo (POEM+F) procedure (Step 3). **b** By closing the endoloop, the distal anchor clips are pulled towards the proximal anchor endoloop is closed tightly and anterior partial fundoplication is achieved. Source for illustration: Kent Sakaguchi|

	POEM+F (n=21)
Age, mean (SD), years	45.4 (14.0)
Sex, male/female, n	10/11
Type, straight/sigmoid, n	18/ 3
Degree of dilation, I/II/III, n	9/10/2
Chicago classification, I/II/III/other, n	13/5/1/2[1]
Preoperative IRP pressure, mean (SD), mmHg	22.8 (12.2)
Duration of disease, mean (SD), years	7.2 (7.4)
Primary procedure, none/PBD/other, n	18/3/0
Baseline Eckardt score, mean (SD)	5.7 (1.8)
Procedure completion rate, n (%)	21 (100)
Total operation time, minutes	
- Mean (SD)	118.9 (20.2)
- Median (range)	115 (92–178)
Fundoplication time, minutes	
- Mean (SD)	51.3 (18.5)
- Median (range)	44 (28–88)
Acute adverse event[2], n (%)	0 (0)
Postoperative stay, mean (SD), days	4.7 (0.8)

IRP, integrated relaxation pressure; PBD, pneumatic balloon dilation; POEM+F, peroral endoscopic myotomy followed by fundoplication.

[1] Ineffective esophageal motility, Jackhammer esophagus.

[2] Bleeding, infection, and any other organ injury.

Endoscopy 2019; 51(02): 161-164

10 anni di POEM: quale bilancio

- Trattamento definitivo, efficace quanto la chirurgia, ma più semplice e meno costoso
- Più elevata incidenza di reflusso gastroesofageo rispetto alla Heller-Dor, ma non c'è evidenza di un rischio maggiore di Barrett o ADK
- Terapia più efficace della chirurgia per l'acalasia di tipo III per la possibilità di fare una miotomia più estesa data l'assenza di vincoli anatomici
- Molto promettente per il ritrattamento dei pazienti con recidiva dei sintomi dopo Heller-Dor
- Trattamento di scelta per i disturbi della motilità esofagea caratterizzati da ipercontrattilità (Jackhammer, SED)
- Nel futuro auspicabile associare una plastica antireflusso endoscopica contestuale alla procedura (POEM-F) o differita in pazienti selezionati