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Conventional clips *vs* over-the-scope-clips for the closure of the entry site in POEM and G-POEM procedures

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ABSTRACT

Background: new alternatives for entry site closure (ESC) in per-oral endoscopy myotomy (POEM) and gastric peroral endoscopy myotomy (G-POEM) have appeared.

Objective: to compare the over-the-scope-clip (OTSC®) and conventional clips (CC) for ESC in POEM and G-POEM.

Material and methods: a retrospective review of a prospective POEM and G-POEM database was performed between January 2015 and August 2019. A description was made of outcomes, using either OTSC® or CC for submucosal tunnel closure.

Results: forty-six POEM and 26 G-POEM were included in the study (23/13 per group [CC/OTSC®]). There were no clinical or procedure differences. ESC was performed with 1 OTSC® *vs* 5 CC and 1 *vs* 6 (p = 0.01) for POEM and G-POEM, respectively. Adverse events associated with clips were 21.7% *vs* 13% (p = 0.01) and 7.7% *vs* 0% (p = 0.02) for CC and OTSC® in POEM and G-POEM, respectively.

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Conclusion: OTSC® represents a safe and effective alternative for entry site closure in POEM and G-POEM cases. Further studies are needed to recommend OTSC® as the first option for submucosal tunnel closure in these procedures.

Keywords: Over-the-scope-clip. Conventional clips. Entry site closure. G-POEM. POEM.

INTRODUCTION

The endoscope-mounted clip, called over-the-scope-clip system (OTSC®, Tubingen, Germany), is an innovative therapeutic tool. It has become popular worldwide due to its excellent results in terms of safety and efficacy for the management of different gastrointestinal wall diseases. These include confirmed indications such as non-variceal upper gastrointestinal bleeding, acute wall perforations and gastrointestinal leaks (1-4). However, more potential uses have recently appeared, with advantages that include lower costs, excellent safety and a similar or even better clinical outcome compared with other traditional treatments (5,6). New potential indications include entry site closure (ESC) in third-space procedures (peroral endoscopy myotomy [POEM], gastric peroral endoscopic myotomy [G-POEM] and Zenker POEM [Z-POEM]), mucosal or submucosal tumor resection and stent fixation (SF) (7-9). ESCs in POEM and G-POEM procedures are usually performed with hemostatic conventional clips (CC). However, some adverse events have been described, such as difficult clip placement, inadvertent dropping of the clips at the entry site, technical problems or even high costs. Therefore, other methods have been described, such as fibrin sealant, cyanoacrylate, endoscopic suture and OTSC® clips (10-12). Limitations include availability and costs. We aimed to evaluate the use of OTSC® *vs* CC for ESC in a cohort of patients that underwent POEM and G-POEM procedures.

MATERIAL AND METHODS

A retrospective review of our prospective POEM and G-POEM databases was performed. Patients that underwent ESC performed with CC or OTSC® in the Endoscopy Department

of the Hospital de Especialidades Centro Médico Nacional Siglo XXI, between January 2015 and August 2019, were included. Patient characteristics, procedural data and clinical outcomes were reported and analyzed. Technical success was considered when no adverse events related with the clip placement were found and clinical success when procedure safety and efficacy was not compromised. Bivariate comparisons were performed using the Student's t-test, Mann-Whitney U test and X^2 test. $p < 0.05$ was considered as statistically significant.

RESULTS

Forty-six and 26 patients were included in the POEM and G-POEM groups, respectively. No differences were found with regard to clinical or demographic data between the closure methods of both procedures.

In the POEM group, the most common clinical characteristics were dysphagia, naïve patients and type II in 74%, 87% and 69.5%, respectively. POEM had a 100% clinical efficacy for both groups, with a decrease in the Eckardt and integrated relaxation pressure (IRP) values, with no differences between both closure methods. There were no differences in POEM characteristics such as tunnel length, myotomy length, incision size and procedure time. However, there were longer clip placement times (6.5 ± 1.1 *vs* 3.2 ± 0.7 minutes; p = 0.01), higher number of clips used (5 *vs* 1; p = 0.01) and more clip related adverse events (21.7% *vs* 13%; p = 0.01) in the CC arm compared with OTSC®. Technical and clinical clip success occurred in 94.5% *vs* 91.7% of cases (p = 0.13) and 91.7% *vs* 100% (p = 0.01) for CC and OTSC®, respectively. Conventional clips could not be placed in two patients due to the inability of facing both sides of the mucosa at the entry site and three patients had a clip dislodgement between 24 and 48 hours after the procedure (cyanoacrylate and OTSC® were used in two and three cases, respectively, as rescue therapies). In the OTSC® arm, the OTSC® clip could not pass throughout the cricopharyngeus in two patients (type A in both) and CC was used. Finally, OTSC® could not be mounted on the endoscope in one patient (cyanoacrylate was used for ESC). Type A was used in 20 (86%) and GC in three (14%) cases (Table 1 and Fig. 1).

Most of the patients in the G-POEM group were male (53% *vs* 69%; p = 0.06) and had nausea and vomiting (53% *vs* 69.2%; p = 0.09) as the predominant symptom in the CC and OTSC® arms, respectively. Clinical G-POEM success was 100%, with no differences in the gastric symptom cardinal index (GSCI) score or scintigraphy assessment between both arms. Procedural characteristics were similar. However, longer clip placement times (6.9 ± 1.4 *vs* 3.1 ± 1.1; p = 0.02), a higher number of clips used (6 *vs* 1; p = 0.01) and more clip related adverse events (7.7% *vs* 0%; p = 0.02) were reported in the CC arm compared with OTSC® group. Technical clip success was 100% in both groups and clinical success was better for OTSC® (100% *vs* 92.3%; p = 0.01). One patient in the CC arm had a clip dislodgement 24 hours after G-POEM and two CC were used for closure, with no clinical G-POEM major complications. Type GC was used in ten cases (77%) and A in three (23%) (Table 2 and Fig. 2).

DISCUSSION

In this study, the safety and efficacy of using OTSC® as an alternative closure method for POEM and G-POEM third space procedures were confirmed. Its use with conventional clips was compared, as it has usually been used for ESC since its first description by Inoue et al. (13). However, several adverse events related to clip placement have been described by different studies, such as clip dislodgement, the inability to place the hemostatic clip and technical problems (7,9-11).

The entry site is the weakest area at the end of the procedure. Therefore, if the closure method is not strong enough or if placement is not adequate, this site could have an accidental mucosotomy secondary to a sudden increase in the intra-abdominal pressure. As a consequence, the safety of the procedure would be compromised (8,10). Different closure methods have been explored. Pescarus et al. (14) performed a retrospective comparison between endoscopic suturing and CC in a cohort of POEM cases. Good clinical results were observed in both procedures, without postoperative leaks, and the closure times were shorter in CC *versus* suturing (16 ± 12 *vs* 33 ± 11min; p < 0.01). Similar clinical results were observed in our study, with no leakage after the procedure in both arms. In

our study, three POEM and one G-POEM cases suffered an inadvertent drop of the clip 24-48 hours after the procedure and were diagnosed based on control fluoroscopy, which is usually performed in our patients before starting oral feeding. The placement time in our study was slightly shorter compared to the CC group of the study by Pescarus et al., 16 ± 12 *vs* 6.5 ± 1.1 min. This was likely due to our experience in clip use. However, OTSC® use improved these times by at least 50% in both arms. In fact, a single clip was used in all procedures, confirming its safety and efficacy.

Other methods such as fibrin sealant and cyanoacrylate have been used to close mucosal injuries during or after procedures (11,12). However, only cyanoacrylate has been used systematically as an ESC method in a cohort of POEM patients with excellent safety, efficacy and low costs (15). In our case, we consider that OTSC® is a good alternative to close the entry site. Saxena P et al. (8) was the first to describe the use of this device in two patients with POEM, with 100% efficacy. In our study, all OTSC® clips were placed correctly and placement was not possible in only in 3/36 (8.3%) cases due to technical problems or patient anatomy.

The main strengths of our study include the fact that this is the first study that directly compares both ESC methods in an area where a better closure method is needed. Second, strict protocols for POEM and G-POEM procedures were performed. Therefore, the detection of clip adverse events was optimal in our cohort. Third, an adequate 1 to 1 comparison of groups was performed in both procedures. Limitations included the retrospective nature, a limited number of cases and OTSC® placement by an experienced endoscopist.

In conclusion, OTSC® represents a safe and effective alternative for entry site closure in POEM and G-POEM cases.

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Table 1. POEM and G-POEM demographic data

Characteristic	*Conventional clips n = 36*	*Over-the-scope-clip n = 36*	*p*
POEM	n = 23	n = 23	
Age, mean (SD), years	43.2 ± 11.3	40.2 ± 9.4	0.15*
Sex, male, n (%)	14 (60.8)	13 (56.5)	0.74†
Type of esophagus, n (%)			
– Normal	1 (4.3)	2 (8.7)	
– Grade I	6 (26.1)	5 (21.8)	
– Grade II	11 (47.8)	9 (39.1)	0.08†
– Grade III	3 (13.1)	6 (26.1)	
– Grade IV	2 (8.7)	1 (4.3)	
Symptoms, n (%)			
– Dysphagia	17	19	
– Weight loss	14	12	0.11†
– Thoracic pain	10	13	
– Reflux symptoms	8	8	
Previous treatments, n (%)			
– Treatment naïve	20	19	0.06†
– Previously treated	3	4	
Achalasia subtype, n (%)			
– Type I	4	4	
– Type II	16	18	0.21†
– Type III	3	1	
Pre-POEM Eckardt score, median (IQR), points	9 (8-12)	9 (7-12)	0.45‡
Post-POEM Eckardt score, median (IQR), points	1 (0-3)	1 (0-2)	0.66‡
Pre-POEM IRP pressure, mean (SD), mmHg	28.8 ± 11.8	26.2 ± 10.2	0.07*
Post-POEM IRP pressure, mean (SD), mmHg	8.8 ± 10.8	9.1 ± 11.1	0.73*

SD: standard deviation; IQR: interquartile range; POEM: peroral endoscopy myotomy; G-POEM: gastric peroral endoscopic myotomy; IRP: integrated relaxation pressure; GSCI: gastroparesis cardinal symptoms index; RPH4: retention percentage four hours; MHET: mean half emptying time. *Student's t-test. †X^2 test. ‡Mann-Whitney U test.

Table 2. OTSC use in POEM and G-POEM procedures

Characteristic	*Conventional clips n = 36*	*Over-the-scope-clip n = 36*	*p*
POEM	n = 23	n = 23	
Tunnel length, mean (SD), cm	12.6 ± 2.9	11.8 ± 3.5	0.09*
Myotomy length, mean (SD), cm	11.1 ± 2.2	10.7 ± 2.6	0.14*
Incision size, mean (SD), cm	1.7 ± 0.35	1.9 ± 0.78	0.08*
Clip placement time, mean (SD), minutes	6.5 ± 1.1	3.2 ± 0.7	0.01*
Procedure time, median (IQR), minutes	55 (38-71)	50 (40-66)	0.06†
Technical clip success, n (%)	94.5	91.7	0.13‡
Clinical clip success, n (%)	91.7	100	0.03‡
Number of clips, median (IQR), number	5 (4-8)	1	0.01†
Adverse events related to clip placement, n (%) – *Inability to place a clip* – *Clip dislodgement after initial successful placement at entry site* – *Inability to pass the clip throughout the cricopharyngeus* – *Technical problems*	5 (21.7) 2 3 0 0	3 (13.0) 0 0 2 1	0.01‡
G-POEM	n = 13	n = 13	
Tunnel length, mean (SD), cm	5.2 ± 0.92	5.5 ± 0.77	0.76*
Myotomy length, mean (SD), cm	4.1 ± 0.72	3.8 ± 0.85	0.38*
Incision size, mean (SD), cm	1.9 ± 0.44	1.8 ± 0.72	0.54*
Clip placement time, mean (SD), cm	6.9 ± 1.4	3.1 ± 1.1	0.02*
Procedure time, median (IQR), minutes	62 (48-77)	66 (51-84)	0.17†
Technical clip success, n (%)	100	100	0.44‡
Clinical clip success, n (%)	92.3	100	0.02‡
Number of clips, median (IQR), number	6 (5-8)	1	0.01†
Adverse events related to clip placement, n (%)	1 (7.7)	0 (0)	

SD: standard deviation; IQR: interquartile range; POEM: peroral endoscopy myotomy; G-POEM: gastric peroral endoscopic myotomy. *Student's t-test. †Mann-Whitney U test. ‡X^2 test.

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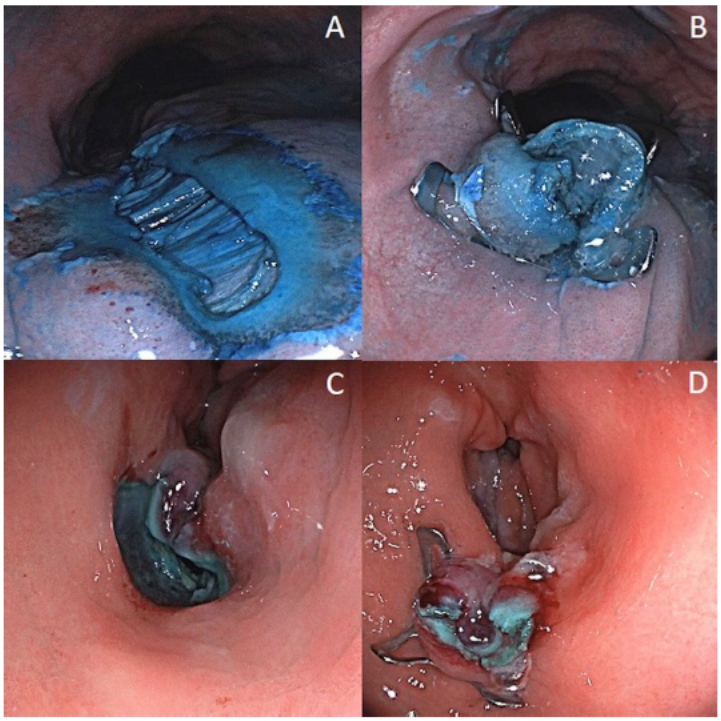

Fig. 1. OTSC placement in POEM and G-POEM cases. A. Entry site in the POEM procedure at the mid-esophagus. B. Closure with an OTSC clip. C. Entry site in a G-POEM case, 5 cm before the pylorus. D. OTSC placement in the G-POEM entry site.

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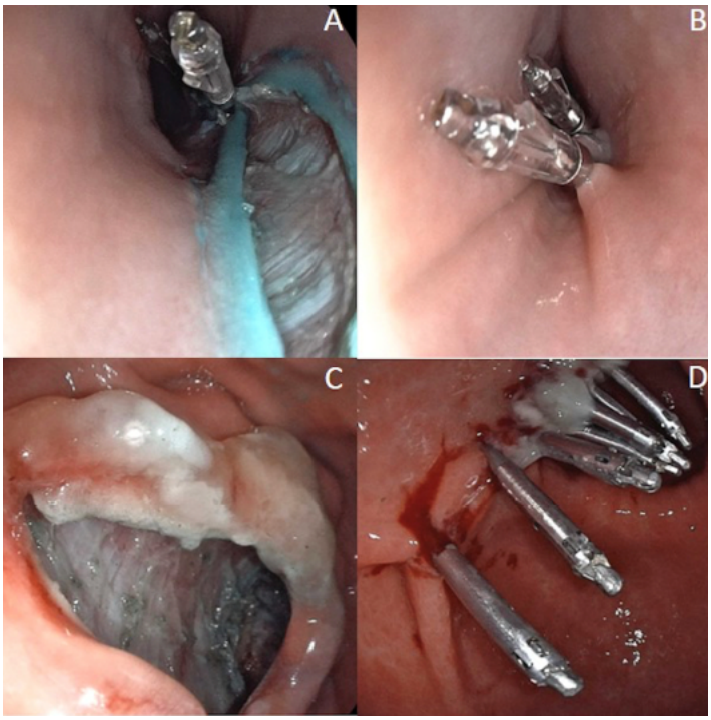

Fig. 2. Conventional clip placement in POEM and G-POEM cases. A. Entry site in the POEM procedure with initial clip placement. B. Final entry site closure with a conventional clip. C. A 20 mm long G-POEM entry site. D. Placement of seven conventional clips in G-POEM.

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