学　位　論　文

Long-term outcomes of Over-The-Scope Clip for refractory gastrointestinal diseases

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医学専攻

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MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
https://doi.org/10.1080/13645706.2020.1867584

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RESEARCH ARTICLE

Long-term outcomes of over-the-scope clip for refractory gastrointestinal diseases

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ABSTRACT

Background: The Over-The-Scope Clip (OTSC) can effectively treat refractory gastrointestinal diseases. However, most reports have focused on short-term effectiveness. We examined clinical outcomes of the deployed clips and long-term characteristics.

Material and methods: Of 47 patients with OTSC treatment, 35 with follow-up periods of ≥3 months were retrospectively examined. The indications were 11 bleedings, 17 perforations, and seven fistulas. The observation period was defined as medium-term (3 to <12 months) or long-term (≥12 months). The primary outcome was the clinical success rate without disease recurrence. The secondary outcomes were the complication rate, survival duration, and clip retention rate.

Results: The medium- and long-term clinical success rates were 100% during the observation period (median, 44 months; range, 3–78 months). The complication rate was 2.9% ($n = 1$). The median survival time was 1,634 days for bleeding, 1,757 days for perforation, and 444 days for fistulas. The overall clip retention rates were 56.4%, 38.1%, 30.9%, and 25.9% after one, six, and 12 months and at the final follow-up, respectively. The average clip retention duration was 244 days in bleeding, 656 days in perforations, and 188 days in fistulas.

Conclusions: Regardless of clip detachment, the OTSC can be effective in long-term.

ARTICLE HISTORY
Received 13 August 2020
Accepted 14 December 2020

KEYWORDS
Endoscopic intervention; Over-the-scope clip; refractory gastrointestinal disease; prognosis

Introduction

Gastrointestinal (GI) diseases that are resistant to conventional endoscopic therapy have traditionally needed surgical repair. Refractory GI bleeding, perforation, anastomotic leakage, and fistulas, which most clinicians encounter in daily practice, may have an especially poor prognosis with high mortality [1]. A full-thickness clipping device, the Over-The-Scope Clip (OTSC; Ovesco Endoscopy AG, Tübingen, Germany), which was released clinically in 2007 [2], has been evaluated for treatment of these refractory diseases worldwide [3]. Full-thickness closure can be achieved using the OTSC during technical procedures such as endoscopic submucosal dissection [4,5] or natural orifice transluminal endoscopic surgery [6,7]. This has contributed to technological advancements [8] and the management of complications related to endoscopic submucosal dissection [9]. The OTSC system has the advantages of rapidity and simplicity. It also has a stronger tissue-grasping force than conventional endoscopic hemoclips. Moreover, two accessory devices for approximating large lesions (Twin Grasper; Ovesco Endoscopy AG) and anchoring the tissue (Anchor; Ovesco Endoscopy AG) can be used to assist with defect closure. The OTSC thus contributes to the accomplishment of minimally invasive therapy, which is beneficial in patients with refractory GI diseases because invasive surgery can be avoided.

According to a recent literature review of 1,517 cases [10], OTSC use provided acceptable clinical success rates (CSRs) of 78% overall, 85% for bleeding, 85% for perforation, 52% for fistulas, 66% for anastomotic leakage, and 95% for other conditions. Additionally, the overall and severe OTSC-associated complication rates were 1.70% and 0.59%,

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respectively. Consequently, the OTSC system is considered a safe and effective device for refractory GI diseases, although it shows limited ability for treatment of fistulas and anastomotic dehiscence with indurated tissues.

Most previous reports of the OTSC have focused on the immediate and short-term effectiveness (observation period of <3 months) [11,12]. Few reports have described the effectiveness and safety of the OTSC after long-term observation (≥1 year). Additionally, the patient survival rates and clip retention rates are still undergoing investigation. In clinical practice, use of the OTSC for hard tissues such as fistulas frequently causes delayed leakage, even if treatment is successful in the short term; i.e. treatment is unsuccessful in the medium to long term. This indicates the need to clarify the true outcomes of treatment with the OTSC by analyzing the medium- and long-term results. Therefore, the present study was performed to evaluate the usefulness and safety of the OTSC and explore the association between deployed clips and baseline characteristics in the medium and long term.

Material and methods

Patient selection

This retrospective study was conducted at three medical centers in the Shikoku area of Japan. In total, 47 patients underwent treatment of refractory GI bleeding, perforations, or fistulas using the OTSC from November 2011 to March 2015. Of these 47 patients, 12 were excluded because of technical failure ($n = 12$), loss to follow-up ($n = 4$), and death by other diseases at <3 months postoperatively ($n = 3$). Thus, 35 patients who underwent follow-up by imaging examinations (abdominal X-ray, computed tomography, or endoscopic imaging) for ≥3 months were included in the present study (Figure 1). The indications for treatment were divided into three groups: intractable bleeding ($n = 11$), perforation ($n = 17$), and fistulas ($n = 7$). The observation period was defined as medium-term (3 to <12 months) or long-term (≥12 months). Key data (patient demographics, indications for the procedure, clinical success of the procedure, and adverse events) were collected prospectively and analyzed retrospectively. When data were lacking or insufficient, the information was confirmed by telephone.

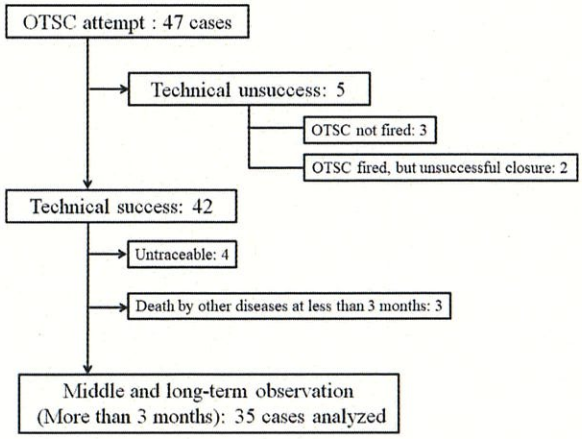

Figure 1. Flowchart of patient enrollment.

OTSC procedure

The OTSC system consists of an OTSC mounted onto an application cap and a hand wheel. First, the endoscope attached to the cap and loaded with the OTSC was inserted into the GI tract either orally or anally. Either a gastroscope (GIF-Q260J, ø9.9 mm or H260Z, ø10.8 mm; Olympus, Tokyo, Japan) or a colonoscope (PCF-Q260AI, ø11.3 mm; Olympus) with a maximum diameter of 9.9 mm and a working channel with a diameter of >2.8 mm was applied. The targeted lesion was centered within the cap of the OTSC, and the lesion was then suctioned into the cap. Finally, the clip was fired by stretching the wire with the hand wheel, and the entire defect of the lesion was completely closed. For patients with GI perforations and leakage, simple suction for small defects and the Twin Grasper for large defects were used to aspirate the defect into the cap. For patients with a fistula with indurated tissues, simple suction or the Anchor assist device was used. The 10-mm gastrostomy closure type of OTSC was used for the gastric wall, and the 10-mm traumatic type of OTSC was used for other organs with thin walls. Four expert endoscopists with experience performing several procedures with the OTSC system, performed the OTSC deployments.

Outcome measures

The primary outcome was the clinical success rate (CSR). Clinical success was defined as a clinically cured, non-recurrence state and was based on the intended treatment, achieving complete hemostasis for GI bleeding or complete closure without delayed leakage for perforations and fistulas. The secondary outcomes were complication rate, survival duration (overall and for each disease), and OTSC clip

retention rate (overall, for each indication, and for each organ). The routine follow-up intervals depended on each individual patient's clinical features and were determined at the clinicians' discretion.

Statistical analysis

The data are mainly presented as median and range. The OTSC clip retention rate was calculated by the Kaplan–Meier method, and the data were analyzed using the log-rank test for between-group comparisons. A p value of $<.05$ was considered statistically significant. All statistical analyses were conducted using JMP version 9.0 (SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics

The patients' detailed clinical data are summarized in Table 1. The 35 consecutive patients comprised 25 male and ten female patients with a median age of 77 years (range, 4–98 years). The observation period was <12 months in four patients and ≥12 months in 31 patients. The medium- and long-term CSR was 100% during the observation period (median, 44 months; range, 3–78 months). There were 15 deaths: five cases of carcinoma, four cases of heart failure, three cases of infection, two cases of hepatic failure, and one case of stroke. The time periods between onsets and performances were defined as immediate (within 1 day), acute (> 1 day, < 7 days), and chronic (> 7 days). Among the 35 cases, there were 14 immediate cases, ten acute cases, and 11 chronic cases.

Outcomes

The median overall survival duration was 1,355 days (range, 90–2,359 days). The overall clip retention rate was 56.4% after one month, 38.1% after six months, 30.9% after 12 months, and 25.9% at the final follow-up. After 24 months, clips remained in the stomach in approximately 30% of patients; this rate was better than that in the other organs (approximately 10%). These outcomes are summarized in Table 2.

The survival rate was significantly different between the bleeding, perforation, and fistula groups ($p = .0143$). The median survival time for each disease was 1,634 days for bleeding, 1,757 days for perforation, and 444 days for fistulas. The rate at 24 months of observation was 0.0% in the esophagus, 33.3% in the stomach, 7.1% in the duodenum plus small intestine, and 12.5% in the colorectum. The average clip duration was 244 days for bleeding, 656 days for perforations, and 188 days for fistulas. The clips for fistulas tended to be lost at the earliest time point, and those

Table 1. Patient characteristics.

Variables	$N = 35$
Age, years	77 (4–98)
Sex, male/female	25/10
Location	
Esophagus	2
Stomach	16
Duodenum	12
Small intestine	1
Colorectum	4
Indications	
Bleeding, N = 11	
Stomach/Duodenum/Small intestine/Colorectum	3/5/1/2
Ulcer/diverticulum /ER complication	8/1/2
Immediate/Acute/Chronic	4/2/5
Median defect size, mm, (range)	12 (5–40)
Perforation, N = 17	
Esophagus/Stomach/Duodenum/Colorectum	2/8/6/1
Endoscopic complication/Boerhaave/iatrogenic stomach tube/Anastomotic leakage	14/1/1/1
Immediate/Acute/Chronic	10/7/0
Median defect size, mm, (range)	25 (5–45)
Fistula, N = 7	
Stomach/Colorectum	5/2
Gastric PEG/pseudo cyst/bladder-rectum fistula/gall bladder-colon fistula	4/1/1/1
Median defect size, mm, (range)	7 (5–15)
Prognosis	
Alive/dead	20/15
Details of deaths	
Cancer/heart failure/infection/hepatic failure/stroke	5/4/3/2/1

Data are presented as median (range) or number of patients. ER: endoscopic resection; PEG: percutaneous endoscopic gastrostomy.

Table 2. Results of outcome measures.

	Outcomes	$N = 35$
Primary	Long-term CSR (≥12 months)	100%
	Medium-term CSR (3–12 months)	100%
Secondary	Complications, *n* (%)	1 (2.9)
	Retention rate (retained clips/total clips)	
	1 month postoperatively	56.4%
	6 months postoperatively	38.1%
	12 months postoperatively	30.9%
	Final	25.9%
	Observation period, months [median (range)]	44 (3–78)
	Overall survival, days [median (range)]	1355 (90–2359)
	Median survival for each indication, days, (range)	
	Bleeding	1634 (90–2010)
	Perforation	1757 (344–2359)
	Fistula	444 (124–1598)

CSR: clinical success rate.

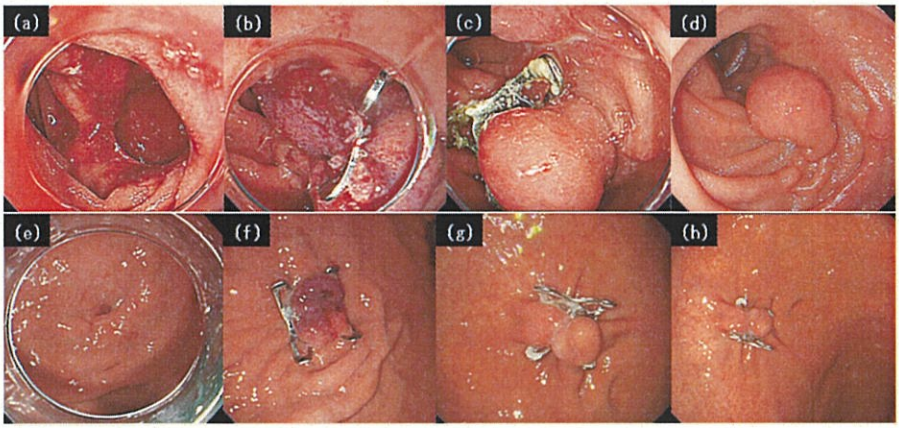

Figure 2. Presentative perforation case and fistula case with long-term clinical success. (a) The perforation during duodenal EMR, which is > 20 mm in size. (b) Successful OTSC closure using two clips. (c) Nine months later (middle term), only one clip had retained. (d) Twenty-four months later (long term), the perforation site was healed and all clips had fallen off. (e) The fistula formed by gastric PEG (3 mm in diameter). (f) Successful OTSC closure. (g) Three months later (middle term), the clip had retained. (h) Twenty-four months later (long term), the clip had still retained.

for perforations were retained the longest. The complication rate was 2.9% in all cases. Only one patient out of 35 experienced a long-term complication of cavity formation at the sigmoid colon.

A representative case of perforation treatment with clinical success is shown in Figure 2(a–d). A representative case of fistula treatment with clinical success is shown in Figure 2(e–h). The only complication case is shown in Figure 3.

Discussion

In this observational study, we investigated long-term patient survival and the organ- and indication-specific results of OTSC. This is the first study to focus on how long the clips are retained for each indication and in each organ. The present study proved the efficacy of OTSC as shown by the excellent short-, medium-, and long-term CSRs. This investigation also showed that the retention or dropping of clips does not affect the patient's clinical status and that clip treatment itself does not compromise the prognosis. In terms of disease-related survival, patients with fistulas had a poorer prognosis than patients with bleeding and perforations. This result was surely influenced by the fact that patients with fistulas included those treated with percutaneous endoscopic gastrostomy tubes and that their general condition was usually poor. The high CSR in this study indicates that the clips themselves sufficiently prevented recurrence of the original disease.

With respect to clip migration, nearly 62% of the OTSC clips tended to fall off within six months, but those that were retained beyond this point stayed in place for much longer than 12 months; this was especially notable with gastric clips. This finding might

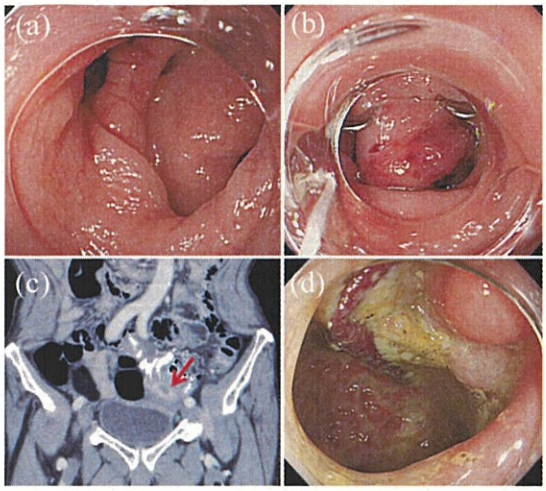

Figure 3. One complication case showing a cavity formation 4 four years after OTSC successful closure for refractory sigmoid diverticular bleed. (a) Intractable diverticular bleeding in sigmoid colon. (b) Successful OTSC deployment and complete hemostasis. (c) Four years later (long-term), CT revealed the occurrence of a non-infectious cavity formation (2 cm in diameter) at the sigmoid (Red arrow). (d) Four years later, the clip had fallen off and the cavity accompanied with granulated tissues appeared.

have been associated with the fact that among the 16 patients who underwent OTSC treatment in the stomach, seven patients had acute perforations. This acute condition with the absence of indurated tissues probably led to the strong defect closure by the OTSC device. Our finding is supported by a recent report. In that investigation of the long-term behavior of OTSC after gastric application, the long-term retention rate of gastric clips was high at 72%, and the indication for treatment in all patients was iatrogenic gastric perforation [13].

These data suggest that the clips tend to be retained in cases involving gastric soft tissues. Further investigations are needed to verify this finding in acute and chronic settings as well as for different organs.

Previous reports described limited success of using the OTSC for fistulas [3,10,14–16]. These results are probably associated with our finding that the fistula clip easily detaches because of its limited power in biting chronically hard tissues. The boundary between successful and unsuccessful clip closure for fistulas is thought to be a lesion diameter of 10 mm, and the success rate is poor even when using the Twin Grasper for lesions with larger diameters [17]. The same difficulties are encountered in patients with bleeding. The OTSC is usually indicated for refractory recurrent bleeding after failure of conventional techniques [18,19]. The ulcer floor becomes indurated as time progresses. Although first-line treatment with the OTSC seems to be a more reasonable option to ensure clinical success [20,21], the instrumental cost is more expensive than that of conventional hemostatic tools.

With respect to the follow-up duration, Haito-Chavez et al. reported a long-term success rate of 60.2% among 188 patients with a median follow-up of 146 days [3]. Additionally, a few case reports and case series have focused on long-term outcomes at $\geq$12 months [22,23]. In the study with the longest-term outcome prior to the present study, Donatelli et al. reported that the overall CSR was 58% (26/45 patients) at a median follow-up of 17 months (range, 1–36 months) [23]. Our study had the longest-term outcome, with a median follow-up period of 44 months (range, 3–78 months). However, our high CSR is not comparable with those in previous studies because cases of technical failure, patients who were lost to follow-up, and patients who died of other diseases in the short term were excluded from the present study. Further clinical trials are needed to clarify the optimal indications for and limitations of the OTSC system.

The OTSC system is recognized as a relatively safe device. Complications such as mis-deployment and endoluminal stenosis can occur during the immediate- and short-term [10]; however, no long-term complications have been reported in PubMed to date. Interestingly, the first-ever case of a complication (diverticulum hemorrhage at the sigmoid colon) associated with OTSC treatment was observed during long-term observation after successful OTSC deployment in the present study. A cavity appeared at the clipping site four years after OTSC treatment. Although the patient remained clinically asymptomatic during the entire observation period, follow-up X-rays and colonoscopy showed the unexpected complication. OTSCs are generally deployed by squeezing the entire layer face-to-face. Blood flow is maintained through the gap between the clips, preventing tissue necrosis. A diverticulum anatomically lacks a muscular layer. Because the clip might suction only the superficial layer, not all layers, the deployed clip may cause mucosal ischemia, a silent perforation sealed by the mesentery, and finally cavity formation as seen in our case. Endoscopic band ligation (EBL) was recently described as an effective treatment method for diverticular bleeding [24]. Delayed perforation has been

described as a rare complication after EBL [25]. The OTSC device has the same mechanical function as the EBL procedure and may therefore have a potential risk of delayed perforation.

In summary, nearly 62% of OTSC clips tend to fall off within six months, but most clips that remain in place for this amount of time are retained for ≥12 months. By the time an OTSC clip falls off, the GI defect is already sealed and completely healed. Accordingly, knowledge regarding clip retention for each indication and organ is very important for effective long-term treatment. In terms of disease-related survival, the survival rate of patients with fistulas is significantly lower, largely because many such patients have severe conditions and a poor prognosis. Even if the clip comes off early, the CSR remains high and the recurrence rate is unaffected; thus, treatment with the OTSC device can be expected to be effective and safe in the medium to long term.

Study limitations

The main limitation of this study is its retrospective design. Additionally, it was conducted in just two centers. Another limitation is that this study does include heterogenous groups with different indications or organs. The main purpose of this study was not only finding long-term clinical outcomes of OTSC but also investigating the clip retention rates. As previous reports [3,10] and a systematic review [17] analyzed clinical outcomes by dividing these indications, OTSC has provided a different outcome on short-term in each indication or organ. Especially, OTSC had a limited ability for chronic fistula with indurated tissues due to delayed leakage and the clip retention rate for fistula was expected to be lower than those for acute bleeding, and immediate perforation. Clip dropping for fistula may be one of the factors associated with the occurrence of delayed leakage. Therefore, this study was conducted to find unknown differences over long-term in heterogenous groups. Moreover, the clip retention may interrupt the evaluation of the healing site when checking a local recurrence of the tumor after endoscopic resection. A dropped clip may also have a concern of stagnancy when an unexpected intraluminal stenosis exists in the intestine. Therefore, tracking clip retention in long-term is clinically meaningful.

In conclusion, although successful closure does not seem to be associated with an improved prognosis in patients with fistulas, regardless of whether clips are dropped, the OTSC can be an acceptable device in the medium to long term.

Acknowledgement

We thank Angela Morben, DVM, ELS, from Edanz Group (https://en-author-services.edanzgroup.com/), for editing a draft of this manuscript.

Declaration of interest

No potential conflict of interest was reported by the author(s).

Compliance with ethical standards

All data were entered into a central database at Kagawa University. This study was approved by the Clinical Ethics Committee of Kagawa University Hospital (Registration number: 2019-187) and the ethics committees of the other two institutions that participated in the study in accordance with the Declaration of Helsinki, and the CONSORT checklist was followed. All patients provided written informed consent to undergo the procedures and participate in the study.

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References

[1] Raithel M, Albrecht H, Scheppach W, et al. Outcome, comorbidity, Hospitalization and 30-day mortality after closure of acute perforations and postoperative anastomotic leaks by the over-the-scope clip (OTSC) in an unselected cohort of patients. Surg Endosc. 2017;31(6):2411–2425.

[2] Kirschniak A, Kratt T, Stüker D, el al. A new endoscopic over-the-scope clip system for treatment of lesions and bleeding in the GI tract: first clinical experiences. Gastrointest Endosc. 2007;66(1):162–167.

[3] Haito-Chavez Y, Law JK, Kratt T, et al. International multicenter experience with an over-the-scope clipping device for endoscopic management of GI defects (with video). Gastrointest Endosc. 2014;80(4):610–622.

[4] Yamamoto Y, Kikuchi D, Nagami Y, et al. Management of adverse events related to endoscopic resection of upper gastrointestinal neoplasms: review of the literature and recommendations from experts. Dig Endosc. 2019;31(S1):4–20.

[5] Tanaka S, Kashida H, Saito Y, et al. Japan Gastroenterological Endoscopy Society guidelines for

colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc. 2020;32(2):219–239.

[6] Khashab MA, Kalloo AN. NOTES: current status and new horizons. Gastroenterology. 2012;142(4):704–710.

[7] Saxena P, Khashab MA. New NOTES clinical training and program development. Gastrointest Endosc Clin N Am. 2016;26(2):385–400.

[8] Aslanian HR, Sethi A, Bhutani MS, et al. ASGE guideline for endoscopic full-thickness resection and submucosal tunnel endoscopic resection. VideoGIE. 2019;4(8):343–350.

[9] Nishiyama N, Mori H, Kobara H, et al. Efficacy and safety of over-the-scope clip: including complications after endoscopic submucosal dissection. World J Gastroenterol. 2013;19(18):2752–2760.

[10] Kobara H, Mori H, Nishiyama N, et al. Over-the-scope clip system: a review of 1517 cases over 9 years. J Gastroenterol Hepatol. 2019;34(1):22–30.

[11] Weiland T, Fehlker M, Gottwald T, et al. Performance of the OTSC System in the endoscopic closure of iatrogenic gastrointestinal perforations: a systematic review. Surg Endosc. 2013;27(7):2258–2274.

[12] Wedi E, Gonzalez S, Menke D, et al. One hundred and one over-the-scope-clip applications for severe gastrointestinal bleeding, leaks and fistulas. World J Gastroenterol. 2016;22(5):1844–1853.

[13] Hu J, Yang Y, Ge N, et al. Long-term assessment of over-the-scope clip (OTSC) behavior after gastric application. Minim Invasive Ther Allied Technol. 2020;29(2):86–89.

[14] Mönkemüller K, Peter S, Toshniwal J, et al. Multipurpose use of the 'bear claw' (over-the-scope-clip system) to treat endoluminal gastrointestinal disorders. Dig Endosc. 2014;26(3):350–357.

[15] Mercky P, Gonzalez JM, Aimore Bonin E, et al. Usefulness of over-the-scope clipping system for closing digestive fistulas. Dig Endosc. 2015;27(1):18–24.

[16] Law R, Wong Kee Song LM, Irani S, et al. Immediate technical and delayed clinical outcome of fistula closure using an over-the-scope clip device. Surg Endosc. 2015;29(7):1781–1786.

[17] Kobara H, Mori H, Fujihara S, et al. Outcomes of gastrointestinal defect closure with an over-the-scope clip system in a multicenter experience: an analysis of a successful suction method. World J Gastroenterol. 2017;23(9):1645–1656.

[18] Winder JS, Kulaylat AN, Schubart JR, et al. Management of non-acute gastrointestinal defects using the over-the-scope clips (OTSCs): a retrospective single-institution experience. Surg Endosc. 2016;30(6):2251–2258.

[19] Manta R, Galloro G, Mangiavillano B, et al. Over-the-scope clip (OTSC) represents an effective endoscopic treatment for acute GI bleeding after failure of conventional techniques. Surg Endosc. 2013;27(9):3162–3164.

[20] Manno M, Mangiafico S, Caruso A, et al. First-line endoscopic treatment with OTSC in patients with high-risk non-variceal upper gastrointestinal bleeding: preliminary experience in 40 cases. Surg Endosc. 2016;30(5):2026–2029.

[21] Wedi E, Fischer A, Hochberger J, et al. Multicenter evaluation of first-line endoscopic treatment with the OTSC in acute non-variceal upper gastrointestinal bleeding and comparison with the Rockall cohort: the FLETRock study. Surg Endosc. 2018;32(1):307–314.

[22] Sagara Y, Shinozaki S, Yano T, et al. Use of an over-the-scope clipping device for closure of a jejuno-sigmoid fistula: a case report with long-term follow-up. Clin J Gastroenterol. 2016;9(6):369–374.

[23] Donatelli G, Cereatti F, Dhumane P, et al. Closure of gastrointestinal defects with Ovesco clip: long-term results and clinical implications. Therap Adv Gastroen0terol. 2016;9(5):713–721.

[24] Yamada A, Niikura K, Yoshida S, et al. Endoscopic management of colonic diverticular bleeding. Dig Endosc. 2015;27(7):720–725.

[25] Takahashi S, Inaba T, Tanaka N. Delayed perforation after endoscopic band ligation for treatment of colonic diverticular bleeding. Dig Endosc. 2016;28(4):484.