Per-oral Endoscopic Myotomy (POEM) for Esophagogastric Junction Outflow Obstruction (EGJOO): A Multicenter Pilot Study

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INTRODUCTION

Esophagogastric junction outflow obstruction (EGJOO) is a rare but increasingly recognized diagnosis as described by The Chicago Classification of Esophageal Motility Disorders version 3.0 (CC v3.0)[1]. On high-resolution manometry (HRM), EGJOO is characterized by elevated integrated relaxation pressure (IRP) of the lower esophageal sphincter (LES), yet with some preserved esophageal peristalsis[2–4]. Little consensus exists on the preferred therapeutic approach[3]. Although conceptually POEM should address the measurable dysfunction in the LES, few data exist to support this[5]. Thus, we aimed to evaluate the safety and efficacy of POEM for the treatment of symptomatic EGJOO.

METHODS

This is a multicenter retrospective analysis of patients with symptomatic EGJOO who underwent POEM between Feb-2014 and Feb-2020. Institutional Review Board approval was obtained at each institution (6 U.S., 1 from Italy). POEM was performed as previously described[5]. All patients underwent pre-POEM HRM and upper endoscopy. Technical and clinical success defined as completion of the POEM and post-POEM Eckardt score ≤ 3 without additional interventions, respectively. Adverse events were graded based on the ASGE lexicon[6].

RESULTS

Fifty-five patients underwent POEM for EGJOO (Table 1). Mean duration of symptoms prior to POEM was 70.1 months. Nearly half of patients (45.5%) had failed prior treatment. The mean baseline Eckardt score and IRP were 7.1 ± 2.64 and 25.34 ± 26.25 mmHg, respectively. Functional lumen imaging probe (FLIP) was abnormal in 88.2% of patients. Barium retention on esophagram was seen in 95.6%.

Technical success was achieved in all patients (100%) with mean procedure time of 73.2± 35.6 minutes (Table 1). Clinical success was attained in 47/55 patients (94%) at median follow-up of 117 days. There were 2 minor (mucosal perforation), 2 mild (pneumoperitoneum requiring decompression) and 1 severe adverse event (1 mucosal perforation treated with esophageal stent with full recovery). Mean post-POEM IRP (n=17) was 8.88±7.03 mmHg, a mean difference of 10.64 (95% CI 5.82-15.46; p=0.0003) from pre-POEM HRM. Post-POEM pH monitoring (n=18) was abnormal in 66%. Twenty-five patients had post-POEM endoscopy and esophagitis was seen in 10/25 (grade A 4/25, grade B 6/25, grade C or D 0/25) (Table 1).

DISCUSSION

Given that EGJOO defining measurable characteristic is failure of LES to relax symptomatic improvement after POEM is expected. Indeed, our preliminary data support POEM as an effective and safe therapy[4]. Our findings expand on earlier report in which POEM was effective for a variety of non-achalasia motility disorders, including EGJOO[5]. Noteworthy, since POEM is an invasive procedure that permanently disrupts the LES, accurate pre-procedure diagnosis with exclusion of secondary causes of mechanical obstruction is essential. Furthermore, it is important to highlight the dynamic nature of symptoms in EGJOO, as spontaneous resolution has been previously documented[3]. In our study, the duration of symptoms pre-POEM averaged 70 months with 45.5% of patients undergoing prior therapy making spontaneous resolution unlikely. As such, POEM should only be considered in patients with persistent symptoms, as those described in this study. Abnormal EndoFLIP results may identify EGJOO patients that would have high success with the current treatments used in achalasia, including POEM[7]. Thus, incorporating EndoFLIP data and stratifying patients based on symptoms into future prospective EGJOO studies is recommended[7]. Similarly, there is accumulating data identifying an association

between opioids and LES mechanics, with many patients exhibiting EGJOO patterns on HRM when opioids were received within 24 hours[1,8]. As this is investigated further, we suggest the discontinuation of all opioids >24 hours prior to HRM during evaluation for POEM.

Our study is not without limitations. At this point in time, there is very limited data on the utility of POEM in EGJOO, thus this study serves as a proof-of-concept. There was no standardized pre- and post-procedure management, thus post-POEM testing was done at the discretion of the performing physician. Subsequently, the observed occurrence of post-POEM GERD may be inaccurately high due to selection bias but there is no reason to believe the frequency of post-POEM GERD to be different for EGJOO than for achalasia.

Nevertheless, we present the largest series to date which serves both as an aid in clinical decision-making and as a springboard for future higher quality studies. Furthermore, our multicenter data provide external validity to our findings. We did not have opioid-use data available, highlighting the necessity of this endpoint in future studies. Despite our relatively short follow-up period, it is reasonable to expect these findings to be similar to that of POEM for achalasia where we have well documented mid- and long-term results. Our findings support the possible role of POEM as safe and effective in everyday practice but also the need for further larger prospective studies.

Table 1. Patient and procedure characteristics (n = 55)

	Pre-POEM	Post-POEM
Age (years), mean ± SD	58.8 ± 16.09	
Female, n= (%)	33 (60)	
Male, n= (%)	22 (40)	
Duration of symptoms (months), mean ± SD	70.1 ± 100.03	
Prior therapy, no. (%)	25 (45.5)	
Pharmacotherapy, total n= (%)	10 (18.0)	2 (3.6)
Botulinum toxin injections, total n= (%)	15 (27.0)	0 (0.0)
Pneumatic dilation, total n= (%)	12 (22.0)	1 (1.8)
Surgical myotomy, n= (%)	0 (0.0)	1 (1.8)
Pharmacotherapy and botulinum toxin injection, n= (%)	7 (13.0)	0 (0.0)
Pharmacotherapy, botulinum toxin injection, and pneumatic dilation, n= (%)	3 (5.0)	0 (0.0)
Botulinum toxin injections and pneumatic dilation, n= (%)	1 (1.8)	0 (0.0)
Esophagitis on endoscopy, n/N= (%)	Grade A 2/55 (2.0) Grade B 0/55 (0.0) Grade C 0/55 (0.0) Grade D 0/55 (0.0)	Grade A 4/25 (16.0) Grade B 6/25 (24.0) Grade C 0/25 (0) Grade D 0/25 (0)
IRP (mmHg), mean ± SD	25.34 ± 26.25	8.88 ± 7.03
Difference from pre- to post-POEM IRP (mmHg), mean (95%CI; p-value)		10.64 (5.82-15.46, 0.0003)
Eckardt score, mean ± SD Distribution - Score 0-1 - Score 2-3 - Score >3	7.1 ± 2.64 4% 3% 90%	1.22 ± 1.50 64% 30% 6%
Abnormal EndoFLIP (EGJ-DI ≤ 2.8 mm2/mmHg), n/N= (%)	15/17 (88.2)	
Barium Esophagram - Retention of liquids n/N= (%) - Retention of tablet n/N= (%)	 21/46 (45.6) 12/25 (48.0)	
Procedural characteristics		
Procedural time (minutes), mean ± SD		73.2 ± 35.6
Anterior/Posterior approach, n (%)		28 (50.9) / 27 (49.0)
Total myotomy length (cm), mean ± SD		12.58 ± 3.33
Post-procedural results		
Technical success, n (%)		55 (100)
Successful clinical response, n (%)		47 (94.0)
Adverse events, n		Minor: 2/55 Mild: 2/55 Severe: 1/55

Adverse events, n (%)		5 (9.6)
Revision of POEM, n (%)		1 (1.8)
Abnormal time pH >4 on 24-hour pH monitoring, n/N (%)		12/18 (66.6)
Duration of follow-up (days), median (IQR)		117 (48-281)

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