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Endoscopy for Nonvariceal Upper Gastrointestinal Bleeding

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Endoscopy for acute nonvariceal upper gastrointestinal bleeding plays an important role in primary diagnosis and management, particularly with respect to identification of high-risk stigmata lesions and to providing endoscopic hemostasis to reduce the risk of rebleeding and mortality. Early endoscopy, defined as endoscopy within the first 24 hours after presentation, improves patient outcome and reduces the length of hospitalization when compared with delayed endoscopy. Various endoscopic hemostatic methods are available, including injection therapy, mechanical therapy, and thermal coagulation. Either single treatment with mechanical or thermal therapy or a treatment that combines more than one type of therapy are effective and safe for peptic ulcer bleeding. Newly developed methods, such as Hemospray powder and over-the-scope clips, may provide additional options. Appropriate decisions and specific treatment are needed depending upon the conditions.

Key Words: Nonvariceal upper gastrointestinal bleeding; Hemostasis; Endoscopy

INTRODUCTION

Acute nonvariceal upper gastrointestinal bleeding (NVUGIB) is a gastrointestinal emergency that has considerable morbidity and mortality. Peptic ulcer bleeding is the most common cause of upper gastrointestinal bleeding (UGIB), and it is responsible for about 31% to 67% of all cases, followed by erosive disease and variceal bleeding. Mallory-Weiss tears, Dieulafoy's lesions, vascular ectasia, and neoplasm comprise the remainder of the possible causes.¹ The mortality rate has remained unchanged at 3.5% to 7.4% over the past several decades.²⁻⁴ Higher mortality is likely associated with one of the following features: hemoglobin <7.0 g/dL, American Society of Anesthesiologists class 4, age >80, renal failure, rebleeding, and failure of endoscopic treatment.^{5,6} Seventy percent of UGIB is recovered spontaneously without recurrence; however, 10% of patients continue to bleed and 20% experience continued or recurrent bleeding in the first 24 to 72 hours.⁷

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Most high-risk stigmata lesions require around 72 hours to regress into a low-risk appearance after endoscopic therapy, and most rebleeding (about 80%) in high-risk patients occurs within the first 72 hours.⁸ Therefore, it is suggested that patients with high-risk lesions be admitted to hospital for the 72 hours of high-dose intravenous proton pump inhibitors (IV PPI) therapy after endoscopic hemostasis.⁸ Furthermore, IV PPI has been found to be cost-effective because it lowers the ration of patients with active bleeding lesions on endoscopic view, thus it reduced the need for further intervention.⁹⁻¹¹

RESUSCITATION, RISK STRATIFICATION, PRE-ENDOSCOPIC MANAGEMENT

Before endoscopy, several preventive management strategies can be used to reduce hemostasis-related adverse effects, including volume replacement, restoration of hemodynamic stability, and amendment of coagulopathy. On presentation with UGIB, immediate evaluation and appropriate resuscitation should be carried out. The nasogastric tube insertion in selected patients should be considered because the findings may have prognostic value. Patients should be stratified into low-risk and high-risk groups by using prognostic scales, laboratory data, and endoscopic criteria, as well as by applying a clinical assessment. Very low-risk patients may be discharged, but all other patients should be hospitalized and categorized as low-risk or high-risk to determine treatment

options.^{12,13}

Blood transfusions should be considered for a patient with a hemoglobin level of 7.0 g/dL or less. Oral PPI therapy can be administered for low-risk patients, but high-risk patients should be treated with endoscopic and IV high-dose PPI. IV

Table 1. Glasgow-Blatchford Score

Variable	Admission risk marker	Score component value
Blood urea, mg/dL	≥6.5 <8.0	2
	≥8.0 <10.0	3
	≥10.0 <25.0	4
	≥25	6
Hemoglobin for men, g/dL	≥12.0 <13.0	1
	≥10.0 <12.0	3
	<10.0	6
Hemoglobin for women, g/dL	≥10.0 <12.0	1
	<10.0	6
Systolic blood pressure, mm Hg	100–109	1
	90–99	2
	<90	3
Other markers	Pulse ≥100 per min	1
	Presentation with melaena	1
	Presentation with syncope	2
	Hepatic disease	2
	Cardiac failure	2

Scores of 6 or more are related to a greater than 50% risk of needing an intervention.

Table 2. Rockall Score

Variable	Scores			
	0	1	2	3
Age, yr	<60	60–79	≥80	-
Shock	No shock	Tachycardia	Hypotension	-
	SBP ≥100 mm Hg	SBP ≥100 mm Hg	SBP <100 mm Hg	
	HR <100 bpm	HR ≥100 bpm		
Comorbidity	No major comorbidity	-	Cardiac failure	Renal failure
			Ischemic heart disease	Liver failure
			Any major comorbidity	Disseminated malignancy
Diagnosis	Mallory-Weiss tear	All other diagnosis	Malignancy of upper GI tract	-
	No lesion identified			
	No stigmata of recent hemorrhage			
Major stigmata of recent hemorrhage	None or dark spot only	-	Blood in upper GI tract	-
			Adherent clot	
			Visible or spurting vessel	

SBP, systolic blood pressure; HR, heart rate; bpm, beats per minute; GI, gastrointestinal.

PPI therapy prior to endoscopy may be considered to downstage the endoscopic lesion and decrease the need for endoscopic intervention but it should not delay endoscopy. All patients should be considered for secondary prophylaxis, including a *Helicobacter pylori* test and treatment, the use of cyclooxygenase-2 antagonists as an alternative to nonsteroidal anti-inflammatory drugs (NSAIDs), and PPI for those taking low-dose aspirin.^{12,13} The Glasgow-Blatchford scoring system may be used at first assessment, but after endoscopy the full Rockall scoring system should be followed.^{14–16} The scores are calculated using the tables below (Tables 1, 2).

ENDOSCOPIC MANAGEMENT

Endoscopy is important for the primary diagnosis and management of acute NVUGIB. Early endoscopy (within 24 hours of presentation) is recommended for most patients with acute UGIB.¹³ Early endoscopy is related to significant reductions in length of hospital stay, as compared to delayed endoscopy and a decreased need for surgery in elderly patients. Rapid endoscopy within 6 hours did not demonstrate advantages in the outcomes of mortality, need for surgery and transfusion requirements compared with endoscopy within 24 hours.^{17,18}

High-risk lesions for rebleeding include actively spurting lesions (Forrest class IA), oozing blood (class IB), a nonbleeding visible vessel (class IIA), and an adherent clot (class IIB). Low-risk lesions include flat pigmented spots (Forrest class IIC) and clean-based ulcers (class III).¹⁹ An endoscopic hemostatic procedure is not required for patients with low-risk stigmata (a clean-based ulcer [III] or a flat pigmented spots [IIC]). A clot in an ulcer bed (IIB) needs to be removed with targeted

irrigation, and appropriate treatment should be performed for the underlying lesion. The necessity of endoscopic therapy for ulcers with adherent clots is still debating. Endoscopic hemostatic therapy is required for patients with high-risk stigmata (active bleeding [IA, IB] or a visible vessel in an ulcer bed [IIA]).¹⁹ Epinephrine injection is not sufficient for complete hemostasis and should be used in combination with other hemostatic modality.^{12,13} Clips or thermocoagulation should be used in patients with high-risk lesions, either alone or in combination with other hemostatic modalities. A second-look endoscopy is generally recommended in cases when rebleeding is suspected.^{13,20,21} Relevant conscious sedation and appropriate use of sedative drugs such as midazolam and propofol during endoscopic hemostasis enhances the success rates and patient's satisfaction.^{11,22}

ENDOSCOPIC HEMOSTATIC METHODS

Many hemostatic methods are available for effective endoscopic hemostasis. These can be categorized based upon their mechanism of action, as follows: 1) injection therapy, 2) mechanical therapy, 3) thermal coagulation, or 4) a combination of these. Several new endoscopic treatments were introduced and applied to control NVUGIB.

Injection therapy

Injection with diluted epinephrine is widely used due to its simplicity. The mechanisms of hemostasis are local tamponade effect and vasoconstriction. It is now clear that injection with diluted epinephrine is a suboptimal treatment.^{8,13} An injection of diluted epinephrine should only be used to stop or slow down bleeding in order to obtain a clear view of the artery. Either hemoclipping or thermocoagulation to the artery should be followed.^{13,21,23} Epinephrine injection is more beneficial than medical therapy in patients with high-risk stigmata, but it is inferior to other monotherapies, such as mechanical therapy or thermal therapy, or to combination therapies that use two or more methods.^{13,24} Other injection therapies using sclerosant (absolute alcohol, polidocanol) or tissue adhesives (cyanoacrylate, thrombin/fibrin glue) have been used for NVUGIB.

Mechanical therapy

One of the most widely used endoscopic mechanical modalities is a hemoclip.²⁵ Clips have been applied for hemostasis and for closing the mucosal defects that result from endoscopic mucosal resection, fistulas and perforations of GI tracts.²⁶ That process commonly starts with the use of hemoclips, particularly where there is a clear vessel head. Effective hemoclipping is difficult if the bleeding site is in the gastric

fundus, the lesser curvature of the stomach, or the posterior wall of duodenal bulb. Hemoclips need precise deployment because inadequate clipping of only the tip of the vessel can result in potentiation or initiation of vigorous bleeding. Tangential approach of hemoclips or their applications with retroflexion of a scope often fail. The deployment of hemoclips on hard or fibrotic ulcer base often difficult.²⁷

Band ligation is another mechanical hemostatic option, and various devices have been introduced each having individual merits. The advantages of using band ligation are: easy application, accessibility to difficult sites, and short procedure time. But it has limitations for poor visual field, unavailability in fibrotic tissue, and narrow indication. Band ligation is useful for a Dieulafoy-like ulcer, angiodysplasia lesions, and Mallory-Weiss tears, and its role is the same as that of mechanical ligation of hemoclipping.^{7,26}

Thermal coagulation

Thermal endoscopic hemostasis is somewhat easier in comparison to hemoclipping.²⁷ It can be classified as either contact or noncontact. Heater probe thermocoagulation and bipolar electrocoagulation are the examples of the thermocoagulation. Contact therapies provide appositional pressure resulting in a heat-sink effect as well as tissue coagulation with contraction of the blood vessels. Among the noncontact methods, argon plasma coagulation is available at many endoscopic facilities. It is safe given the depth of penetration (<1 mm) and relatively easy to use. However, it has a limitation due to the fact that it only provides superficial coagulation, which may miss larger deeper vessels.²⁷

Endoscopic combination therapy

Hemoclips and thermocoagulation were found to be similar in their hemostatic efficacies.^{28,29} Combination therapy may have an additive effect for each modality and different mechanisms of action for each technique.^{28,30} However, combination therapy (injection plus second injectate, thermal, or clips) was not found to be superior to hemoclips or thermal therapy alone.^{28,30}

NEW ENDOSCOPIC TREATMENTS

Hemospray powder

A new endoscopic application is the use of Hemospray powder (Cook Medical Inc., Winston-Salem, NC, USA). that has an ability to increase the concentration of coagulation factors, to activate platelets, and to form a mechanical plug on an injured blood vessel.³¹ Upon contact with blood, the powder becomes aggregated and forms a stable mechanical plug on the bleeding site. Hemospray powders were applied for

peptic ulcer bleeding, cancer-associated gastrointestinal bleeding, and in patients taking antithrombotic agents. The initial reports are feasible, but there are still have a small sample size limitation. More studies should be followed to confirm the efficacy of Hemospray in the management of UGIB.^{27,32,33}

Over-the-scope clip

Recent invasive endoscopic treatments, such as endoscopic submucosal dissection and natural orifice transluminal endoscopic surgery, have provided alternative approaches to surgery. An over-the-scope clip (OTSC; Ovesco Endoscopy, Tübingen, Germany) is designed for tissue approximation.³⁴ Retrospective studies have shown the preliminary safety and feasibility of the OTSC for the treatment of UGIB and fistulae as well as for the closure of acute GI perforations. The OTSC system shows great potential for use in endoscopic treatments that require speed and simplicity.^{27,34-37}

OTHER CONSIDERATIONS

Complications during endoscopic hemostatic procedure, including aspiration pneumonia and perforation, have been minimal. A pooled analysis for all modalities has shown a complication rate of 0.5% (95% confidence interval, 0.4 to 0.8).³⁸ Clips and epinephrine injection had the lowest rates of perforation, while the heater probe group had the highest rate.³⁹ Other factors, such as the quality of the endoscopist's skill, unstable patient, poor sedation, poor visual field due to blood, and difficult area of reach, can affect the complications.³⁹

Despite studious attempts with different modalities, endoscopic hemostasis therapy is sometimes unsuccessful. Factors that could predict the failure of endoscopic hemostasis include: large ulcers (2 cm in size), located at the bulbar duodenum or the lesser curvature of the stomach, active bleeding, hemodynamic instability, and the presence of comorbid illnesses.⁴⁰⁻⁴² Angiographic embolization may be used as a rescue therapy when there is refractory bleeding to any endoscopic hemostasis. Perforation, uncontrolled bleeding, or unstable vital signs despite repeated hemostasis would be indications of emergent surgery.⁴³

CONCLUSIONS

Early endoscopic approachment is important in the identification and management of NVUGIB, especially for patients with high-risk lesions such as active bleeding and visible vessels. Endoscopic hemostatic therapy has been considered as the pivotal treatment for NVUGIB as it has been shown to reduce rebleeding, the need for surgery, morbidity, and mortality. Many safe and effective devices are available for endo-

scopic hemostasis. Although epinephrine injection provides more beneficial effects than pharmacological methods, the use of clips, thermocoagulation, or a therapeutic option that combines more than one treatment approach is more effective than injection treatment alone. Promising results have recently been reported for the application of hemostasis using Hemospray powder or OTSCs. Selection of the optimal hemostatic device depends upon the characteristics of the lesion, the physician's ability, the availability of the equipment, the patient's clinical conditions, and cost. In addition, adequate *H. pylori* eradication, PPI therapy, and the withdrawal of NSAIDs can further reduce the rebleeding and mortality rates.^{1,44}

Conflicts of Interest

The authors have no financial conflicts of interest.

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