Endoscopic Bleeding Control

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Gastrointestinal bleeding (GIB) can occur at different locations and different intensities throughout the intestine. Gastrointestinal bleeding is subdivided based on the location (upper, lower, middle GIB). The upper GI tract comprises the esophagus, stomach, and duodenum (up to the papilla of Vateri). Middle GIB relates to that part of the GI tract located below the papilla Vateri up to the terminal ileum. Lower GIB is defined as a bleeding within the colon and rectum. Upper GIB is diagnosed with esophagogastroduodenoscopy, middle GIB with capsule endoscopy or enteroscopy, and lower GIB with colonoscopy.

3.1 Introduction

Upper gastrointestinal bleeding (GIB) has an incidence of 50/100,000 persons and is a common gastroenterological emergency. Endoscopic techniques for bleeding control as well as intensive care treatment have greatly evolved in recent years. However, the mortality of GIB is still high at 5–14% (Czernichow et al. 2000). Bleeding ulcers of the duodenum are the most common causes of upper GIB. They account for up to 50% of all cases with GIB (Thomopoulos et al. 2004). Ulcers within the stomach and duodenum are more often seen in the elderly. They are induced by infection with *Helicobacter pylori* or the use of nonsteroidal anti-inflammatory drugs (NSAIDs). Most of the ulcer bleedings stop spontaneously. If not, immediate medical treatment is required. Endoscopic, radiological, or surgical techniques are available for bleeding control. The most commonly used intervention is endoscopic therapy.

A special entity is the so-called Dieulafoy's lesion. It is difficult to diagnose, because an aberrant vessel reaches the mucosa and can lead to strong arterial bleeding based on erosion of the superficial vessel. The typical endoscopic feature is a bleeding vessel without surrounding mucosal damage (Fig. 3.1).

Mallory-Weiss lesions, esophageal varices, and malignancies within the upper GI tract are other sources of GIB (Table 3.1).

Lower GIB shows a strong association with aging. The incidence is 20.5–27/100,000 persons per year. Lower GIB is less common than upper GIB. Common causes of lower GIB are diverticula, malformation of vessels (angiodysplasia), polyps, cancer, and inflammatory bowel disease (IBD). Most GIB (85–90%) is self-limiting. However, strong bleedings can also rapidly occur with hypotension and shock (Longstreth 1997).

The least common form of GIB is middle GIB. Middle GIB accounts for about 10% of all GIB. Causes are malformations of vessels, ulcerations, neoplasia, and IBD. Diagnosis of middle GIB can be challenging. Here, capsule endoscopy and balloon-assisted enteroscopy (single or double) are used to identify the source of bleeding. Capsule endoscopy is more used for occult bleeding, whereas balloon-assisted enteroscopy is used for diagnosing and treating overt bleedings.

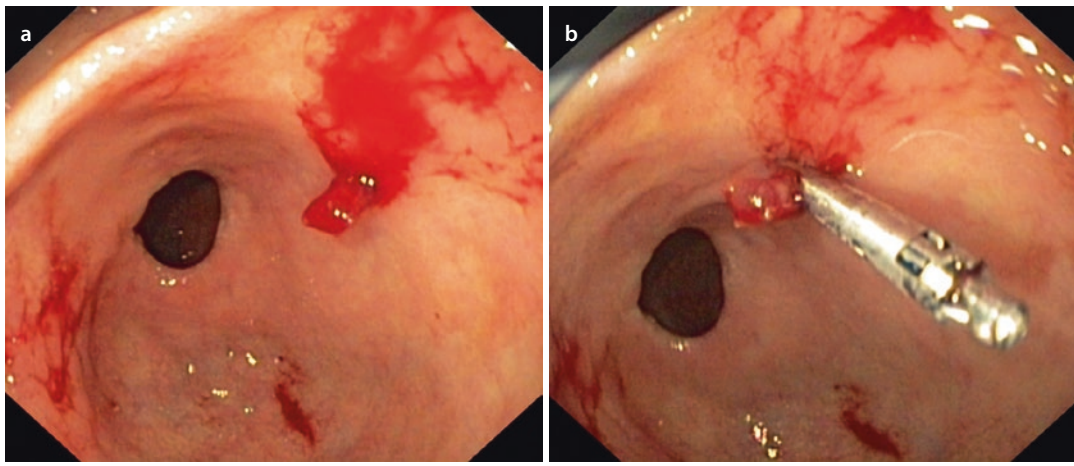

Fig. 3.1 **a** Visible vessel within a Dieulafoy's lesion of the antrum. **b** Endoscopic bleeding control with clip application

Table 3.1 Causes and frequencies of gastrointestinal bleeding

	Etiology	Frequency (%)
Upper GI bleeding	Peptic ulcers	50
	Erosions	16
	Variceal hemorrhage	10
	Mallory-Weiss lesion	5
Lower GI bleeding	Diverticula	42
	Hemorrhoids	16
	Colitis	18
	Post-polypectomy bleeding	13
	Vessel malformation	3

3.2 Ulcer Bleeding

Classification of peptic GI bleeding is based on Forrest classification (Table 3.2). The classification differentiates between acute, recent (with risk of re-bleeding), and almost-healed ulcerations. The goal of the Forrest classification is the immediate judgment of the risk of re-bleeding and the need for endoscopic intervention (Forrest et al. 1974).

Risk Stratification and Pharmaceutical Options of Therapy

First, thorough clinical evaluation is needed to define the health situation of the patient. Several scores can be used to define the need for hospitalization and treatment under intensive care. Measurement of vital parameters is the first and most important step of clinical evaluation. Hemodynamic instable patients require infusions and transfusions. However, red blood cells should only been given in otherwise healthy patients if the hemoglobin value is below 7 g/dl. Patients with coronary heart disease might require transfusions earlier, and the expected hemoglobin level should be above 10 g/dl.

Tip

Blood transfusions should be initiated in otherwise healthy patients if the hemoglobin value drops below 7 g/dl.

Table 3.2 Forrest classification of peptic ulcer bleeding

Forrest classification		Morphology of ulceration	Risk of re-bleeding
Forrest I	A	Active bleeding (pulsating)	High 5–20%
	B	Venous bleeding	
Forrest II	A	Visible vessel	
	B	Blood clot	
	C	Hematin based	Low 3–10%
Forrest III		Fibrin-based ulceration	

Active bleeding from the upper GI tract has to be considered as a medical emergency. Typical clinical signs are hematemesis and melena. Strong upper bleeding might lead to perianal bleeding with red color (hematochezia). Occult bleeding leads mainly to fatigue, dizziness, weakness, and cardiac symptoms (Peura et al. 1997).

Prognostic Scores

Differential risk stratification can be achieved with different prognostic scores (e.g., Rockall score, AIMS65 score; see Tables 3.3 and 3.4).

The different scores are scientifically evaluated. However, they are not all embedded into clinical practice. Here, simple parameters can be used to judge the overall blood loss. Melena is associated with an average blood loss between 50 and 100 ml. Hypotension develops after blood loss between 10 and 25% of the overall blood volume. Stable vital signs are seen if less than 10% of the blood volume is lost.

Medical Therapy of Gastrointestinal Bleeding

Endoscopic therapy of peptic ulcer bleeding should always be combined with medical treatment. Here, proton pump inhibitors (PPI) are the drugs of choice. The imbalance between aggressive and protective factors within the gastric mucosa can be treated with PPI. PPI therapy should be initiated prior to endoscopy. This regimen will lead to less active bleedings and will ease endoscopic therapy. PPI therapy after endoscopy is associated with lower re-bleeding. PPI can be given intravenously or orally. Patients with ulcer bleeding of the

Table 3.3 Rockall score: score below 3 is associated with a good prognosis, and scores above 8 predict high mortality risk

Variable	0 Points	1 Point	2 Points	3 Points
Age	<60	60–79	>80	
Hemodynamic	Normal	Pulse > 100 bpm Sys. RR >100 mmHg	Sys. RR <100 mmHg	
Comorbidity	None		Heart/circulation	Organ failure
Diagnosis	Mallory-Weiss	Other sources	Malignancy	
Forrest	III		I, II	

Table 3.4 AIMS65 score

Risk factor	Value
Albumin	<3 g/dl
INR	>1.5
GCS (mental status)	<14
Sys. RR	<90
Age	>65

Mortality risk:
No risk factor: 0.3%
1 risk factor: 1%
2 risk factors: 3%
3 risk factors: 9%
4 risk factors: 15%
5 risk factors: 25%

small bowel without intake of NSAIDs do profit from immediate eradication of *Helicobacter pylori* (Chan et al. 2007; Kahi et al. 2005).

Tip

Endoscopic therapy of peptic ulcer bleeding should always be combined with PPI treatment. Re-bleeding will be reduced.

Rapid pH elevation is mandatory for stabilization of blood coagulation and leads to reduced recurrence of GI bleeding. Cellular and plasmatic coagulation is only sufficiently active if pH values are between 4 and 5. There is inconsistency with regard to the route of administration of PPI (orally or intravenously) to be used. Oral administration may be sufficiently effective in patients with stable bleeding. Eradication of *Helicobacter pylori* if present is an additional benefit. The recurrence of ulcerations of the stomach and duodenum is accordingly reduced (less than 5%). Prokinetic agents such as erythromycin and metoclopramide can be of benefit in preparing for endoscopic diagnosis and therapy (Altraif et al. 2011). The stomach will be freed of blood clots by prokinetic therapy, and the visibility of blood lesions will be improved. In contrast, the vasoconstriction of the splanchnic vessels which can be achieved with somatostatin does not play a role in endoscopic bleeding management or therapy (Imperiale and Birgisson 1997).

Tip

Prokinetic agents prior to endoscopic examination ease the visibility of the mucosa and improve endoscopic diagnosis and therapy.

Surgery does not play an important role in treatment of GI bleeding nowadays. Endoscopy, radiological interventions, and medical treatment have almost replaced surgical interventions. Resection methods such as Billroth were performed in the past but are no longer necessary. However, surgery is needed if recurrent bleeding is present. Complications such as perforation or stenosis still require surgery.

Co-medication with anticoagulation increases the risk of GI bleeding and can lead to more severe bleedings. However, cardiovascular mortality can be increased if anticoagulation is stopped based

on GI bleeding. Thus, close interaction between cardiologists and gastroenterologists is needed to define optimal treatment of the patients.

Endoscopic Therapeutic Methods

The main diagnostic step for diagnosing upper GI bleeding is EGD. EGD should be performed within 24 h after onset. Ideally, EGD should be done right after stabilization of the patient. Early endoscopy is associated with a higher diagnostic yield, and almost 90% of upper GI bleedings can be identified with EGD (Zuccaro 1998). Endoscopic therapy depends on size, severity, location, and experience of the examiner. There are several endoscopic therapy options:

Endoscopic Therapy Options for Upper GIB

- Injection therapy:
  - Epinephrine
  - Histoacryl
  - Aethoxysklerol
  - Fibrin glue
- Thermal therapy:
  - Electrocoagulation
  - Heater probe
  - Laser coagulation
  - Argon plasma coagulation (APC)
- Mechanical therapy:
  - Rubber band ligation
  - Hemoclip
  - Over-the-scope clip
- Hemostatic powder:
  - Hemospray
  - EndoClot (Hegade et al. 2013, Huang et al. 2014)

It is mandatory to use two types of endoscopic therapy to sufficiently treat GI bleeding (Sung et al. 2007). Most commonly, injection therapy is combined with clipping.

Indications

Upper endoscopy is recommended in every patient with GIB. Informed consent should be obtained if possible (stable patient). Emergency upper endoscopy is needed in clinically unstable patients. The lab parameters should be analyzed. However, it should be taken into account that dilution due to infusion therapy might play a role.

Personnel

Sufficient and experienced personnel are required to perform high-quality endoscopic diagnosis and therapy. EGD is performed on the left lateral position, or the patient is intubated and can stay on the back. Patient with severe bleeding and hematemesis requires intubation. This minimizes the risk of aspiration. Emergency EGD should be performed by an experienced examiner and experienced nurse. Ideally, the team is highly familiar with all endoscopic techniques for stopping GI bleeding. The team should already have performed all kinds of endoscopic interventions in elective patients. Intensive care treatment is needed if the patient is highly unstable. A physician and a nurse who are familiar with intensive care treatment should be part of the team to treat the patient properly and sufficiently. Endoscopy can be performed in the emergency room, the endoscopic suite, or within the intensive care unit. Interdisciplinary interaction is needed to receive the best results.

Tip

Acute GIB is an emergency, which requires interdisciplinary interaction to achieve best treatment for the patient.

Organizational Requirements

Organizational requirements depend on the severity of the bleeding. It has to be ensured that indication is clarified and informed consent is obtained. Coagulation parameters and vital signs have to be measured and optimized (if possible). In general, any endoscopic service should be able to offer diagnostic and therapeutic endoscopy. The structure of the team and the suite has to be adapted to the needs of the patients. Therapeutic algorithms and post-interventional follow-up have to be defined — within the endoscopic suite as well as in the hospital.

Knowledge of the working method as well as the technical application of endoscopic therapies is mandatory to perform sufficient endoscopy and proper endoscopic hemostasis. Medical device requirements and law have to be taught to the team, and reliable handling of the different devices has to be ensured. Maintenance of the equipment is also mandatory.

Instrumentation Requirements

In general, the use of therapeutic endoscopes with larger working channels (3.8–4.2 mm) is recommended. A second endoscope should be available in case malfunction of the used endoscope occurs or if the working channels become blocked due to the aspiration of blood clots. Intensive care treatment should be available depending on the severity of the bleeding. Monitoring of the patient is essential. Here, noninvasive measurement of the blood pressure, continuous measurement of the oxygen saturation, and pulse oxymetry are recommended.

Necessary Preparations for Endoscopic Diagnosis and Therapy

- Absorbent sheets
- Detergent flushing fluid (e.g., Dimethicone and Aqua) (Fig. 3.2)
- Lubricant
- Adequate amount of container for suction and exchange material
- Suction pump
- Adequate amount of rinsing fluid for the optical system

Fig. 3.2 Lubrication cream and antifoam agents are standard for endoscopic care

- Two i.v. cannulas with safe fixation and large diameter
- Mouthpiece
- Oxygen applicator with humidification
- Emergency chest (with regular controls) nearby
- Endoscopic injection needles
- Saline solution 0.9%, adrenaline solution(1:10,000)
- Clips (according to the manufacturer)
- Devices for thermal hemostasis

Types of Intervention

The highest level of success can be achieved if the endoscopic team is experienced and has performed the interventions many times before. Ideally, emergency interventions should be performed by the most experienced examiners. The different forms of endoscopic interventions are now explained.

Injection Therapy

Injection therapy is performed with different agents (see Table 3.5). Here, mechanical compression of the vessel is the main mode of action. Vasoconstriction might play an additional role. Compression lowers the blood flow and thus activates the coagulation system (Fig. 3.3).

The use of diluted epinephrine solution is most common. Several circumstances are in favor for this type of agent:

- High tolerance
- Low costs compared to fibrin glue
- No tissue destruction or damage

Table 3.5 Substances for injection therapy of peptic ulcer bleeding

Substance	Mode of action
Epinephrine solution 1:10,000–1:100,000	Vasoconstriction and compression
Polidocanol	Sclerosing and scar formation
Fibrin glue	Multiple component activator of coagulation
Saline	Compression
Alkyl cyanocrylat	Polymerization

Fig. 3.3 Substances used for injection therapy. The dilution of epinephrine is carried out using saline solution

Injection with diluted epinephrine (1:10,000) is highly effective. The source of bleeding is treated by injecting several doses (1–2 ml) of epinephrine toward the bleeding vessel. Complication rates are below 1%. Bleeding control can be achieved in 75–90% of cases.

Technical note: The catheter covering the needle is gently passed over the working channel of the endoscope. The nurse moves the needle forward out of the catheter if the distal tip of the catheter becomes clearly visible. The syringe with the diluted epinephrine is connected with the catheter. The examiner moves the needle forward into the tissue. Ideally, injection is done within four quadrants surrounding the bleeding vessel. The nurse states aloud the amount of applied epinephrine and also whether the injection can be done easily or resistance occurs; the examiner can reposition the needle based on this information.

The diluted epinephrine can be further diluted, or pure saline can be used in patients with coronary heart disease to further minimize the risk for systemic side effects.

Injection therapy is an easy and basic endoscopic intervention and can be learned quickly. It can be performed also by less experienced examiners.

Tip

Injection therapy with diluted epinephrine is aimed mainly at mechanical compression of the bleeding vessel. Pharmacological vasoconstriction might play an additional role. Epinephrine can be further diluted, or pure saline can be used in patients with known coronary heart diseases. This will further minimize the risk of systemic side effects.

The mode of intervention is similar for polidocanol, alkyl cyanoacrylate, and fibrin glue. However, the preparation of compounds using components such as fibrin glue requires special attention. The eyes and mouth of the patient and the examiners should be protected.

Fibrin glue has been stated to be superior in single studies (compared to epinephrine injection). However, further studies and meta-analysis could not confirm this observation. Additional injection of sclerosing agents for peptic ulcer bleeding has no additional benefit. Indeed, it is associated with a higher complication rate due to risk of necrosis and is not recommended.

Combination of injection therapy and thermal ablation or treatment has also shown no convincing benefit. Mortality, risk of re-bleeding, and need for surgery were comparable. However, mechanical treatment (hemoclip) in combination with injection therapy has shown advantages. Here, re-bleeding is less frequent mainly because of the prolonged compression of the bleeding vessel.

Figure 3.4 shows an 88-year-old patient with melena. The endoscopic examination revealed a continuously bleeding ulcer (Forrest I b) in the duodenal bulb. Hemostasis was done with two hemoclips Fig. 3.4b.

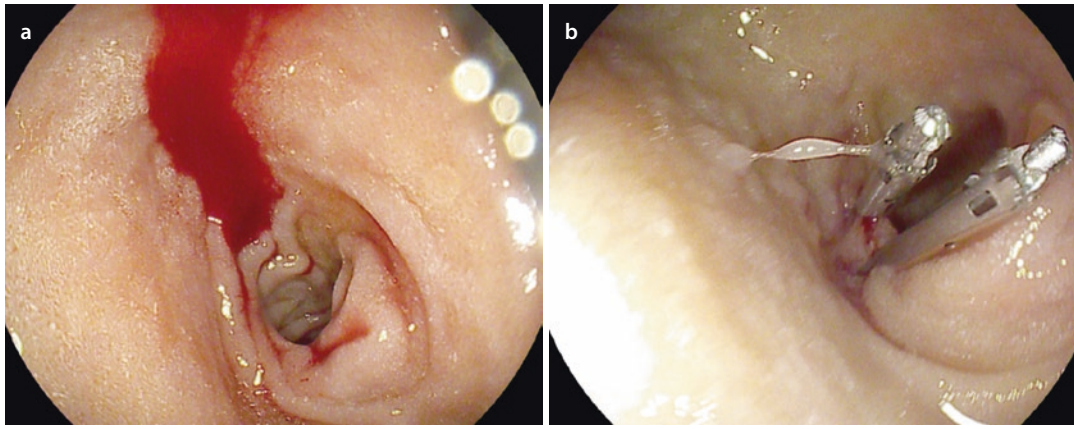

Fig. 3.4 **a** Bleeding ulcer in the duodenal bulb. **b** Hemostasis with two hemoclips

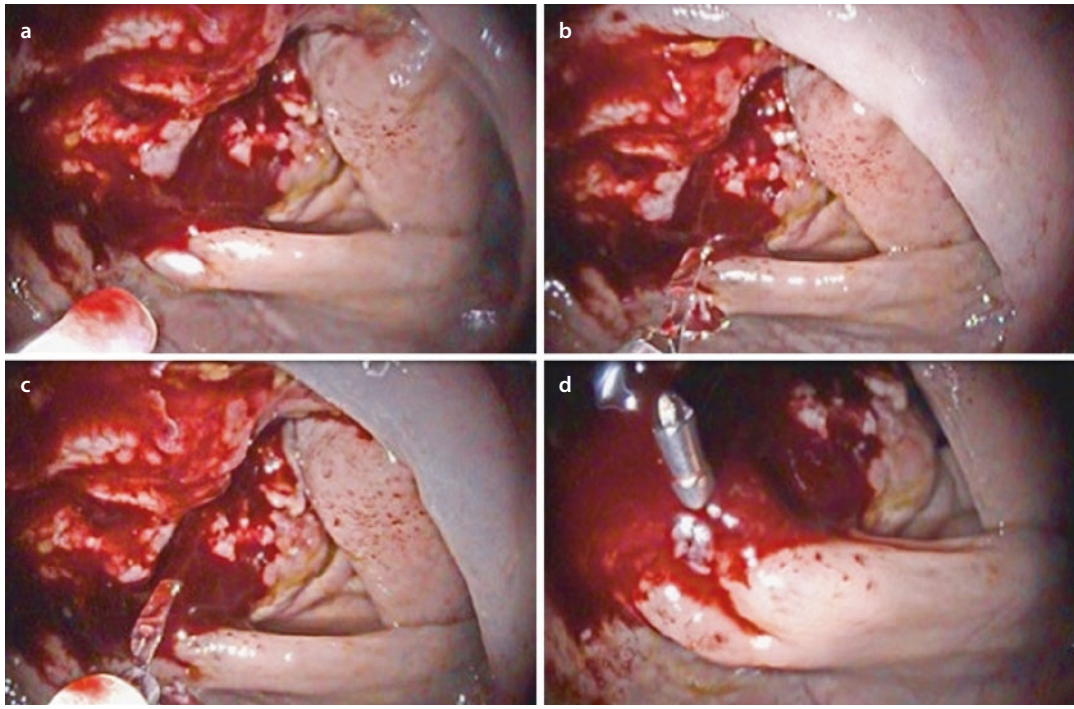

Fig. 3.5 Preoperative marking with hemoclip in a patient with colonic cancer. First the clip is advanced **a**, **b**, and then it is tautened **c** and finally applied **d**

Furthermore, hemoclips have also proved themselves useful for marking (Fig. 3.5) and for closure, for example, of small fistulas and perforations. All studies to date have demonstrated the significant superiority of hemoclips compared with injection methods with regard to primary hemostasis.

Nowadays, different single-use and reusable clips with different designs are available. The QuickClip (Olympus Medical Systems) is a single-use metallic clip which can be rotated within the endoscopic examination. The clip is available with varying opening angles and lengths of branches. In contrast to others, it cannot be reopened.

A reloadable system is available for more than 20 years. Another single-use product, the TriClip (Cook Medical), is a metal pin with three branches which can be closed only once after placement.

The manufacturer regards rotation as unnecessary due to the trilateral application.

The Resolution clip (Boston Scientific Corporation) is suitable for hemostasis, for closure of small perforations, and for the fixation of jejunal nutrition tubes according to the manufacturer's instructions. Furthermore, this clip can be reopened after closure.

The Over-The-Scope Clip (Ovesco Endoscopy AG, Tübingen, Germany) has been available for interventional endoscopy since 2007. While all other clips are introduced through the instrumentation channel of the scope, this clip is fitted at the tip of the scope (Schurr et al. 2008). Due to its design, it can grasp much more tissue and apply a higher pressure than conventional clips. This allows a targeted placement of the clip.

For proper and safe placement, the tissue can be sucked out, or a special tissue anchor can be used which is provided by the same manufacturer.

Case Study

Figure 3.6 shows a 69-year-old man with melena and vomiting of blood as an emergency case. Due to leg thrombosis, he was under Marcumar medication.

A gastric antrum ulcer with Forrest Ia bleeding was diagnosed. The endoscopic treatment was done with an OTS Clip solely (no injection). Testing for *Helicobacter pylori* was negative.

Therapy was successful, and no re-bleeding occurred. Patient was discharged 5 days after OTSC treatment.

Figure 3.6c, d demonstrates endoscopic controls after 3 days and after 6 weeks.

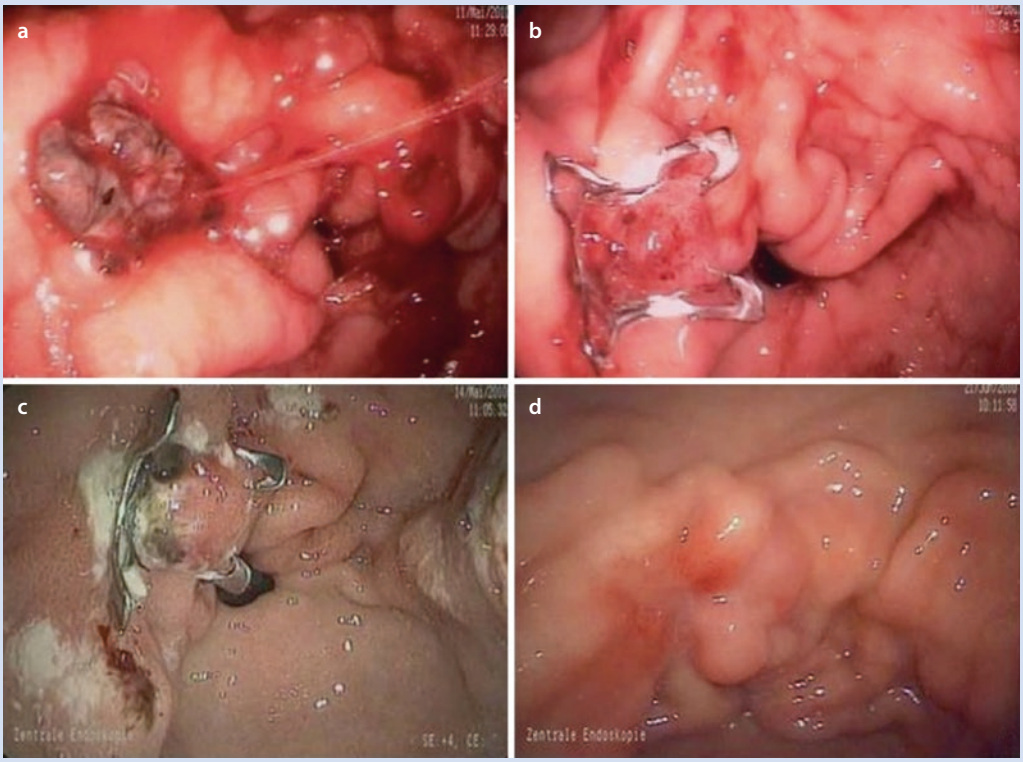

Fig. 3.6 **a** Forrest 1a bleeding in the gastric antrum. **b** Endoscopic therapy with OTSC without further treatment. **c** Postoperative day 3, **d** 6 weeks after intervention (With kind permission from Dr. Thomas Kratt)

The use of hemoclips in endoscopy provides a lot of advantages. All the abovementioned systems combine the positive aspects of low rebleeding rates and are superior to most of the injection methods. The handling and the related success rate depend on the experience of the endoscopist. Recommendations concerning follow-up endoscopies are conflicting. An international consensus from 2010 does not give a general recommendation for a control.

Mineral Powders

Just recently, endoscopic Hemospray (Cook Medical, Ireland) became available as an alternative to traditional methods (Holster et al. 2014; Smith et al. 2014; Yau et al. 2014). EndoClot (MicroTech Europe) is another mineral powder which can achieve homeostasis in GI bleeding. Hemospray (Fig. 3.7) is an inorganic silicate crystal (powder) which is provided in a cartridge. It is applied with a catheter through the instrumentation channel of the scope directly to the bleeding source.

The mode of operation of the powder is not clear in detail. In addition to a mechanical barrier, there seems to be another really significant component. On one hand, the powder causes a plasma separation and thereby an increased concentration of coagulation factors; on the other hand, electrostatic loading of the crystals activates intrinsic blood coagulation.

This noninvasive mode of functioning also works in patients with full anticoagulation. This is a clear advantage, in particular in emergency situations.

Few data exist about the use of Hemospray. In 2011, the first published study demonstrated a high level of safety and no side effects due to Hemospray.

With the exclusive use of Hemospray, after 72 h a hemostasis could be achieved in 89% of cases. In a European Register study (SEALS), the superiority of Hemospray was registered in particular in those cases in which other methods failed. Here, a hemostasis rate of 70% could be achieved.

The use of this method for peptic ulcer bleeding is promising (Fig. 3.8). In addition, it can be used in tumor-related bleedings and in patients with gastrointestinal bleeding and medical anticoagulation. In Europe, Hemospray is approved for nonvariceal upper GI bleeding. In Canada, it is approved also for lower GI bleeding (Fig. 3.9).

Even thermal treatment methods can be used in gastrointestinal bleedings, in particular the heater probe and argon plasma coagulation (APC) (▶ Sect. 3.4).

Complications

Aspiration of blood and overdosage of sedative medications are the most common complications before and during endoscopic therapy. A decrease in blood pressure can be caused not only by a hemodynamic complication by the bleeding itself but also by the sedation. Furthermore, perforations are possible complications. The complication rate is higher with aggressive monotherapy, in particular with thermoablation, compared with a combination of thermal ablation with clipping. For rare cases with failing of endoscopic hemosta-

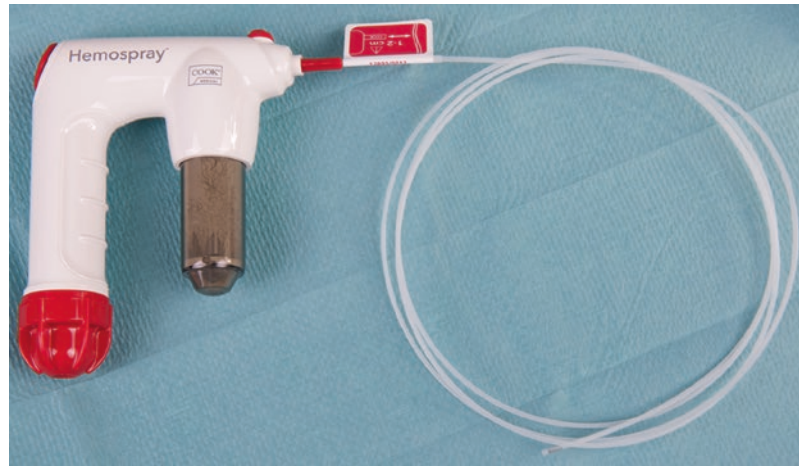

Fig. 3.7 Hemospray: the powder is applied by twisting the red button at the handle and opening of the outlet channel (*red lever*)

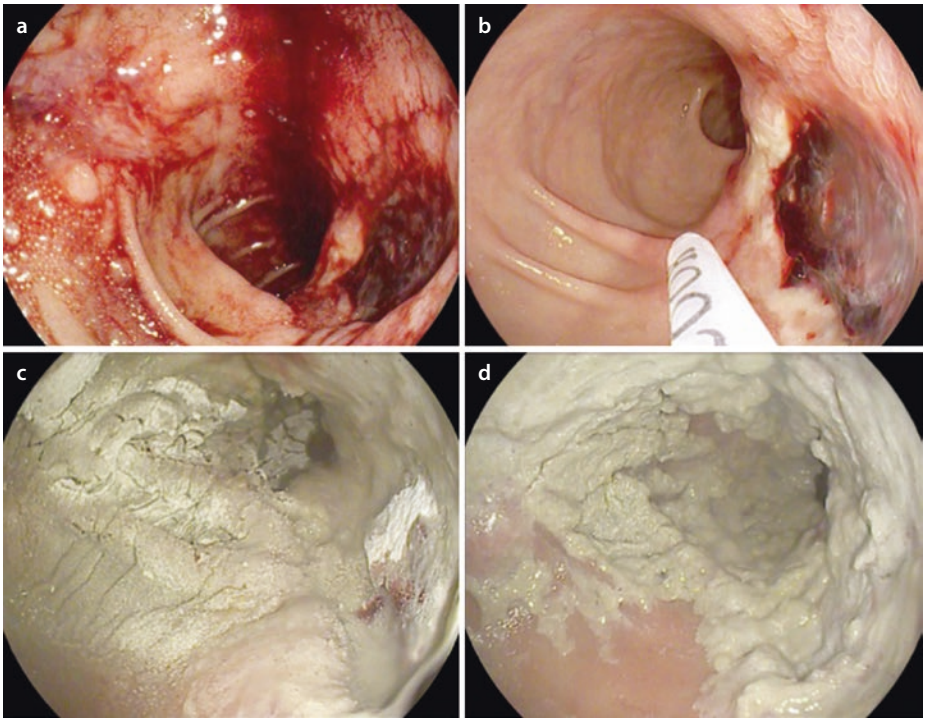

Fig. 3.8 A 76-year-old man with melena and hemorrhagic shock. The patient had a partial gastrectomy (Billroth I) with a non-bleeding ulcer with visible vessel stump (Forrest II a) (**a**). The endoscopic therapy was done with Hemospray and intensive care. Hemostasis could be achieved and the patient could be stabilized (**b**–**d**)

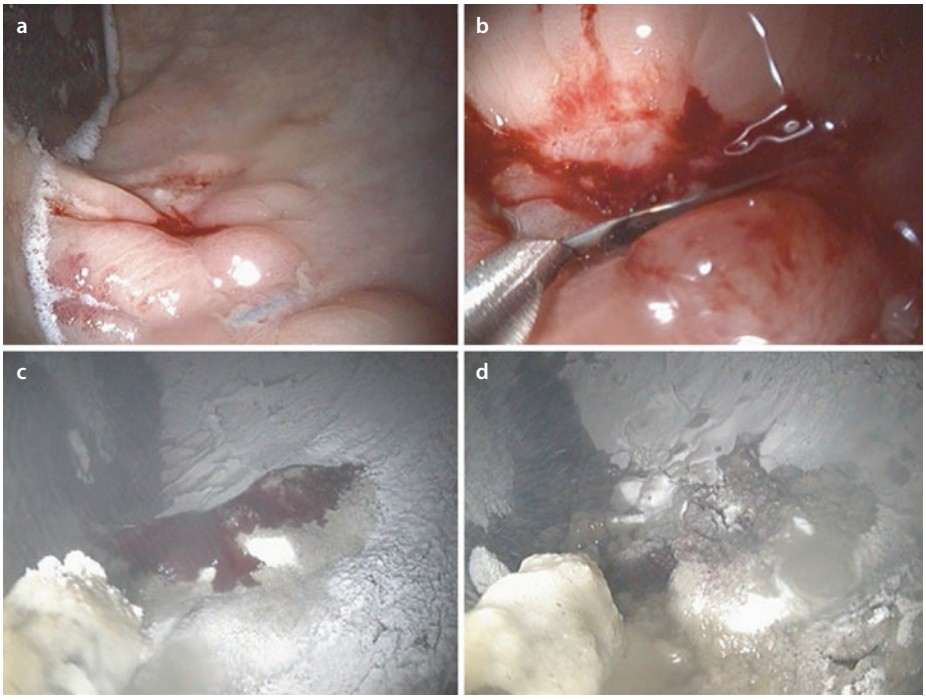

Fig. 3.9 A 71-year-old female with continuous perianal blood loss after (outpatient) hemorrhoidectomy some days before. **a** Endoscopic finding: bleeding from operation site. **b** Applied clips could not fix the mucosa. **c**, **d** Hemostasis after repeated Hemospray application till final surgery

sis, a transarterial chemoembolization should be undertaken (if appropriate radiologic expertise is available) before surgical therapy.

An overdosage of analgosedation can cause severe complications during endoscopy.

Tip

Analgosedation with propofol (e.g., Diprivan) should be started by titration. Administration of 0.5–1 mg/kg KG is usually sufficient to start sedation.

3.3 Variceal Bleedings

Esophageal and gastric varices are indicators of portal hypertension, which is the consequence of a pressure gradient between the portal vein and hepatic veins exceeding 12 mm Hg. Approximately one third of patients with liver cirrhosis succumb to variceal bleeding. In these patients, this variceal bleeding is responsible for 50–90% of upper gastrointestinal bleeding episodes. A spontaneous stop of variceal bleeding is observed in less than 50% of cases. Bad coagulation capacity also favors bleeding. Following variceal bleeding, the patient runs a high risk of re-bleeding within the first 6 weeks, the risk being highest during the first 24–73 h after the bleeding event. Therefore, the 30-day mortality from variceal bleeding ranges up to 20%.

Risk Factors of Acute Variceal Bleeding

- Age >60 years
- Kidney failure
- Large variceal convolutes
- Initial hemoglobin <8g/dl

In order to predict a variceal bleeding, other than due to localization, clinical circumstances, and intra-variceal pressure, the size of the varices and the morphology are relevant. Apart from the endoscopic therapy of bleeding-prone varices, primary prophylaxis by beta-blockers (carvedilol) represents the most important medical action.

Medical Therapies

Before attempting endoscopic diagnosis and therapy, a supportive medical treatment for the variceal bleeding must be started (Gawrieh and Shaker 2005; Schepke et al. 2004). Even if there is only a suspicion of a variceal bleeding, taking account of potential contraindications such as severe coronary disease, a vasoactive therapy should be started immediately, e.g., by 1 mg terlipressin intravenously every 4–6 h in a normal-weight patient. It should be continued in hemodynamically stable patients for 2–5 days. Furthermore, in addition to the hemodynamic stabilization of the patient, prevention and treatment of complications are integral parts in a therapeutic concept for variceal bleedings. A frequent monitoring of hemoglobin is essential. If values fall below 7 g/dl, the administration of an erythrocyte concentrate should be considered. However, hemoglobin levels should not exceed 9 g/dl because this could trigger re-bleeding episodes. Crystalloid liquids should be infused at a speed which maintains a urinary output of 50 ml/h; an excess infusion should be avoided. Correcting coagulation and thrombocytes may be useful.

Patients should be regularly checked for signs of sepsis. In patients with liver cirrhosis, infections are frequent, and a prophylactic administration of antibiotics has shown a survival advantage in most studies. Therefore, in these patients, an antibiotic therapy (gyrase inhibitors) even before endoscopic intervention is recommended. The currently available data suggest that both mortality and recurrent bleeding rates are thereby lowered. Depending on the clinical situation, airway safety must be guaranteed. Intensive care surveillance of pulmonary and cardiac function and a regular metabolic monitoring of potential electrolyte disturbances and base/acid imbalances are also integral parts of the therapeutic management.

Tip

In variceal bleeding situations, careful management of volume and blood transfusion is advisable; the hemoglobin value should not exceed 9 g/dl.

Tranexamic acid, which is already a well-established part of the emergency room management, was able to show an improvement of mortality in meta-analyses. However, it has failed to show this benefit in cases of upper GI bleedings.

Table 3.6 Grade of varices according to the endoscopic finding

Grade	Endoscopic finding
I	Small, flat varices
II	Enlarged tortuous variceal convolutes, comprising less than 1/3 of the esophageal lumen
III	Large, snail-shaped variceal convolutes, comprising more than 1/3 of the esophageal lumen

Endoscopic Therapeutic Procedures

The endoscopic ligation of varices (multiband ligation) not only is a successful step in the treatment of acute bleedings but also serves as primary prophylaxis of repeat bleedings. Endoscopically, the varices are classified into three different grades of severity (Table 3.6, Fig. 3.10).

Endoscopic primary prevention, however, has not shown superiority as compared to medical beta-blocker therapy as of today. A combination of both modalities has not been investigated yet. An endoscopic sclerosing therapy of varices is no longer recommended, since pulmonary embolism and sepsis have been reported. But it may still be helpful as an action of last resort.

Endoscopic multiband ligation is the treatment of choice in acute esophageal variceal bleedings. As soon as the suspicion has been raised of this type of bleeding, it should be rapidly prepared for and carried out in all patients. Long-term studies have revealed that rubber band ligation is superior to sclerosing therapy. This ligation procedure, since its first description in 1986, has been further developed and may today be regarded as a routine measure in the treatment of patients with esophageal varices.

One of the biggest steps forward was the development of the multiband ligator (Six-Shooter and Speedband) which made the treatment easier and safer. Esophageal variceal ligation is achieved by occlusion of the varix and subsequent thrombosis. This leads to necrosis of the tissue which then—after some days to weeks—will be discharged while the mucosa is healing. Unlike with sclerotherapy, injuries to the deeper layers of the esophagus are rare.

Recently, soft endoluminal stents have been used for compression of the varices. There is, however, only limited experience with this novelty, and case reports are rare. Acute variceal bleeding is always a life-threatening situation, where the bleeding and other complications endanger the patient's life (Table 3.7).

Endoscopic therapy of varices of the gastric fundus has to be looked upon separately from the treatment of esophageal varices. Here, for primary hemostasis, histoacrylic tissue glue is used. The application is done by injecting the histoacrylic solution via an injection needle which is forwarded through the working channel of the endoscope. By doing so, an immediate clotting of the blood inside the varices is achieved (Fig. 3.11). There is a

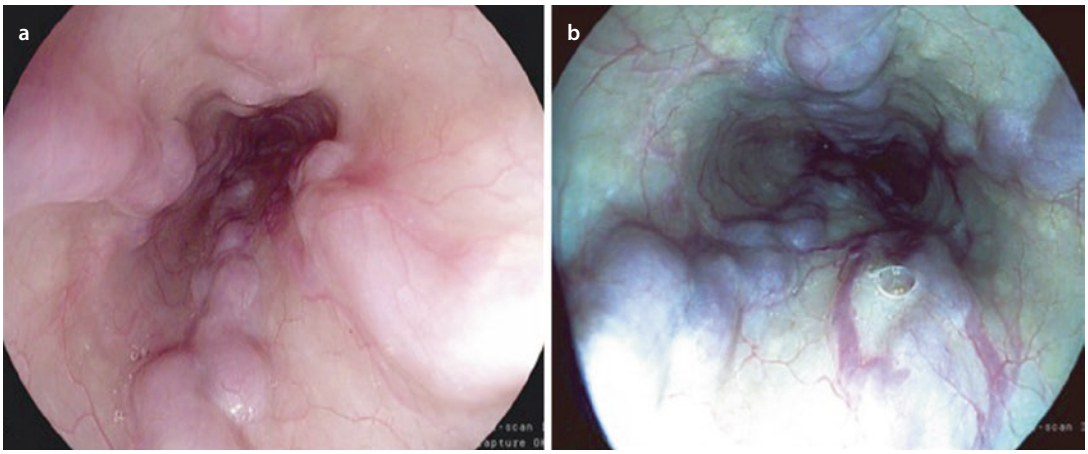

Fig. 3.10 Endoscopic aspect of esophageal varices II° without stigmata of imminent bleeding or red colour signs. **a** i-scan 1 mode. **b** i-scan 3 mode in virtual chromoendoscopy

Table 3.7 Potential complications of endoscopic therapy for variceal bleeding

Type	Complication
Local	Ulcerations, bleedings, strictures, motility disorders, pain, odynophagia, lacerations
Regional	Perforation, mediastinitis, pleural injuries
Systemic	Sepsis, aspiration, ARDS, spontaneous bacterial peritonitis, hypoxemia, portal vein thrombosis
For the physician	Eye injuries during sclerosing action

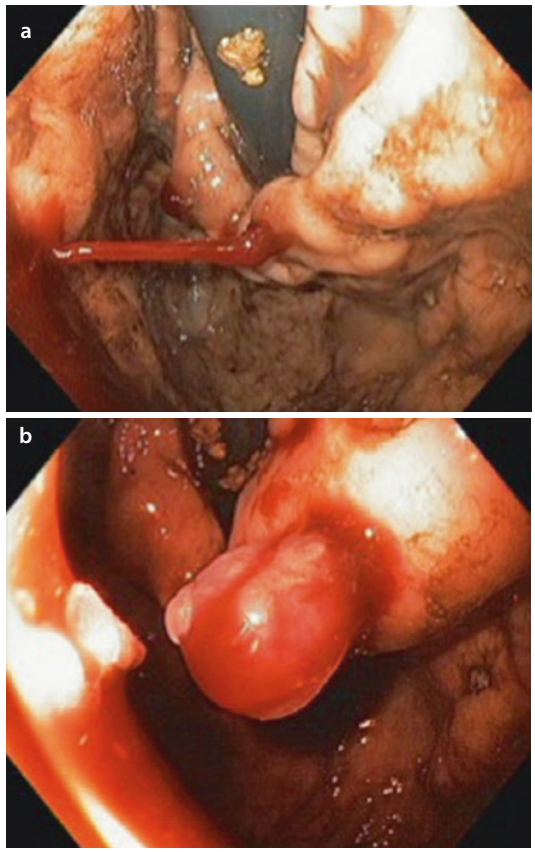

Fig. 3.11 **a** Endoscopic view in retroflexion onto an active spurting fundal variceal bleeding. **b** The bleeding stopped after the injection of n-butyl-cyanoacrylate

great variation as far as volume of the glue and frequency of injections are concerned. We usually take 1–2 ml of morrhuate sodium 5% per single injection, with a total of 12–20 injections per session. It is mandatory to wear protective goggles for eye protection. In addition, during retraction of the catheter, it is important to avoid the working channel of the endoscope being damaged or occluded by residual histoacrylic glue.

In those patients where endoscopic attempts to stop the acute variceal bleeding are unsuccessful, there remains the possibility of a transjugular intrahepatic portosystemic stent shunting (TIPSS). Placement of this shunt type makes it possible to avoid an emergency shunt operation in most patients.

Indications

The indication for an elective variceal band ligation is made following a diagnostic esophagogastroscopy in patients with large third-degree varices or varices ready to bleed («cherry-red spots»). The elective variceal band ligation is supposed to prophylactically reduce bleeding complications in these patients, while studies show a similar effect as compared to medical primary prophylaxis. Informed consent of the patient is obligatory. As of today, however, uncertainty exists concerning the post-ligation time frame until the next prophylactic endoscopy. Expert opinion recommends a repeat endoscopy, possibly with further band ligations, within 7–10 days. An additional interval therapy is helpful after 3/6/12 months.

Personnel Requirements

The requirements are similar to those necessary in patients with non-variceal gastrointestinal bleedings which were described previously. In the case of an elective variceal ligation, a standardized sequence of events should be prepared and carried out. Endoscopist as well as assisting personnel should be experienced in ligation and injection therapy. The elevated risk for significant blood loss during the intervention should be in everybody's mind.

Organizational Requirements

The organizational requirements for the elective treatment by variceal ligation are by no means

completely different from other endoscopic procedures and interventions. After a correct indication, the localization of the intervention and the personnel should be chosen according to their ability to react to possible complications in an adequate and timely fashion. For the event of an emergency intervention because of an acute variceal bleeding, every endoscopy unit should work out clear procedural rules which not only focus on endoscopy but well beyond on consequences for interaction in the whole hospital. Among these there are not only commitments of the intensive care unit and the blood transfusion lab but also the identification of adequate transportation services.

Instrumentation Requirements

The instrumentation requirements are also similar to those necessary in patients with nonvariceal gastrointestinal bleedings. In case of a rubber band ligation, nearly every standard endoscope has an additional device which may be mounted on the tip of the scope. The rubber bands are hung up under tension and may be mechanically released by the endoscopist.

The instrumentation requirements for histoacrylic glue injection are similar to injection therapy with adrenaline. Care has to be taken to prepare the correct mixture.

During injection of tissue glues, self-protection is always mandatory. The endoscopist must wear protective masks and goggles.

Practical Execution

In the case of an acute variceal bleeding, the endoscopic examination should commence fast, even if coagulation might be impaired (Fig. 3.12).

Parallel to that, achieving optimal coagulation parameters should be an essential goal. In order to avoid any aspiration of blood, patients should lie on their side. In acute bleedings, a protective intubation might be required. The first step of the endoscopy is a diagnostic esophagogastroscopy to identify the type and localization of the bleeding.

The treatment of esophageal variceal bleeding should start at the distal end, since the placed rubber bands will narrow the esophageal lumen. Practically, a varix for ligation is identified, the scope positioned, and the varix then sucked into the tip of the augmented scope. Then the rubber band is released (Fig. 3.13). It is important to suck in sufficient mucosa in order to avoid a slippage of the rubber band provoking an additional bleeding. In order to avoid exactly this issue, sufficient distance between ligations should be planned. Although theoretically there is no upper limit for the number of placed rubber bands, during index endoscopy, the number should be restricted to maximally ten. Studies have shown that more than six ligations placed during the first endoscopy have no benefit anymore for the course of the disease.

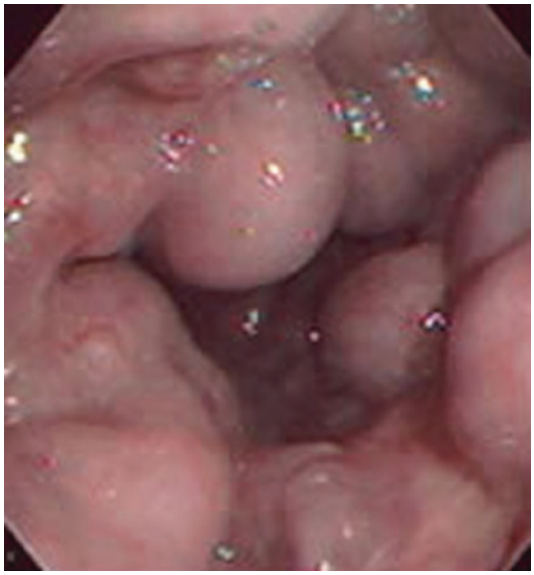

Fig. 3.12 Esophageal varices with signs of imminent bleeding

Tip

Variceal ligations in the esophagus should always start distally and move proximally.

There is a risk of iatrogenic variceal bleedings caused by endoscopy.

When the bleeding site is unclear, the blind attempt to place one or more ligations in the region of the gastroesophageal junction might reduce a more proximal bleeding. Studies have shown that rubber band ligations may achieve hemostasis in 80–100% of cases.

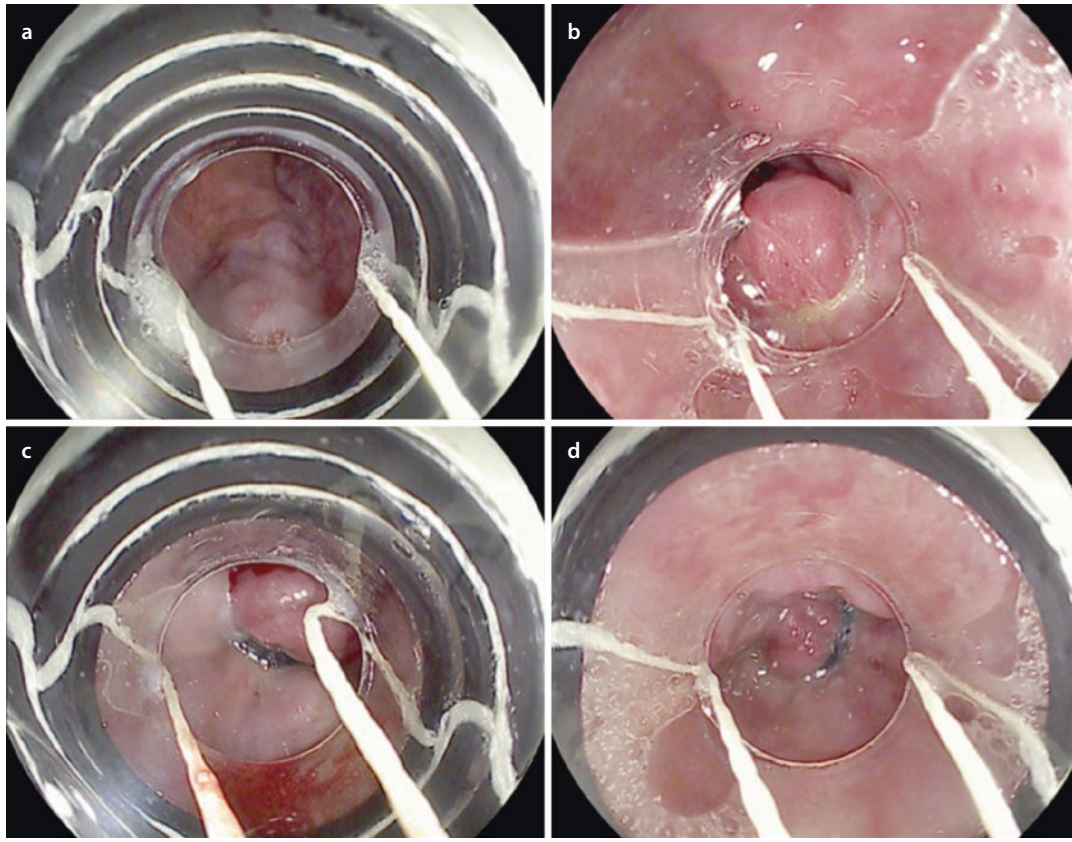

Fig. 3.13 Variceal band ligation with a cap into which the varix is suctioned **a**, **b** before the rubber band is released at the base of the pseudopolyp **c**, **d**

Currently, the following rubber band ligation sets are available: Conmed (Steigmann-Goff endoscopic ligator and Clearvue ligator), Boston Scientific (Speedband Super View Super 7), and Wilson-Cook (four, six, and ten multi-shooter speedband ligators). In acutely bleeding varices, the multi-shooter has definite advantages, whereas single shooters may be used in elective ligations. A combination of ligation and injection has not yet shown a better course in several studies. Furthermore, the combination of ligation and thermotherapy has not been sufficiently investigated and cannot be recommended for routine use. There are early reports on the successful use of Hemospray to treat variceal bleeding (Mostafa et al. 2015) although the license is pending.

Tip

In the treatment of variceal bleedings, antibiotic prophylaxis has to be carried out.

Complications

On the basis of current evidence, the complication rate of ligation therapy is less than that of injection therapy, most likely a transient bacteremia may be observed in patients with variceal ligation. As a consequence of the closure of esophageal varices the hypertensive gastropathy may aggravate. With regard to the instruments, the ligation device of the endoscope may lead to a poorer view within the esophagus. In addition, coagulated blood in the suction chamber can reduce orientation, thereby increasing the risk for secondary bleedings. Quite often, following ligation, the patients complain of retrosternal pain. Esophageal stenoses, strictures, or motility disorders—especially after multiple ligations—are only rare events. A transient bacteremia may be observed. The closure of esophageal varices may worsen the hypertensive gastropathy.

It should be recommended to fast during the following day and to eat soft food only for a couple of days. The healing process of the naturally

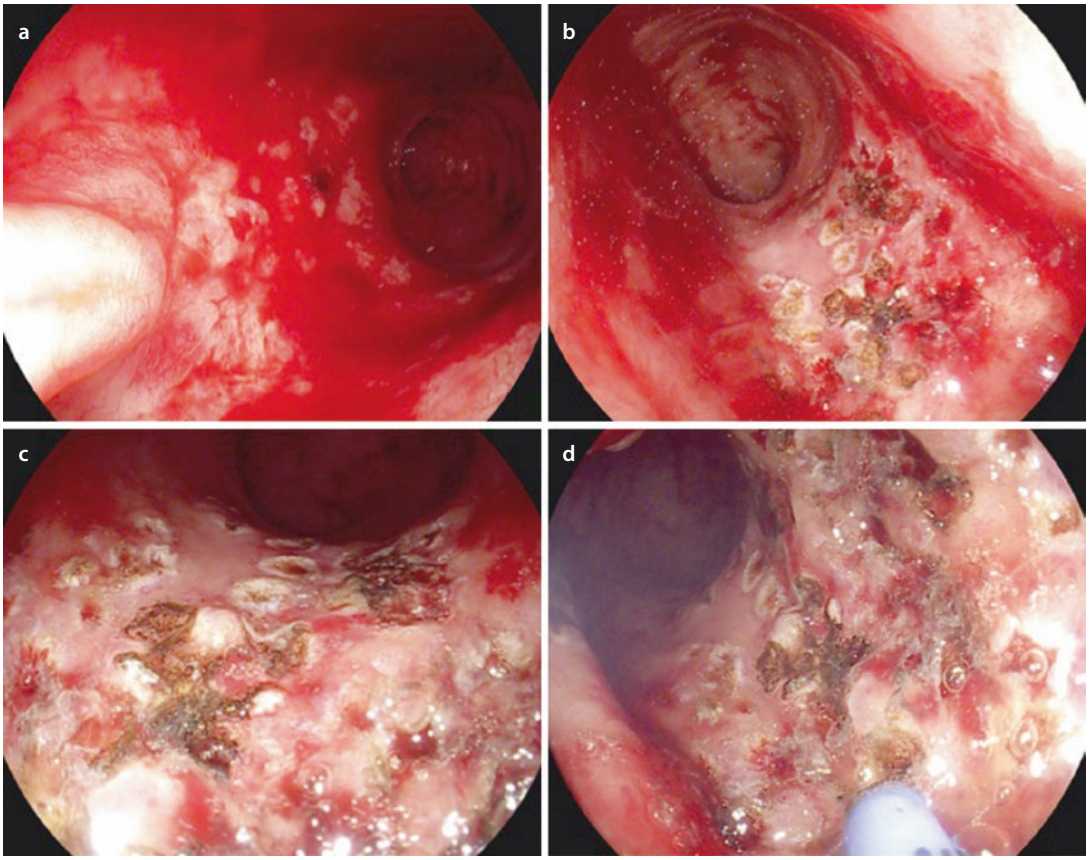

Fig. 3.14 A 72-year-old patient presenting with hematochezia after irradiation of an ovarian cancer. **a–c** Endoscopic finding of broad oozing from multiple rectal and sigmoid erosions. **d** Hematostasis achieved by APC

occurring tissue necroses in the esophagus may be supported by proton pump inhibitors.

3.4 Diffuse Bleedings

The endoscopic therapy of diffuse bleedings from mucosal defects in the gastrointestinal tract is a challenge to the endoscopist. Quite often they are the result of endoscopic mucosa resection or large polypectomies. Ischemic colitis, postirradiation colitis, and tumor bleedings may also contribute to diffuse upper and lower gastrointestinal bleedings (Fig. 3.14).

Here, patients with advanced carcinomas, e.g., of the colon, may develop severe bleedings due to erosions and ulcerations at the tumor surface (Fig. 3.15). So far, the endoscopic possibilities for hemostasis have been limited, since established procedures such as clipping bear an increased risk of perforation and often the tumor surface appears to be too hard. Thermotherapy for hemostasis is an alternative. The biggest potential may be given to the Hemospray, although our positive experience is primarily based on case reports rather than on prospective studies.

▪ Endoscopic Therapies: Thermotherapy for Hemostasis

Diffuse bleedings may be successfully stopped by thermal methods. Here, monopolar and bipolar (BICAP) electrocoagulation, argon plasma coagulation (APC), heat coagulation (heater probe), and laser coagulation are currently available methods (Table 3.8).

Contrary to laser or argon plasma coagulation, which is executed without direct contact to the bleeding site, in electrocoagulation, the mechanical compression of the bleeding vessel is relevant. The coagulation by electric current is only the second step. To reduce the danger of a deeper lesion in the mucosa with subsequent perforation, frequently bipolar electrocoagulation methods are in use today. Here the well-defined flux of the current from one electrode to the other at the tip of the instrument allows for a limitation

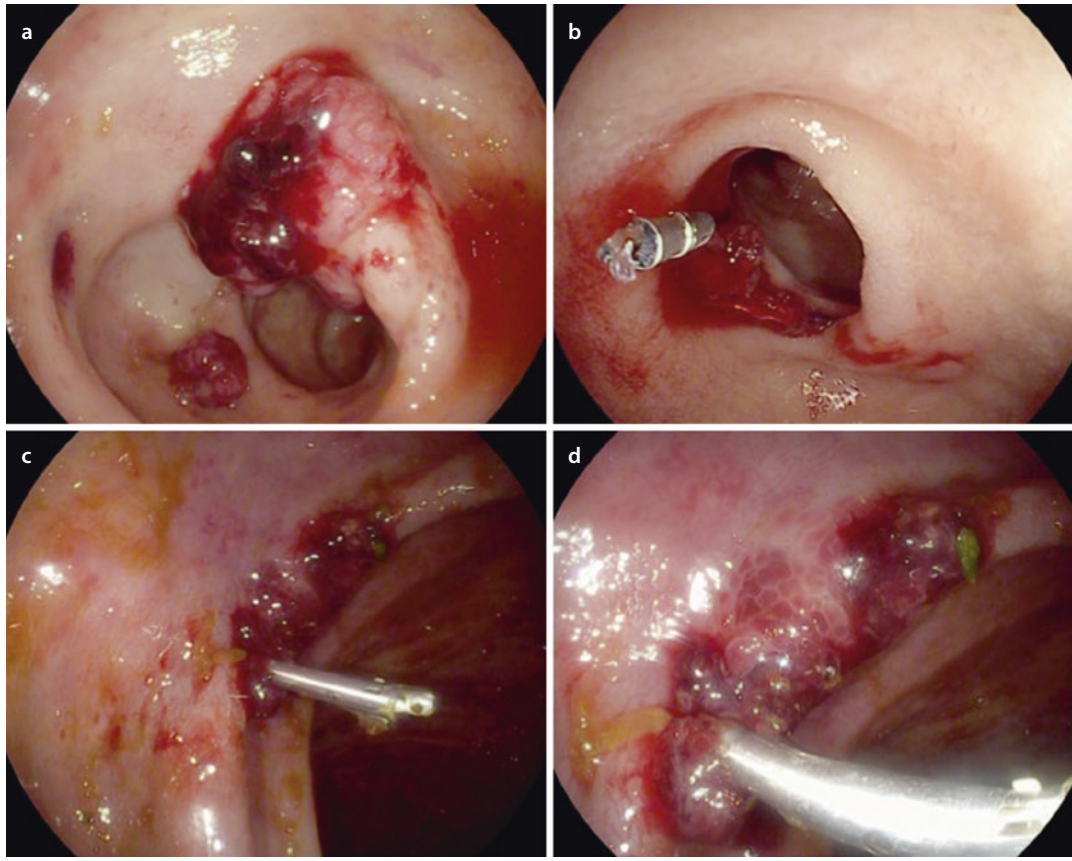

Fig. 3.15 **a–d** Bleeding from a tumor that was treated by application of a single hemoclip

Table 3.8 Different thermic procedures for endoscopic hemostasis

Type of procedure	Function
Electrocoagulation	Heat Coagulation with electricity (mono-/bipolar)
Heater-probe	Coaptive coagulation with high-frequency generator
Laser coagulation	Heat coagulation by energetic lasers
Argon plasma coagulation	Coagulation by ionized argon plasma

of the heated area and the depth of the heating effect. The use of hemostatic powders is comparable to its use in ulcer bleeding (▶ Sect. 3.2).

Indication: Argon Plasma Coagulation (APC)

Argon plasma coagulation was first described in 1994 to control bleeding in gastrointestinal tumors. Further use of this method has since been extended to diffuse superficial mucosal bleedings. Following polypectomy of sessile polyps in piecemeal technique, the application of APC provides a prophylaxis against re-bleeding and might coagulate potential residual polyp tissue. In cases of angiodysplasia, a hemostasis success of 85–100% is described in the literature (Fig. 3.16) (Kwan et al. 2006). The repeated treatment of the GAVE syndrome by APC is able to reduce the need for blood transfusion. The clinical appearance of postradiation proctitis is characterized by telangiectasias and hemorrhagic changes in the mucosa of the rectum. APC may serve here both therapeutically and prophylactically.

Indication: Thermal Contact Coagulation

Heat coagulation by electric current (mono- and bipolar) and coaptive coagulation by means of a high-frequency generator (heater) are in use for stopping acute bleedings. The currently available studies do not show an advantage of one method over the other. In patients with cardiac pacemakers, bipolar coagulation may have the least influence on pacemaker function and should therefore be preferred.

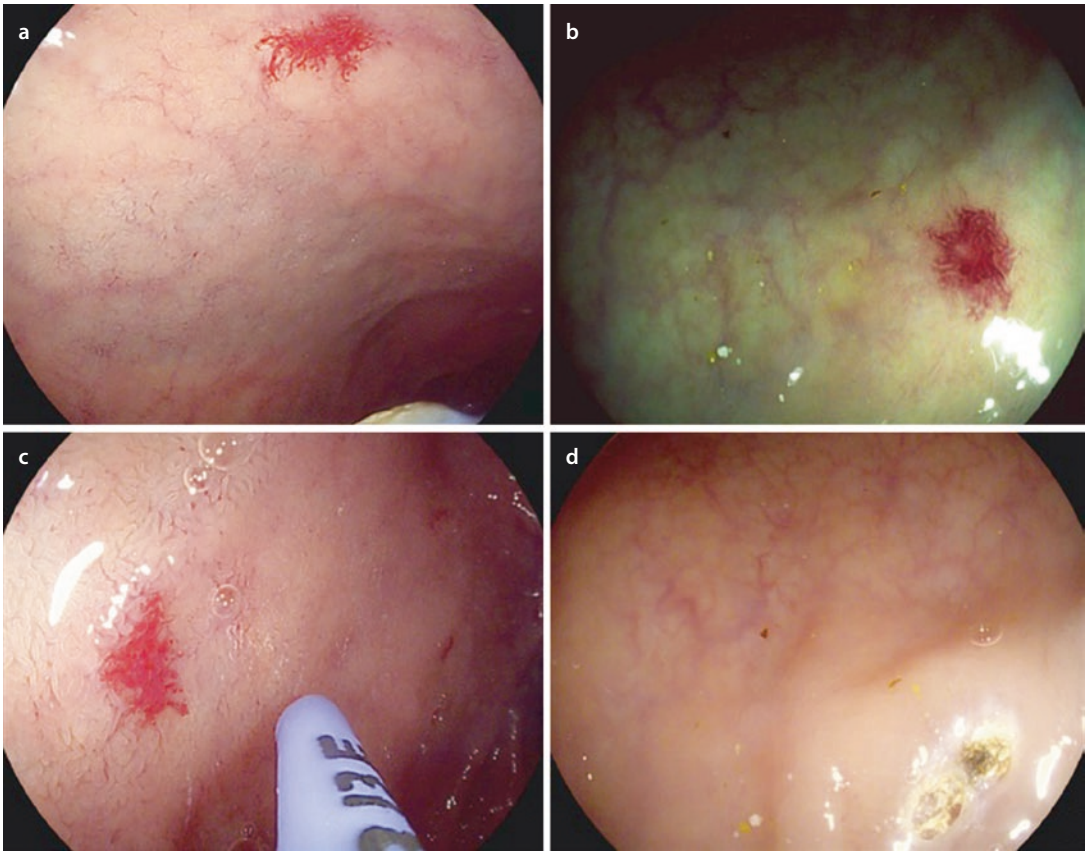

Fig. 3.16 Angioodysplasias are potential sources of gastrointestinal bleeding **a**, **b**. Preventive APC application **c** results in coagulation **d** of the superficial vessel

Personnel Requirements

For the use of all procedures, respecting the recommendations for sedation in endoscopy, next to the investigator, one experienced assistant should be sufficient. Both should be familiar with both preparation and execution of the chosen procedure. Our personal experience indicates that APC and Hemospray in particular are easily manageable after a few applications, provided there was sufficient guidance during the learning phase.

Tip

APC and Hemospray are suitable for inexperienced endoscopists, too, and may be used swiftly and safely.

Organizational Requirements

The organizational requirements are equivalent to those previously described for treatment of variceal and non-variceal bleedings in the gastrointestinal tract.

Instrumentation Requirements: APC

For APC, depending on the localization within the gastrointestinal tract, several sizes of catheters should be at hand. They are available in three different diameters (1.5 mm, 2.3 mm, and 3.2 mm) and two different lengths (220 cm and 300 cm). Following a pre-setting procedure, the further maneuver is steered by a pedal. After starting the instrument, a self-test is usually run automatically. Of course, a sufficient filling status of the argon gas reservoir has to be secured before the examination (► Chap. 2).

Instrumentation Requirements: Thermal Contact Coagulation

For this procedure, a therapeutic endoscope with a large-bore working channel should be used. Alternatively, an endoscope with two working channels serves the same purpose. This allows for simultaneous coagulation and rinsing of the procedural

field. The different probes for a mono- or multipolar electrocautery system (MPEC) or the so-called heat probe have to be at hand, together with the electrosurgical instruments that are typically required. The diameters of the probes are 3.2 mm or 10F. Since thermal contact coagulation procedures are often used in combination with other methods, additionally, hemoclips, loops, injection needles, and diluted adrenaline solution 1:10,000 should lie ready for use.

Practical Execution: Argon Plasma Coagulation

Argon plasma coagulation, in comparison to other thermal methods, is easy to use. Its specific advantage is that the mucosa does not require direct contact to the device. Argon gas is put under high voltage and sprayed onto the mucosa, invading it to a depth of 2–3 mm. As soon as a lesion suitable for APC has been identified, a grounding patch is glued to the thigh of the patient. The catheter for coagulation is then forwarded through the working channel. The generator is started, and a flux rate of the argon gas of 0.8–1 l/min is adjusted. The gas is applied periodically, not continuously. Depending on the extension of the lesion, the magnitude of wattage is chosen. In thinner parts of the gastrointestinal tract, it will range from 20 to 30 W and in thicker areas from 30 to 50 W. The depth of invasion depends both on duration of gas application and on the wattage. Usually the generators have programs in their software which adjust to localization and type of intervention. A visible mark at the end of the APC catheter indicates when the correct position is reached, so as to avoid damage to the endoscope. Successful use is only possible if the distance between catheter tip and mucosa is not more than 1 cm. By repetitive use while varying the catheter position, a calibration by the endoscopist is feasible. As during the whole process, any direct contact to the mucosa must be prevented by all means since this may lead to deep lesions with perforations. The currently available device leaves the choice between three application modalities.

Thermal interventions with too intense punctual coagulation may cause perforations in the gastrointestinal tract.

Practical Execution: Thermal Contact Coagulation

Unlike APC, here a direct contact with pressure on the target area is required. The combination of this direct contact with electric coagulation will affect hemostasis. Frequently, this method is used in combination with injection therapy. This may have the advantage of a more precise coagulation, since adrenaline can achieve hemostasis by itself, thereby clearing the vision for the endoscopist. This effect is similarly desirable in an acute bleeding. Already, pressure onto the bleeding source may reduce the bleeding intensity. The additional coagulation has a higher chance to achieve definite hemostasis. We choose in acute bleedings of average intensity an energy application of 15–20 W over 10 s, repeated 3–5 times. In less severe cases, lower wattage of 10–15 W may be tried first.

When using coaptive coagulation with a high-frequency generator (heat probe), an energy of 20–30 joules is used with similar duration and frequency to that for heat coagulation.

Complications: APC

The APC is a safe method with few complications. When used at the right colon, a perforation risk of 0.2% has to be considered. Further potential complications comprise subcutaneous emphysema and pneumoperitoneum. In one case report, an argon gas explosion triggered a colon perforation.

Complications: Thermal Contact Coagulation

In addition to secondary bleedings caused by the intervention itself, perforations are possible. The complication rate depends on the experience of the endoscopist and the depth of penetration of the thermal procedure. A so-called post-endoscopic submucosal dissection electrocoagulation syndrome (PEECS) is observed if the thermal application reaches down to the muscular and serosal layers without the signs of perforation with fever, muscular defense, and leukocytosis being apparent. In patients with ESD, this complication has been reported in up to 40% of procedures. Risk factors appear to be lesions >3 cm and all localizations outside the rectosigmoid colon.

In the case of combined therapies with adrenaline injections, systemic side effects such as tachycardia and arrhythmia are possible.

3.5 Summary

Today, the treatment of gastrointestinal bleedings is the preferred domain of gastrointestinal endoscopy. Depending on localization, the bleedings

Table 3.9 Type of bleeding and preferred endoscopic hemostatic technique

	Bleeding type	Endoscopic hemostatic technique
Upper GI	Ulcer	Injection, clipping, powder
	Esophageal varices	Ligation, injection, powder (off-label)
	Gastric varices	Injection, powder (off-label)
Lower GI	Diverticula	Injection, powder, thermal, clipping
	Hemorrhoids	Ligation
	Post-polypectomy	Clipping, thermal, powder (off-label)
	Angiodysplasias	Thermal
	Diffuse	Thermal, powder (off-label)

are classified as upper, middle, or lower gastrointestinal bleedings. Further differentiations group the bleedings as peptic, variceal, and diffuse or as tumor bleedings. Several endoscopic hemostatic techniques are available which are often used in combination (Table 3.9). The success rate of endoscopic hemostatic techniques is 80–100%.

Gastrointestinal bleedings are interdisciplinary challenges requiring endoscopic, medical, and intensive care therapies. Knowledge about the total spectrum of available diagnostic and therapeutic procedures is essential to provide a targeted and effective therapy to patients involved.

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