Endoscopic Interventions for Anastomotic Leaks and Fistulas

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Despite continuing evolution of surgical procedures, anastomotic leaks in the gastrointestinal tract still give rise to a significant morbidity and mortality. By now, interventional endoscopic techniques allow a nonsurgical management of these complications in many cases. Stent therapy has become the standard in the management of anastomotic leaks in the upper gastrointestinal tract, and endoscopic vacuum therapy has become the standard for leaks of rectal anastomoses. Recently, two novel techniques have been added to the methods for endoscopic management of leaks and fistulas: endoscopic vacuum therapy in the upper gastrointestinal tract, which has been introduced into routine application, and the placement of over-the-scope clips (OTSC).

6.1 Anastomotic Leaks in the Upper and Lower Gastrointestinal Tract

R. Mennigen

Classification

Although anastomotic leaks in the gastrointestinal tract are a quite heterogeneous field, we will present a rough classification of anastomotic leaks before discussing endoscopic therapeutic options. This is important, as endoscopic therapy depends on localization of the leak, grade (Table 6.1), time point of occurrence, and further factors.

Table 6.1 Clavien–Dindo classification of surgical complications (Clavien et al. 2009)

Grade 1: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
Grade 2: Requiring pharmacological treatment with drugs other than those allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
Grade 3: Requiring surgical, endoscopic, or radiological intervention
Grade 4: Life-threatening complication (including CNS complications) requiring IC/ICU management
Grade 5: Death of a patient
Complications are graded depending on their clinical consequences and necessary therapies

Anastomotic leaks can be classified by the following criteria:

- Localization [upper versus lower GI (gastrointestinal) tract]
- Type of previous operation and anastomotic technique (e.g., esophageal resection with gastric conduit, gastrectomy, rectal resection)
- Time point of postoperative diagnosis: acute versus chronic leak
- Size of leak (given in percent of circumference)
- Presence or absence of a leak cavity
- Severity of the complication (Clavien–Dindo classification, Table 6.1)

Therapeutic Algorithms: Operation, Endoscopy, or Conservative Management?

The severity of the complication and the condition of the patient determine if endoscopic therapy is an option for the management of a postoperative leak. With regard to the Clavien–Dindo classification, the domain of endoscopic therapy are grade 3 complications. These are anastomotic leaks which cannot be managed by parenteral nutrition, antibiotic therapy, and placing of a gastric tube alone. The patient is in a septic condition, but does not fulfill criteria for a grade 4 complication (organ dysfunction). A partial dehiscence of an esophagogastric anastomosis following esophagectomy with viable gastric conduit is a typical example. This is a situation in which endoscopic therapy has replaced surgical management in most cases and has become the gold standard. In this example, endoscopic stent placement is a well-defined standard procedure; recently, endoscopic vacuum therapy is increasingly used in such cases. A typical example of a grade 3 complication in the lower gastrointestinal tract is the rectal anastomotic leak with a leak cavity in the small pelvis with the presence of a diverting ileostomy. In this case, endoscopic vacuum therapy is the accepted standard therapy.

The success of endoscopic therapy combined with low morbidity and mortality of these procedures has even shifted the indications toward grade 4 complications. By now, critical patients with organ dysfunction and ICU therapy are managed by endoscopic means in selected cases.

However, in these cases it has to be critically evaluated if endoscopic therapies are sufficient to manage the life-threatening sepsis. If the septic condition cannot be controlled by endoscopic means or if the local condition of the anastomosis is not suitable for endoscopic therapy (e.g., necrosis of the gastric conduit after esophagectomy), surgical management is still mandatory.

In case an endoscopic therapy is indicated, the choice of method depends on the abovementioned criteria, especially localization of the leak (stent or endoscopic vacuum therapy in the upper gastrointestinal tract, endoscopic vacuum therapy in the lower gastrointestinal tract), the local condition of the anastomosis, and the presence of an infected leak cavity. These aspects are discussed in the context of the respective endoscopic techniques.

6.2 Stent Therapy

M. Colombo-Benkmann

Indication, Evidence, and Significance of Endoluminal Stenting

Implantation of self-expanding endoprotheses, i.e., stents, is indicated in the treatment of leakages of esophagogastrostomies as well as esophagojejunostomies, perforations of the esophagus (van Boeckel et al. 2011), and leakages after bariatric operations (Puli et al. 2012). So far, stenting is not established in the therapy of leaks or perforations of the duodenum, jejunum, or ileum.

At present, stents are made of wires of alloys, e.g., nitinol with a memory effect, which are woven as a cylindrical mesh. Stents can be covered either partially or over their total length by a silicone sheet to prevent ingrowth of the mucosa into the mesh. Each end of the stent should contain a circular thread to allow stretching. This will result in simultaneous reduction of the diameter of the stent, enabling adjustments of its intraluminal position or its removal. The advantage of nitinol stents is that they can be implanted easily without the need for any preparation, in contrast to former endoprostheses made exclusively from plastic.

Further advantages comprise their ability to cover multiple leaks of suture lines such as after sleeve gastrectomy, as well as easy endoscopic removal and amendment in case of a misplacement.

The most common indications of stent insertion are anastomotic leaks after esophageal resections (51%), followed by iatrogenic perforations due to diagnostic or interventional endoscopy (25%) occurring during gastroscopic balloon dilatation or bougienage of stenoses after endoscopic mucosal resection or endoscopic retrograde cholangiopancreaticography, Boerhaave syndrome (17%), and benign fistula, e.g., to the trachea and bronchi (4%) (van Boeckel et al. 2011). Even anastomotic dehiscences comprising up to 100% of the luminal circumference can be treated successfully. This holds true also for leaks after bariatric surgery such as gastric bypass, gastric sleeve, and biliopancreatic diversions (Puli et al. 2012).

Covered stents represent a physical barrier between leakage and lumen, preventing contact of endoluminal secretions with the leak. This represents a crucial prerequisite of leak closure. In addition, patients can receive enteral nutrition 24–48 h after implantation, initially by a simultaneously implanted jejunal tube followed by natural ingestion of food. This prevents the necessity of parenteral nutrition and its associated complications (Puli et al. 2012).

Despite low levels of evidence due to the lack of prospective not to mention randomized studies and due to small patient cohorts, endoluminal stents are the gold standard in the treatment of postoperative leaks and fistula.

Requirements of Manpower, Instrumentation, and Organization

Implantation of intraluminal stents requires at least two, ideally three, persons with expertise in endoluminal stenting: the implanting physician and two assistants who are knowledgeable in the technique of implantation.

Instruments include a gastroscope and a stiff guide-wire with a flexible spiral tip (e.g., Eder–Puestow) which yields when coming into contact with the tissue. Due to the soft spiral tip, the risk of incidental perforation of the hollow organ reduces. The guide-wire should have a length of 200 cm.

Sterile warm water should be injected into the core of the delivery system, to ensure fast expansion of the stent once it is released. In our practice, stents are delivered under fluoroscopic guidance. Thus epicutaneous radiopaque pins, e.g., made from lead, are needed to mark the position of the leak, the eophageal introitus in case of leaks in the

vicinity of the upper esophageal sphincter, the esophagogastric junction, or the pylorus depending on the location of the leak. If adjustment of the stent's position after delivery is required, an alligator forceps should be used.

Ideally, stents should be implanted using a fluoroscopy system. This allows monitoring and documentation of the respective phases of stent implantation from the positioning of the leak until expansion of the stent in its final position.

Implantation is carried out in a supine position of the patient in analgosedation. Intubation should be used to avoid aspiration if there is significant reflux, in case of respiratory failure or fistulas. Constant monitoring of oxygen saturation is mandatory; electrocardiography should be used additionally in patients with cardiac failure or significant cardiac risk factors.

In general, patients who breathe spontaneously during stent implantation should be given oxygen continuously during the procedure by a nasal applicator. This can prevent decrease of oxygen saturation during the procedure. Since many patients already suffer from pre-existent cardiopulmonary morbidity, sedation may result in respiratory failure during implantation. As a consequence, the equipment for manual resuscitation such as a respiratory mask, a resuscitation bag with oxygen supply, and an emergency case with the possibility of endotracheal intubation are to be provided at the site of the procedure.

In case of extraction of the stent, disconnection of the grasping forceps from the stent on the level of the pharynx can result in acute respiratory obstruction, resulting in asphyxia. The attempt of immediate endoscopic extraction by an endoscopic forceps is unlikely to be successful. Instead, we recommend instant insertion of a laryngoscope as used for endotracheal intubation, for visualization of the stent, and a strong needle holder to enable immediate stent removal. Thus, we recommend having these instruments ready to hand.

With regard to selection of specific type of stent, it should be taken into account that in case of the treatment of leaks, it is recommended to remove stents 6 weeks after implantation. Fully covered stents have the advantage that they can be extracted generally without damaging the mucosa. In partially covered stents, there is a significant risk of ingrowth of the mucosa into the mesh. This impedes not only stent extraction, but can result in considerable trauma to the mucosa. Thus, single cases of leak caused by extraction of partially covered stents have been described.

On the other hand, fully covered stents have a significant risk of dislocation, due to their smooth surface allowing them to slide on the mucosa. Choosing an adequate diameter of the shaft and the ends of the stent may impede dislocation. In general, we use fully covered stents with diameters of the shaft of 25 mm and of both ends of at least 30 mm.

Procedure

At first a diagnostic endoscopy is carried out in the sedated or intubated patient. This should comprise not only the esophagus, but all parts of the digestive tract which can be reached by the gastroscope. Independent from the endoscopic verification of a leak, water-soluble contrast dye during fluoroscopy should be applied, since this enables reliably the detection of fistulas in the respiratory tract. The contrast dye is applied by a catheter, which is inserted into the gastroscope. After aspiration of the contrast dye, the leak is marked under fluoroscopy by epicutaneous markers (Fig. 6.1). These have to be attached onto the patient's skin by an adhesive tape. Markers should not be attached onto the patient's clothing. If the leak is close to the upper esophageal sphincter, the latter should be marked in the same way as well, to avoid misplacement of the upper end of the stent, e.g., into the pharynx. When using stents in the treatment of a leak after sleeve gastrectomy, the pylorus should be marked as well, to ensure that the aboral end of the stents is positioned reliably beyond the pylorus.

In the meantime, warm sterile water is instilled into the delivery systems through a respective opening. Subsequently, a guide-wire (Eder–Puestow) is introduced through the gastroscope. The end of the wire is placed aborally to the intended position of the aboral end of the stent. The wire is secured by the assisting staff during retraction of the endoscope, to prevent an incidental dislocation of the wire. Very importantly, the risk of facial and eye injury by the extracorporeal end of the wire is to be considered.

The well-lubricated delivery system is introduced over the wire, and the stent is delivered in a

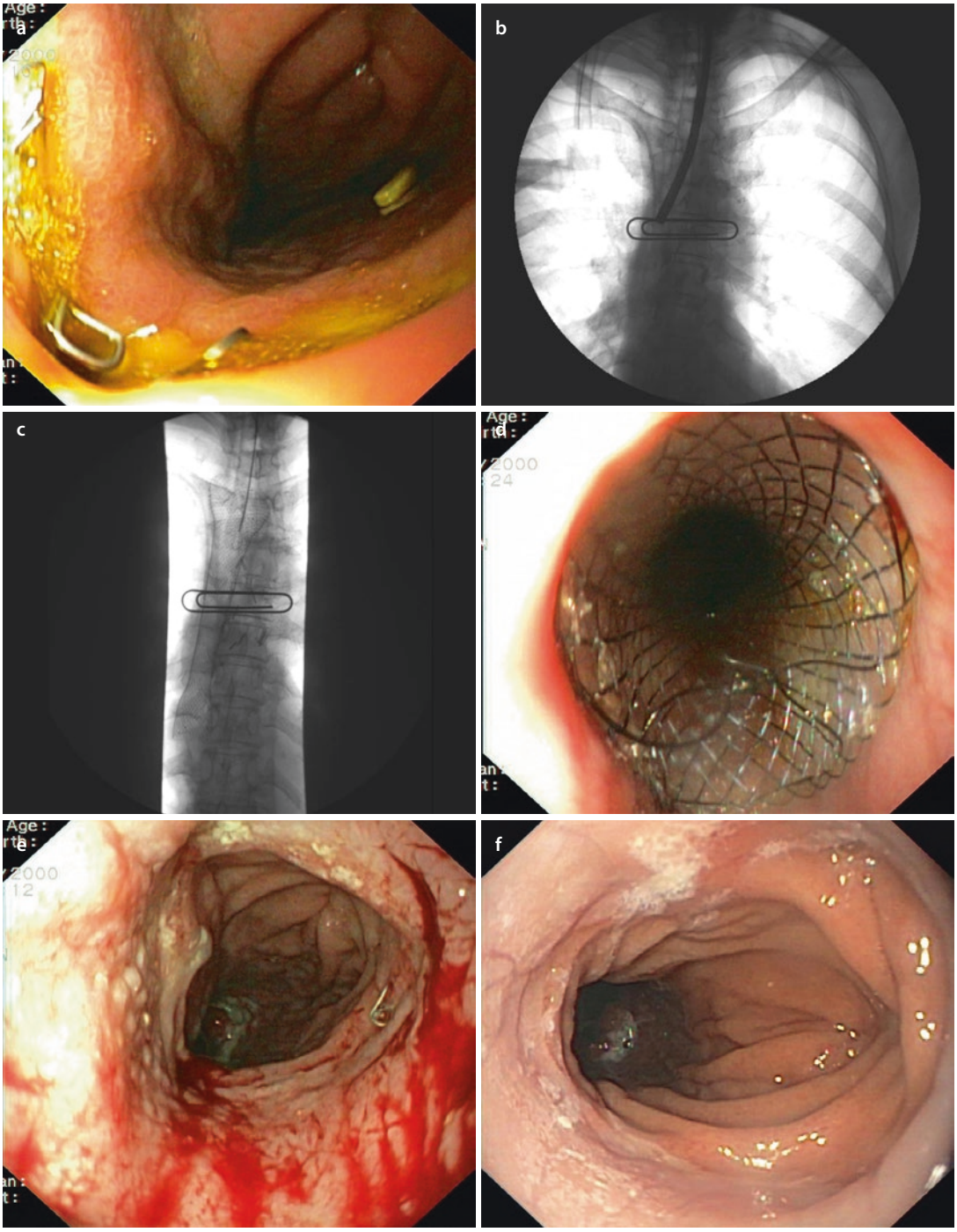


Fig. 6.1 Procedure of stent implantation. **a** Anastomotic leak following esophagectomy with gastric conduit, located at 7 o'clock. **b** The level of anastomosis is indicated by an epicutaneous marker. **c** The stent is placed with the leak being located in the middle portion of the stent. **d** Endoscopic view on the upper opening of the stent. **e** Immediately after stent removal which was performed 6 weeks later: multiple erosions can be seen, and the leak is completely closed. **f** Endoscopic view 3 weeks later: all erosions have resolved, and the anastomosis is healed

way that leak or fistulas are covered with a sealing effect. After the stent has disconnected from the delivery system during its expansion, the latter is pulled out together with the guide-wire. Care has to be taken that the stent is not dislocated by this maneuver. If dislocation occurs or if the position of the stent has to be corrected, an endoscopic grasper should be used.

The final endoscopic exam should be limited to documenting the distance of the upper end of the stent from the front teeth in centimeters, to verify dislocation if it should occur. It is not necessary to intubate a stent not fully expanded, since this carries a high risk of dislocation. Exceptions are the necessary adjustments of the stent's position.

If there is suspicion of a newly occurred stent dislocation, it can be verified by endoscopy or fluoroscopy. Insufficient sealing of the leak can be confirmed by fluoroscopy and water-soluble contrast dye. Occasionally if the diameter of the chosen stent is too small, the failure of sealing can be recognized by a gap between the stent and the hollow organ.

There is no need for a special follow-up if the patient is asymptomatic and receiving his habitual nutrition.

Stent removal is carried out by an endoscopic grasper pulling at the upper thread. If the stent is adherent to the inner layer of the stent due to mucosal overgrowth of the ends of the stent, these adhesions can be eliminated either mechanically by graspers or thermically.

Technical success of stent implantation with complete sealing of leaks and fistulas in non-bariatric patient is between 98% and 100% (van Boeckel et al. 2011).

In non-bariatric patients, the time the stent is left in place is 6 weeks on average, published times are between 3 and 17 weeks on average (van Boeckel et al. 2011) and between 6 and 8 weeks in bariatric patients (Puli et al. 2012).

If the interval chosen to leave the stent in place is too short, this will result in incomplete closure of the leak, while choosing an excessively long interval may result in stent migration or mucosal overgrowth by epithelial cell. This significantly impedes removal of the stent and contains a considerable risk of injury to the hollow organ. In addition to this, if too long intervals are chosen, this can lead to dysphagia.

Removal of fully covered stents in non-bariatric patients is almost completely without any complication. After removal of a partially covered stent, 8% of patients will experience complications (van Boeckel et al. 2011). In bariatric patients, successful stent extraction occurs in 92% of patients (Puli et al. 2012).

The objective of complete closure of leaks and fistulas solely by stents can be achieved in 85% of non-bariatric patients and in 88% of bariatric patients. In this context, successful treatment is defined by complete closure of leaks and fistulas as shown by fluoroscopy with contrast dye, if after stent removal no extraluminal contrast dye can be seen.

If leaks are persistent, re-stenting can be carried out without any problems in general.

Possible Complications and Treatment

Complications associated with implantation of stents such as intraluminal bleeding or perforation are rare and occur in only 3% of patients (van Boeckel et al. 2011).

Dislocation of the stent is one of the most common complications. In fully covered stents, this occurs in 26% and in partially covered stents in 13% of non-bariatric patients. In bariatric patients, the dislocation rate is 16% and 9% (Puli et al. 2012). In bariatric patients, stents can migrate into the jejunum. In such cases, surgery is required to remove the stent; occasionally, stents have been egested by defecation. If repositioning is not successful, a stent with a larger diameter should be chosen or another method is to be applied.

In contrast, partially covered stents are more often overgrown by the epithelium (12%) than fully covered stents (7%) (van Boeckel et al. 2011). As a consequence, the stent cannot be removed (Puli et al. 2012).

Endoscopic reinterventions are necessary in 26% of patients with fully covered stents and in 13% of patients with partially covered stents (van Boeckel et al. 2011). Occasionally, stents are obstructed by food (Puli et al. 2012). If possible, the bolus should be dislocated aborally, to be digested. If this is not possible nor indicated, extraction should be strived.

Surgical therapy is necessary in 13% of non-bariatric patients, since leaks do not close and due to complications associated with the procedure or the stent (van Boeckel et al. 2011). Mortality after stent implantation is due to septicemia associated with the leakage and not due to the endoprostheses. Its incidence in non-bariatric patients is 18% (van Boeckel et al. 2011).

Endoluminal stenting has been the standard treatment of the abovenamed complications for more than 10 years. However, new therapies are becoming available due to the technological progress in medicine. Thus, it can be expected that in the next few years, indications for specific treatment options will be specified, especially if they become more available.

6.3 Endoscopic Vacuum Therapy (EVT)

M.G. Laukoetter

Indication and Evidence

Vacuum therapy (endoscopic vacuum therapy (EVT), VacuSeal, vacuum-assisted closure [VAC] therapy, negative pressure wound therapy [NPWT]) for wound healing simply consists of a sponge-based drainage system connected to negative pressure, leading to decrease of bacterial contamination, secretion, local edema, and promotion of granulation tissue (Holle et al. 2007). Since introduction of this treatment technique in the early 1990s, endoscopic vacuum therapy, as an alternative treatment option for even desolate wounds in almost every localization, has been established in nearly all surgical disciplines (Argenta and Morykwas 1997). After initially being considered and established as a treatment modality for infected superficial skin defects of different sizes and extent (Argenta and Morykwas 1997; Vikatmaa et al. 2008), the first intracorporeal endoscopic vacuum therapy was established successfully for anastomotic leaks after rectal resection (Weidenhagen et al. 2008; Willy et al. 2006). The close proximity of the sphincter and of the anastomotic region in such cases leads to permanent congestion of infected secretion and intestinal gas, leading to potential severe local peritonitis in the pelvic region. In such cases where there is local lower abdominal peritonitis with an endoscopically accessible cavity, the Endo-SPONGE treatment can be applied (Fig. 6.2). An overtube is placed into the cavity,

Fig. 6.2 Endo-SPONGE® system (By courtesy of Braun Melsungen AG)

and, after the endoscope has been withdrawn from the overtube, the sponge is brought down by a pusher. The cavity is drained subsequently by the endoscopically introduced Endo-SPONGE® system. The open pores of the sponge allow the suction to be transferred over all tissues in contact with the sponge surface.

The insertion of a polyurethane sponge into the defect zone, connected transanally to an external vacuum system, does, in contrast to the treatment of superficial skin defects, not require the presence of an airtight sealing, since the pelvic wound cavity seals itself after start-up of the drainage system. Closure rates of >90% avoid reoperations in those patients characterized by a complicated postoperative course (Glitsch et al. 2008; Weidenhagen et al. 2008). Perforations and fistulas of the upper gastrointestinal (GI) tract occur as postoperative complications (anastomotic dehiscence or fistula), during diagnostic or interventional endoscopy, iatrogenic as a consequence of other therapeutic measures (e.g., gastric tube placement, percutaneous endoscopic gastrostomy, transesophageal echocardiography), or spontaneously (ulcers, tumors, Boerhaave syndrome, and others). These perforations often lead to severe septic conditions which are difficult to treat and give rise to a high morbidity and mortality, especially if leading to mediastinitis or peritonitis (Junemann-Ramirez et al. 2005). In particular, reported leak rates after esophagectomy vary widely from 1% to 30% (Ahrens et al. 2010; Whooley et al. 2001). Anastomotic leakage accounts for approximately 40% (Miller et al. 1997; Pross et al. 2000) of all postoperative fatalities and is highly challenging to treat: control of the septic focus is essential; thus, the already critically ill patient often requires intensive additional measures that themselves are associated with high morbidity, adding to the clinical burden (Junemann-Ramirez et al. 2005).

A number of competing treatment modalities ranging from conservative to surgical approaches are available for the management of this situation. The surgical treatment options include revision of the anastomosis, closure of the defect and perifocal drainage, or complete surgical deviation and creation of a cervical stoma. These procedures are usually difficult and carry a high risk for severe complications associated with high morbidity and mortality rates. Therefore reoperation is not always a reasonable option.

In this context, numerous minimally invasive treatment options have more recently become available to treat a variety of secondary surgical complications. Conservative management may be advantageous if reliable endoscopic methods are available. Endoscopic clips (Mennigen et al. 2013; Rodella et al. 1998), fibrin glue injection, absorbable plugs, and endoscopic suturing (EndoCinch) (Adler et al. 2001; Fritscher-Ravens et al. 2010) have been used to close smaller defects. At present, the placement of completely covered metal or plastic stents (Doniec et al. 2003; Hunerbein et al. 2004) is still the favored conservative treatment option for esophageal leakage. The implantation of these stents has been thoroughly studied and has been proven to be effective (Tuebergen et al. 2008; van Boeckel et al. 2011). However, stent implantation does not always lead to a sufficient sealing of the leakage (van Boeckel et al. 2011), and dislocation rates of up to 40% (Kauer et al. 2008) have been reported. Another important complication is failure of stent extraction due to ingrowth of granulation tissue and/or secondary strictures due to scarring (Doniec et al. 2003; Loske and Muller 2009; Schubert et al. 2005). While stents bridge the defect intraluminally and prevent further leakage, continuous local drainage is necessary to prevent inflammatory fluids from remaining in the perianastomotic tissues and maintaining inflammation. The well-established stent therapy is now being challenged increasingly by endoscopic vacuum therapy (EVT). While it can already be considered as standard therapy for leakages of lower colorectal anastomoses, its use in the upper GI tract only evolved several years later. Yet soon after first reports of the technical feasibility of endoscopic vacuum therapy in the upper GI tract, several case series with good success rates in the management of esophageal leaks were published. However, most series include heterogeneous types of leaks and are not focused on anastomotic leaks. All publications report excellent success rates (healing of leaks and perforations in 84–100%) and virtually no procedure-related complications in these patient cohorts. The technique appears to have potential as a first-line therapy for postoperative upper GI leaks (Table 6.2).

Table 6.2 Endoscopic vacuum therapy (EVT) for leaks of different etiology

Literature	Patients (*n*)	Indication for EVT	Success rate (closure of leak by EVT)
Weidenhagen et al.	6	6× a. l.	6/6 (100%)
Wallstabe et al.	1	1× a. l.	1/1 (100%)
Brangewitz et al.	32	30× a. l. 1× perf. 1× b. s.	27/32 (84%)
Schniewind et al.	17	17× a. l.	15/17 (88%)
Bludau et al.	14	8× a. l. 6× perf.	12/14 (87%)
Smallwood et al.	6	1× a. l. 5× perf.	6/6 (100%)
Schorsch et al.	35	21× a. l. 7× perf. 1× b.s. 6× o.o.	32/35 (91%)
Kuehn et al.	21	11× a. l. 8× perf. 2× b.s.	19/21 (91%)
Seyfried et al.	1	1× b. surg.	1/1 (100%)
Total	**133**	**95× a. l.** **27× perf.** **4× b. s.** **1× b. surg.** **6× o. o.**	**119/133** **89.5%**

Synopsis of studies to date which have reported EVT, with number of treated patients and success rates of closure of the defect in total and percentage
a. l. anastomotic leakage, *perf.* perforation, *b. s.* Boerhaave syndrome, *b. surg.* bariatric surgery, and *o. o.* other origin

Since its first description by Wedemeyer et al. and Loske et al. the abovementioned principle is used by all authors, with only small variations in the procedure. Recently, a commercially available and certified drainage system using the overtube principle has been distributed (Eso-SPONGE®, Braun Melsungen AG).

Resources and Organizational Requirements

In case of anastomotic leakage or perforation in the upper gastrointestinal tract, interventional endoscopy has evolved as an effective alternative treatment modality (Maish et al. 2005). Endoscopic vacuum therapy requires a competent, experienced endoscopic team and a well-equipped endoscopic unit permitting additional perinterventional radioscopy as well as an examiner who is well trained in the field of EVT. EVT can be done under conscious sedation or general anesthesia, depending on the general condition of the patient.

The following tools and equipment have to be provided (Fig. 6.3a):

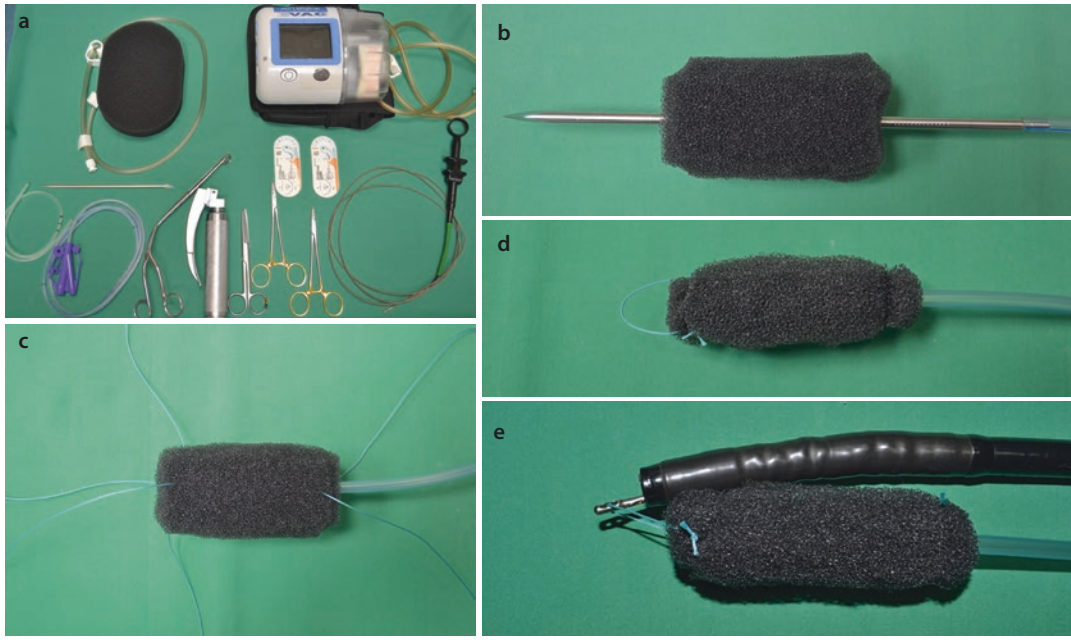


Fig. 6.3 Endoscopic vacuum therapy (EVT) in the upper gastrointestinal tract. **a** Arrangement of the necessary materials. **b** Open-pore polyurethane sponge—sponge preparation. **c** Sponge mounted on a gastric tube for endoscopic vacuum therapy. **d** Mounted sponge—L loop for easy positioning. **e** Principle of sponge drainage insertion into the esophagus using a forceps in a «backpack method»

Materials

- 1× open-pore polyurethane sponge (e.g., VivanoMed® Foam, Paul Hartmann AG, Heidenheim, Germany; V.A.C. GranuFoam, KCI-Kinetic Concepts, Inc., TX, USA)
- 1× electronic vacuum pump system(e.g., VivanoTec®, Paul Hartmann AG, Heidenheim, Germany)
- 1× polyvinyl chloride (PVC) gastroduodenal tube (e.g., Covidien™ Salem Sump™, 14 Fr/Ch (4.7 mm) × 114 cm, Covidien™, MA, USA)
- 2× suture material (e.g., Ethibond Excel, Ethicon, Johnson & Johnson MEDICAL GmbH)
- 1× scissors, 1× clamp, 1× needle holder, 1× Magill forceps, 1× laryngoscope, 1× metal pin for the Redon drainage, 1× tube for nasal diversion, 1× endoscopic forceps, and lubricant

Endoscopic Vacuum Therapy (EVT): Procedure

EVT is performed under conscious sedation or general anesthesia, depending on the general condition of the patient. After endoscopic assessment of the geometry of the leakage and the cavity, a polyurethane foam sponge is cut into the corresponding shape (Fig. 6.3b). The sponge is fixed to the tip of a polyvinyl chloride (PVC) gastroduodenal tube with a suture at the proximal and distal ends of the sponge (Fig. 6.3c) allowing communication between the side ports of the tube with the sponge. An additional suture loop (L loop) is placed at the tip of the sponge (Fig. 6.3d). Thus, the additional loop at the tip of the sponge serves as a purchase for the endoscopic forceps and facilitates manipulation of the sponge into difficult-to-access cavities and hollow spaces. After final shaping of the sponge (Fig. 6.3d), the loop is grasped with a forceps (Fig. 6.3e) and pulled close to the endoscope, and the sponge is placed in the leakage cavity under direct endoscopic vision. If the defect is initially not wide enough to accommodate the endoscope (<10 mm) and an abscess cavity is suspected, the opening can be dilated by endoscopic balloon dilatation (Esophageal Balloon Dilatation Catheter, 10–12 mm, Boston Scientific, Ratingen, Germany) to allow extraluminal inspection by the standard endoscope and examination of the extraluminal septic focus. After sponge placement, the vacuum drainage tube is diverted through the nose. Continuous suction of 100–125 mmHg generated by an electronic vacuum pump system (e.g., VivanoTec®, Paul Hartmann Ag, Heidenheim, Germany) is connected to the drainage tube,

allowing the sponge to stay in position due to continuous suction. Optionally, with the sponge drainage system in place, parenteral feeding, a transnasal enteral feeding tube, a percutaneous endoscopic gastrostomy (PEG,) or a jejunostomy feeding tube ensure enteral nutrition (Fig. 6.4a). A scheduled change of sponges should take place every 3rd to 5th day; and at each session, the size of the defect has to be assessed and be treated with an individually prepared sponge, cut to fit the lesion's dimensions. After each discontinuation of suction, the tube has to be diverted through the mouth and removed simply by pulling. It is advisable to flush the tube with 0.9% saline solution to dissolve the granulation tissue from the pores of the sponge prior to removal. In some cases, remnants of the sponge have to be removed by endoscopic forceps. Over the course of the treatment and with diminishing defect size not allowing an access with the scope, sponge placement can be changed from its initial intracavitary position to intraluminal position onto the defect at any time. Secretion is then drained endoluminally, and the continuous suction force results in temporary complete occlusion of the intestinal passage. Especially in the absence of an extraluminal wound cavity (e.g., with early diagnosis of a transmural defect in case of a Boerhaave syndrome), it is advisable to

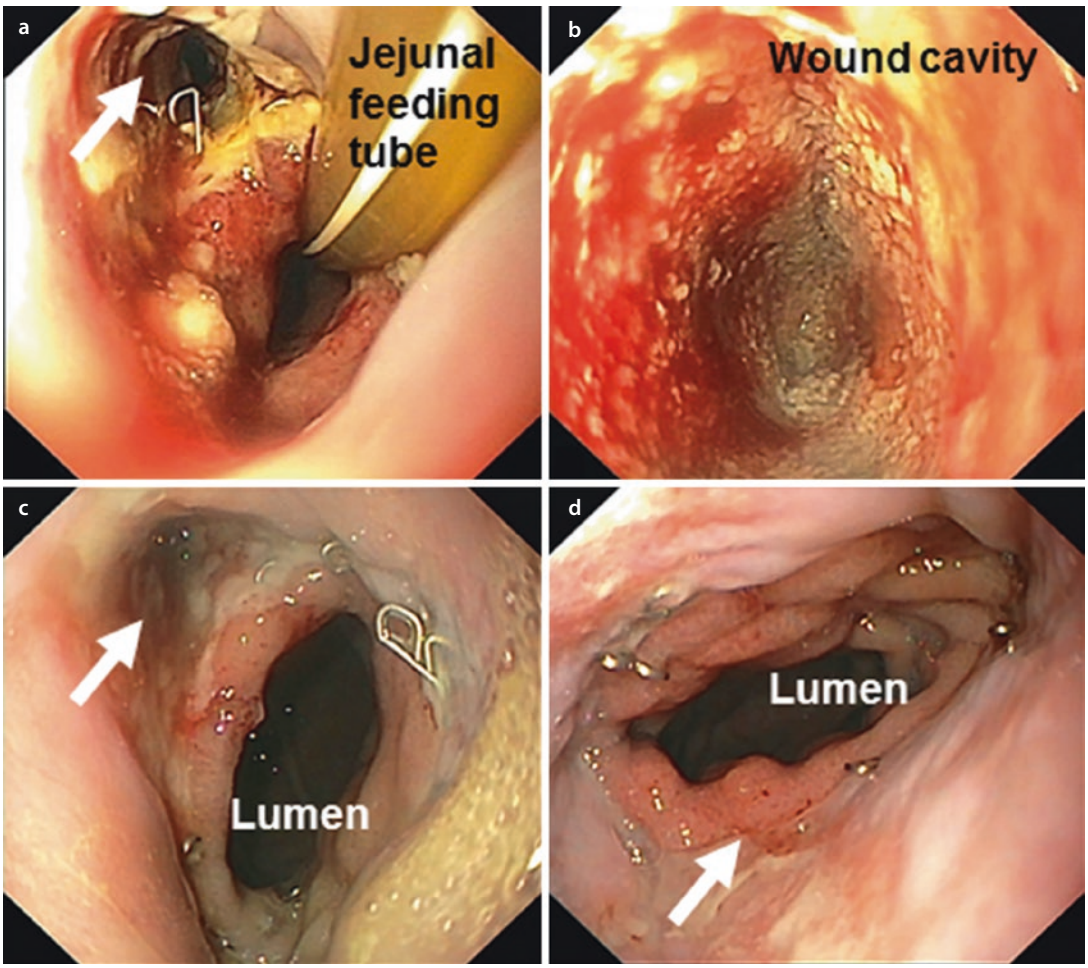


Fig. 6.4 Endoscopic vacuum therapy (EVT) in a case of anastomotic dehiscence after esophagectomy with esophagogastric anastomosis. **a** Mediastinal cavity lateral to the anastomotic ring (*arrow*). Detection on postoperative day 3. **b** Formation of granulation tissue within the cavity after 3 days of endoscopic vacuum therapy. **c** Residual finding and granulation tissue (*arrow*) after four sponge changes. **d** Completely healed anastomosis 3 weeks after initiated endoscopic vacuum therapy and seven sponge changes in total

use an intraluminal sponge drainage covering the whole defect zone within the lumen of the upper GI tract. EVT can be stopped when the defect size becomes too small for further sponge placements and the defect is finally lined with surface epithelium (Fig. 6.4b–d). Complete healing of the anastomosis should be assessed by endoscopy and additional X-ray contrast study showing no clinical signs of persistent leakage. Usually the defect completely closes within 1–2 weeks.

Control of Possible Complications

EVT in the upper GI tract seems to be not only feasible but superior to previous therapeutic procedures such as surgical revision and stent placement for esophageal defects. Although EVT requires multiple endoscopic procedures (every 3–4 days), its advantages with regard to previous treatment options are the regular visualization of the wound cavity and the optimal drainage provided by the vacuum system. This leads to effective sepsis control and final closure of the defect.

Although previous studies reporting heterogeneous types of upper GI tract leakages reported excellent success rates without procedure-related complications (Table 6.2), every sponge change can be associated with minor or major complications. In our prospective single-center study, comprising 52 consecutive patients, we experienced two severe critical events of fatal hemorrhage in patients suffering from a late anastomotic insufficiency after distal esophagectomy. Therefore, we strongly recommend that EVT for esophageal perforations should be performed combined with a CT scan of the thorax done directly before or after every first endoscopic placement of the sponge, to exclude close proximity of the sponge to cardiovascular structures with subsequent risk of erosion bleeding. Patients who show no intermediate tissue layer between the sponge and major thoracic vessels defining a close proximity to cardiovascular structures, and revealing a major complication risk for EVT in the upper GI tract in these patients, should be evaluated critically in terms of potential different therapy regimes and exit strategies such as stent placement.

Minor EVT-associated complications such as sponge dislocation due to swallowing and coughing or minor bleedings after sponge removal usually do not need additional therapy, and EVT can be successfully continued. It is advisable in these cases to fix the sponge properly to the tube and in the case of minor superficial bleedings to interrupt the course of therapy for 1 or 2 days.

In the case of insufficient drainage or large mediastinal cavities, up to two separate sponge drainage systems can be used. Sometimes, even an additional external drainage might be necessary and does not interfere with a successful course of therapy.

6.4 Over-the-Scope Clip

R. Mennigen

Indication, Evidence, and Value of the Technique

Endoscopic clipping of gastrointestinal leaks and fistulas has been tried for many years. Usually, through-the-scope clips (TTSC) have been used which were designed for hemostasis. These procedures were only successful in very small lesions or mucosal defects, and despite several successful case reports, clipping of leaks did not reach widespread use. The small wingspan and especially the low compression force of the TTS clips are the main reasons for this, as they do not allow a full-thickness closure of gastrointestinal leaks with sufficient compression force.

The over-the-scope clip (OTSC; Ovesco Endoscopy AG, Tübingen, Germany) has changed the basic principle of clip placement, thereby overcoming these limitations. The nitinol clip has a «bear-claw» shape and is loaded on a transparent distance cap which is mounted on the endoscope tip.

First, tissue is pulled into the cap. This can be achieved by simple suction, or special instruments introduced via the working channel are used. Then, the clip is deployed by pulling on a string connected to a handwheel mounted on the endoscope—this is basically the same technique used for application of rubber band ligations. The clip application with the cap allows much larger wingspans, and full-thickness closures of defects have become possible with the high compression force of 8–9 Newton that is delivered by the closed clip.

In addition to closure of gastrointestinal leaks, OTSCs are used for hemostasis and for special indications such as marking of endoscopic findings for subsequent operations or for the creation of pseudopolyps for subsequent mucosectomy. These applications are discussed in the respective chapters.

There are no randomized trials on OTSC closure of gastrointestinal leaks, and the evidence is based on retrospective series with heterogeneous indications and applications. Reporting the clinical results to registries, such as the «CLIPPER Study Group,» ensures that the increasing use of OTSCs for leak closure is accompanied by a steady evaluation of the clinical results.

Table 6.3 presents an overview of published case series with overall 301 patients. Reported long-

Table 6.3 Literature review for the closure of gastrointestinal leaks using the OTSC system

Author	Year	*N*	Overall success	Postoperative leaks	Acute endoscopic or interventional perforations	Chronic fistulas and leaks
Albert	2011	12	8/12 (66%)	5/6 (83%)	2/2 (100%)	1/4 (25%)
Arezzo	2012	14	12/14 (86%)	12/14 (86%)		
Baron	2012	36	24/36 (67%)	10/14 (71%)	4/5 (80%)	10/17 (59%)
Jacobsen	2012	10	5/10 (50%)	5/10 (50%)		
Disibeyaz	2012	9	5/9 (56%)	4/7 (57%)	1/1 (100%)	0/1 (0%)
Galizia	2012	3	3/3 (100%)	3/3 (100%)		
Gubler	2012	14	13/14 (93%)		13/14 (93%)	
Hagel	2012	17	11/17 (65%)	2/3 (67%)	7/10 (70%)	2/4 (50%)
Jayaraman	2013	21	12/21 (57%)			
Kirschniak	2007	4	4/4 (100%)		4/4 (100%)	
Kirschniak	2011	19	14/19 (74%)	1/2 (50%)	11/11 (100%)	2/6 (33%)
Manta	2011	12	11/12 (92%)	11/12 (92%)		
Mennigen	2013	14	11/14 (79%)	10/12 (83%)		1/2 (50%)
Mönkemüller	2013	7	3/7 (43%)	1/3 (33%)		2/4 (50%)
Nishiyama	2013	13	11/13 (85%)		7/8 (88%)	4/5 (80%)
Parodi	2010	10	8/10 (80%)	4/6 (67%)	1/1 (100%)	3/3 (100%)
Pohl	2010	2	1/2 (50%)	1/2 (50%)		
Repici	2009	2	2/2 (100%)		2/2 (100%)	
Sandmann	2011	10	9/10 (90%)	2/3 (67%)	3/3 (100%)	4/4 (100%)
Schlag	2013	6	6/6 (100%)		6/6 (100%)	
Seebach	2010	7	5/7 (71%)	2/3 (67%)	3/4 (75%)	
Surace	2011	19	8/19 (42%)	7/18 (39%)		1/1 (100%)
Voermans	2012	36	32/36 (89%)	1/1 (100%)	31/35 (89%)	
Von Renteln	2010	4	2/4 (50%)	0/1 (0%)		2/3 (67%)
Overall		**301**	**220/301 (73%)**	**81/120 (68%)**	**95/106 (90%)**	**32/54 (59%)**

Mennigen et al. (2013), Albert et al. (2011), Arezzo et al. (2012), Baron et al. (2012), Jacobsen et al. (2012), Disibeyaz et al. (2012), Galizia et al. (2012), Gubler and Bauerfeind (2012), Hagel et al. (2012), Jayaraman et al. (2013), Kirschniak et al. (2007), Kirschniak et al. (2011), Manta et al. (2011), Monkemuller et al. (2013), Nishiyama et al. (2013), Parodi et al. (2010), Pohl et al. (2010), Repici et al. (2009), Sandmann et al. (2011), Schlag et al. (2013), Seebach et al. (2010), Surace et al. (2011), Voermans et al. (2012), and von Renteln et al. (2010)

term success rates range from 42% to 100%; the average success rate was 73% (220/301). However, follow-up was quite short in most studies.

There are three different types of indications:

1. Acute endoscopic or interventional perforations being diagnosed immediately during the procedure, like colonic perforation during polypectomy
2. Postoperative leaks and fistulas, especially anastomotic leaks
3. A very heterogeneous field of chronic fistulas and leaks not belonging to the first two groups. This, for example, includes enterocutaneous fistula, perforated ulcers, or persistent gastrocutaneous fistulas after removal of PEG tubes.

Acute Endoscopic or Interventional Perforations

The success rate of OTSC closure in acute endoscopic or interventional perforations is 90% (95/106), meaning that most perforations occurring during endoscopic interventions can be managed by OTSC applications. From the technical point of view, acute perforations are the ideal indication for OTSC closure: the acute lesion is free from infection or scarring and is not contaminated by luminal contents, and the patient usually is already located in a specialized endoscopy unit. The OTSC application can avoid a surgical management in these cases, and some authors already claim «sparing the surgeon.» However, a certain amount of patients still undergo operations for safety reasons, with the finding of a sufficient OTSC closure of the leak in most cases.

OTSC closure of acute endoscopic perforations requires special care and caution.

After OTSC closure of an endoscopic perforation, the sufficient closure must be proven by endoscopic aspect and, if possible, by contrast study (application of contrast dye via the endoscope).

There is one fatality in the literature after dislocation of an OTSC placed on a colonic leakage, leading to a fatal peritonitis.

After OTSC closure of acute perforations, intensive clinical monitoring of the patient is mandatory. If in doubt, safety of the patient is the highest priority, even if this means an exploratory laparotomy.

Tip

Massive pneumoperitoneum is a frequent problem after OTSC closure of endoscopic perforations. Therefore, CO_2 insufflation should be used for interventions with a risk of perforation. After closure of the perforation, pneumoperitoneum can be easily drained by a cannulation of the peritoneum. This usually leads to a rapid improvement of symptoms. With the occurrence of a perforation being treated by OTSC, broad-spectrum antibiotic therapy should be initiated.

Postoperative leaks

Postoperative leaks and fistulas are another important indication for OTSC application. There are reports of successful closure of chronic fistulas following gastric sleeve resection, of fistulas at esophagojejunal and esophagogastric anastomoses, of fistulas at colorectal anastomoses, and in some cases of acute anastomotic leakage. The overall success rate is 68% (81/120), which is substantially lower than for acute endoscopic perforations. Fibrosis and acute inflammation at the site of leak are the most mentioned reasons for OTSC failure in these cases. In cases of early postoperative anastomotic leaks, the OTSC closure can be impaired by progressive necrosis or dehiscence at the anastomosis.

Despite these limitations, the OTSC closure of leaks and fistulas has a low risk and does not impair subsequent therapies in case of OTSC failure. The exact place of the OTSC in therapeutic algorithms for postoperative leaks and fistulas still has to be determined. Possible indications are summarized in the following box:

Suitable Indications for OTSC Closure of Postoperative Leaks

- Leaks which can be closed with one single OTSC (in selected cases, closure can be done with two or even more adjacent clips).
- No acute inflammation of the leak area.
- Little fibrosis and scarring.
- Chronic fistulas, especially residual fistulas after stent or endoscopic vacuum therapy.

- Under favorable circumstances, possibly acute anastomotic leaks. In these cases, alternative endoscopic vacuum therapy should be evaluated, as it provides sufficient drainage and debridement of the leak cavity.

Chronic Leaks and Fistulas

The field of chronic leaks and fistulas naturally is very heterogeneous. Chronic fistulas are often difficult to manage; stent therapy or application of fibrin glue is frequently not successful. The OTSC is a valuable alternative in these cases and should be considered before surgical management. Chronic fistulas usually show a lot of fibrosis, which makes it more difficult to get enough tissue into the clip. In this respect, the success rate of 59% (32/54) is lower than for acute endoscopic perforations. The value of the OTSC, however, is high in this setting, e.g., even esophagobronchial fistulas can be closed by OTSC, which significantly reduces morbidity and mortality compared to redoing thoracotomy for fistula repair.

Requirements of Staff, Instrumentation, and Organization

The endoscopist must be familiar with the application of the OTSC system, as well as with the different assist devices like twin grasper and anchor. The procedure requires, at least one, better two assisting persons who are not occupied with the sedation and monitoring of the patient.

The OTSC system consists of a clip loaded on a transparent cap; this system is placed on the tip of the endoscope (Fig. 6.5). A string is pulled through the working channel and connected to a handwheel. The clip is placed by pulling the target tissue into the cap (by suction or by using the twin grasper or the anchor), and by turning the handwheel, the string pulls the clip off the cap resulting in the closure of the leak (Fig. 6.6).

Ovesco provides OTSCs in different specifications. There are three different cap diameters (11, 12, and 14 mm), so any standard endoscope can be used. There are two different heights of the cap (3 and 6 mm). This cap height determines how much tissue can be pulled into the cap. Finally, there are three different shapes of the teeth of the clip (Fig. 6.7): «a» for atraumatic, blunt teeth, «t» for sharp teeth with improved anchoring, and a special clip geometry «gc» (gastric closure) for the closure of gastric full-thickness defects, e.g., during NOTES surgery.

The cap diameter is selected according to the endoscope used. For most purposes, a cap height of 6 mm is appropriate, as this allows the clip to grasp more tissue. The "t" shape with its sharp teeth possibly provides a more solid anchoring at the application site, and it can be used for most indications (Fig. 6.7).

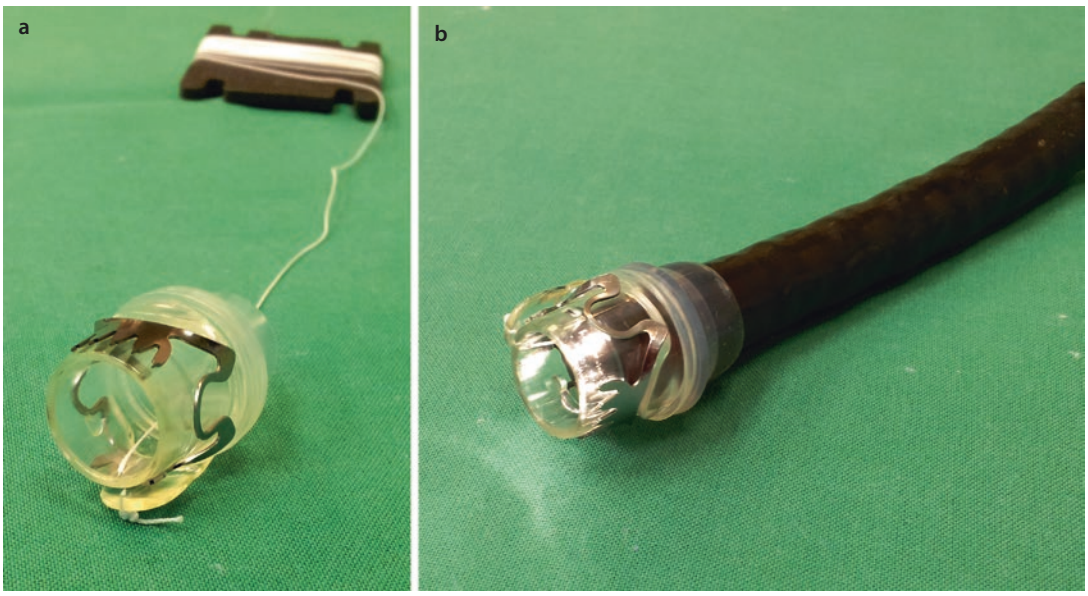


Fig. 6.5 **a** OTSC loaded on cap, the attached string is pulled through the working channel before mounting the cap. **b** OTSC system mounted on the endoscope

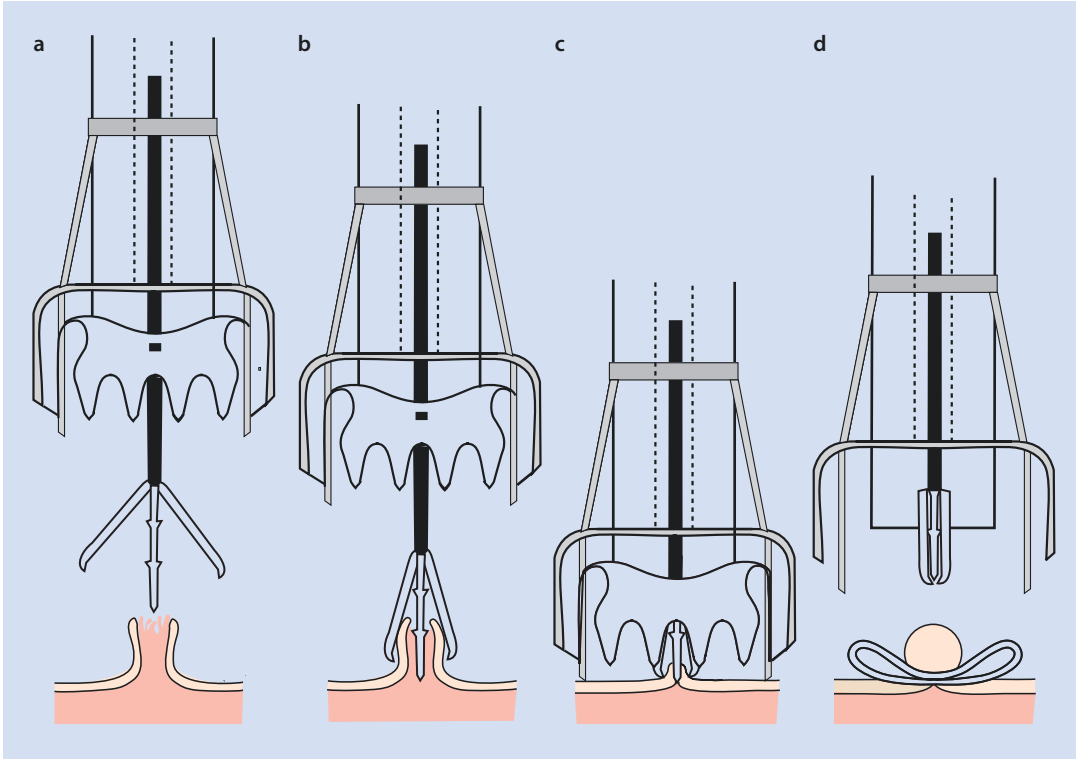


Fig. 6.6 OTSC application (here using a twin grasper). The defect is pulled into the cap by the twin grasper, before firing the clip. **a** Aiming at the lesion. **b** Pulling the tissue into the cap. **c** Firing the clip by turning the handwheel. **d** The clip is placed

Fig. 6.7 OTSC in different specifications («a,» «t,» and «gc») (Ovesco Endoscopy AG, Tübingen, Germany, with kind permission)

Fig. 6.8 Anchor and twin grasper (Ovesco Endoscopy AG, Tübingen, Germany, with kind permission)

The easiest way of clip application is certainly to bring the tissue into the cap by suction with subsequent firing of the clip. Ovesco provides two optional devices which can be introduced via the working channel: the anchor and the twin grasper (Fig. 6.8). The anchor basically is a probe which has three hooks («anchors») which can be moved out by the assisting person. This system is very valuable when dealing with small fibrotic fistulas. After introduction of the anchor into the fistula, the fistula can be pulled into the cap. The twin grasper is a forceps with two independently opening branches on each side, so both edges of a defect can be grasped separately, thus making possible the closure of larger defects.

Procedure

The applications of an OTSC on fistulas and leaks include the following steps:

OTSC Application on Fistulas and Leaks

- Diagnostic endoscopy with assessment of exact localization of the leak, check of endoscopic accessibility, and check of stable endoscope position at the planed application site
- If necessary: lavage of the leak, debridement
- Positioning the mounted cap on the leak or fistula site
- Pulling the leak site into the cap (by suction, by twin grasper, or by anchor)
- Firing the OTSC
- Endoscopic visual control of successful closure
- When indicated, contrast study to ensure a sufficient closure of the leak

Before placing an OTSC, the leak site must be thoroughly inspected. After assessment of leak type, its localization, the grade of fibrosis, and inflammation, the indication for a possible OTSC application should be evaluated using the above-mentioned criteria. Especially chronic leaks or fistulas should undergo a debridement, e.g., with a brush, prior to OTSC application.

Always check if there is a relevant cavity behind the leak. This prohibits OTSC application, as the cavity would then be without drainage, which inevitably would lead to an abscess.

In these situations, an additional drainage of the leak cavity is mandatory, or an alternative therapy, such as endoscopic vacuum therapy, should be used. All fistulas and cavities should be intensively rinsed.

During this preparatory endoscopy, the following aspects are important:

- Can the leak site be reached with the mounted OTSC system? Is there a stenosis preventing the passage of the system?
- Will it be possible to place the cap onto the leak site?

Tip

At some sites it is quite difficult to place the cap onto the leak, especially in the esophagus or duodenum. In such situations, it is good advice to check the accessibility with a standard distance cap mounted on the endoscope. The OTSC system is only opened if this test is successful. This avoids unnecessary costs for mounted OTSC systems which finally cannot be placed at the intended site.

After mounting the OTSC system, the endoscope again has to be introduced to the site of leak. With the cap mounted, this has to be done very carefully.

In particular, the passage of the mounted OTSC system through the upper esophageal sphincter has to be done very carefully; an iatrogenic perforation of the proximal esophagus is one of the most severe complications reported in the literature.

The optimal placement of the cap onto the leak site is not always easy. The assisting person fixing or pushing the endoscope can be of great help in these situations. Optimal communication within the team is important. Once the tissue is pulled into the cap, the assisting person has to ensure that the endoscope remains in exactly the correct position.

The application of the OTSC by suction of the tissue is the easiest and usually most suitable technique. The cap is placed on the leak site; the assisting person holds the endoscope in this exact position, allowing the endoscopist to use both hands for the following clip application. While applying continuous suction with his left hand, he turns the handwheel with his right hand. The OTSC drop-off can usually be visualized.

Small fibrotic fistulas often cannot be sucked into the cap. In these situations, the anchor is a good instrument. Its application is quite easy: the anchor is introduced into the fistula. While the assisting person ensures the position of the endoscope and of the cap on the fistula, the hooks of the anchor are extended, and the endoscopist can pull the fistula into the cap. This procedure can be facilitated by applying suction.

Larger defects can be closed using the twin grasper, which makes it possible to grasp both edges of the defect separately and to pull them together into the cap before firing the clip.

Before firing the OTSC, it has to be checked that the device (anchor or twin grasper) is completely pulled into the cap. Otherwise the instrument is fixed to the surrounding tissue by the fired OTSC.

After placing the OTSC, the former leak site is endoscopically assessed:

- Is the clip exactly positioned on the leak?
- Is the leak completely closed?
- Is the OTSC sufficiently anchored?
- Is the remaining lumen (especially in the esophagus, duodenum, and small bowel) still wide enough?

Documenting the sufficient sealing of the leak by contrast study during endoscopy is advisable; it is mandatory in cases of acute endoscopic perforations which otherwise would make an operation necessary. If this contrast study cannot be done during endoscopy, it can be subsequently be done by CT scan with oral or rectal application of contrast dye.

Two clinical cases demonstrating the OTSC closure of postoperative leaks are shown in Figs. 6.9 and 6.10.

Possible Complications and Their Management

Only a few complications have been described in the available literature; some of these, however, were severe.

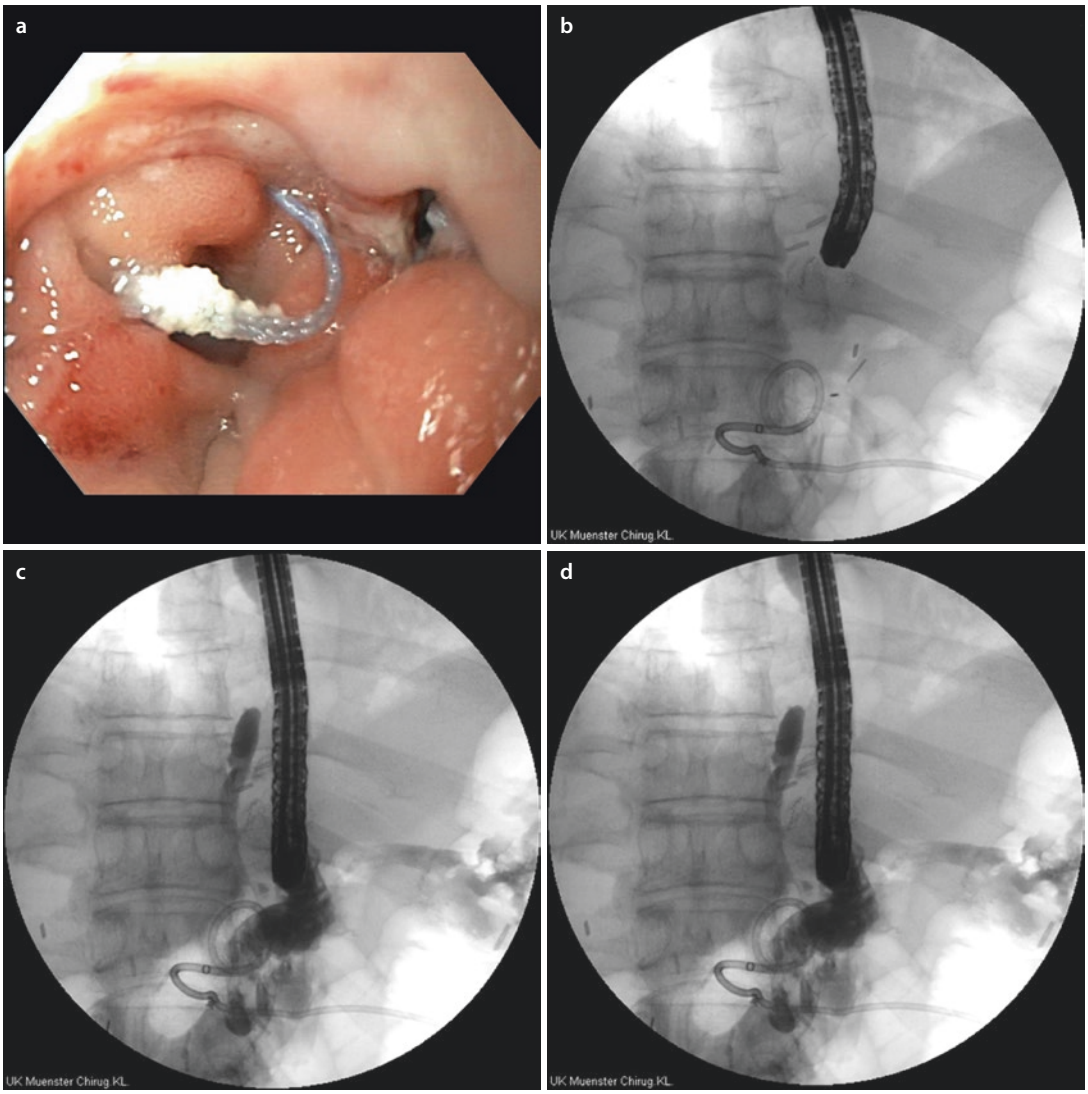
The introduction of the mounted OTSC system can induce injuries, especially at the upper esophageal sphincter or in the anal canal. Frequently, these are superficial mucosal tears; the published case of proximal esophageal perforation has already been mentioned before.

If not retracted completely, the assist devices «twin grasper» or «anchor» can be fixed to the gastrointestinal wall by the fired OTSC. Pulling on the device is the only option in this situation (after retracting the hooks of the anchor), and this usually is quite unproblematic, as the surface of the instruments is smooth and they can slip out of the clip. This procedure of course impairs the safety of the OTSC leak closure; special attention has to be paid to a possible displacement of the clip or to a persistent leak.

Wrong positioning of the OTSC can give rise to complications, too. If the lesion is not centered correctly, a persistent leak can be the result. In some cases, a second OTSC can be placed next to the first one. However, this is technically demanding. After application of OTSCs in duodenum and small bowel, unintended complete or subtotal closure of the lumen has been reported in some cases; these cases were managed by surgery. When using the OTSC in the distal rectum, special attention has to be paid not to place the OTSC in the sensitive anoderm. Placing an OTSC in this sensitive area is only possible under anesthesia. For this

purpose, Ovesco offers a special «OTSC proctology» device allowing the closure of anal fistulas.

The removal of wrongly positioned OTSCs is not trivial; therefore, they should be placed with utmost caution. Before the introduction of a special device, authors reported the successful removal of OTSCs by Nd:YAG lasers. Recently, Ovesco developed a special device for the purpose of OTSC removal (remOVE, Ovesco Endoscopy AG, Tübingen, Germany; ◘ Fig. 6.11.). It is a bipolar forceps with a DC generator connected to it. The instrument is introduced via the working channel. The clip is grasped at its thinnest point. A short electric impulse melts the nitinol between the branches. Due to the bipolar construction, no relevant electric current runs through the patient. The divided clip can then be extracted by a forceps under protection of a soft cap.



◘ **Fig. 6.9** OTSC closure of an anastomotic leak following gastrectomy. **a** After gastrectomy with stapled esophagojejunostomy, the patient developed an anastomotic fistula. **b** Fluoroscopy: a CT-guided pigtail drain is located in the leak cavity. **c** Contrast dye application into the fistula via a cannula, showing a bizarre leak cavity. **d** Contrast dye application into the jejunum. **e** Rinsing the fistula via a cannula. **f** OTSC placed onto the fistula. **g** Endoscopic aspect after 2 months: enduring closure of the fistula. **h** Contrast study after 2 months: no leakage present, clip in situ

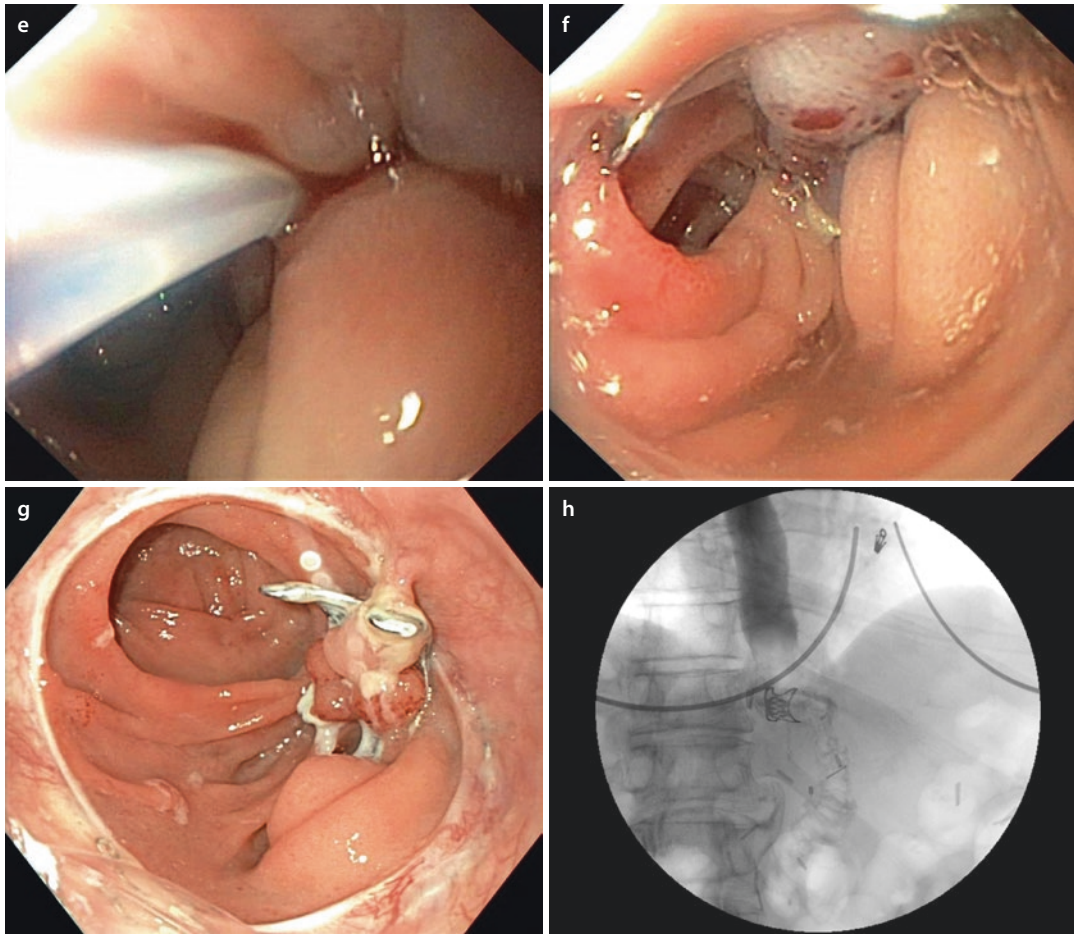


Fig. 6.9 (continued)

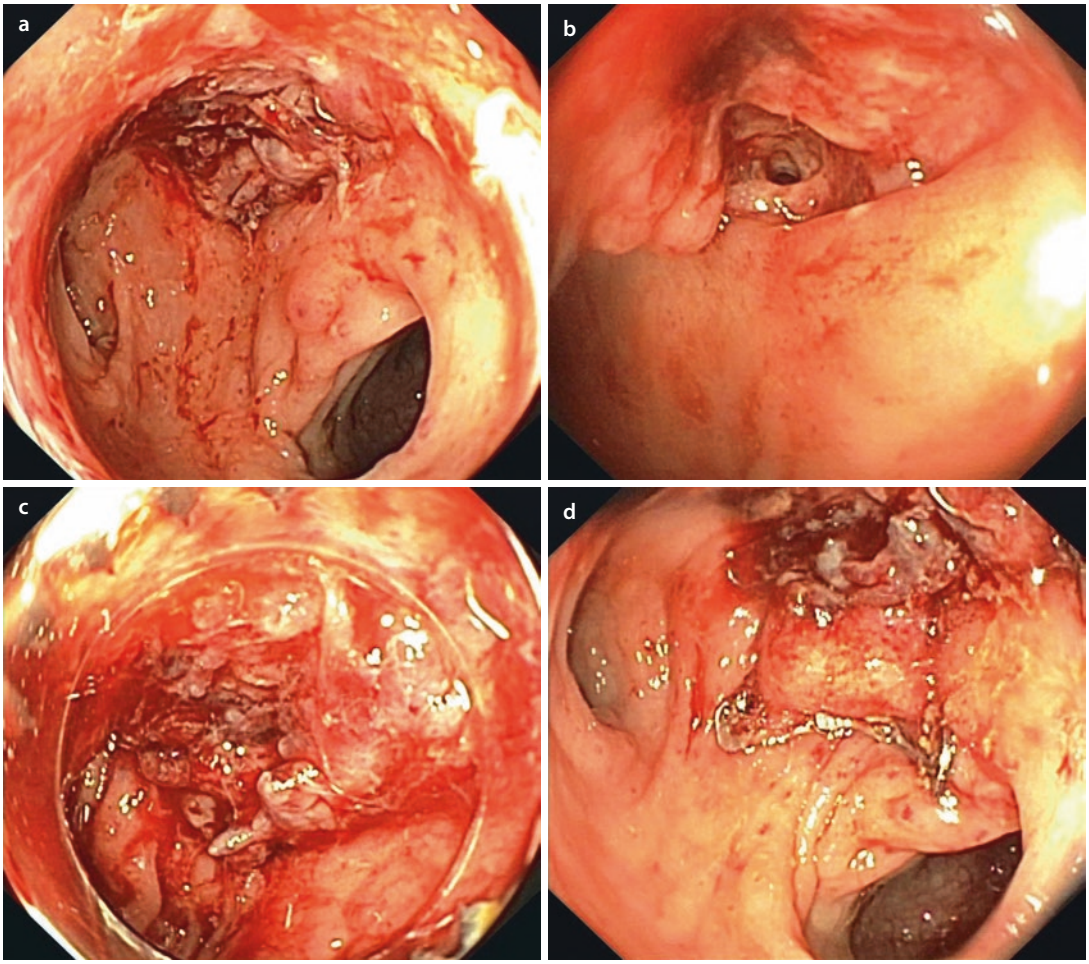


Fig. 6.10 OTSC closure of an anastomotic fistula following rectal resection (residual fistula after endoscopic vacuum therapy). **a** Side-to-end anastomosis of descending colon and rectum. Fistula located at 12 o'clock. **b** Closer view of the fistula. **c** Placing the cap onto the fistula. **d** OTSC placed correctly on the fistula

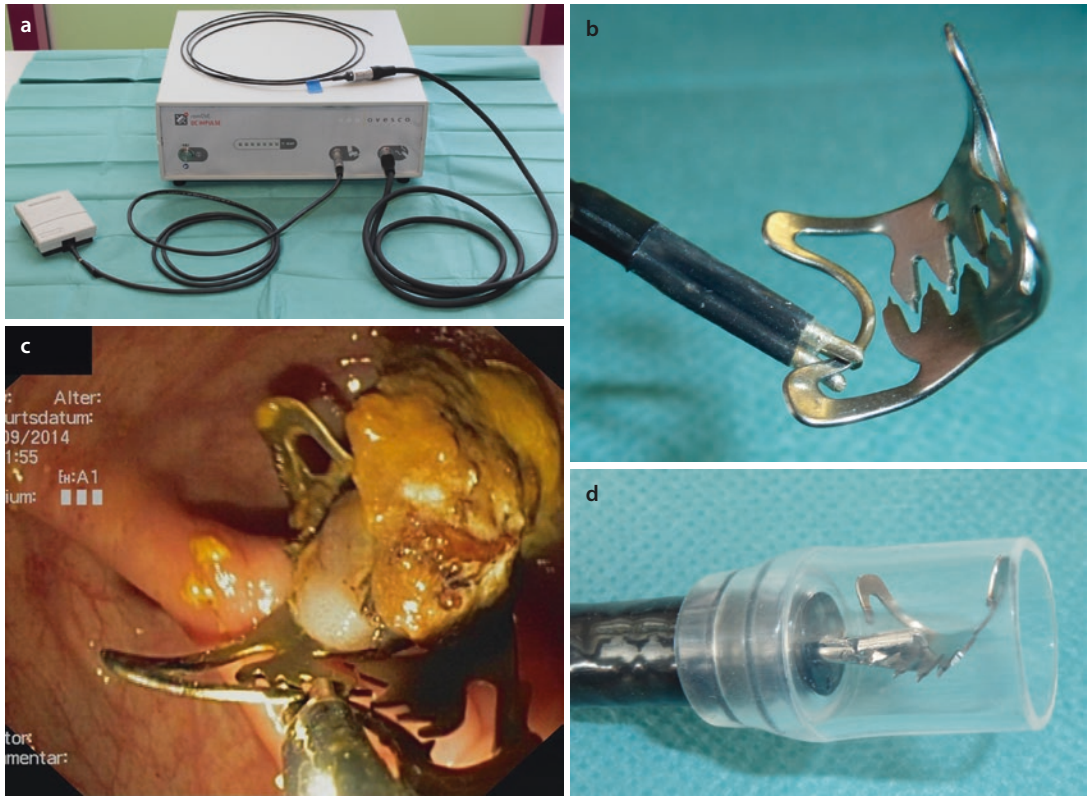


Fig. 6.11 Removal of an OTSC with the remOVE system. **a** DC generator. **b** Bipolar forceps allowing the fragmentation of the OTSC. **c** Clinical case: removal of an OTSC at the appendix base in order to allow a control biopsy after former full-thickness resection with the FTRD System (Ovesco). **d** Extraction of the divided clip within a covering soft cap (**a**, **b**, **d** with kind permission of Ovesco Endoscopy AG, Tübingen, Germany; **c** with kind permission of Dr. Arthur Schmidt, Klinikum Ludwigsburg, Germany)

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