International Journal of
Science Inventions Today
www.ijsit.com
ISSN 2319-5436
Review Article

MANAGEMENT OF NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: A REVIEW

Dr. Laxmi Narayan Goit[1 *] and Prof. Dr. Yang Shaning[2]

[1]*Department of Cardiology, the first affiliated Hospital of Yangtze University, Jingzhou, Hubei, P.R China.*

[2]*Department of Cardiology, clinical college of Yangtze University and the first affiliated hospital to Yangtze University, Jingzhou, Hubei, P.R china*

ABSTRACT

Acute upper gastrointestinal bleeding (AUGIB) is one of the most common medical emergencies. AUGIB due to peptic ulcer bleeding remains an important cause of emergency presentation and hospital admission. Despite advancement in technology the management of AUGIB remains a challenge. The clinical community recognizes the need for improvement in the treatment of these patients. Pre-endoscopy erythromycin appears to improve outcomes and is probably underused. High-dose oral proton pump inhibition (PPI) for 11 days after PPI infusion is advantageous in those with a Rockall score of 6 or more. Oral is as effective as parenteral iron at restoring hemoglobin levels after a peptic ulcer bleed. Endoscopic therapy is the gold standard treatment. The mortality in AUGIB is rarely related to the presenting bleed but significantly associated with concurrent comorbidities. The cost of blood transfusion in the management of patients with AUGIB is significant and misuse of blood products has been documented nationally. Risk stratification tools such as Glasgow-Blatchford Score, Rockall Score and the AIMS65 score have allowed clinicians to triage patients appropriately in order to deliver endoscopic therapy within a suitable time frame. Endoscopic therapeutic modalities such as epinephrine injection, heat Thermocoagulation and mechanical clips have had a positive impact on patient's management. However, in order to continue to improve patient's outcomes, further developments are needed

Keywords: Acute upper gastrointestinal bleeding, peptic ulcer, Protons pump inhibitors, Endoscopic therapy.

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is of the most common acute gastrointestinal emergency and remains an important clinical problem. The incidence of non-variceal acute upper GI bleeding is approximately 85 per 100,000 per year [1]. The majority of the upper GI bleeding is (80-90 %) are non variceal. Although the specific mortality associated with acute variceal bleeding is higher [2], peptic ulcer bleeding (PUB) remains the commonest cause of acute GI bleeding overall and significant bleeding requiring transfusion [2]. Patients may present with symptoms such as hematemesis, coffee grounds vomit, drops in hemoglobin, melaena and with or without hemodynamic instability [3]. The presence of pre-existing comorbidities is a significantly contributors to mortality in elderly patients UGIB [4]. Despite considerable advances in many aspects of the management of PUB, the overall mortality remains significant (approximately 10%) and endoscopic therapy remains the gold standard treatment. Common causes of non variceal upper GI bleeding are peptic ulcer disease, oesophagitis, gastritis, Mallory-Weiss tear, Gastric carcinoma, gastro-esophageal varices and hemophilia [5-9].

There are several evidence-based guidelines to aid the management of PUB [10, 11] although comprehensive audits have shown that all aspects of management do not always reliably follow guidelines. Impacted bed stay, endoscopy provision and blood product transfusion are the main contributors to the overall cost of UGIB. Early endoscopy within 24 hours is recommended for most patients with AUGIB; in order to achieve prompt diagnosis, provide risk stratification and haemostasis [12].

Mortality in AUGIB is rarely related to acute hemorrhage but rather to coexisting comorbidities. Recent studies show that about 18 % of the total mortality is directly related to GI hemorrhage with majority of death caused by concurrent comorbidities. Pulmonary disease (24%), multiorgan failure (24%) and terminal pregnancy (34%) are the most common comorbidities [13].

Diagnosis:

Usually the presentation of acute upper GI bleeding is obvious to the clinician, certainly once the presence of blood in the vomitus or melaena passed rectally is detected. One significant dilemma remains over the likely site of bleeding for profuse, hemodynamically significant fresh rectal bleeding. Is this from a colonic source or very rapid transit from an upper GI source? This has implications for the investigative process. The presence of a pulse rate greater than the systolic blood pressure was associated with an upper GI source for fresh rectal bleeding and although further studies examining this index in a prospective way are required, it certainly seems reasonable to perform a gastroscopy initially before lower GI endoscopy in these patients showing that degree of circulatory compromise after appropriate resuscitation.

Resuscitation:

Despite the high prevalence of PUB, there are few data on any specifics of fluid resuscitation in this context. The general clinical principles on restoring circulating fluid volume and adequacy of organ perfusion are employed; although it seems inevitable that there will be individual choice in terms of fluids used and rate given. The blood transfusion recommended when hemoglobin dropped below 7.0 g/dL [14]. The European society of Gastrointestinal Endoscopy recommends a restrictive blood transfusion strategy that aims for target

hemoglobin between 7.0 and 9.0 g/dL. Higher target hemoglobin should be considered in patient with significant comorbidities (ischemic cardiovascular disease) [11]. At the time of discharge, the target hemoglobin should be 8.o -10.0 g/dL, has shown to have better outcomes in those presenting with AUGIB [15].

Risk stratification:

Early patients risk stratification will be allowing the planning and timing of lifesaving procedure such as endoscopic therapy. The primary aim of the initial assessment is to determine whether endoscopy is required urgently or it can be delayed [16]. There are many systems that have been used to stratify risks in upper GI bleeding. At present, three such score exists and are used in clinical practice.

Glasgow-Blatchford Score:

The Glasgow-Blatchford score(GBS) used both clinical(Pulse, systolic blood pressure, presence of melaena, presentation with syncope, presence of hepatic disease and heart failure) and serological parameters(urea and hemoglobin), which are easily available at initial assessment, which allow the clinician to identify patients who is suitable for management in the outpatient setting table 1 [17]. The ESGE and the National Institute for Health and Care Excellence recommend the use of the GBS for pre-endoscopy risk stratification. Patients with the score of 0 or 1 do not require hospital admission and can be safely discharged and managed with outpatient endoscopy [11]. A GBS of 7 or more was best at predicting the need for endoscopic treatment [18].

Parameters	Scores Value
1. Blood Urea:	
• 6.5-7.9 mmol/L	2
• 8.0-9.9 mmol/L	3
• 10-25 mmol/L	4
• > 25.o mmol/L	6
2. Hemoglobin for men:	
• 12-12.9 g/dL	1
• 10-11.9 g/dL	3
• < 10 g/dL	6
3. Hemoglobin for women:	
• 10-11.9 g/dL	1
• < 10 g/dL	6
4. Systolic blood pressure:	
• 100-109 mm Hg	1
• 90-99 mm Hg	2
• < 90 mm Hg	3
5. Other marker:	

• pulse ≥ 100 beat/minutes	1
• presentation with melaena	1
• presentation with syncope	2
• hepatic disease	2
• Cardiac failure	2

Table 1: Glasgow-Blatchford scores for Gastrointestinal Bleeding.

• Known history or clinical and laboratory evidence of acute or chronic hepatic disease.

• Known history or clinical and echocardiography evidence of cardiac failure.

Rockall score:

In contrast, the Rockall Score (RS) combines clinical parameters with endoscopic findings in order to predict the risk of mortality (table 2). Lack of endoscopic findings in the initial assessment of a patient with AUGIB may deter the clinician from using the RS; however, full post endoscopy RS remains an important tool in predicting mortality rate [19].

	0	1	2	3
Initial score criteria:				
• Age	< 60 years	60-79 years	> 80 years	
• Shock	no Shock	HR > 1oo b/min	HR > 100, SBP	< 100 mm Hg
•Comorbidity			CHF, IHD	RF, LF, DM
Additional criteria for full score:				
• Diagnosis:	Mallory Weiss, no lesion. No stigmata of recent hemorrhage.		All other diagnosis.	Cancer of UGIT
• Stigmata of recent hemorrhage:	none or dark spot.		Fresh blood, adherent clot, visible vessel.	

Table 2: Rockall score for gastrointestinal bleeding.

HR= heart rate. CHF= congestive heart failure. IHD= Ischemic heart disease. RF= Renal failure.

LF= Liver failure. DM= Disseminated malignancy. UGIT= Upper gastrointestinal tract. SBP= systolic blood pressure.

Maximum additive score prior to diagnosis=7.

Maximum additive score after diagnosis= 11.

The AIMS65 score:

The AIMS65 score is designed to predict in-hospital mortality, length of stay and cost of GI bleeding (tables 3 and 4). In comparison to GBS and RS, it is superior in predicting inpatient mortality [20]. AIMS65 score is inferior to GBS and RS in predicting rebleeding. GBS, RS and AIMS65 are similar in predicting length of hospital stay [20, 21]. GBS is more accurate in terms of detecting transfusion need, rebleeding rate and endoscopic intervention rate [18, 20]. The AIMS65 score has requiring only on a 5-point score for each of the following factors: albumin of less than 30 g/l, international normalized ratio (>1.5), Glasgow coma scale score of less than 14, systolic blood pressure of less than 90 mmHg, and age of more than 65.

Parameters	score
• Age > 65 years	1
• Systolic BP: < 90 mm Hg	1
• Altered mental status:	1
• INR > 1.5	1
• Albumin: < 3.0 g/L	1

Table 3: AIMS 65 Score.

INR= International normalised score. BP= Blood pressure.

A further score based on seven factors—systolic blood pressure of less than 100 mmHg, syncope, hematemesis, hemoglobin of less than 100 g/l, blood urea of 22.4 mg/dl, estimated glomerular filtration rate of less than 60 mL/min per 1.73 m2, and the use of anti-platelet medications—was recently proposed [22]. This score was superior to the pre-endoscopy Rockall and AIMS65 scores in pre-dicting clinical intervention.

Total score	Mortality rate (%)
• 0	0.30
• 1	1.20
• 2	5.30
• 3	10.30
• 4	16.50
• 5	24.50

Table 4: In-hospital mortality rate based on AIM65 Score

Optimal timing of Endoscopy:

The benefit of early endoscopy in the management of NVUGIB remains controversial [12] however; endoscopy has an important role in obtaining diagnosis with a sensitivity of 90%–95% at locating the bleeding site. In hemodynamically stable patients with ASA grade 1 or 2, early endoscopy within 12 hours of presentation has no effect on mortality or recurrent bleeding [23, 24], however; more high-risk endoscopic lesions are identified [25] in those receiving early endoscopy and these patients tend to have a shorter length of hospital stay [26-28]. Early endoscopy in hemodynamically stable patients with ASA grades 3–5 is associated with lower in-hospital mortality. In patients with hemodynamic instability, early endoscopy is associated with lower in-hospital mortality [26]. Although 2%–10% of patients with AUGIB can die from their AUGIB, mortality in 80% of these patients is due to other non-bleeding comorbidities.

The Forrest Classification:

The endoscopic management of UGIB has evolved in recent decades as therapeutic modalities available to the endoscopist have evolved, driven by innovations in new techniques and accessories. Endoscopy in patients with AUGIB is effective in diagnosing and treating most causes of UGIB [16]. The Forrest Classification categorizes the lesion morphology at the time of index endoscopy, allowing the endoscopist to decide when to intervene and prognosticate the risk of rebleeding. This categorisation has also been shown to correlate with

the need for surgery and mortality [29]. However, there is significant interobserver disagreement in categorizing the bleeding site, hence accurate photographic documentation is paramount [30].

Stages	Forrest classification	Re-bleeding
I a	Spurting bleed	60-100 %
I b	Oozing bleed	50 %
II a	Non-bleeding visible vessel	40-50 %
II b	Adherent Clot	20-30 %
II c	Flat spot in ulcer crater	7-10 %
III	Clean base ulcer	3-5 %

Table 5: Forrest Classification of different type of bleed

Endoscopy and endoscopic therapy:

Endoscopic haemostatic techniques:

Several endoscopic treatment modalities have been developed; these include injection methods, heat cauterization and mechanical therapy.

Epinephrine injection therapy:

This includes injection of dilute epinephrine (1:10 000) at the site of bleeding. It reduces blood flow by temporary creating local tamponade and vasoconstriction of blood vessels. Injection of large volume of epinephrine (>13 mL) can reduce the rate of recurrent bleeding in patients with high-risk peptic ulcer and is superior to injection of lesser volumes [31, 32].

Thermocoagulation:

Thermocoagulation uses direct contact with the bleeding site with thermal energy delivered via a variety of devices. Heater probe consists of a Tefloncoated hollow aluminum cylinder with inner heating coil. It uses electrical current to generate heat. The Gold Probe has a rounded gold distal tip with good conductivity and has irrigation and injection capability, in addition to delivering heat for Thermocoagulation.

Argon plasma coagulation is a non-contact ablative modality that uses steam of ionised gas to conduct electricity for the coagulation of bleeding tissue [33].

Mechanical therapy clips:

Mechanical therapy is an attractive method for achieving endoscopic haemostasis. It has a significant impact on achieving haemostasis in difficult and challenging cases and a significant impact on outcomes [34].

Mechanical therapy with endoscopic clips has been shown to be effective by physically obstructing the blood flow in the vessel; however, this technique will require direct visualization of the bleeding point and culprit vessel. Successful application of clip is better in achieving haemostasis when compared with injection therapy alone but similar to Thermocoagulation [35].

The over-the-scope clip (OTSC) has been reported to effectively achieve haemostasis and significantly reduces rebleeding and rebleeding-associated mortality in NVUGIB. A recent multicentre study was able to

show a haemostasis rate of 92.4% with OTSC as monotherapy in the treatment of acute NVUGIB with significant reduction in the occurrence of bleeding and mortality of rebleeding [36].

Drug therapy:

Proton Pump Inhibitors (PPI):

Pre-endoscopy PPI infusion is recommended by some guidelines but not by all [37]. Pre-endoscopic use of PPI reduces the detection rate of high risk stigmata during endoscopy and need for endoscopy therapy [16]. Post-endoscopy PPI treatment after endoscopic therapy to high-risk ulcers has repeatedly been shown to be better than placebo at reducing rebleeding and surgery [38].

Many clinicians use the original 'Hong Kong' regimen (bolus followed by continuous infusion of omeprazole, pantoprazole, or esomeprazole) for 72 hours. Other dose regimens, including intermittent parenteral dosing and even high-dose oral PPI, have also been shown to be effective, and it is not clear what the optimal regimen is [39, 40]. After endoscopic therapy and 72 hours intravenous PPI, high-dose oral acid suppression seems to be beneficial for highest-risk patients. It is reported that 11 days of double-dose oral esomeprazole (40 mg twice daily) in this context was superior to once daily esomeprazole 40 mg (with 40 mg once daily subsequently for both groups) in preventing rebleeding in patients with a full Rockall score of 6 or more.

There was no significant difference in mortality, hospital stay, or blood transfused. Thus, there is a rationale for treating the higher-risk patients (Rockall score of 6 or more) with higher-dose PPI for the period after initial stabilisation. PPI have significantly reduces the incidences of peptic ulcer disease [41].

Prokinetics Drugs:

There is a sound rationale for using Prokinetics before endoscopy in upper GI bleeding to clear the stomach and improve both the endoscopic views and probably safety. The trials showed that intravenous erythromycin before endoscopy was associated with meaningful clinical benefit in terms of improved mucosal visualization, reduction in repeat endoscopy, and blood transfused as well as length of stay but that metoclopramide was less effective [41-43]. Erythromycin is probably under used and seems to be a simple intervention that would improve outcomes.

Tranexamic Acid:

Tranexamic acid, a derivative of the amino acid lysine, has an antifibrinolytic effect by preventing the degradation of fibrin networks. Studies have shown that it decreases rebleeding and mortality in AUGIB, without increasing the thromboembolic adverse effects; however, its routine use in clinical practice has not been recommended as further clinical trials are needed [44, 45].

New Anticoagulation Drugs:

The emergence of the direct oral anticoagulants(DOAC: Dabigatran, rivaroxaban, apixaban and edoxaban)has reduced regular serum monitoring that is required for patients on warfarin; however, there is a 25%–30% increased risk of GI bleeding with the use of DOAC when compared with warfarin[46, 47]. The risk

is mostly relevant in the elderly and those with hepatic disease, renal disease and patients on concomitant antiplatelet agents.

In the case of an AUGIB, reversal agents can be used; however, different assays are needed to indirectly quantify DOAC level prior to reversal. These assays include the dilute thrombin time and ecarin clotting time for Dabigatran and the drug-specific calibrated anti-Xa factor assay for rivaroxaban, edoxaban and apixaban [48]. Reversal agents exist (prothrombin complex concentrate (PCC), activated PCC, idarucizumab) with many others currently on clinical trials [47].

Acute upper GI bleeding is a significant drain on the iron stores of the body, and many patients are anemic after initial management. Iron therapy—oral ferrous sulphate 200 mg daily—was more effective than placebo at restoring hemoglobin levels to normal. There was no difference in the rates of improvement in anemia between parenteral and enteral iron groups, although higher ferritin levels were seen in the parenteral group [49].

Dual and triple therapy is better than monotherapy:

Dual endoscopic therapy is superior to monotherapy with epinephrine injection alone in the management of patients with high-risk bleeding peptic ulcer; dual therapy reduces the risk of recurrent bleeding, the risk of emergency surgery [34] and mortality [50]. The possible adverse events from dual therapy include perforation and gastric wall necrosis, with very low occurrence rate. Dual therapy remains to be superior to monotherapy with epinephrine [51].

Interventional radiology suitable for GI bleeding:

Interventional radiology (IR) has shown to provide diagnostic imaging and endovascular therapeutic interventions that can localise the source of bleeding and provide endovascular embolisation to achieve haemostasis successfully when conventional endoscopic haemostasis has been unsuccessful [52]. IR can control UGIB and achieve haemostasis with the use of minicoils for the embolisation of bleeding vessels with reduced risk of serious complications [53].

Optimum postprocedure management:

Post endoscopic treatment with high-dose infusion of PPI (bolus of 80 mg followed by 8 mg/hour for 72 hours) in bleeding peptic ulcers significantly reduces the risk of recurrent bleeding [54]. Rebleeding rate has also been shown to be associated with the Hb at the time of discharge. The rebleeding rate in patients with a discharge Hb between 80 and 100 g/L is not significantly different when compared with patients with higher Hb at discharge [15]. In addition, a discharge Hb between 80 and 100 g/L is associated with a lower consumption of red blood cells [15].

Rebleeding is more common in patients with high stigmata lesions at the time of endoscopy, hence repeat endoscopy and treatment should be considered in all high-risk bleeds, in particular those with the need to recommence anticoagulation and patients who have had limited endoscopic therapy at the initial endoscopy. Surgery should be considered in those not responding to endoscopic therapy or radiological embolisation, taking into account patient's status and comorbidities.

Newer Approach for Bleeding Control:

Video capsule endoscopy:

The use of video capsule endoscopy (VCE) in the emergency department (ED) as a risk stratification tool for identifying high and low-risk patients with UGIB has been evaluated. It has shown potential to identify high and low-risk patients presenting with signs of AUGIB, helping to determine the need for intervention with significant reduction in the time to emergent endoscopic therapy[55]. VCE in the ED is safe and effective in identifying AUGIB [56]. The used of VCE in the ED performed by a gastroenterologist or a VCE-trained clinician and the aim was to determine whether patients with signs and symptoms of upper GI bleeding can be discharged without patient follow-up endoscopy.

A total of 25 subjects were enrolled with excellent tolerance to the VCE. The study was able to show a sensitivity of 88% with a specificity of 64% for the detection of fresh blood in the upper GI tract [57]. Similar studies have shown significant reduction in hospital admissions with no difference in the clinical outcome in terms of recurrent bleeding and 30-day mortality in the VCE group and those receiving standard treatment [58].

Hemospray:

Hemospray is a novel proprietary mineral blend that forms a mechanical barrier over the bleeding site when applied endoscopically. It gives the endoscopist the opportunity to apply therapy in challenging anatomies. The multicentre European Survey to Evaluate the Application of *Hemospray* in the Luminal tract (SEAL) study [59] showed high haemostasis rates with the use of Hemospray as monotherapy and in combination with conventional methods. Expansion of this study is currently in progress and shall provide further evidence on the use of Hemospray monotherapy, dual therapy and rescue therapy in various pathologies.

EndoClot:

The EndoClot (EndoClot Plus, Santa Clara, CA) is a polysaccharide haemostatic powder that can be delivered endoscopically to the site of bleeding in the GI tract without the need for direct mucosal contact. It is composed of absorbable polymer particles that absorb water from the blood on the surface of the bleeding site, hence increasing the concentration of platelets and clotting factors, resulting into haemostasis [60, 61]. Further clinical trials are waiting.

Management of refractory bleeding:

Despite advances in endoscopic and pharmacological therapies, a significant minority of patients experience significant rebleeding. Surgery has traditionally been regarded as the appropriate approach. As increasingly the interventional radiology is regarded as the initial therapeutic approach before surgery. It is believed that overall the safety of interventional radiological embolization is significantly better than surgery and hence most guidelines now advocate radiological embolization as the rescue therapy of choice.

Follow-up and prevention:

An understanding of the major causes of PUB naturally leads to developing strategies for both primary and secondary prevention. The major ameliorable causes of PUB are *Helicobacter pylori* and drugs. So for *H. pylori* eradication regimes must be effective in the population being treated and 14-day courses of four agents (either bismuth-containing or not) are now standard in Europe and the USA, although 7-day clarithromycin containing regimens are used.

Although aspirin and other anti-platelet agents are clearly associated with an increased risk of PUB, in many cases these agents are indicated because of the underlying vascular disease, and it is now accepted that where indicated aspirin should be continued (or interrupted for a minimal interval of fewer than 3 days) in acute PUB [62]. A small risk in early rebleeding is more than offset by a significantly reduced risk of vascular events and death.

The most appropriate treatment after an aspirin-induced bleed is aspirin plus a PPI [63]; this is superior to the P2Y12 antagonist Clopidogrel alone as secondary treatment. Patients with drug-eluting coronary artery stents do need to continue dual anti-platelet therapy for a year; PPI co-treatment reduces bleeding in those taking aspirin plus Clopidogrel [64].

The patients taking dual anti-platelet agents with PPI cover, the risk of lower GI bleeding is now approximately three times higher than that of upper GI-bleeding [65]. In general, PPI co-treatment has been advocated with aspirin for primary and secondary prevention [62]. In recent studies show that famotidine was equivalent to rabeprazole [66]. Previous data suggested that PPI treatment was better [67], and until more data in wider populations are available, PPI treatment remains the treatment of choice. Anticoagulation therapy for atrial fibrillation after a PUB is beneficial; again, a risk of rebleeding is more than offset by reductions in stroke and death. The selective COX-2 inhibitors are safer than traditional non-selective NSAIDs in terms of GI-complications [62]. The combination of celecoxib plus a PPI is associated with the lowest risk of rebleeding after an NSAID induced PUB, when reintroduction of anti-inflammatory therapy is required [62]. More recent data suggest that the increased cardiovascular risk is common to all cyclooxygenase inhibitors.

PPI co-treatment would be usual after a PUB, and primary prevention of PUB in higher-risk patients taking anticoagulants is usually advocated by some but not all guidelines [68]. The omeprazole co-treatment reduced rebleeding in warfarin-treated patients, although this effect was significant only in those also taking anti-platelet drugs or NSAIDs [69].

A further observational study showed that concurrent use of PPIs or H2-receptor antagonists were both associated with a reduced risk of acute upper GI bleeding and this effect was most marked in those with a history of peptic ulcer disease [70]. Therefore, despite the relative lack of evidence, co-prescription of gastro protection with anticoagulant therapy would seem to be indicated in secondary prevention; for primary prevention, a case- and risk-based approach seems sensible pending further data. Those with highest risk of bleeding are most likely to gain from the use of acid suppression.

Studies from disparate geographical regions have shown an important increase in apparently idiopathic peptic ulcers as the cause of upper GI bleeding. Although continued acid suppression with a PPI is the logical intervention for this idiopathic ulcer group). They showed that acid suppression did not alter rebleeding or mortality in this group [71]. Other approaches, perhaps with alternative mucosal protectant agents such as misoprostol, would seem to be warranted.

CONCLUSIONS

GI bleeding remains to be a challenging clinical emergency with significant mortality and morbidity that remains unchanged these past two decades; however, with adequate service planning and adherence to robust guidelines, improved and desirable out comes can be achieved. Patients with AUGIB should be admitted to units that provide a 24/7 GI bleed service with anesthetic support and access to IR and surgery. Risk stratification and adequate resuscitation prior to any endoscopic therapy are paramount and must supersede the interventional endoscopy as the key initial process in the management of patients with AUGIB. The timing of endoscopy is dependent on the presenting signs, taking into account the clinical status of the patient. For endoscopic treatment, the haemostatic powders and over-the-scope clips are useful tools when standard modalities are ineffective or impractical. The endoscopic therapy of all acute NVUGIB should not rely on monotherapy alone but a combination of injection therapy with other modalities such as clips, Thermocoagulation or both. Second-look endoscopy is recommended in patients with signs of rebleeding. Further developments of new techniques will assist future generations in the management of AUGIB; however, all endoscopists must acquire sufficient training in order to provide the best treatment options. Finally, the focus of treatment should not only be the endoscopic therapy and a holistic approach is encouraged in order to optimize treatment by managing multiorgan failure and comorbidities.

Abbreviations:

AUGIB: Acute upper Gastrointestinal Bleeding.

PPI: Proton pumps inhibitors.

GI: Gastrointestinal.

PUB: Peptic Ulcers Bleeding.

GBS: Glasgow-Blatchford score.

RS: Rockall score.

NVUGIB: Non-variceal upper gastrointestinal bleeding.

DOAC: Direct oral anticoagulation.

IR: Interventional Radiology.

VCE: Video capsule endoscopy.

ED: Emergency department.

Conflicts of Interest:

There authors have no Conflicts of interest to declare.

Acknowledgements:

This review article is supported by the National Natural Science Foundation of China (31700736), Hubei Province Natural Science Foundation of China (2016CFB180), Hubei Province Health and Family Planning Scientific Research Project (WJ2016Y07), Hubei Province Scientific and Technological Research Project (Q20171306), Jingzhou Science and Technology Development Planning Project (JZKJ15063) and the Yangtze Fund for Youth Teams of Science and Technology Innovation (2016CQT04).

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