



# Gastrointestinal Bleedings and Advances in the Endoscopic Therapies

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## INTRODUCTION

Upper GI bleeding is a common medical presentation in gastroenterology practice and approximately 90% of gastrointestinal bleeds are from the upper digestive tract. It is estimated that greater than 350,000 hospital admissions for UGI bleeding occurs annually with an overall mortality rate of 10%.<sup>1</sup> During the past decade endoscopic hemostatic therapy has simplified the management of upper GI bleeding. In fact endoscopy is considered a primary and pivotal early intervention in establishing the source and cause of bleeding. It also allows estimation of an individual's risk for recurrent bleeding and therapeutic intervention accordingly. Early endoscopy with therapeutic interventions is associated with lower cost of care and improved medical outcomes.

The causes of upper GI bleeding could be classified as follows:

- Duodenal ulcer (30-37%)
- Gastric ulcer (19-24%)
- Esophageal varices (6-10%)
- Gastritis or duodenitis (5-10%)
- Esophagitis or esophageal ulcer (5-10%)
- Mallory Weiss tear (3-7%)
- Gastrointestinal malignancy (1-4%)
- Dieulafoy's lesion (1%)
- Arteriovenous malformation
- Angiodysplasia of the stomach or duodenum

This chapter attempts to discuss the recent advances and consensus on endoscopic management of upper GI bleeding.

Endoscopic management strategies differ based on the cause of bleed and can be classified into two primary divisions:

- Variceal Bleeding
- Non-variceal bleed

## ENDOSCOPIC MANAGEMENT OF VARICEAL BLEEDING

### Epidemiology

Bleeding from esophagogastric varices is a major complication of portal hypertension. Varices are identified in about 30% of patients with well-compensated cirrhosis and 60% of patients

with decompensated cirrhosis.<sup>2</sup> Small varices are at low risk of hemorrhage compared to bigger ones. Varices increase in size from small to large at the rate of 10-20% per year.<sup>2,3</sup> Variceal bleeding takes place at the rate of 10-20% per year but rises to 20-30% per year in patients with large varices.<sup>4</sup> The statistics are important because bleeding from varices is responsible for more than a quarter of deaths in patients with cirrhosis.<sup>5</sup>

### Therapeutic Endoscopy for variceal bleeding

The goal of therapeutic endoscopy is to stop acute variceal bleeding by creating an intravariceal thrombus. Repeated procedures may induce variceal obliteration. Two techniques are now standardized:

#### *Endoscopic sclerotherapy*

Sclerotherapy involves injecting an irritant solution (e.g., sodium morrhuate, ethanolamine or polidocanol) or a dehydrating chemical (sodium tetradecyl sulphate) into the esophageal varix or its adjacent supporting tissues. This results in acute induction of vascular spasm, with subsequent development of intravariceal thrombosis, intimal thickening and perivenous thrombosis.<sup>6</sup>

Although sclerotherapy was introduced as early as 1939, it was only with the advent of fibre optic endoscopy in the mid 1970's that sclerotherapy was accepted as an effective mode of management of esophageal varices. It is now recognized that sclerotherapy can achieve early hemostasis in up to 95% of patients suffering from variceal bleeding.<sup>2</sup>

However sclerotherapy has a number of drawbacks. These are summarized as follows:

1. It usually takes 3-6 ES sessions to obliterate esophageal varices.<sup>7</sup>
2. ES has no role in the control of bleeding from portal hypertensive gastropathy.
3. It is rarely successful in the emergent control of bleeding from large gastric varices.
4. Complication rates have ranged from 10% to 20% and associated mortality rates as much as 1% to 2%. Post-sclerotherapy esophageal ulcer is the commonest complication of ES. These ulcers may be further complicated by esophageal dysmotility and esophageal stricturing which is seen in 1.6%-3% of patients.<sup>8</sup>

**Table 1 : Rockall numerical risk scoring system**

	0	1	2	3
Age (years)	<60	60-79	>80	
Shock	None	Tachycardia	Hypotension	
Comorbidity	None	None	IHD or CHF	Hepatic/renal failure
Diagnosis	No lesion/SRH/MWT	All others	UGI malignancy	
Major SRH*	None/ dark spot only	Blood, adherent clot, visible or spurting vessel		

\*SRH: Stigmata of recent hemorrhage; \*\* Source: Rockall et al<sup>23</sup>

Risk of rebleeding and mortality respectively were 4.3% and 0 when the score was <2;14% and 4.6% when it was 3-5 and 37% and 22% when >6.

Other complications including esophageal perforation (0.5%), systemic infections, pleural effusion, mediastinitis, portal and mesenteric vein thrombosis and adult respiratory distress syndrome has been reported.

5. Sclerotherapy is known to worsen portal hypertensive gastropathy and increase the size of gastric varices seen at sites above the level of variceal obstruction.<sup>9</sup>

### **Endoscopic variceal ligation (EVL)**

EVL is a promising alternative to sclerotherapy. The basic principle of this procedure is similar to and derived from a hemorrhoid banding procedure. A special ligating chamber is fitted to a standard endoscope. The varix is suctioned into the ligating chamber and an elastic O ring released around the neck of the varix creating a polyp.<sup>10</sup> This results in the coagulative necrosis of the ensnared polyp, with eventual sloughing. Varices in the adjacent submucosa subsequently thrombose. Additionally acute inflammation of the superficial mucosa leads to shallow ulcers followed by healing, granulation tissue and resultant obliteration of variceal channels.<sup>11</sup>

The original band ligating device could employ only one "O" ring at a time. Technical problems were encountered with this system including a limited field of view and the need to reload bands. Multi-band ligating devices are now available. The multiband ligator has obviated the need of passing an overtube prior to starting an EVL and only one passage of the endoscope is needed. This has in turn reduced the risks of esophageal laceration and perforation and increased the safety of the procedure.

Endoloop ligation with detachable endoloops is the latest modification to overcome drawbacks associated with the use of band ligators.<sup>12</sup> This is the only method that can stop bleeding from vessels 3-5mm in diameter because it exerts a greater compressive force on tissue compared to elastic bands. Also, because endoloops attach more tightly to tissue, it could be the treatment of choice for junctional varices in the cardia of the stomach where the tissues are thicker compared to the esophageal mucosa.<sup>13</sup>

**Table 2 : Modified Forrest Criteria**

Type 1: Actively bleeding ulcer
1a. Spurting
1b. Oozing
Type 2: Non-actively bleeding ulcer
2a. Non-bleeding visible vessel
2b. Ulcer with surface clot
2c. Ulcer with red or dark blue spots
Type 3: Ulcer with clean base

### **EVL vs. ES vs. Endoloop**

The first randomized trial comparing EVL with ES was reported in 1992.<sup>14</sup> By 1995 at least seven randomized trials underwent meta-analysis. Other long term data have subsequently been published comparing the two.

Compared to ES, EVL significantly reduced the rebleeding rate, the mortality rate, and the death rate due to rebleeding.<sup>15</sup> On an average it took lesser number of EVL sessions to obliterate varices than ES. Also, there were fewer treatment-induced ulcers and complications associated with EVL. In fact, only 1.0% of EVL procedures were associated with fatal complications compared to 3.3% with ES. Some studies have however reported higher frequency of variceal recurrence (48%) compared with sclerotherapy (30%).<sup>16</sup>

Comparative studies between EVL and endoloop ligation have shown both to be equally effective in achieving hemostasis. There are no statistically significant difference in recurrent bleeding between the two groups. However variceal eradication after the initial treatment appears to be higher in the endoloop group as compared to the band group. Also, technically the chances of damage to the endoscope are lesser with the endoloop as the connecting thread between the cap and trigger in the multiband ligation device exerts a strain on the endoscope throughout the procedure.<sup>17</sup>

### **Alternative endoscopic approaches and the future**

Endoscopic management of gastric varices is the current focus of research. One approach uses sclerotherapy technique to inject the tissue adhesive N-butyl-2-cyanoacrylate. Cyanoacrylate injections with simultaneous sclerotherapy have shown promising results.

Other recent advances include the use of endoscope to deploy detachable clips and detachable snares in an effort to entrap esophageal varices and induce thrombosis.<sup>18,19</sup>

Ligation therapy is considered the endoscopic treatment of choice for esophageal variceal bleeding. However ligation may be technically difficult in patients with a large amount of blood in the esophagus and treatment of active bleeding at initial endoscopy is more easily accomplished by sclerotherapy. Sclerotherapy is also useful near the end of a course of treatment when only small varices remain and proper degree of aspiration of the varices into the ligation chamber is not possible. Additional clinical experience with detachable endoscopic clips, snares and the newer techniques are required to standardize endotherapy of varices.

**Table 3 : Endoscopic modalities available for management of UGI bleed**

Injection	Thermal	Mechanical
Adrenaline	Heater probe	Haemoclips
Fibrin glue	Bicap probe	Banding
Human thrombin	Gold probe	Endoloops
Sclerosants	Argon plasma coagulation	Staples
Alcohol	Laser therapy	Sutures

## ENDOSCOPIC MANAGEMENT OF NON-VARICEAL UPPER GI BLEED

### Epidemiology

Peptic ulcer accounts for about 50-70% of all cases of upper GI hemorrhage as diagnosed on upper GI endoscopy.<sup>20</sup> A Dieulafoy lesion accounts for up to 5% of cases of GI hemorrhage and is another important cause of upper GI bleeding.<sup>21</sup> Upper GI vascular ectasias including gastric antral vascular ectasias (GAVE) and angiodysplasia are also being recognized as increasingly important sources of GI bleeding.

Bleeding from peptic ulcer stops spontaneously in 70-80% of cases.<sup>22</sup> However mortality from peptic ulcer bleed ranges from 5-10% and could be as high as 50% in case of rebleed.<sup>22</sup> Clinical and endoscopic stratification of patients into low and high risk categories is thus crucial to decide the line of management. The Rockall score is an accepted clinical scoring system for predicting outcome (Table 1).

The modified Forrest criteria are internationally accepted for endoscopic risk stratification of peptic ulcer (Table 2). Type 2c & 3 require no endotherapy as risk of rebleed is only 5-10%. Type 1 & 2 require endotherapy with a rebleed risk of 43-55%.

Endoscopic haemostasis is thus the key therapeutic tool for management of all high-risk cases of non-variceal bleed. In two meta-analyses comprising over 30 randomized trials involving over 2400 patients, endoscopic therapy significantly reduced rebleeding, need for emergency surgery, and mortality.<sup>24,25</sup> In parallel these improved health outcomes are associated with significant cost benefit both to the patient and the healthcare system.<sup>26</sup>

Hemostatic techniques available at the time of endoscopy could be classified as shown in Table 3. Selection of the optimal hemostatic device would depend primarily on the characteristics of the lesion, local expertise, and equipment availability and of course cost of the procedure.

### Thermal hemostatic devices

All thermal devices generate heat either directly (heater probe) or indirectly by tissue absorption of light energy (laser) or passage of electric current through tissue (multipolar probes, argon plasma coagulator). Heating leads to edema, coagulation of tissue protein and contraction of vessels resulting in a haemostatic bond.

The conventional gold probe is reasonably effective, cheaper and widely available. Laser therapy is the precise, effective albeit expensive alternative. Laser systems may additionally be cumbersome requiring 220V power source and with limited portability. Both these methods however have the potential

to cause unintentional injury to the adjacent as well as deeper tissues. The rate of perforation following treatment of GI bleeding ranges from 1.8-3% and precipitation of bleeding has been reported in up to 5%.<sup>27</sup> Complications may be related to power setting, duration of application, and distance of the probe tip from the tissue.

Argon plasma coagulation has an inherent advantage in that it produces superficial tissue coagulation with a penetration depth of only 1 to 2 mm. Also, it is easier to use particularly in the duodenum and is cheaper than the laser.<sup>28</sup>

At the Asian institute of gastroenterology we have recently used the "spray coagulation" system endoscopically with encouraging results. This method is normally used in surgery to control bleeding e.g. from the gallbladder fossa after cholecystectomy. It may be a useful alternative in that it involves no new equipment and thus is very cost-effective.

### Injection needles

Injection needles are devices passed through the working channel of an endoscope that allow the injection of liquid agents into target tissue. They consist of an outer sheath (plastic, Teflon or stainless steel) and an inner hollow-core needle and are available in lengths of 200 to 240cm. Solutions administered via these needles achieve haemostasis by mechanical tamponade, induction of vasospasm and thrombosis of vessels.

Injection therapy is simple to perform and is the cheapest available diagnostic modality. A large range of injection materials has been used including dilute adrenaline (1in10000), fibrin glue, thrombin, alcohol and a variety of sclerosants have been used. Current evidence suggests that dilute adrenaline is effective and safe for active hemorrhage. Rebleeding rates are reduced by the addition of agents such as thrombin or a thrombin-fibrinogen mixture. Sclerosants and alcohol should be used only sparingly because of the risk of serious complications including rebleeding, sclerotherapy ulcers and perforation.<sup>28</sup>

### Mechanical devices

These arrest bleeding by applying a direct pressure in case of minor injuries or by applying ligature when a larger vessel is involved. A range of metallic clips (haemoclips), bands and loops are now available.

Endoscopic haemoclips have achieved hemostasis in 84 to 100% of patients with a variety of upper GI bleeding sources peptic ulcers, Mallory Weiss tears, Dieulafoy lesions, gastric angiectasias, gastric tumors and following polypectomy, sphincterotomy and biopsy.<sup>29</sup> The advantages of haemoclips are that they cause no tissue injury, do not impair tissue healing and can be applied relatively quickly and safely using improved applicators. Clips are particularly well suited for the treatment of arterial bleeding and visible vessels and appear to be the treatment of choice in such situations.

Other mechanical methods like band ligation and endoloops are usually used for small focal bleeders like Dieulafoy's lesions. Newer mechanical suture devices are now being introduced but further clinical experience is needed to prove its practicability and long term results.

## Combined modalities

There is trend towards combined use of two endoscopic modalities using injection and mechanical or injection and thermal probe therapy in actively bleeding peptic ulcer. Adrenaline injection and thermocoagulation combined have shown lesser rebleed rates than injection alone in some studies whereas others have not been as conclusive.<sup>30,31</sup> Larger comparative trials are necessary for a definite answer

## Consensus Recommendations for Endoscopic Management of Non-variceal upper GI bleed<sup>32</sup>

- Early endoscopy (within the first 24 hours) with risk classification by clinical and endoscopic criteria allows for safe and prompt discharge of patients classified as low risk; improves outcomes for patients classified as high risk; reduces resource utilization for patients classified as either low or high risk.
- A finding of low-risk endoscopic stigmata is not an indication for endoscopic hemostatic therapy. A finding of a clot in an ulcer bed warrants targeted irrigation in an attempt at dislodgement, with appropriate treatment of the underlying lesion.
- No single solution for endoscopic therapy is superior to another for haemostasis.
- No single method of thermal coaptive therapy is superior to another.
- Monotherapy with injection or thermal coagulation, is an effective endoscopic haemostatic technique for high risk stigmata; the combination is superior to either alone.
- The placement of clips is a promising endoscopic hemostatic therapy.
- Routine second look endoscopy is not recommended.
- In cases of rebleeding, a second attempt at endoscopic therapy is generally recommended.

As it stands today, optimal use of endoscopic therapeutic modalities shall continue to play a pivotal role in the management of UGI bleed in the years ahead.

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