INTRODUCTION

In 2007, Kirschniak et al. first described treating 11 patients with so-called over the scope clips (OTSC) for a variety of GI conditions such as bleeding, deep wall lesions, and perforations. These devices are supplied on caps that fit over the end of a flexible endoscope and are much larger than traditional through the scope (TTS) clips. Since then, OTSC use has taken off worldwide and has even spread to new indications including, but not limited to, stent anchoring and endoscopic full thickness resections.

One OTSC (Ovesco Endoscopy GmbH, Tübingen, Germany) system consists of an applicator cap with mounted clip, hand wheel, thread retriever. The clip is deployed when a hand wheel is turned which pulls the thread connected to the applicator cap. This system is quite intuitive to a GI physician as it is similar to the devices used to band esophageal varices. The clip is made of nitinol which is a biocompatible, MRI conditional alloy. The jaws of the clip are supplied open at 90 degrees in contrast to the closed jaws of the TTS clips. This allows for the strong compression force when the jaws of the clip are closed. The OTSC system has two auxiliary forceps which are the twin grasper (TG) and anchor (AC) forceps. The TG forceps allow approximation of both sides of a lesion as it has two arms that close separately from each other. The AC forceps are tri-pronged with three needles that can simultaneously grab a lesion.2

Another OTSC is the Padlock Clip™ (Aponos Medical, Kingston, NH). This clip is a nitinol ring with six pre-affixed dagger-shaped needles pointing towards each other. The clip is preassembled in an open position and loaded onto an applicator cap. The design of the cap allows for efficient suction and adhesion of the tissue to the instrument cap, avoiding the need for other instrumentation. The trigger wire used to deploy the clip does not go through the working channel of the endoscope and is instead outside of the endoscope along the shaft and is connected to a trigger handle. Pressing the trigger causes the wire to be pushed within the cable. This causes release to the clip by the delivery system™ (Aponos Medical, Kingston, NH). Once the clip is deployed, it goes back to its original form, an 11mm hexagonal ring. The prongs of the six dagger-shaped needles penetrate and pull the tissue inwards. The tissue controllers (the crossguards of the daggers) moderate penetration depth and tissue-on-tissue pressure.5
Device and Accessory Selection
Choosing the equipment for OTSC placement is important for clinical success. Asokkumar et al.\(^3\) reported using a therapeutic endoscope (3.7mm) and water jet or CO2 insufflation to visualize a target before placing an OTSC. This author also reported adjusting the cap depth onto the tip of the endoscope based on the amount of tissue needed to be grasped. A cap depth of 3mm is appropriate for most types of targeted tissue as it potentially avoids excessive tissue capture.\(^3\) For GI perforations or lesions that need additional tissue to be grasped a 6mm cap depth may be more appropriate. Usually the OTSC will be deployed using the suction technique, but an accessory like the forceps described above may be needed for additional traction.

Indications

**GI Bleeding (Non-Variceal)**
One common use of the OTSC system is to treat patients with non-variceal GI bleeding (NVGIB). While OTSC used to be used to close GI perforations, they are now being increasingly used to treat upper GI bleeding. (Figure 1) One study randomized patients into two arms, with one group receiving standard hemostasis treatment and the other an OTSC with the possibly of adjunctive treatment with epinephrine. The OTSC were shown to be superior in comparison to standard treatment in patients with recurrent GI bleeding. Immediate hemostasis was achieved in 94% of patients in the OTSC group but in only 58% of controls. Clinical success, defined as no further bleeding, was also significantly higher in the OTSC group.

OTSC are useful in treating refractory bleeding. These instances of bleeding are often associated with high risk features. One high risk feature is involvement of a large artery, either a visible large artery or bleeding along the distribution of a large artery. Another high risk feature is a lesion that has suspicion for perforation such as one that is deeply penetrating or fibrotic. In this case, thermal intervention will be harmful. According to one study, there is as high as a 40% rebleeding rate for these lesions with standard therapy. Another study found that there was a true success rate of the OTSC in 81.3% of patients which was in line with comparable smaller studies showing a success rate between 77.8% and 100%.\(^3\) The authors concluded that OTSC could be a valuable tool in both primary and rescue therapy for NVGIB.

Another variable to consider when deciding to treat a GI bleed with an OTSC is the location of the bleed. Lower success rates, especially after 30 days, were found when OTSC were deployed in the esophagus or small bowel. One theory for this is that the clip has to be deployed tangentially given the limited diameter of the GI lumen in these locations. Nonetheless, OTSC have been shown to be superior in comparison to standard treatment...
be more effective than traditional clips in posterior duodenal lesions. OTSC are easier to apply in these situations because the cap at the end of the scope allows for good visualization and less distance is needed between the clip and tissue for application of the clip.\textsuperscript{8} There is also a difference between OTSC success rates in iatrogenic and spontaneous bleeding. Iatrogenic bleeding is defined as bleeding due to a medical procedure while spontaneous bleeding is due to other causes such as an ulcer. One study reported a lower rate of success in spontaneous bleeding.\textsuperscript{10} The reason for this could be that the tissue surrounding a spontaneous bleed is less favorable for OTSC as it contains more fibrotic and inflammatory tissue which is harder to suction neatly or approximate with forceps.

\textbf{Full Thickness Resection}

Another indication for OTSC is to perform full thickness resections of GI lesions including adenomas and submucosal tumors. This procedure can also be performed when a transmural wall sample is needed for pathologic analysis. This procedure can be performed with the Full Thickness Resection Device (FTRD, Ovesco Endoscopy, Tubingen, Germany). The FTRD consists of a transparent cap that is mounted over a standard endoscope. The cap is 13mm in diameter and is longer than a standard cap. When resecting a colonic lesion, this device comes with a 14mm OTSC mounted over the cap and a polypectomy snare attached to the tip of the colonoscope. Instead of putting the snare through the endoscope, this snare runs on the outer surface of the endoscope under a plastic sheath. Before attempting the full thickness resection, diagnostic endoscopy is done to identify the lesion and its lateral margins are marked with a high frequency probe (Ovesco Endoscopy). For the resection itself, either grasping forceps or an anchor device (Ovesco Endoscopy) is advanced through the scope. The lesion is grasped and pulled into the scope until the previously marked lateral margins can be seen. This creates a pseudopolyp. The OTSC is then deployed across the base of the pseudopolyp and the snare is then used to resect the target lesion. The goal is a complete full thickness resection (R0).

Standard treatment for colorectal neoplasms includes routine polypectomy, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). However, most of these techniques rely on being able to separate the submucosal layer from the underlying muscularis propria. FTRD and OTSC can be used in more difficult lesions where standard treatments are unable to remove the lesion due to technical or anatomic constraints.

The major endpoints of resection of lesions when using FTRD are technical success and R0 resection. Technical success refers to the removal of the lesion in one piece and no macroscopic residual lesion as determined by the endoscopist. An R0 resection refers to complete histological removal of the lesion with positive margins. One study of 181 patients who had colorectal lesions treated with FTRD found a technical success rate of 89.5% and a R0 resection rate of 76.9%. Comparatively, in a meta-analysis, R0 resection rates were found to be 42.3% with EMR and 80.3% with ESD. In the FTRD study, 11% of the patients had to undergo surgery due to adverse events or non-curative resection\textsuperscript{12} while 5.8 to 9.9% of patients receiving standard EMR or ESD treatment underwent additional surgical intervention.\textsuperscript{13} The majority of patients receiving FTRD treatment were considered to have lesions that were difficult to resect and would likely have needed surgical intervention if FTRD was not performed. Only 2.2% of patients receiving FTRD had to go to surgery specifically due to procedure-related adverse events.\textsuperscript{12}

One limit of FTRD is lesion size as larger lesions will not fully fit into the cap. R0 resection rates in lesions less than 2cm were 81.2% while those in lesions larger than 2cm were 58.1% (p=0.0038).\textsuperscript{12} Another limit of FTRD is the long cap which has an outer diameter of 21mm. This makes it difficult to advance the endoscope to the target lesion since the cap may impair visibility and endoscope tip flexibility. Resection of the lesion is also difficult as this long cap may impair the ability to see the lateral margins of the target.\textsuperscript{12}

\textbf{Stent Anchoring}

Esophageal self-expanding metal stents (SEMS) are used for a wide variety of benign and malignant esophageal and upper GI pathologies. Fully covered SEMS are often preferred because they have a
lower rate of tissue ingrowth than partially covered or uncovered SEMS. Fully covered SEMS are also generally removable. Partially covered SEMS still can be removed but this can be technically challenging, with special maneuvers being required at times. The biggest liability of SEMS is their high migration rate. One large multicenter retrospective study found the migration rate in fully covered SEMS to be 30% in benign strictures and 23% in malignant strictures. However, the clinically relevant migration rate was 17% and 12% in benign and malignant strictures respectively. Clinically relevant migration was defined as migration that warranted reintervention with stent replacement. In comparison, a study examining the migration rate of partially covered SEMS in benign conditions found a migration rate of 11%.14

Prevention of stent migration usually takes one of two forms: either external or internal fixation. External fixation, which is only rarely performed, includes silk sutures or umbilical tape which can be used to secure the SEMS against the back of the ear or nasal septum. However, discomfort is a limiting factor for this. Internal fixation can be accomplished via the use of endoscopic full thickness suturing, TTS clips, and OTSC. Full thickness sutures can decrease the stent migration rate to 1 in 6 but can significantly add to the total procedure cost. The average procedure time with suturing has been found to be 12.5 minutes. On the other hand, securing the stent with an OTSC takes 3.5 minutes on average.14 TTS clips are rarely used to fix fully covered SEMS in place.17 The placement of TTS clips is limited by their superficial degree of attachment.

In cases where a stent needs fixation, the OTSC is advanced to the proximal end of the stent and suction is applied so that the clip will be 50% attached to the stent and 50% attached to the esophageal wall. (Figure 2) Studies examining the efficacy of OTSC in stent anchoring have generally had a small sample size but have shown positive outcomes. In a study of 13 patients, only 2 (15%) were found to have stent migration and even in those patients the median dwell time of the stent increased from 3.5 days to 32 days. This group of 13 patients notably were high risk for stent migration as all of them had previous stent migration and 8 of them had stent migration even with conventional

![Figure 2. An esophageal stent that has been clipped into position by an OTSC in an effort to reduce migration.](image)

Perforations, fistulae, leaks
Diagnostic endoscopic procedures have a low risk of perforation with an incidence of 0.01 to 0.6%. However, therapeutic endoscopic procedures have a higher risk of perforation (0.6% to upwards of 5%). Besides iatrogenic perforations, there are spontaneous perforations which occur due to wide variety of pathologies including ulcers, tumors, and Boerhaave’s syndrome. Conventional treatment for GI perforation has traditionally been surgery but this has not yielded good results with a post-operative mortality rate of 7%. Other alternative treatments include hemoclip suturing and TTS clips. Hemoclip suturing involves placing multiple clips to close a perforation. Two clips will be placed at the distal ends of the perforation and additional clips in the center as necessary to further close

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the gap between the tissue. Hemoclip sutures are limited in that only lesions under 10mm can be successfully sutured. TTS clips are limited by the low opening width and closure strength. On the other hand, ex-vivo experiments have shown that strengths of OTSC are comparable to the gold standard of surgical suturing. Therefore, OTSC are now commonly used to close esophageal, gastric, small intestinal, and colonic perforations.

To set up the OTSC device, a nitinol clip is loaded onto a cap which is mounted on the tip of the endoscope. Clip size can range from 9 to 14mm depending on the size of the endoscope tip and/or the size of the lesion. There are three types of clips that can be used. The atraumatic clip (type a) has a blunt distal end used for tissue compression while the traumatic clip (type t) has small spikes distally used for compression and anchoring and the gastric closure clip (type gc) has large distal spikes used for tissue closure. The defect or perforation can be prepared for closure in a number of ways. One way is to use suction to pull the lesion into the cap, which is appropriate for adequately mobile tissue. Another device that can be used is the “twin grasper” forceps whose mechanism was described earlier. Some endoscopists prefer using accessories such as a rat toothed forceps to grasp and retract tissue. It is important to avoid excessive suction since this can cause luminal restriction and can catch structures from outside of the bowel wall. Examples of this include small bowel fixation during closure of a colonic fistula and ureteral capture while closing a sigmoid fistula. Once the clip is deployed, it exerts 8-9 N of force onto the tissue which is similar to rubber band ligation.

OTSC are widely effective in treating GI perforations and leaks. (Figure 3 and Figure 4) A meta-analysis including 301 patients from 24 publications found that the long-term overall success rate for treating GI perforations with OTSC ranged between 42% and 100% with a pooled success rate of 73%. This analysis also found a discrepancy in success rate depending on the etiology of the lesion. Endoscopic and procedural-based perforations had a 90% success rate followed by post-operative perforations at 68% and chronic leaks and fistulas at 59%. This could be attributed to the fact that a procedural lesion, if acted on in short order, is more likely to present without fibrosis, inflammation, or other complications. The lower success rates seen in patients with fistulae have been noted in other studies. A multinational retrospective study found only a 42.9% success rate when OTSC were used for the closure of fistulae. Gastrogastric fistulae after Roux-en-y gastric bypass surgery appear to be especially challenging to close; a small study on this topic demonstrated long term success in only 33% of patients. Khater et al. analyzed closure of iatrogenic perforations before and after the advent of OTSC. Technical success was achieved in 100% of cases meaning that the OTSC was deployed in all cases with successful closure of the perforation without...
leakage. The overall clinical success rate was 82% as 18% of patients (2/11) had to undergo surgery. These authors also found a similarly high success rate of OTSC closing iatrogenic perforations at 75-100%. Additionally, the rate of surgeries needed dropped from 62.5% before the introduction of the OTSC system to 12.5% afterwards.

**Complications**

In one meta-analysis, the overall adverse event (AE) rate for OTSC was found to be 1.3% (4/301). In another meta-analysis, the AE rate was found to be 1.7% with a severe AE rate of 0.6%. Complications can happen during device setup, endoscope insertion, OTSC deployment, endoscope removal, or in the post procedure setting. During device set up, participants have been seen to accidently release the clip into the air or onto their fingers given that there is no safety or locking mechanism to prevent inadvertent deployment. When the endoscope is inserted, resistance can be felt when navigating through any luminal narrowing. Forceful advancement of the endoscope could result in mucosal injury or even perforation.

When deploying the clip, it is important to be cognizant of technique, surrounding structures, and orientation. Misplacement or superficial placement of OTSC have been reported in instances where the entire lesion is not suctioned into the cap. Additionally, placement of OTSC in thin-walled areas of bowel can result in perforation with resulting peritonitis, pneumoperitoneum, and fistulae.

In some cases, surrounding structures have been caught with the OTSC. There has been a report of inadvertent capture of the right ureter with the gastrointestinal wall. Loss of orientation during OTSC deployment can also cause luminal stenosis.

Occasionally, the OTSC will fail to release if the endoscope is severely angulated even with multiple hand wheel rotations. Post procedurally, there have been reports of detachment of the OTSC which led to delayed surgery.

**Follow Up and Removal of OTSC**

One of the biggest advantages of OTSC is that it has a powerful clamping ability and broader range...
for closure of GI bleeds, leaks, and fistulae. On the other hand, the OTSC does not spontaneously detach from the mucosa. Rates of spontaneous detachment range from 13% in the gastric fundus to 75% in the gastric body with a follow up time of 20 months. A systematic review reported that between 0 and 44.4% of OTSC detached with a follow up of 1-12 weeks. The FTRD includes a 14mm clip with more teeth than the standard OTSC, potentially making it even harder to detach. The low rate of OTSC detachment is generally considered a positive development. Generally, the OTSC should stay in place for 4-8 weeks. For endoscopic full thickness resection, the FTRD device should stay in place for 2-3 months.

Some indications for OTSC removal include need for further treatment, adverse events, poor healing, recovery from the initial GI condition that warranted treatment, misplacement of the clip, and patient preference. OTSC removal methods involve damaging the clip so it can be removed including endoscopic lasers, argon plasma coagulation (APC), and the remOVE system (Ovesco Endoscopy, Tubingen Germany), EMR/ESD, and ice-cold saline solution.

In general, removal of an OTSC involves two procedure phases: clip fragmentation and fragment retrieval. The remOVE system uses a bipolar grasping device with three distal electrodes and uses DC current to burn through the clip. The DC impulse is applied to the thinnest part of the clip in order to dislodge it. The electrical current is programmed to stop when the device is no longer in contact with nitinol, which reduces risk of thermal mucosal injury. One study showed a pooled success rate of 97% and 89% for fragmentation and retrieval respectively. The most cited reason for failure was mucosal overgrowth where the clip was buried so deep in the tissue that it could not be fragmented or retrieved.

OTSC removal via EMR/ESD involves cutting away the clip with the tissue it is attached to. This can only be performed in clips that are attached to the mucosal or submucosal level as major bleeding and perforation is a concern if the muscular layer is involved. The theory behind the ice-cold saline solution is that nitinol, the material OTSC is made of, changes stiffness at various temperatures. At temperatures under 10 degrees C, nitinol changes to its martensitic grid structure; this means that one can change its shape with application of low force. Therefore, at this temperature, it is easier to deform and remove the clip. This method has only been described in case reports, so its safety, efficacy, and criteria for usage is uncertain.

Adverse events to OTSC removal tend to be mild with minor bleeding, superficial thermal damage, and superficial mucosal tears being the most common.

**CONCLUSION**

OTSC have the potential to change management and outcomes for many patients. The mechanism for using these clips is intuitive for endoscopists as it is like the mechanism to deploy esophageal bands. OTSC also have several benefits over alternative treatments. Indications for OTSC include NVGIB, perforations, fistulae, tissue resection, and stent anchoring. AEs do occur and can include creating a perforation, fistula, or stenosis in the bowel or capture of structures outside of the bowel wall. However, the AE rate is low overall. OTSC can be removed in some situations. Overall, understanding the mechanism of OTSC and its advantages and disadvantages can help endoscopists improve their practice.

**References**

Over the Scope Clips: Current Indications, Uses and Outcomes


