

Reviewer #1

Comment 1

This article offered a thorough overview of the current approaches to managing upper gastrointestinal hemorrhage. It discussed a range of pharmacological, endoscopic, and angiographic therapies, as well as innovative methods like Hemospray and Endoclot, showcasing the multifaceted nature of treating GI hemorrhage. The article also mentioned advances in endoscopic techniques, such as over-the-scope clips (OTSCs) and the Gold probe, while underscoring the importance of assessing the combination of different methods for safety and efficacy. It's clear that advancements in endoscopic imaging techniques, such as the Olympus X1500 endoscope model with Rapid Diagnostic Imaging (RDI), were crucial for more precise and effective bleeding control. The need for ongoing research to establish standardized indications and methods for diagnosing and managing hemorrhages was clearly highlighted. In sum, this review provided a comprehensive understanding of the current landscape of hemostatic treatments for upper GI hemorrhage and underscored the need for continued research and development in this critical area. The article would be more informative if it included discussions about the specific scenarios in which each method is most effective.

Response 1

We are deeply grateful for the positive reception of our manuscript and the valuable insights provided. Following your advice, we have incorporated specific scenarios regarding hemostasis techniques into the discussion section of the text.

Page 4, lines 15 – Page 4, line 19

In 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.

Reviewer #2

The paper provides a detailed and exhaustive overview of the management of upper gastrointestinal (UGI) hemorrhages and the various strategies used in clinical practice. Overall, the paper is well-written and structured, presenting relevant and up-to-date information in the field. Here are some positive aspects: 1) Clarity and Structure: The paper follows a logical structure, first presenting the importance of the problem, followed by management strategies and innovations in technologies. This facilitates reader comprehension. 2) References: Bibliographic references are provided to support the presented claims and data, which is essential in a scientific context. 3) Content Breadth: It covers a wide range of therapeutic approaches, from medical strategies to endoscopic and surgical interventions, providing a comprehensive view of the topic. However, there are some areas that could be improved.

Comment 2-1

While the paper is well-written, in some points, it may feel dense due to the amount of technical information. It would be beneficial to simplify some sentences to enhance accessibility and understanding, especially for non-specialist readers.

Respond 2-1

Thank you for the helpful advice. Following your suggestion, I have revised some parts of the text to make it more accessible to non-specialist readers, while maintaining its scientific integrity.

Page 4, lines 4 – Page 4, line 12

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, 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. On the other hand, 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, covering the majority of ulcer bleeding^[9]

Comment 2-2

Concept Clarification: Some technical terms could benefit from a brief explanation for readers not familiar with advanced medical terminology. This would improve overall text comprehension.

Respond 2-2

Thank you for the advice. Following your suggestion, I have rephrased and elaborated on some technical terms to make them more understandable to readers.

Page 4, lines 4 – Page 4, line 12

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, 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. On the other hand, 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, covering the majority of ulcer bleeding^[9]

Page 4, lines 19 – Page 4, line 24

An innovative approach involves the use of a powder, specifically Hemospray (HS, TC-325, Cook Medical, Bloomington, Indiana, United States). Essentially, when this

powder comes into contact with blood, it absorbs water and works together to create a sort of mechanical barrier by acting cohesively and adhesively to form a mechanical tamponade. This process helps to stop bleeding effectively.

Comment 2-3

Emphasis on Conclusions or Key Points: Towards the end of the paper, it might be helpful to summarize or highlight key points, such as emerging trends, current challenges, and future directions in the research and treatment of upper gastrointestinal hemorrhages. In summary, the paper provides a well-referenced and detailed review of the management of upper gastrointestinal hemorrhages. Some improvements in clarity and structure could make the information more accessible to a broader audience

Response 2-3

Thank you for the kind feedback. Following your advice, I have integrated both a summary and future directions into the conclusion section.

Page 7, lines 1 – Page 7, line 7

In conclusion, endoscopic hemostatic techniques, much like the once-prominent but now less-utilized 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. 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.

Reviewer #3:

Comment 3-1

Can you illustrate your editorial about management of gastro-intestinal bleeding by an iconography illustrating the different probes and devices described (OTSCs, EC and TC-325).

Response 3-1

We appreciate your valuable advice. At our center, we frequently use the over-the-scope clip (OTSC), especially in cases of bleeding associated with the risk of perforation. Conversely, TC-325 is utilized particularly after procedures such as ESD, when there is significant bleeding or when the depth of post-procedural ulcers suggests a risk of delayed bleeding. We have added this information to the manuscript accordingly.

Page 5, line 19 – Page 5, line 20

Our endoscopy team primarily employs OTSCs in cases of bleeding where perforation is suspected.

Page 5, lines 1 – Page 5, line 3

In our team, we primarily used TC-325 particularly after procedures such as ESD, when there is significant bleeding, or when the depth of post-procedural ulcers suggests a risk of delayed bleeding.

Comment 3-2

Can you enrich your article with more recent references? (The more recent is from 2015).

Respond 3-2

Regarding the use of over-the-scope clips (OTSC), we have incorporated references to recent materials, including data from meta-analyses, to provide a comprehensive overview and support our practices

Page 5, lines 18 – Page 5, line 19

Given meta-analysis findings that OTSCs reduce 30-day rebleeding in UGIB, their use has increased^[16]

Reference 16: Bapaye, J., et al., *Safety and efficacy of over-the-scope clips versus standard therapy for high-risk nonvariceal upper GI bleeding: systematic review and meta-analysis*. *Gastrointest Endosc*, 2022. **96**(5): p. 712-720.e7.