How Can We Maximize Skills for Non-Variceal Upper Gastrointestinal Bleeding: Injection, Clipping, Burning, or Others?

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Endoscopy has its role in the primary diagnosis and management of acute non-variceal upper gastrointestinal bleeding. Main roles of endoscopy are identifying high risk stigmata lesion, and performing endoscopic hemostasis to lower the rebleeding and mortality risks. Early endoscopy within the first 24 hours enables risk classification according to clinical and endoscopic criteria, which guide safe and prompt discharge of low risk patients, and improve outcomes of high risk patients. Techniques including injection therapy, ablative therapy and mechanical therapy have been studied over the recent decades. Combined treatment is more effective than injection treatment, and single treatment with mechanical or thermal method is safe and effective in peptic ulcer bleeding. Specific treatment and correct decisions are needed in various situations depending on the site, location, specific characteristics of lesion and patient's clinical conditions.

Key Words: Non-variceal UGI bleeding; Endoscopy; Hemostasis

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is the most common gastrointestinal emergency, with 0.1% of annual incidence of hospital admission for UGIB. Major causes included peptic ulcer bleeding (PUB) accounting for 31% to 67% of all cases, followed by erosive disease and variceal bleeding. Less frequent causes are oesophagitis, Mallory Weiss tears, neoplasm and vascular lesions.[1] Mortality rate has remained unchanged at 6% to 8% due to patients' specific situations such as older age, more concurrent illnesses, and higher chance of hospitalization. We can expect that 70% of UGIB is relieved spontaneously without recurrence, 10% bleed continuously, and 20% experience continued or recurrent bleeding in the first 24 to 72 hours.

Endoscopy has clearly defined role in the primary diagnosis and management of acute non-variceal UGIB (NVUGIB). The main role of endoscopy is identifying high risk stigmata lesion, and endoscopic hemostasis lowers rebleeding and mortality risks. Several techniques, including injection therapy, ablative therapy and mechanical therapy have been studied over the recent decades.[2,3] Depending on the appearance of the bleeding focus and specific characteristics of each lesion, a suitable technique should be chosen. Related risk and history of persistent or recurrent bleeding can be a deciding factor when choosing an endoscopic hemostasis method. This review covers the various endoscopic techniques as well as its suitable application methods and useful tips to maximize skills for NVUGIB.

INDICATIONS OF ENDOSCOPIC HEMOSTASIS

The Endoscopic hemostatic therapy is indicated for patients with high risk ulcers including active bleeding stigmata and nonbleeding visible vessel, while patients with low-risk stigmata can be treated with pharmacotherapy alone. Endoscopists can choose endoscopic hemostasis according to the type, size, base, and location of a lesion. Recently, pre-endoscopy

proton pump inhibitor (PPI) was found to lower the stage of bleeding stigmata and improve the final clinical outcomes. A Cochrane review shows odds ratio of 0.67. PPI administration before endoscopy decreased the chance of endoscopic therapy.[4] During 24 hours, introduction of endoscopic hemostasis is adequate to control hemostatic outcome. Emergent endoscopy had controversial results.

Upon detecting bleeding stigmata during endoscopy, it is necessary to irrigate or remove the blood clot to find the culprit vessel. Controversial data were reported on differentiation between the clot and the exposed vessel.[5] So far, endoscopic therapy should be considered, although intensive PPI therapy may be sufficient among patients with adherent clots resistant to vigorous irrigation.

Characteristics of exposed vessel of high risk should be evaluated in terms of its color, size, and location. Exposed vessel changes its color generally from red color to white and then to black color, sequentially. Sizes of vessels are relatively large and confluent in the lesser curvature of the upper body. What endoscopic hemostasis methods are most suitable on specific situation of each vessel remains to be determined in future studies.

TECHNIQUES FOR ENDOSCOPIC THERAPY

Endoscopic therapies are classified into injection therapy, ablative therapy, mechanical therapy, and combination therapy.

INJECTION THERAPY

Injection therapy is an easy and most simple method to any NVUGIB. This form of therapy aims at controlling bleeding by means of hydrostatic tamponading pressure, vasoconstriction, and/or possibly a secondary inflammatory reaction. Usually 2 to 10 mL of solution is used for one lesion, which can be changeable by location, size, or characteristics of the lesion.

The advantages of this technique are easiness to learn and economic merit of using not expensive equipment such as sclerotherapy needle. The disadvantages are that missed injection can result in a brisk bleeding and subsequently mask the visible area for treatment. Furthermore, the effects are short lasting, as the injected fluid gradually dissipates.

There are various injection materials and their reported initial hemostasis ranges from 80% to 100%. Most common form of injection material is epinephrine mixture, which is diluted (1:10,000) and administered through a 25-gauge retractable sclerotherapy needle. This solution can be injected in increments of 0.5 to 1.5 mL targeting near the ulcer. There are no clear guidelines as to the ideal volume. Non-constrictive agents such as distilled water, normal or hypertonic sa-

line, and 50% dextrose have been also introduced. Studies show that initial hemostasis rates are comparable to that of epinephrine; however, when compared to hemoclips, the recurrent bleeding rates are generally higher in the injection group. These agents work by their local compressive action. Other agents including sclerosants such as ethanol and polidocanol have been used but side effects such as tissue necrosis have resulted in complications including even perforation. Alcohol injection dehydrate exposed vessel by direct injection to vessel. Epinephrine injection makes vessel disappear on the base of ulcer after several days. Tissue adhesives (cyanoacrylate) and fibrin glue are other injectable solutions which have yielded variable results.

MECHANICAL THERAPIES

The endoscopic mechanical modality currently available is hemoclip, a metallic device designed to grasp the mucosa as well as seal and approximate vessels without interfering with underlying mucosal regeneration and healing. They need precise deployment since inadvertent clipping of only the tip of the vessel can result in potentiation or initiation of vigorous bleeding. End on clipping with axial push of surrounding tissue resulting in better anchoring is preferred over tangential clipping, which may slip on fibrotic ulcer bases. Difficult areas such as the gastric fundus, lesser curvature, and posterior duodenal bulb present challenging territories for effective clip application. Similarly, clipping in the setting of underlying coagulopathy can also aggravate bleeding. Most clips slough off within days or weeks of deployment, which may vary depending on the type of clip.

The followings are several practical tips for perfect hemoclipping. Final dislodgement of clips is better at proximal or most near site from the tip of endoscope. Endoscopists have to decide the object of clipping; stigmata, surrounding vessel, or the entire lesion. We have to decide suitable size of clip based on the characteristics of lesion. Timely opening or closing of clip without hesitation or slowness is also important. We have to think perpendicular angle and correct direction of clip arm, and have to decide compression or stay introducer during final clipping. Sites that are difficult to approach, such as post wall and lesser curvature aspect of body, post wall of duodenal bulb, or duodenal second portion, can be accessed by cap fitted method. Cap fitted method can change angle from horizontal to perpendicular approach, from oblique to direct visualization, and from unstable to stable position. Multi-bending endoscope can be introduced to approach and ligate lesions at these specific locations with better flexibility than common endoscopes.

Currently available endoclip was introduced by Olympus

Co. (Tokyo, Japan). This is a rotatable clip device produced in various sizes with various degrees of tip and arm length, designed for specific condition of each size and characteristics of tissue. Its advantages include small tissue damage, repeated procedure, and wide indication with reasonable cost-effectiveness. Disadvantages include limitations in sites with low accessibility and in severe fibrotic tissue as well as the risk of malfunction. There are several new clips such as Resolution Clip (Boston Scientific Co., Natick, MA, USA) which can be reopened for repositioning after closure, TriClip (Wilson Cook Inc., Winston-Salem, NC, USA) with a three-pronged clip, and Inscope (Ethicon Endo-Surgery Inc., Cincinnati, OH, USA) multiclip applicator with four endoclips.

Band ligation is another option for endoscopic hemostasis, and various devises are introduced with their individual merits. Advantages of band ligation are: easy application, accessibility to difficult sites, shorter procedure time, and deeper ligation. Disadvantages are poor visual field, unavailability in fibrotic tissue, the risk of perforation, and narrow indication. Band ligation methods are useful in case of Dieulafoy like ulcer or angiodysplasia lesions, and its role is the same as mechanical ligation of hemocipping. Degree of suction has to be modified by site; deep suction is suitable for esophagus and distal stomach while shallow suction is suitable for proximal stomach and duodenum. Target point has to be corrected by angle so that the target point should be at the center on the frontal view, contrary to proximal lesion on the oblique view.

Chiu et al.[6] studied the endoscopic plication using Eagle Claw VII (Olympus Co.) in a porcine bleeding ulcer model and showed success of endoscopic stitching. It is expected to be used for severe or nearly perforated ulcer or operational field, but it needs human studies in advance.

We can summarize the strategies of mechanical hemostasis as follows: In peptic ulcer, if fibrosis is prominent, deep clipping by short clip is suitable. Wide clipping by long clip is suitable on soft tissue. Cap fitted method and positional change are good alternative methods in locations difficult to access. In Mallory Weiss syndrome, according to experience, band ligation should be selected by a non-expert, while clipping can be chosen by expert endoscopists. In Dieulafoy lesion, band ligation is suitable for difficult locations, and clipping is suitable for easy sites.

THERMAL COAGULATION

Thermal endoscopic hemostasis can be classified by contact and noncontact methods. Contact method is classified by heater probe (HP) thermocoagulation and electrocoagulation such as bipolar. Noncontact methods include argon plasma coagulation (APC) and yttrium aluminum garnet (YAG) laser coagulation.

Contact therapies

These ensure appositional pressure resulting in a heat-sink effect in addition to tissue coagulation with contraction of blood vessels. These include the bipolar probe or the HP which can weld arteries (coaptive coagulation) as large as 2.5 mm in diameter in controlled laboratory conditions.[7]

The two currently available bipolar probes include Gold Probe (Microinvasive; Boston Scientific Co.) and BICAP or bipolar circumactive probe (Circon-ACMI, Stamford, CT, USA). The probes are available in diameters of 2.4 to 3.2 mm and have alternating positive and negative electrodes which concentrate diathermic coagulation concentrated around the tip providing lesser depth of tissue injury and lower risk for perforation.

The HP (Olympus Co.) uses a simple heating device in a teflon-coated hollow aluminum cylinder with an inner coil rather than electric current. The generated heat can be given directly or tangentially by the distal tip. Probes are available in diameters of 2.3 to 3.2 mm. The probe temperature can rise up to 250°C (482°F). Four to five bursts of energy of 30 J/pulse are applied for adequate coagulation.[7]

Non-contact therapies

The use of neodymium:YAG laser for endotherapy is rarely used today primarily owing to the increased depth of coagulation resulting in high rates of perforation as well as the excessive maintenance costs. The underlying mechanism of action is the conversion of light to heat energy by the directed beam which coagulates the bleeding site.

APC as a non-contact thermoablative technique is now available at many endoscopic units. It has advantages of being safe given the depth of penetration (<1 mm) and relative ease of use. However, there is a disadvantage of providing only superficial coagulation which may thus miss larger deeper vessels.

Advantages of thermal coagulation are easiness of application, accessibility to difficult sites, shorter procedure time, and immediate confirmation of hemostasis. Disadvantages are high cost of equipment, problem of coagulated tissue, high perforation risk, and narrow indication.

As for the tips for thermal coagulation, contact method with direct approach is suitable on gastric body and distal stomach. Non-contact method with side approach is suitable on esophagus, proximal stomach and duodenum. Contact method should be selected on large vessels and spurting from a protruding vessel. Non-contact method can be selected on oozing or diffuse bleeding from a vague vessel.

ENDOSCOPIC COMBINATION THERAPY

Endoscopic therapy using a combination of the methods discussed above is favored to monotherapy, considering the theoretical additive effect of each modality and different mechanisms of action of each technique. The benefits of dual therapy have been studied in several trials with most studies offering an additional hemostatic therapy to epinephrine injection.[8] A second procedure further reduced the bleeding rate from 18.8% to 10.4% (odds ratio [OR], 0.51), and the need for emergency surgery from 10.8% to 7.1% (OR, 0.63).The mortality fell by half from 5% to 2.5% (OR, 0.50). Another study by Marmo et al.[9] comparing dual versus monotherapy in high-risk ulcer patients suggested that single endoscopic treatment by means of thermal probes or clips (non-injection-based monotherapies) is as effective as dual treatments and probably safer. These results encourage endoscopists to use more than one modality other than injection alone, especially in patients with high risk of ulcer bleeding.

ENDOSCOPIC SPRAY METHOD

A new promising endoscopic application is the use of a chemical compound which covers bleeding ulcer with a layer of nanopowder when sprayed and leads to immediate hemostasis. In a pilot study of 15 patients with active ulcer bleeding treated with this nanopowder, immediate hemostasis was achieved in 93%, and only one patient had recurrent bleeding. No adverse events were reported during the 30-day follow-up.[10] Several considerations such as time to spray, situation, amount, and method to confirm hemostasis should be established. Further studies with this product or other hemostatic material are ongoing and will elucidate if the endoscopic spary is also beneficial for other causes of NVUGIB.

LIMITATIONS AND OTHER CONSIDERATIONS

Complications of endoscopic therapy are limited and include aspiration pneumonia and perforation. A pooled analysis for all these modalities revealed a complication rate of 0.5% (95% confidence interval, 0.4 to 0.8).[11] Clips and epinephrine injection had the lowest rates of perforation while the HP group had the highest rate. Endoscopic therapy is limited by factors such as an unstable condition of patients, poor sedation, inadequate visualization due to blood, and areas difficult to reach such as the posterior wall of duodenum, junction between the first and second part of duodenum, and lesser curvature side.

Transarterial embolization as a rescue therapy can be se-lected for refractory bleeding to any endoscopic hemostasis in high risk patients for operation. Indications for operation in UGIB have been known as more than three times of endoscopic hemostasis and large amount of transfusion more than 10 pints of packed red blood cell. Uncontrolled bleeding, unstable vital sign despite repeated hemostasis, and possibility of perforation can be other indications for operation.

CONCLUSIONS

NVUGIB is the most common gastrointestinal emergency. Early endoscopy is important in management and prognosis of NVUGIB. Endoscopic therapy is indicated for patients with high-risk stigmata, in particular those with active bleeding and visible vessels. Endoscopic therapy has main role in every NVUGIB. Combined treatment is more effective than injection treatment alone, and single treatment with mechanical or thermal method is safe and effective for PUB. Specific treatments and correct decisions are needed depending on various situations including site, location, and specific characteristics of lesion and patient's clinical conditions. The application of an ulcer-covering hemospray and endoscopic suturing are new promising tools. Various hemostatic methods can be selected optimally in each cause of NVUGIB.

Conflicts of Interest

The author has no financial conflicts of interest.

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