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## Advancements in hemostatic strategies for managing upper gastrointestinal bleeding: A comprehensive review

Ah Young Lee, Joo Young Cho

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### Abstract

Upper gastrointestinal (GI) hemorrhage presents a substantial clinical challenge. Initial management typically involves resuscitation and endoscopy within 24 h, although the benefit of very early endoscopy (< 12 h) for high-risk patients is debated. Treatment goals include stopping acute bleeding, preventing rebleeding, and using a multimodal approach encompassing endoscopic, pharmacological, angiographic, and surgical methods. Pharmacological agents such as vasopressin, prostaglandins, and proton pump inhibitors are effective, but the increase in antithrombotic use has increased GI bleeding morbidity. Endoscopic hemostasis, particularly for nonvariceal bleeding, employs techniques such as electrocoagulation and heater probes, with concerns over tissue injury from monopolar electrocoagulation. Novel methods such as Hemospray and Endoclot show promise in creating mechanical tamponades but have limitations. Currently, the first-line therapy includes thermal probes and hemoclips, with over-the-scope clips emerging for larger ulcer bleeding. The gold probe, combining bipolar electrocoagulation and injection, offers targeted coagulation but has faced device-related issues. Future advancements involve combining techniques and improving endoscopic imaging, with studies exploring combined approaches showing promise. Ongoing research is crucial for developing standardized and effective hemorrhage management strategies.

**Key Words:** Upper gastrointestinal bleeding; Hemostasis; Endoscopy; Probe; Spray; Clip

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**Core Tip:** Endoscopic hemostasis for nonvariceal upper gastrointestinal bleeding primarily involves electrocoagulation and heater probes, though monopolar electrocoagulation raises tissue injury concerns. Newer methods such as Hemospray and Endoclot offer mechanical tamponade but with limitations. First-line treatments currently include thermal probes and hemoclips, with over-the-scope clips gaining traction for larger ulcers. The gold probe, merging bipolar electrocoagulation and injection, targets coagulation effectively but has device-related issues. Future progress lies in integrating techniques and enhancing endoscopic imaging. Research is vital to establish standardized, effective hemorrhage management strategies.

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## INTRODUCTION

Upper gastrointestinal (GI) hemorrhage is a substantial clinical challenge that often necessitates urgent medical intervention. Notably, bleeding from ulcers halts spontaneously in at least 80% of cases without specific intervention[1]. However, the annual incidence of upper GI bleeding (UGIB) ranges from 0.05% to 1%, with several patients succumbing to this condition[2]. This underscores the critical need for effective hemostatic treatments and the importance of ongoing research in this area.

Initial management of GI hemorrhage typically involves resuscitation and subsequent decisions regarding therapeutic interventions. Current guidelines advocate endoscopy within 24 h for patients with UGIB. Whether high-risk patients would benefit more from very early endoscopy (within 12 h) remains open to debate[3,4]. Studies have indicated that restrictive fluid resuscitation (employing a delayed or smaller fluid volume) is not inferior to more aggressive fluid resuscitation strategies (involving early or larger fluid volumes) in terms of mortality[5].

The primary goals of treating GI hemorrhage are two-fold: Halting acute bleeding episodes and preventing rebleeding. Achieving these goals requires a multimodal approach that includes endoscopic, pharmacological, angiographic, and surgical therapies. Various pharmacological agents, such as vasopressin, secretin, prostaglandins, somatostatin, and proton pump inhibitors have been effectively employed for the management of GI hemorrhage[6]. However, studies have also highlighted that the increasing incidence of combined pharmacological agents such as antithrombotics has increased the morbidity from GI bleeding, indicating that direct intervention is often essential[1]. Angiographic therapies, including gel foam and vasopressin, have been used, although they can potentially lead to complications, such as ischemia, stenosis, infarction, perforation, and abscess formation[7].

Endoscopic hemostasis has become the accepted standard of care for individuals presenting with acute nonvariceal upper GI hemorrhage. Techniques such as monopolar electrocoagulation, bipolar electrocoagulation, and heater probes have also been used. Although effective, monopolar electrocoagulation can cause a greater degree of tissue injury than bipolar electrocoagulation, which has been a source of concern[8]. This technique uses a single electrical circuit to heat and stop the bleeding, which can sometimes harm surrounding tissues. However, bipolar electrocoagulation, which uses two electrical points to create a more focused and less damaging heat, and heater probes, are particularly useful for arterial bleeding of < 2 mm, which addresses the requirements of the majority of patients with ulcer bleeding[9].

Injection strategies vary depending on the agent used, with mechanisms of action that may include vasoconstriction, tamponade effects, induction of platelet aggregation, sclerosis, thrombosis, and/or tissue desiccation[10]. At our center, during endoscopic submucosal dissection (ESD) and peroral endoscopic myotomy procedures, we initially apply injection techniques when the bleeding source is unclear, primarily to induce vasoconstriction and tamponade effects, thereby reducing bleeding before proceeding to precise clipping. An innovative approach involves the use of a powder, specifically Hemospray (HS, TC-325; Cook Medical, Bloomington, IN, United States). When this powder comes into contact with blood, it absorbs water and works together to create a mechanical barrier by acting cohesively and adhesively to form a mechanical tamponade. This process helps to stop bleeding effectively. By absorbing fluid, HS enhances clot formation by deforming and packing erythrocytes, concentrating activated platelets with clotting factors, and interacting with the fibrin matrix[11]. However, its residence time is limited to 24 h or less, and it does not induce tissue healing. Consequently, TC-325 monotherapy might not be adequate for treating ulcers with high-risk stigmata but can be useful as a temporary measure to halt bleeding. In such cases, a second-look endoscopy or an additional hemostatic technique is recommended[12]. Our team primarily uses TC-325 particularly after procedures such as ESD, when there is substantial bleeding, or when the depth of post-procedural ulcers suggests a risk of delayed bleeding.

Endoclot (EC; Micro-Tech Europe, Düsseldorf, Germany) is made of starch-derived compounds composed of absorbable hemostatic polysaccharides. Similar to HS, upon contact with blood, EC initiates a dehydration process that leads to a concentration of clotting factors, platelets, and erythrocytes, thereby accelerating the physiological clotting cascade and the formation of a mechanical shell of the gelled matrix that adheres to the bleeding tissue[13].

Currently, the first-line therapy for ulcer-related GI bleeding includes the use of thermal probes and through-the-scope clips with or without the adjunctive use of submucosal epinephrine injection[14]. However, there are limitations to achieving hemostasis during active hemorrhage, especially in cases of large and/or cratered fibrotic ulcers in anatomically challenging locations. Recently, over-the-scope clips (OTSCs) have emerged as a promising alternative. These

larger-caliber clips, composed of nitinol, a metal known for its shape memory effect and high-grade elasticity, allow high-pressure closure of larger mucosal areas. OTSCs capture deeper tissue layers and may enhance hemostasis[15]. Given meta-analysis findings that OTSCs reduce 30-d rebleeding in UGIB, their use has increased[16]. Our endoscopy team primarily employs OTSCs in cases of bleeding where perforation is suspected.

The gold probe (Microvasive, Boston, MA, United States) represents a considerable advancement in this field of research. This probe combines bipolar electrocoagulation with an internal injection mechanism, which makes it particularly useful for targeting specific coagulation sites. When positioned perpendicular to the mucosa, the probe at 20 W and 40 W for less than 6 s caused coagulation confined to the mucosal layer, whereas at 9 s, submucosal coagulation occurred, and at 80 W for more than 15 s, coagulation extended to the muscular layer[17]. The design of the gold probe aims to reduce kinking, thus facilitating its advancement and providing better en face and tangential tamponades. The integration of injection and thermal hemostasis into a single catheter is intended to reduce catheter exchange and the procedural time. The precise spacing of the electrode pairs helps to control the coagulation depth, and the rounded distal tip is designed to facilitate effective coagulation at various tip positions. However, issues have arisen with gold probes, particularly when used with or without injection, including energy delivery, followed by material separation, fracture of the probe tip, arcing, missing components, bending of the tips, and device detachment.

Given these frequent device-related problems, the use of a gold probe, even without adverse effects on patients, might not be advisable. In endoscopic hemostasis therapy, two major complications, i.e., uncontrollable bleeding and viscus perforation, are rare; however, their potential occurrence must be considered in every case.

The future direction for advancement in hemostatic techniques involves evaluating the combination of different methods for their safety and effectiveness. One study explored a conventional combined technique involving saline adrenaline injection followed by heater probe application. This method involved injection of saline adrenaline, followed by application of a heater probe to the ulcer at the site of the visible vessel. Subsequent energy pulses up to 30 J were delivered until the vessel was completely flattened or ablated. This approach was superior to TC-325 monotherapy. One potential strategy involves the application of TC-325 multiple times over the first few days following a conventional combined technique. Furthermore, the combination of OTSCs with various hemostatic tools merits further investigation to determine their efficacy. Advancements in endoscopic imaging techniques are crucial for more accurate and effective bleeding control. For example, the recent introduction of the Olympus X1500 endoscope model and its use of rapid diagnostic imaging (RDI) is a step quicker identification of bleeding sites. However, there is no complete consensus on the diagnosis and management of hemorrhages, highlighting the need for ongoing research to develop standardized and quantified indications and methods.

## CONCLUSION

In conclusion, endoscopic hemostatic techniques, much like the once-prominent but now less used gold probe, are evolving. While methods such as injection and clipping have been consistently employed in the past, there is a growing scope for newer techniques such as OTSCs and hemostatic powder for managing UGIB. The introduction of the Olympus X1500 with its RDI adds another dimension to diagnosing and managing bleeding foci. Continuous research is necessary to further explore and optimize the application of these hemostatic techniques.

## FOOTNOTES

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