Hemostasis of Acute Nonvariceal Upper Gastrointestinal Bleeding

11

Amir Klein and Ian M. Gralnek

Introduction

The causes of acute non-variceal upper gastrointestinal bleeding (NVUGIB) include gastroduodenal peptic ulcer (20–50 %), gastrointestinal erosions (8–15 %), erosive esophagitis (5–15 %), Mallory-Weiss tear (8–15 %), angiodysplasia/gastric antral vascular ectasia (GAVE) (5 %), and benign and malignant tumors of the upper gastrointestinal (GI) tract (5 %) [1–3]. Upper endoscopy in patients presenting with acute NVUGIB is effective for both diagnosis of the bleeding cause and for therapy, as indicated. Endoscopic hemostasis significantly reduces rebleeding rates, blood transfusions, length of hospital stay, need for surgery, and/or mortality [4–13]. Furthermore, early upper endoscopy, performed within 24 h of presentation, improves patient outcomes [5]. This chapter will highlight the role of endoscopic evaluation and risk stratification, as well as the various endoscopic modalities available for hemostasis of acute NVUGIB.

Timing of Endoscopy in Acute NVUGIB

After correction of coagulopathy and hemodynamic stabilization with intravenous fluid resuscitation, patients with presumed acute upper GI bleeding should undergo early endoscopy [6, 7]. Early endoscopy is defined as esophagogastroduodenoscopy (EGD) performed within 24 h of patient presentation. Although early endoscopy is advocated in most patients, select high-risk patients, such as those with severe coagulopathy, acute coronary syndrome, or suspected bowel perforation, should have their upper endoscopy examination deferred until the clinical situation is fully evaluated and stabilized. In contrast, low-risk patients, identified by clinical pre-endoscopy risk stratification scores (e.g., Glasgow-Blatchford Bleeding Score or the Clinical Rockall Risk Score), may be considered for outpatient management [11–13].

Very early or emergent upper endoscopy (defined as within 2–12 h of patient presentation) has not been shown to confer additional benefit or

Electronic supplementary material: The online version of this chapter (doi:10.1007/978-1-4939-3085-2_11) contains supplementary material, which is available to authorized users. Videos can also be accessed at http://link.springer.com/chapter/10.1007/978-1-4939-3085-2_11.

A. Klein, M.D.
Department of Gastroenterology, Rambam Health Care Campus, Haifa, Israel

Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

I.M. Gralnek, M.D. M.S.H.S., F.A.S.G.E. (✉)
Department of Gastroenterology and Hepatology, Ha'Emek Medical Center, Afula, Israel

Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
e-mail: ian_gr@clalit.org.il

L.M. Wong Kee Song et al. (eds.), *GI Endoscopic Emergencies*,
DOI 10.1007/978-1-4939-3085-2_11

alter patient outcomes. A review of meta-analyses on the subject found no significant difference between urgent (1–12 h) and early (>12 h) endoscopy in terms of rebleeding rates, need for surgery, or mortality [8]. One controlled study, however, reported significantly shorter hospital length of stay and lower costs in favor of very early (1–2 h) as opposed to elective (1–2 days) upper endoscopy [14]. Endoscopy performed within hours of presentation will likely reveal more high-risk bleeding stigmata, such as active bleeding, a non-bleeding visible vessel, or an adherent clot. However, these endoscopic findings, which invariably lead to more therapeutic interventions, are not clearly beneficial with regard to patient outcomes [14, 15].

Early upper endoscopy may actually confer additional risk to the patient when the procedure is performed during off hours (nights and weekends). An increased risk in oxygen desaturation has been described in patients undergoing urgent (within 2 h) versus early (2–24 h) endoscopy [16]. Moreover, a large cohort study from the United Kingdom showed a strong correlation between increased mortality and the practice of after-hours endoscopy [17].

Endoscopic Hemostatic Modalities for NVUGIB

A variety of endoscopic devices for hemostasis exists for the management of acute NVUGIB, including injection therapies, thermal modalities, mechanical devices, or a combination thereof. This section will focus on the technical aspects and applications of these various techniques.

Injection Therapy

The primary mechanism of action of injection therapy is local tamponade resulting from the volume effect. The addition of epinephrine (1:10,000 or 1:20,000 dilution) in saline solution has a secondary pharmacological effect that produces local vasoconstriction [18]. Agents, such as normal saline or dilute epinephrine, are usually injected in 1–2-ml aliquots around the bleeding stigmata in a 4-quadrant fashion, if feasible. There are data to suggest that higher injected volumes of dilute epinephrine (>10–20-ml total) are superior to small volume injection for achieving hemostasis in peptic ulcer bleeding (Video 11.1) [19]. Care is needed, however, to avoid over-injection on the side of the lesion closest to the tip of the endoscope as this may elevate the lesion away from the field of view and hamper access for subsequent therapy.

Sclerosing agents, such as ethanol, ethanolamine, and polidocanol, produce hemostasis by causing direct tissue injury and vascular thrombosis. However, the injection of a sclerosant is associated with an unpredictable depth of injury, which can lead to delayed perforation. Sclerosing agents are not commonly used for NVUGIB due to the availability of safer and equally effective alternatives for hemostasis. Tissue adhesives, such as thrombin, fibrin sealant, and cyanoacrylates, are another class of injectable agents that can be used to create a primary seal at the site of bleeding. These agents, however, are not commonly used in the treatment of NVUGIB and are not approved by the US Food and Drug Administration (FDA) for this purpose.

Endoscopic injection is performed using catheter needles, which consist of an outer sheath and an inner hollow-core needle (19–25 gauges). By actuating a handle on the end of the sheath, the endoscopist or assistant can retract the needle into the sheath for safe passage through the working channel of the endoscope. With the catheter needle in position near the site of bleeding, the needle is extended out of the sheath, and the agent is injected using a syringe attached to the catheter handle after needle puncture into the submucosal space [18]. Table 11.1 lists available injection needles.

Thermal Therapy

Thermal devices used in the treatment of GI bleeding include contact and noncontact modalities (Table 11.2). Contact thermal devices include heater probes, which generate heat directly at the tip of the probe, and bipolar electrocoagulation

Table 11.1 Injection needles[a]

Manufacturer	Device name	Sheath diameter (French)	Sheath length (cm)	Needle gauge	Needle length (mm)
Boston Scientific (Natick, MA)	Interject sclerotherapy needle	7	200, 240	23, 25	4, 6
ConMed Endoscopic Technologies (Chelmsford, MA)	Click-Tip injection needle	7	180, 230	19, 22, 25	4, 6
	Flexitip disposable sclerotherapy needle	7	180, 230	4, 5	
	Sure shot injection needle	7	160, 230	5	
Cook Medical (Winston-Salem, NC)	Acujet variable injection needle	7	220	23, 25	
	Injectaflow variable injection needle	7	220	23, 25	
Olympus America (Center Valley, PA)	Injector force injection needle	7	230	21, 23, 25	4, 5, 6, 8
US Endoscopy (Mentor, OH)	Articulator injection needle	7	160, 230, 350	25	4,5
	Carr-Locke injection needle	7	230	25	5
	Vari-Safe injection needle	7	230	23	4, 5, 7
Kimberly-Clark (Roswell, GA)	Injection needle catheter	7	160, 200, 240	23, 25	4, 6
Telemed Systems (Hudson, MA)	Sure-Stop sclerotherapy needle	5,7	160, 240	25	4, 5

[a]Adapted from Conway JD, Adler DG, et al. Endoscopic hemostatic devices. Gastrointest Endosc 2009;69:987–96

Table 11.2 Contact and noncontact thermal devices[a]

Manufacturer	Device name	Sheath diameter (French)	Sheath length (cm)	Special features
Boston Scientific (Natick, MA)	Gold probe	7, 10	300, 350	
	Injector gold probe	7, 10	210	Integrated injection needle
ConMed Endoscopic Technologies (Chelmsford, MA)	Bicap superconductor, multielectrode bipolar probe	5, 7, 10	200, 300, 350	
	Palladium tip bipolar hemostasis probe	7, 10	300	
	Beamer argon probe	5, 7, 10	160, 230, 320	
Cook Medical (Winston-Salem, NC)	Quicksilver bipolar probe	7, 10	350	
Olympus America (Center Valley, PA)	Solar probe	7, 10	350	
	Heat probe	7, 10	230, 300	Reusable
	Coagrasper	7	165	
US Endoscopy (Mentor, OH)	Bipolar hemostasis probe	7, 10	350	
Canady (Hampton, VA)	Canady plasma GI probe	5, 7	230, 340	Straight, side fire
ERBE (Marietta, GA)	APC probe	5, 7, 10	50, 220, 300	Straight
	FiAPC probe	5, 7, 10	50, 220, 300	Side circumferential fire

[a]Adapted from Conway JD, Adler DG, et al. Endoscopic hemostatic devices. Gastrointest Endosc 2009;69:987–96

probes, which generate heat indirectly by passage of an electrical current between closely spaced electrodes at the tip of the probe. Noncontact thermal devices include argon plasma coagulation and laser therapy, although the latter is rarely used nowadays.

Heat generated from these thermal devices leads to edema, coagulation of tissue proteins, contraction of vessels, and indirect activation of the coagulation cascade, resulting in a hemostatic bond [18, 20]. Heater and bipolar probes also benefit from local tamponade (mechanical pressure of the probe tip directly onto the bleeding site) combined with heat or electrical current to coagulate blood vessels, a process known as "coaptive coagulation." This process minimizes the heat sink effect, whereby energy is lost due to blood flow through a non-compressed vessel.

The heater probe consists of a Teflon-coated hollow aluminum cylinder with an inner heating coil. A thermo-coupling device at the tip of the probe maintains a constant temperature. A foot pedal controls heat activation as well as water-jet irrigation through the probe. Heater probe activation delivers energy to the diode in the probe tip. Once the pulse has been initiated, the duration of activation is predetermined and cannot be stopped until the entire amount of preselected energy is delivered [21]. A setting of 30 J is suggested for peptic ulcer bleeding (Video 11.1) and gastric Dieulafoy lesions. A setting of 15 J is recommended for other lesions, such as a bleeding Mallory-Weiss tear and vascular ectasias.

The bipolar probe delivers thermal energy by completion of an electrical circuit between positive and negative electrodes on the tip of the probe as current flows through non-desiccated tissue. In contrast to monopolar devices, the electrical circuit is confined to the tip of the probe, and so no grounding pad is required. As the targeted tissue desiccates, there is decrease in electrical conductivity, thereby limiting the maximum temperature, depth, and area of tissue injury. A foot pedal controls the delivery of the energy in watts [20]. The usual setting for peptic ulcer bleeding and gastric Dieulafoy lesions is 20 W delivered in 7–10 s application (referred to as tamponade stations) prior to removal of the probe. Several applications, with moderate to firm probe-tissue contact pressure, may be required until active bleeding is controlled and/or white coagulum formation with shallow cavitation of the treated site is observed. A lesser amount of energy (12–15 W) and shorter application duration (3–5 s) are recommended for other lesions, such as a bleeding Mallory-Weiss tear and vascular ectasias. Similar to the heater probe, built-in water-jet irrigation in the bipolar probe facilitates identification and precise targeting of the actively bleeding point prior to coagulation and aids in sliding the probe off the coagulated, sticky tissue.

Argon plasma coagulation (APC), a noncontact device, uses high-frequency monopolar alternating current conducted to the target tissue through a stream of ionized argon gas to achieve coagulation of superficial tissue [22]. As the coagulated tissue surface loses its electrical conductivity, the plasma stream shifts to adjacent non-desiccated (conductive) tissue, which again limits the depth of tissue injury [18]. If the APC catheter is too far from the target tissue, there is no ignition of the gas, and depression of the foot pedal results only in flow of inert argon gas. Coagulation depth is dependent on the generator power setting, duration of application, and distance from the probe tip to the target tissue [22, 23]. The optimal distance between the probe and target tissue ranges from 2 to 8 mm [24]. Commercially available APC systems (ERBE USA, Marietta, GA; ConMed Electrosurgery, Centennial, CO; Canady Technology, Pittsburgh, PA; Genii, St. Paul, MN) include a specialized electrosurgical generator capable of high-frequency monopolar current, an activation foot pedal, an argon gas cylinder, disposable grounding pads, and flexible single-use APC probes. An adjustable gas flowmeter allows argon gas flow rates of 0.5–7 l/min. APC probes are composed of Teflon with a ceramic tip encasing the tungsten electrode and are available as end-firing, side-firing, and circumferential-firing probes. APC is primarily used for the treatment of superficial mucosal vascular lesions, such as vascular ectasias and GAVE (Video 11.2). Suggested settings are a power of 30–45 W (depending on the APC generator utilized) and an argon flow rate of 1 l/min.

Table 11.3 Clipping devices[a]

Manufacturer	Device name	Sheath diameter (French)	Sheath length (cm)	Jaw opening width (mm)	Special features
Boston Scientific (Natick, MA)	Resolution clip	7	155, 235	11	2-prong clip
Cook Medical (Winston-Salem, NC)	Triclip	7,8	207	12	3-prong clip
	Instinct clip	7	230	16	2-prong clip rotatable
Olympus America (Center Valley, PA)	Quickclip 2	7	165, 230	9	2-prong clip rotatable
	Quickclip 2 long	7	165, 230	11	2-prong clip rotatable
	QuickClipPro	7	165, 230	11	2-prong clip rotatable

[a]Adapted from Conway JD, Adler DG, et al. Endoscopic hemostatic devices. Gastrointest Endosc 2009;69:987–96

Mechanical Therapy

Endoscopic mechanical therapies include clips (Table 11.3) and band ligation devices. Through-the-scope (TTS) endoscopic clips are deployed directly onto the bleeding site (e.g., active bleeding, non-bleeding visible vessel) and typically fall off within days to weeks after placement [1, 25]. All endoscopic clipping devices have three primary components: a metallic double- or triple-pronged preloaded clip, a delivery catheter, and a handle to operate and deploy the clip. Clips are available in a variety of jaw lengths and opening widths. The delivery catheter consists of a metal cable with or without a protective sheath. The tip of the metal cable has a hook onto which the clip is attached. The handle consists of two sliding components: the first allows advancement of the metal cable holding the clip out of the protective sheath, if present, and the second is the plunger that controls the opening, closing, and deployment of the clip. After insertion of the clip through the working channel of the endoscope, the clip is extended out of the sheath, if one is present. The clip is then positioned over the target area and opened with the plunger handle. A rotation mechanism on the handle is available on some commercially available clips, and this allows the endoscopist to change the orientation of the clip at the site of bleeding. The jaws of the clip are applied with pressure and closed onto the target tissue by using the device handle [25, 26]. Some clips have reopening capabilities and can be repositioned, whereas others are permanently deployed and released upon clip closure. Similarly, some clips are automatically released on deployment, while others require repositioning of the plunger handle to release the deployed clip from the catheter. Hemostasis is achieved by mechanical compression of the bleeding site (Video 11.3). Both the operator and assistant should be well acquainted with the various clip deployment mechanisms so as to facilitate easy and efficient utilization. Clip selection is mostly dependent on device availability, operator preference, and familiarity with a particular clip.

Emerging data suggest that the over-the-scope clip (OTSC; Ovesco, Tübingen, Germany), developed for closure of small mural defects, may also be effective for the management of focal nonvariceal GI bleeding lesions (e.g., peptic ulcer, Dieulafoy lesion, post-polypectomy bleeding site) (Figs. 11.1 and 11.2) [27–29]. The OTSC may prove superior to standard TTS clips because of its ability to grasp more surrounding tissue and apply a greater compressive force (Video 11.4). However, no comparative data are available at this time. The OTSC device includes an applicator cap carrying the clip, a memory-shaped nitinol clip in the form of a bear claw when released, and a rotating hand wheel for clip deployment. The applicator cap with the mounted nitinol clip is affixed to the tip of the endoscope in a manner similar to that of a variceal band ligation device. Caps are available in three sizes to accommodate various endoscope diameters: 11 mm (designed for endoscope diameters 9.5–11 mm), 12 mm (for endoscope diameters 10.5–12 mm), and 14 mm (for endoscope diameters 11.5–14 mm). Caps are also available in two depths (3 and 6 mm) to allow variation in the amount of tissue desired during

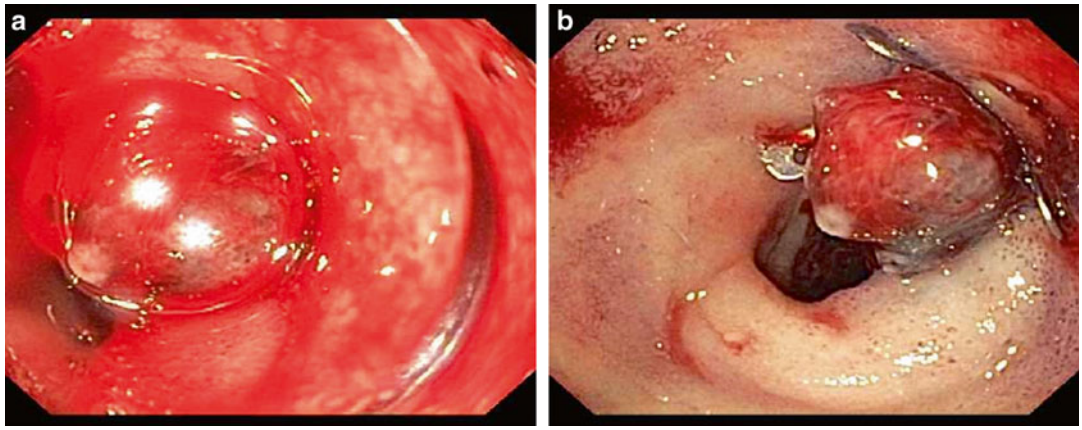

Fig. 11.1 (**a**) Cap-assisted access to an actively bleeding duodenal ulcer in a difficult location. (**b**) Successful hemostasis achieved with placement of an over-the-scope clip

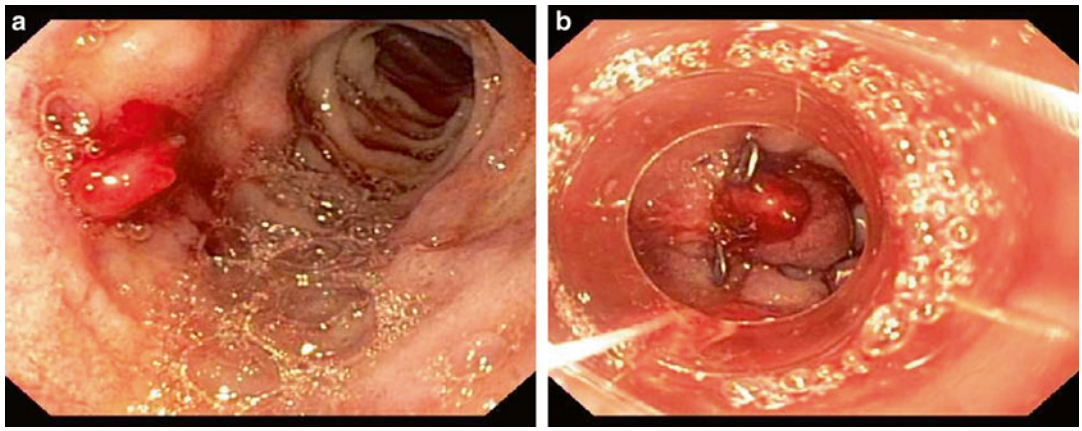

Fig. 11.2 (**a**) Duodenal Dieulafoy lesion. (**b**) Hemostasis achieved with placement of an over-the-scope clip

suction. Clips come in three different sizes to match the cap sizes and also in three different shapes of teeth: type A (rounded teeth), type T (pointed teeth), and type GC (longer pointed teeth). Clips with rounded teeth are used when the goal is tissue compression for hemostasis, particularly in the thinner-walled esophagus and colon. The applicator cap incorporates a clip release thread, which is pulled retrograde through the working channel of the endoscope and fixed onto a hand wheel mounted on the working channel access port of the endoscope. The clip is released by turning the hand wheel, in a manner similar to deploying a variceal ligation band [27].

Endoscopic band ligation (EBL) devices, commonly used in esophageal variceal bleeding, can also be effective at treating select NVUGIB lesions. EBL involves placement of elastic bands under the suctioned target tissue to produce mechanical compression and tamponade (e.g., Dieulafoy lesion) (Fig. 11.3 and Video 11.5) [30].

Emerging Endoscopic Techniques for NVUGIB

Video Capsule Endoscopy

Recently, video capsule endoscopy has been shown to be an effective method to identify acute upper GI bleeding in the emergency department. Capsule endoscopy identified gross blood in the

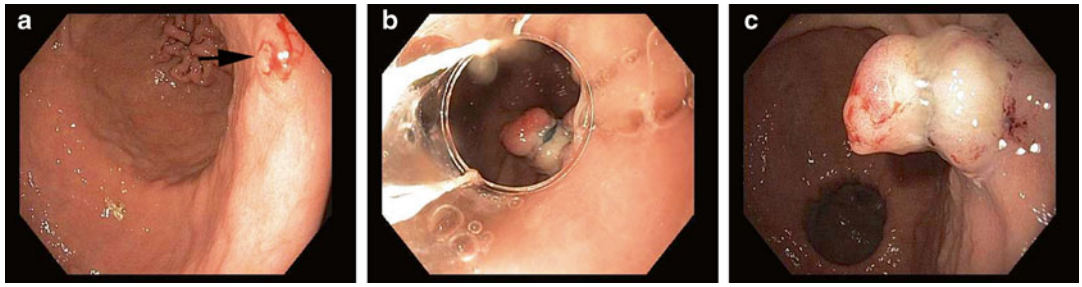

Fig. 11.3 (**a**) Gastric Dieulafoy lesion. (**b**) Band ligation performed. (**c**) Post band ligation appearance

upper GI tract, including the duodenum, significantly more often than nasogastric tube aspiration, and identified inflammatory lesions to a similar degree as EGD. Capsule endoscopy may also facilitate patient triage and earlier endoscopy but at this point in time should not be considered a substitute for EGD [31].

Capsule endoscopy only offers diagnostic capabilities and cannot offer the dual diagnostic and therapeutic advantage of EGD in the hands of a skilled endoscopist for the treatment of NVUGIB. The role of real-time capsule endoscopy might be in a setting where endoscopic services are not readily available and to ascertain the presence of upper GI bleeding before a patient is referred to a tertiary facility.

Topical Hemostatic Agents

Hemostatic sprays have been used thus far in a limited number of patients with acute upper and lower GI bleeding, with good results overall [32]. The advantages of noncontact spray catheter delivery of hemostatic agents include ease of use, lack of need for precise lesion targeting, access to lesions in difficult locations, and the ability to treat a larger area (Video 11.6). Various granules or powders have been used in military combat situations to treat compressible external hemorrhage in battlefield casualties. One of these compounds, TC-325 (Hemospray; Cook Medical Inc., Winston-Salem, NC), is currently undergoing evaluation as a hemostatic agent for endoscopic use [32, 33]. TC-325 is a proprietary, inorganic, absorbent powder that rapidly concentrates clotting factors at the bleeding site, forming an adherent coagulum. Hemospray is a handheld device consisting of a pressurized CO2 canister for delivery of the powder, a TTS delivery catheter, and a reservoir for the powder cartridge. The powder is delivered via push button in 1–2-s bursts until hemostasis is achieved. The maximum amount of TC-325 that can be safely administered during a single treatment session has not yet been established [32]. The coagulum typically sloughs within 3 days and is naturally eliminated. Hemospray has received regulatory clearance in some countries but is not yet approved by the US FDA.

Hemostatic sprays derived from plant products have also been evaluated. Clinical experience with these agents for endoscopic hemostasis is currently limited to the off-label use of the Ankaferd Blood Stopper (ABS; Ankaferd Health Products Ltd, Istanbul, Turkey), a mixture of extracts from several plants that is approved in Turkey for topical treatment of dental and postsurgical external bleeding [34–39]. ABS promotes formation of a protein mesh that acts as an anchor for erythrocyte aggregation without significantly altering coagulation factors or platelets. The ABS solution, available in 2-mL vials, is delivered onto the bleeding site via an endoscopic spray catheter until an adherent coagulum is formed [35]. EndoClot (EndoClot Plus Inc., Santa Clara, CA) consists of absorbable modified polymers and is intended to be used as an adjuvant hemostatic agent to control bleeding in the GI tract. It is a biocompatible, non-pyogenic, starch-derived compound that rapidly absorbs water from serum and concentrates platelets, red blood cells, and coagulation proteins at the

bleeding site to accelerate the clotting cascade. The particles are subsequently cleared from the bleeding site with no remaining residue a few hours to days later. There are only scant data on this product's safety or efficacy [35]. The current limited data demonstrate the potential for hemostatic sprays to be used as definitive or bridge therapy. The efficacy of these agents is unknown in brisk arterial bleeding and may be limited because of the rapid "wash-away" effect of the hemostatic agent by ongoing blood flow. The exact role and overall safety of hemostatic sprays remain to be delineated. Additional data and prospective comparative studies involving a larger number of subjects are needed.

Preprocedural Considerations

In addition to fluid resuscitation and correction of coagulopathy, as previously mentioned, an assessment should be made for preemptive endotracheal intubation for airway protection, particularly in the setting of active hematemesis, encephalopathy, and/or difficult airway (e.g., short, thick neck). The procedure should also be aborted temporarily if a large amount of retained blood and clots is found in the stomach at the time of endoscopy to enable airway protection for prevention of aspiration.

A dual channel or therapeutic channel (3.7 mm) upper endoscope is recommended for the assessment of acute upper GI bleeding. The larger working channel enables better suction capability and the passage of large (10 Fr) rather than small (7 Fr) diameter thermal probes for hemostasis. A pedal-activated water-jet irrigation device coupled to the entrance port of the working channel or built in the endoscope facilitates washing the mucosa of adherent bloody material and aids in precisely identifying the actively bleeding point for targeted hemostasis.

Common Causes of NVUGIB

Peptic Ulcer

Gastroduodenal ulcer remains the leading cause of acute NVUGIB. Mortality rates associated with peptic ulcer bleeding are still about 5–10 %. Endoscopic findings in peptic ulcer bleeding associated with increased morbidity and mortality include ulcer location (e.g., high lesser gastric curve, posterior duodenal bulb), ulcer size $\geq$ 2 cm, pulsatile arterial bleeding, and large bleeding vessel ($\geq$2 mm) [6, 9]. Endoscopic assessment and risk stratification prior to application of a specific hemostatic technique are essential in guiding the appropriate endoscopic treatment of patients with acute upper GI bleeding due to peptic ulcer.

The endoscopic stigmata of an ulcer provide prognostic information regarding the risk of ongoing bleeding or rebleeding and the necessity for therapeutic intervention (Table 11.4). In Europe and Asia, the Forrest classification for stigmata of recent hemorrhage (Fig. 11.4) is

Table 11.4 Rates of rebleeding before and after endoscopic therapy and rates of surgery and mortality with no endoscopic therapy, stratified by endoscopic stigmata

Endoscopic stigmata	Forrest classification	Prevalence (%)	Persistent bleeding or rebleeding with no endoscopic treatment (%)	Rebleeding after endoscopic hemostasis (%)	Surgery for bleeding with no endoscopic treatment (%)	Mortality with no endoscopic treatment (%)
Active bleeding	I	12–18	55–90	15–30	35	11
Non-bleeding visible vessel	IIa	8–22	43–50	15–30	34	11
Adherent clot	IIb	8–17	22–33	0–5	10	7
Flat pigmented spot	IIc	16–20	8–10	NA	6	3
Clean base	III	42–55	5	NA	0.5	2

Data from Refs. [1, 6, 10, 40]

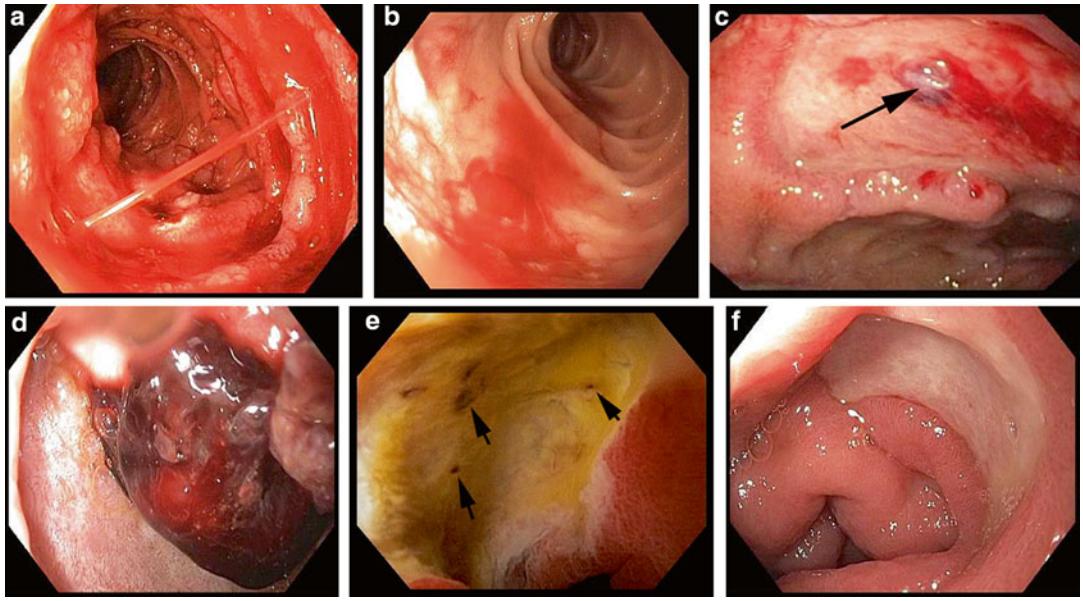

Fig. 11.4 Endoscopic stigmata of bleeding peptic ulcer. High-risk lesions include (**a**) Forrest 1A, spurting blood; (**b**) Forrest 1B, oozing blood; (**c**) Forrest IIA, non-bleeding visible vessel; (**d**) Forrest IIB, adherent clot. Low-risk lesions include (**e**) Forrest IIC, flat pigmented spots, and (**f**) Forrest III, clean base

commonly used, whereas in North America, descriptive terms are the norm. Most patients with ulcer bleeding have low-risk stigmata (flat pigmented spot or clean base) and thus do not require endoscopic hemostasis. High-risk stigmata (active bleeding, non-bleeding visible vessel, or adherent clot) are encountered in up to 35 % of patients with acute peptic ulcer bleeding [10, 40]. Active bleeding is subcategorized as spurting or oozing, although most studies of prevalence have combined these categories into "active ulcer bleeding" [41]. Results from prospective trials, however, suggest they should likely be viewed separately because the risk of further bleeding with spurting bleeding is higher than with oozing bleeding [42, 43].

Deeply penetrating, indurated ulcers with high-risk stigmata are problematic to treat endoscopically. They are usually located in the high lesser curve of the stomach or the posteroinferior wall of the distal duodenal bulb, supplied by large vessels originating from the left gastric artery or gastroduodenal artery, respectively (Video 11.7). Furthermore, these are difficult locations to access at endoscopy. In some cases, a clear cap placed at the tip of the endoscope aids in maintaining a more stable position and provides a working window for passage of hemostatic accessories. This technique is particularly helpful for accessing lesions at the duodenal angle in the setting of an edematous, shortened duodenal bulb. However, the application of firm tamponade pressure using a thermal probe on a (usually large) vessel within a penetrating ulcer base may result in perforation. Clip placement is also of limited value in this setting since the clip does not have sufficient compression force to close the indurated ulcer base. Moreover, an attempt at clip closure may result in avulsion of the vessel and precipitation of torrential bleeding (Fig. 11.5). Thus, ulcers with high-risk stigmata in deeply fibrotic bases are generally not amenable to endoscopic therapy and should be referred for angiographic embolization or surgical intervention.

Esophagitis

Erosive esophagitis can cause up to 8 % of acute upper GI bleeding. It is more commonly seen in patients who are already in hospital for another reason and with an indwelling nasogastric tube.

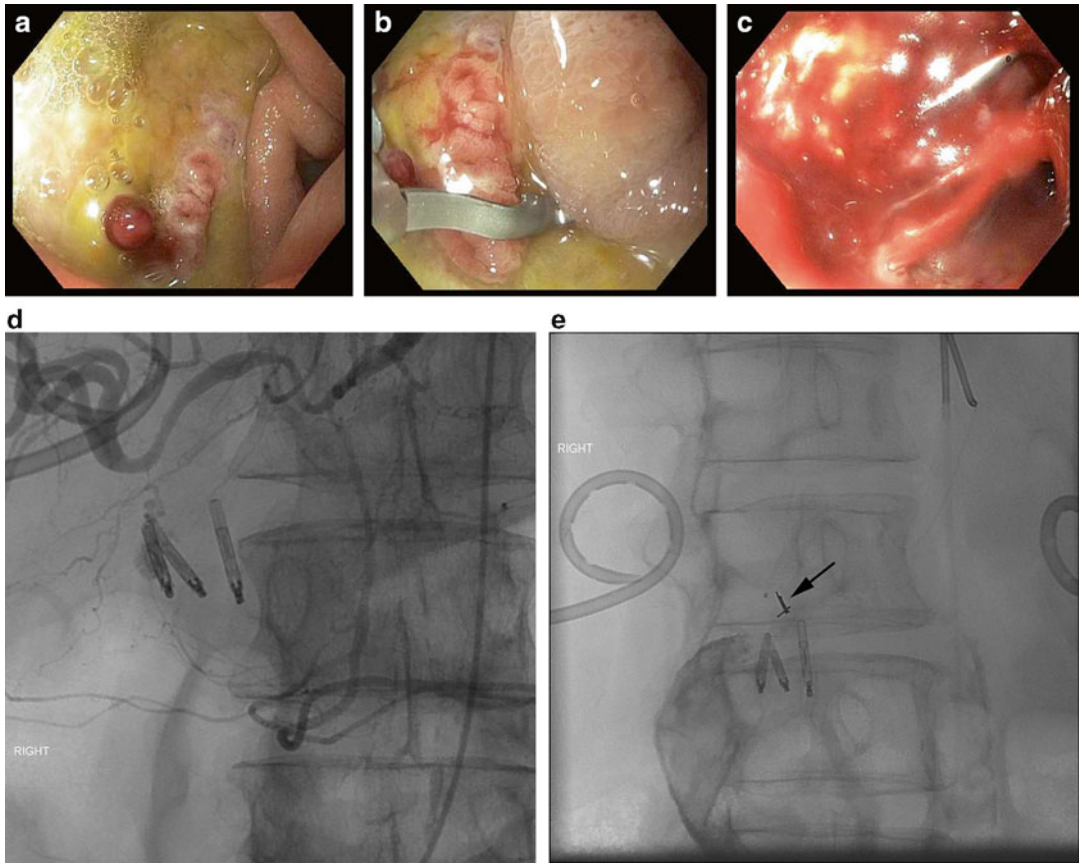

Fig. 11.5 (**a**) Large penetrating duodenal ulcer with prominent visible vessel. (**b**) Attempted clip closure of visible vessel in a fibrotic base. (**c**) Failed clip placement with precipitation of torrential bleeding. (**d**) Emergent angiogram performed for superselective embolization, aided by visualization of endoscopic clips. (**e**) Coil embolization of feeding vessel (*arrow*)

Upper endoscopy is important for diagnosis, although endoscopic hemostasis is rarely required unless a focal ulcer with high-risk stigmata of recent hemorrhage is found. The application of a thermal probe (e.g., bipolar probe at 15 W for 3–5 s with moderate contact pressure) and placement of clips are reasonable endoscopic treatment options. These patients should be treated with a proton pump inhibitor (PPI) for 8–12 weeks, followed by repeat endoscopy to rule out underlying Barrett's esophagus [10].

Mallory-Weiss Tear

A mucosal laceration at the gastroesophageal junction (more often located on the gastric side as seen on retroflex endoscopic view) is usually, but not always, due to antecedent vomiting or retching. Bleeding is usually self-limited and the rate of rebleeding approximates 10 % [10, 44]. Patients with active bleeding require endoscopic therapy. Bipolar coagulation and clips (Video 11.8), with or without epinephrine injection, as well as band ligation have all been used successfully [45–49]. In patients with portal hypertension and/or concomitant esophageal varices, band ligation is the preferred modality.

Dieulafoy Lesion

A Dieulafoy lesion is a large submucosal artery (1–3 mm in size) that protrudes through the mucosa and can be a cause of massive upper GI bleeding. The lesion is usually located in the

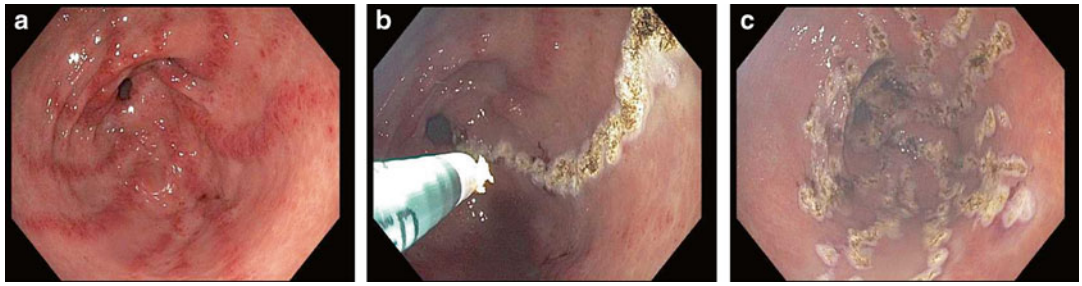

Fig. 11.6 (**a**) Gastric antral vascular ectasia (watermelon stomach). (**b**) Ablation of the stripes of vascular ectasias using argon plasma coagulation. (**c**) Endoscopic appearance following argon plasma coagulation

stomach, most often in the fundus, but can be present anywhere in the GI tract [10]. It may be difficult to locate a Dieulafoy lesion by the time upper endoscopy is performed because the lesion can retract back into the mucosa leaving no telltale sign. Dieulafoy lesions can be managed successfully by a variety of endoscopic techniques, including band ligation (Video 11.5), clip placement, contact thermal coagulation, sclerosant injection, and cyanoacrylate injection. Epinephrine injection alone is not recommended since it is associated with high rates of rebleeding [50, 51].

Sporadic Vascular Ectasias and Gastric Antral Vascular Ectasia

These mucosal vascular lesions are more likely to cause chronic blood loss with resulting iron deficiency anemia rather than overt upper GI bleeding. They can be isolated or associated with comorbidities such as cirrhosis, chronic renal failure, collagen vascular disease, valvular heart disease, and Osler-Weber-Rendu syndrome. Although these lesions can be treated by a variety of hemostatic techniques, APC is usually the preferred treatment modality due to ease of use (Fig. 11.6) [52–54].

Upper Gastrointestinal Tumors

Benign or malignant tumors of the upper GI tract are responsible for up to 5 % of cases of acute upper GI bleeding. Endoscopic hemostasis is less effective in this setting, with higher rates of rebleeding compared to bleeding from peptic ulcer [55–58]. Various endoscopic treatment modalities have been described with no clear recommendations [1]. Endoscopic control of bleeding is usually short-lived, and these lesions generally require angiographic embolization, radiotherapy, or surgical intervention for definitive hemostasis. Successful preliminary experience with Hemospray for tumor bleeding has been reported, although long-term efficacy remains to be seen [59].

Comparison of Available Techniques

Studies comparing various modalities for NVUGIB have focused mostly on peptic ulcer bleeding. The following, therefore, relates primarily to ulcer hemostasis.

Injection Therapy

Epinephrine

Dilute epinephrine is comparable to other monotherapies in achieving primary hemostasis of active bleeding. However, a meta-analysis of three trials with 212 patients, without second-look endoscopy, revealed that epinephrine was inferior in preventing rebleeding and surgery when compared to bipolar coagulation, clips, or fibrin glue [8]. Furthermore, when epinephrine was combined with another modality—an

injectable sclerosant, bipolar electrocoagulation, heater probe, thrombin glue, or fibrin glue—there was a significant reduction in rebleeding and surgery compared with epinephrine injection alone. A combined analysis of epinephrine plus another modality (bipolar coagulation, sclerosant, or clip) was shown to be significantly more effective in reducing rebleeding and surgery (RR 0.34 [95 % CI 0.23–0.5]; NNT=5) [6, 8]. Current consensus statements and technology reviews state that epinephrine injection alone is inadequate (unless no other hemostatic modality is available to the endoscopist) for definitive hemostasis and should be used in combination with another modality [6–9].

Sclerosing Agents

Compared to no therapy, the use of sclerosants alone (e.g., absolute alcohol) has been shown to be superior with regard to outcomes of primary hemostasis, need for urgent intervention, surgery, and mortality [6]. A meta-analysis comparing thermal therapy with a sclerosant showed no significant differences in rebleeding rate, surgery, or mortality [8]. Sclerosant injection, however, is rarely used for NVUGIB due to the perceived risk of serious tissue damage.

Thrombin/Fibrin Glue

Thrombin and fibrin glues have been shown to be more effective than no endoscopic therapy in preventing rebleeding. Fibrin glue was only comparable to epinephrine injection for primary hemostasis, and additional studies revealed no significant differences between fibrin glue and polidocanol, or a combination of dilute epinephrine plus fibrin versus dilute epinephrine plus polidocanol [8, 40].

Contact Thermal Therapy

A meta-analysis of 15 trials [8] showed thermal contact therapy with heater probe or bipolar probe to be significantly more effective than no therapy for reducing ulcer rebleeding (RR 0.44 [95 % CI 0.36–0.54]; NNT=4), need for surgery (RR 0.39 [95 % CI 0.27–0.55]; NNT=8), and mortality (RR 0.58 [95 % CI 0.34–0.98]; NNT=33). No difference was observed between the two thermal devices. A benefit of combination therapy with epinephrine plus contact thermal therapy versus thermal coagulation alone was suggested in two trials. A study comparing thrombin injection plus heater probe versus heater probe alone found no superiority for the combination arm [8].

Clips

No studies have evaluated endoscopic clips versus sham therapy. Several studies have compared clips with alternative hemostatic modalities—epinephrine, heater probe, bipolar coagulation plus epinephrine, and sclerosants. Clips were found to be more effective than epinephrine alone in reducing rebleeding and surgery. A summary of the comparative trials against other modalities found no significant differences in rates of rebleeding or surgery [8].

Endoscopic Therapy of High-Risk Versus Low-Risk Lesions

Several well-conducted clinical trials, meta-analyses, and consensus statements have determined that endoscopic hemostasis significantly reduces ulcer rebleeding rates, need for surgery, and mortality in patients with high-risk endoscopic stigmata (i.e., active bleeding, non-bleeding visible vessel, and adherent clot) [7–9]. All methods of endoscopic hemostasis have been shown to be superior to no endoscopic intervention. As previously mentioned, the addition of a second hemostatic modality, such as contact thermal therapy, to injection of dilute epinephrine further reduces the rebleeding rate, need for surgery, and mortality compared with epinephrine injection alone.

Endoscopic therapy for the ulcer with an adherent clot has been advocated, yet remains controversial [6–8, 10, 60–66]. An adherent clot is red, maroon, or black in color, amorphous in texture, and unable to be dislodged from the

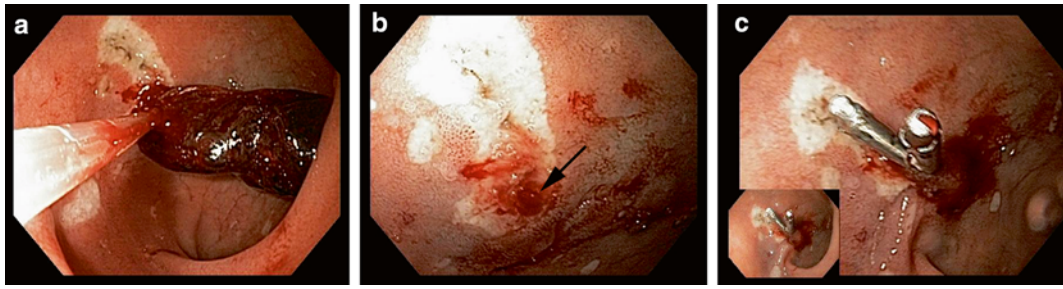

Fig. 11.7 (**a**) Epinephrine injection around duodenal ulcer with adherent clot. (**b**) Clot removal revealed an underlying visible vessel (*arrow*). (**c**) Clip placement performed for definitive hemostasis

ulcer bed by suction or forceful water irrigation. Vigorous irrigation of a clot in an ulcer bed successfully exposes underlying stigmata in 26–43 % of cases and high-risk stigmata in 70 % of those cases [64–66]. The risk for rebleeding with clots that remain adherent after vigorous washing without endoscopic therapy (with or without PPI therapy) has been reported to be as low as 0–8 % in some studies and as high as 25–35 % in others [60–66]. If endoscopic therapy is entertained, the recommended approach is to inject dilute epinephrine (1:10,000 or 1:20,000) around the clot, followed by cold snare guillotine to shave down the clot without disrupting the pedicle of the clot, and finally apply definitive therapy (e.g., bipolar coagulation or clip placement with or without additional epinephrine injection) to any underlying stigmata of hemorrhage (Fig. 11.7 and Video 11.9). A meta-analysis [8] of randomized trials in ulcer patients with an adherent clot did not show a significant benefit for endoscopic therapy over medical treatment (RR 0.31, 95 % CI 0.06–1.77). Similarly, endoscopic therapy did not significantly reduce rebleeding (RR 0.48, 95 % CI 0.18–1.30) compared with medical therapy in another meta-analysis [66]. However, significant heterogeneity was present among the studies, with some trials reporting significant benefit in favor of endoscopic hemostasis [8, 66]. The disparity in the data has led to ongoing controversy regarding the optimal management of adherent clots in peptic ulcers (endoscopic hemostasis vs. high-dose PPI only).

Patients with low-risk stigmata (e.g., ulcer with clean base or flat pigmented spot) have a low likelihood of recurrent bleeding and, therefore, do not benefit from endoscopic therapy [6–9]. Findings from randomized and retrospective trials have shown that, following endoscopy, low-risk patients who are otherwise stable and without significant anemia and comorbidities can be discharged home on the same day [67–71].

Second-Look Endoscopy

Planned second-look endoscopy that is performed within 24 h after initial endoscopic therapy is not recommended [6–9].

A meta-analysis of randomized trials assessing second-look endoscopy reported a small but significant reduction in rebleeding in patients undergoing the procedure (absolute risk reduction 6.2 % [95 % CI 1.3–11.1 %]; NNT=16), with no significant benefit, however, in reducing surgery or mortality rates [72]. A subsequent meta-analysis found no significant benefit when therapy for hemostasis involved epinephrine injection or fibrin glue injection but did identify a significant difference in rebleeding in the two randomized trials employing thermal therapy (RR 0.29, 95 % CI 0.11–0.73) [73]. However, these studies were performed prior to the era of intensive PPI therapy. In a randomized trial of single endoscopy plus high-dose intravenous PPI versus routine second-look endoscopy without PPI, rebleeding rates were similar at 8.2 and 8.7 %, respectively (RR 1.1, 95 % CI 0.4–2.7) [74]. A meta-analysis was published on the effectiveness of routine second-look endoscopy in peptic ulcer bleeding that included four randomized trials encompassing

938 patients [75]. The rebleeding rate was significantly decreased with routine second-look endoscopy (OR 0.55, 95 % CI 0.37–0.81), as was surgery (OR 0.43, 95 % CI 0.19–0.96), but not mortality (OR 0.65, 95 % CI 0.26–1.62). The only trial in which high-dose PPI was used did not show a benefit of second-look endoscopy. When the two trials that included patients at the highest risk of rebleeding were removed, no significant benefit for second-look endoscopy was found (OR 0.65, 95 % CI 0.42–1.00). Also, planned second-look endoscopy may not be cost-effective when medical therapy with intravenous high-dose PPI is used [76].

Repeat upper endoscopy should be considered on a case-by-case basis, particularly when recurrent bleeding is suspected or there is uncertainty regarding the effectiveness of hemostasis during initial endoscopy.

Conclusions

The endoscopic treatment of a patient presenting with acute overt upper GI bleeding is a multi-step process. Following initiation of resuscitative measures with hemodynamic stabilization and clinical risk stratification, most patients should undergo upper endoscopy within 24 h of presentation. In patients who are found to have bleeding due to peptic ulcer, the endoscopic stigmata are critical in directing further management. Patients with high-risk stigmata, such as active bleeding or non-bleeding visible vessel, should receive endoscopic therapy, whereas those with an adherent clot should be considered for endoscopic therapy. Ulcers with flat pigmented spots or clean bases do not require endoscopic therapy. Currently, the best outcomes for endoscopic hemostasis are achieved using a combination of dilute epinephrine injection and a more definitive treatment modality, such as contact thermal therapy or clip placement. Recurrent ulcer bleeding after initial endotherapy should be considered for a second attempt at endoscopic therapy, but if bleeding persists or recurs, referral to interventional radiology or surgery should be undertaken.

In the majority of patients presenting with ulcer- and non-ulcer-related NVUGIB, endoscopic therapy is an effective means of achieving long-term hemostasis. The selection of the most appropriate hemostatic device(s) for a particular lesion, recognition of caveats of endotherapy, and familiarity and proficiency in using the various devices available are important determinants for the safe and effective application of endoscopic hemostasis in NVUGIB.

References

1. Hwang JH et al. The role of endoscopy in the management of acute non-variceal upper GI bleeding. Gastrointest Endosc. 2012;75(6):1132–8.
2. Rockall TA et al. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. Steering committee and members of the national audit of acute upper gastrointestinal haemorrhage. BMJ. 1995;311(6999):222–6.
3. Boonpongmanee S et al. The frequency of peptic ulcer as a cause of upper-GI bleeding is exaggerated. Gastrointest Endosc. 2004;59(7):788–94.
4. Chak A et al. Effectiveness of endoscopy in patients admitted to the intensive care unit with upper GI hemorrhage. Gastrointest Endosc. 2001;53(1):6–13.
5. Lin HJ et al. Early or delayed endoscopy for patients with peptic ulcer bleeding. A prospective randomized study. J Clin Gastroenterol. 1996;22(4):267–71.
6. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107(3):345–60. quiz 361.c.
7. Barkun AN et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152(2):101–13.
8. Laine L, McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence-based approach based on meta-analyses of randomized controlled trials. Clin Gastroenterol Hepatol. 2009;7(1):33–47. quiz 1–2.
9. Gralnek IM, Barkun AN, Bardou M. Management of acute bleeding from a peptic ulcer. N Engl J Med. 2008;359(9):928–37.
10. Fordtman SA, editor. Sleisenger and Fordtran's gastrointestinal and liver disease, vol. 1. 9th ed. Philadelphia: Saunders/Elsevier; 2010.
11. Masaoka T et al. Blatchford scoring system is a useful scoring system for detecting patients with upper gastrointestinal bleeding who do not need endoscopic intervention. J Gastroenterol Hepatol. 2007;22(9):1404–8.
12. Robins GG et al. Evaluation of the need for endoscopy to identify low-risk patients presenting with an

acute upper gastrointestinal bleed suitable for early discharge. Postgrad Med J. 2007;83(986):768–72.
13. Stanley AJ et al. Outpatient management of patients with low-risk upper-gastrointestinal haemorrhage: multicentre validation and prospective evaluation. Lancet. 2009;373(9657):42–7.
14. Spiegel BM, Vakil NB, Ofman JJ. Endoscopy for acute nonvariceal upper gastrointestinal tract hemorrhage: is sooner better? A systematic review. Arch Intern Med. 2001;161(11):1393–404.
15. Tsoi KK, Ma TK, Sung JJ. Endoscopy for upper gastrointestinal bleeding: how urgent is it? Nat Rev Gastroenterol Hepatol. 2009;6(8):463–9.
16. Yen D et al. Arterial oxygen desaturation during emergent nonsedated upper gastrointestinal endoscopy in the emergency department. Am J Emerg Med. 1997;15(7):644–7.
17. Hearnshaw SA et al. Acute upper gastrointestinal bleeding in the UK: patient characteristics, diagnoses and outcomes in the 2007 UK audit. Gut. 2011;60(10):1327–35.
18. Conway JD et al. Endoscopic hemostatic devices. Gastrointest Endosc. 2009;69(6):987–96.
19. Lin HJ et al. A prospective, randomized trial of large- versus small-volume endoscopic injection of epinephrine for peptic ulcer bleeding. Gastrointest Endosc. 2002;55(6):615–9.
20. Laine L. Therapeutic endoscopy and bleeding ulcers. Bipolar/multipolar electrocoagulation. Gastrointest Endosc. 1990;36(5 Suppl):S38–41.
21. Fullarton GM et al. Controlled trial of heater probe treatment in bleeding peptic ulcers. Br J Surg. 1989;76(6):541–4.
22. Ginsberg GG et al. The argon plasma coagulator: February 2002. Gastrointest Endosc. 2002;55(7): 807–10.
23. Watson JP et al. The tissue effect of argon plasma coagulation on esophageal and gastric mucosa. Gastrointest Endosc. 2000;52(3):342–5.
24. Cipolletta L et al. Prospective comparison of argon plasma coagulator and heater probe in the endoscopic treatment of major peptic ulcer bleeding. Gastrointest Endosc. 1998;48(2):191–5.
25. Raju GS, Gajula L. Endoclips for GI endoscopy. Gastrointest Endosc. 2004;59(2):267–79.
26. Chuttani R et al. Endoscopic clip application devices. Gastrointest Endosc. 2006;63(6):746–50.
27. Banerjee S et al. Endoscopic closure devices. Gastrointest Endosc. 2012;76(2):244–51.
28. Kirschniak A et al. A new endoscopic over-the-scope clip system for treatment of lesions and bleeding in the GI tract: first clinical experiences. Gastrointest Endosc. 2007;66(1):162–7.
29. Monkemuller K et al. Utility of the “bear claw”, or over-the-scope clip (OTSC) system, to provide endoscopic hemostasis for bleeding posterior duodenal ulcers. Endoscopy. 2012;44(Suppl 2 UCTN):E412–3.
30. Alis H et al. Is endoscopic band ligation superior to injection therapy for Dieulafoy lesion? Surg Endosc. 2009;23(7):1465–9.
31. Gralnek IM et al. Capsule endoscopy in acute upper gastrointestinal hemorrhage: a prospective cohort study. Endoscopy. 2013;45(1):12–9.
32. Sung JJ et al. Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. Endoscopy. 2011;43(4):291–5.
33. Giday SA et al. Long-term randomized controlled trial of a novel nanopowder hemostatic agent (TC-325) for control of severe arterial upper gastrointestinal bleeding in a porcine model. Endoscopy. 2011;43(4):296–9.
34. Alpay A et al. Use of a novel haemostatic agent: ankaferd blood stopper in conjunctival incisions. Clin Exp Ophthalmol. 2011;39(8):793–8.
35. Barkun AN, Moosavi S, Martel M. Topical hemostatic agents: a systematic review with particular emphasis on endoscopic application in GI bleeding. Gastrointest Endosc. 2013;77(5):692–700.
36. Baykul T, Alanoglu EG, Kocer G. Use of Ankaferd blood stopper as a hemostatic agent: a clinical experience. J Contemp Dent Pract. 2010;11(1):E088–94.
37. Huri E et al. First clinical experience of Ankaferd BloodStopper as a hemostatic agent in partial nephrectomy. Kaohsiung J Med Sci. 2010;26(9):493–5.
38. Leblebisatan G et al. Topical Ankaferd hemostat application for the management of oral cavity bleedings in children with hemorrhagic diathesis. Blood Coagul Fibrinolysis. 2012;23(6):494–7.
39. Teker AM et al. Prospective, controlled clinical trial of Ankaferd Blood Stopper in children undergoing tonsillectomy. Int J Pediatr Otorhinolaryngol. 2009;73(12):1742–5.
40. Laine L, Peterson WL. Bleeding peptic ulcer. N Engl J Med. 1994;331(11):717–27.
41. Enestvedt BK et al. An evaluation of endoscopic indications and findings related to nonvariceal upper-GI hemorrhage in a large multicenter consortium. Gastrointest Endosc. 2008;67(3):422–9.
42. Sung JJ et al. Intravenous esomeprazole for prevention of recurrent peptic ulcer bleeding: a randomized trial. Ann Intern Med. 2009;150(7):455–64.
43. Chung SC et al. Endoscopic injection of adrenaline for actively bleeding ulcers: a randomised trial. Br Med J (Clin Res Ed). 1988;296(6637):1631–3.
44. Bharucha AE, Gostout CJ, Balm RK. Clinical and endoscopic risk factors in the Mallory-Weiss syndrome. Am J Gastroenterol. 1997;92(5):805–8.
45. Gunay K et al. Endoscopic ligation for patients with active bleeding Mallory-Weiss tears. Surg Endosc. 2001;15(11):1305–7.
46. Huang SP et al. Endoscopic hemoclip placement and epinephrine injection for Mallory-Weiss syndrome with active bleeding. Gastrointest Endosc. 2002; 55(7):842–6.
47. Morales P, Baum AE. Therapeutic alternatives for the Mallory-Weiss Tear. Curr Treat Options Gastroenterol. 2003;6(1):75–83.
48. Myung SJ, Kim HR, Moon YS. Severe Mallory-Weiss tear after endoscopy treated by endoscopic

band ligation. Gastrointest Endosc. 2000;52(1): 99–101.
49. Yamaguchi Y et al. Endoscopic hemoclipping for upper GI bleeding due to Mallory-Weiss syndrome. Gastrointest Endosc. 2001;53(4):427–30.
50. Gadenstatter M et al. Dieulafoy's disease of the large and small bowel. J Clin Gastroenterol. 1998;27(2): 169–72.
51. Norton ID et al. Management and long-term prognosis of Dieulafoy lesion. Gastrointest Endosc. 1999;50(6):762–7.
52. Wong RM et al. Endoscopic ligation for non-esophageal variceal upper gastrointestinal hemorrhage. Endoscopy. 1998;30(9):774–7.
53. Sebastian S, O'Morain CA, Buckley MJ. Review article: current therapeutic options for gastric antral vascular ectasia. Aliment Pharmacol Ther. 2003;18(2): 157–65.
54. Pavey DA, Craig PI. Endoscopic therapy for upper-GI vascular ectasias. Gastrointest Endosc. 2004;59(2): 233–8.
55. Savides TJ et al. Severe upper gastrointestinal tumor bleeding: endoscopic findings, treatment, and outcome. Endoscopy. 1996;28(2):244–8.
56. Loftus EV et al. Endoscopic treatment of major bleeding from advanced gastroduodenal malignant lesions. Mayo Clin Proc. 1994;69(8):736–40.
57. Mathus-Vliegen EM, Tytgat GN. Analysis of failures and complications of neodymium: YAG laser photocoagulation in gastrointestinal tract tumors. A retrospective survey of 18 years' experience. Endoscopy. 1990;22(1):17–23.
58. Suzuki H et al. Endoscopic laser therapy in the curative and palliative treatment of upper gastrointestinal cancer. World J Surg. 1989;13(2):158–64.
59. Chen YI et al. Use of the endoscopically applied hemostatic powder TC-325 in cancer-related upper GI hemorrhage: preliminary experience (with video). Gastrointest Endosc. 2012;75(6):1278–81.
60. Lin HJ et al. Natural history of bleeding peptic ulcers with a tightly adherent blood clot: a prospective observation. Gastrointest Endosc. 1996;43(5):470–3.
61. Laine L, Stein C, Sharma V. A prospective outcome study of patients with clot in an ulcer and the effect of irrigation. Gastrointest Endosc. 1996;43(2 Pt 1): 107–10.
62. Sung JJ et al. The effect of endoscopic therapy in patients receiving omeprazole for bleeding ulcers with nonbleeding visible vessels or adherent clots: a randomized comparison. Ann Intern Med. 2003; 139(4):237–43.
63. Lau JY et al. The evolution of stigmata of hemorrhage in bleeding peptic ulcers: a sequential endoscopic study. Endoscopy. 1998;30(6):513–8.
64. Bleau BL et al. Recurrent bleeding from peptic ulcer associated with adherent clot: a randomized study comparing endoscopic treatment with medical therapy. Gastrointest Endosc. 2002;56(1):1–6.
65. Jensen DM et al. Randomized trial of medical or endoscopic therapy to prevent recurrent ulcer hemorrhage in patients with adherent clots. Gastroenterology. 2002;123(2):407–13.
66. Kahi CJ et al. Endoscopic therapy versus medical therapy for bleeding peptic ulcer with adherent clot: a meta-analysis. Gastroenterology. 2005;129(3):855–62.
67. Hay JA et al. Prospective evaluation of a clinical guideline recommending hospital length of stay in upper gastrointestinal tract hemorrhage. JAMA. 1997;278(24):2151–6.
68. Lai KC et al. A retrospective and prospective study on the safety of discharging selected patients with duodenal ulcer bleeding on the same day as endoscopy. Gastrointest Endosc. 1997;45(1):26–30.
69. Moreno P et al. Efficacy and safety of an early discharge protocol in low-risk patients with upper gastrointestinal bleeding. Am J Med. 1998;105(3): 176–81.
70. Lee JG et al. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. Gastrointest Endosc. 1999;50(6):755–61.
71. Cipolletta L et al. Outpatient management for low-risk nonvariceal upper GI bleeding: a randomized controlled trial. Gastrointest Endosc. 2002;55(1):1–5.
72. Marmo R et al. Outcome of endoscopic treatment for peptic ulcer bleeding: Is a second look necessary? A meta-analysis. Gastrointest Endosc. 2003;57(1):62–7.
73. Tsoi KK et al. Second-look endoscopy with thermal coagulation or injections for peptic ulcer bleeding: a meta-analysis. J Gastroenterol Hepatol. 2010;25(1): 8–13.
74. Chiu PW et al. Effect of scheduled second therapeutic endoscopy on peptic ulcer rebleeding: a prospective randomised trial. Gut. 2003;52(10):1403–7.
75. El Quali S et al. Is routine second-look endoscopy effective after endoscopic hemostasis in acute peptic ulcer bleeding? A meta-analysis. Gastrointest Endosc. 2012;76(2):283–92.
76. Spiegel BM et al. Minimizing recurrent peptic ulcer hemorrhage after endoscopic hemostasis: the cost-effectiveness of competing strategies. Am J Gastroenterol. 2003;98(1):86–97.