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Expert consensus on emergency diagnosis and treatment procedures for acute upper gastrointestinal bleeding

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ABSTRACT

Acute upper gastrointestinal bleeding is one of the most common life-threatening diseases. Standardized diagnosis and treatment of acute upper gastrointestinal bleeding are of great importance for improving the prognosis. In 2015, the Emergency Physician Branch of the Chinese Medical Doctor Association updated an expert consensus statement on the emergency diagnosis and treatment procedures for acute upper gastrointestinal bleeding. Based on the 2015 consensus statement, members of the expert panel decided to reconvene and draw up a 2020 update on the advancements in the clinical care for acute upper gastrointestinal bleeding. The 2020 expert consensus statement is summarized in 10 sections: emergency assessment, diagnosis, stratified treatment, emergency treatment, comprehensive assessment, medication management, endoscopy, interventional radiology, multidisciplinary treatment, and evaluation of prognosis. The consensus statement is based on experts' opinions combined with the latest relevant medical evidence.

1. Background

Acute upper gastrointestinal bleeding is one of the most common life-threatening diseases. The incidence in adults ranges from 100 to 180 cases per 100 000 population per year[1], with mortality between 2% and 15%[2]. Standardization of its diagnosis and treatment is of great importance for improving the prognosis. In the past five years, many advancements in clinical care have been made for this condition. Based on the 2015 consensus statement, the Emergency Physician Branch of the Chinese Medical Doctor Association organized experts from departments of emergency medicine, gastroenterology, interventional radiology, and surgery to develop the 2020 update (3rd edition) on the emergency diagnosis and treatment procedures for acute upper gastrointestinal bleeding.

2. Methods

Evaluation of patient condition, hemodynamic stabilization, drug selection, and hemostatic treatments for acute upper gastrointestinal bleeding were the key points of the previous 2015 expert consensus statement. The 2020 statement was based on the 2015 version but focused on optimizing relevant diagnostic and treatment procedures. The consensus content was developed after extensive discussions and revisions regarding risk stratification, dynamic evaluation, therapeutic strategies, the timing of endoscopy, and management of medications for special populations.

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Table 1. Criteria for grading evidence levels.

Evidence level	Description
Low	Future research is very likely to have an important impact on the current assessment results, which will very likely change the current recommendations
Moderate	Future research is likely to have an important impact on the current assessment results, which may change the current recommendations
High	Future research is unlikely to change the current assessment

This update aimed to reference the latest evidence-based domestic and foreign guidelines and literature as well as the emergency clinical situation in China[3-18]. The consensus statements were reached through a modified Delphi method[12]. The content of each statement was required to be approved by 80% or more of all the experts. This update took evidence-based medicine into account, and after discussion among all experts, grades of evidence were classified into three levels (Table 1).

3. Consensus contents

3.1. Emergency diagnosis and treatment procedures

This consensus statement adhered to the concept of "prioritizing life-saving interventions before further diagnostic testing" in Chinese emergency medicine. It also has developed the key emergency diagnosis and treatment procedures into a "three evaluations and two treatments" structure. Both clinical operability and practicality were considered in providing a useful reference for emergency physicians to treat patients with acute upper gastrointestinal bleeding (Figure 1).

3.2. Emergency assessment, diagnosis, and stratified treatment

3.2.1. Emergency assessment

Statement 1: Patient consciousness, airway, breathing, and circulation should be evaluated first. If acute upper gastrointestinal bleeding can be preliminarily diagnosed and differentiated, then the risk level should be assessed in combination with the Glasgow Blatchford Score (GBS) (evidence level: high, agreement: 100%).

Consciousness assessment: Consciousness should be evaluated primarily. Altered mental status not only indicates potentially serious blood loss but also puts the patient at a high risk of aspiration.

Airway assessment: Airway patency and the risk of airway obstruction should be evaluated.

Breathing assessment: Respiratory frequency, rhythm, effort, and blood oxygen saturation should be evaluated.

Circulatory assessment: Heart rate, blood pressure, urine output, and peripheral perfusion should be monitored. Invasive hemodynamic monitoring should be performed if conditions permit.

3.2.2. Diagnosis

Patients with typical hematemesis, melena, or hematochezia can be diagnosed easily. Gastric aspirate, vomitus, or fecal testing positive for occult blood could reveal suspected patients. Acute upper gastrointestinal bleeding should be suspected when patients present with dizziness, weakness, syncope, or other atypical symptoms, in particular those with unstable vital signs, pallor, or an unexplained acute decrease in hemoglobin. Dangerous acute upper gastrointestinal bleeding should be considered if any one of the following manifestations is present: active bleeding, circulatory failure, respiratory failure, altered mental status, aspiration, or GBS>1 (Appendix 1), which would necessitate emergency diagnosis and treatment[19]. Severe pallor, persistent hematemesis or hematochezia, syncope, hypotension or a low hemoglobin level suggest severe blood loss. When the volume of hematemesis or hematochezia is not consistent with the extent of anemia, occult massive upper gastrointestinal bleeding should be considered. A critical condition is implied if a patient vomits bright red blood or coffee-ground material[20,21].

3.2.3. Stratified treatment

Statement 2: Stratified treatment should be performed based on the patient's risk level, and dangerous bleeding should be treated in the emergency department (evidence level: high, agreement: 100%).

On the premise of a comprehensive analysis of clinical manifestations, the patient's risk level can be divided into five categories: very high risk, high risk, medium risk, low risk, and very low risk. According to risk level, patients would then be referred to a corresponding area for appropriate diagnosis and treatment[16] (Table 2). Dangerous bleeding should be treated in the emergency department. Cardiopulmonary resuscitation should be performed immediately for those patients who have lost consciousness and who have unpalpable pulses in their major arteries[1,22]. In addition, patients should be taken to the "resuscitation room" of the emergency department or other similar area for immediate resuscitation[1,4] in the following situations: patients presenting with syncope, persistent hematemesis or hematochezia, cold and diaphoretic extremities, heart rate>100 beats/min, systolic blood pressure<90 mmHg, a relative decrease from their baseline systolic blood pressure>30 mmHg, or having a hemoglobin level (Hb)<70 g/L. Patients with stable vital signs can be treated in the general area of the emergency department. GBS $\leqslant$1 represents a very low risk of dangerous hemorrhage (*i.e.* only 1.2% of patients with this score will need a blood transfusion or an emergency intervention). Patients with such a low score can pursue further evaluation and treatment as an outpatient[19,23-25].

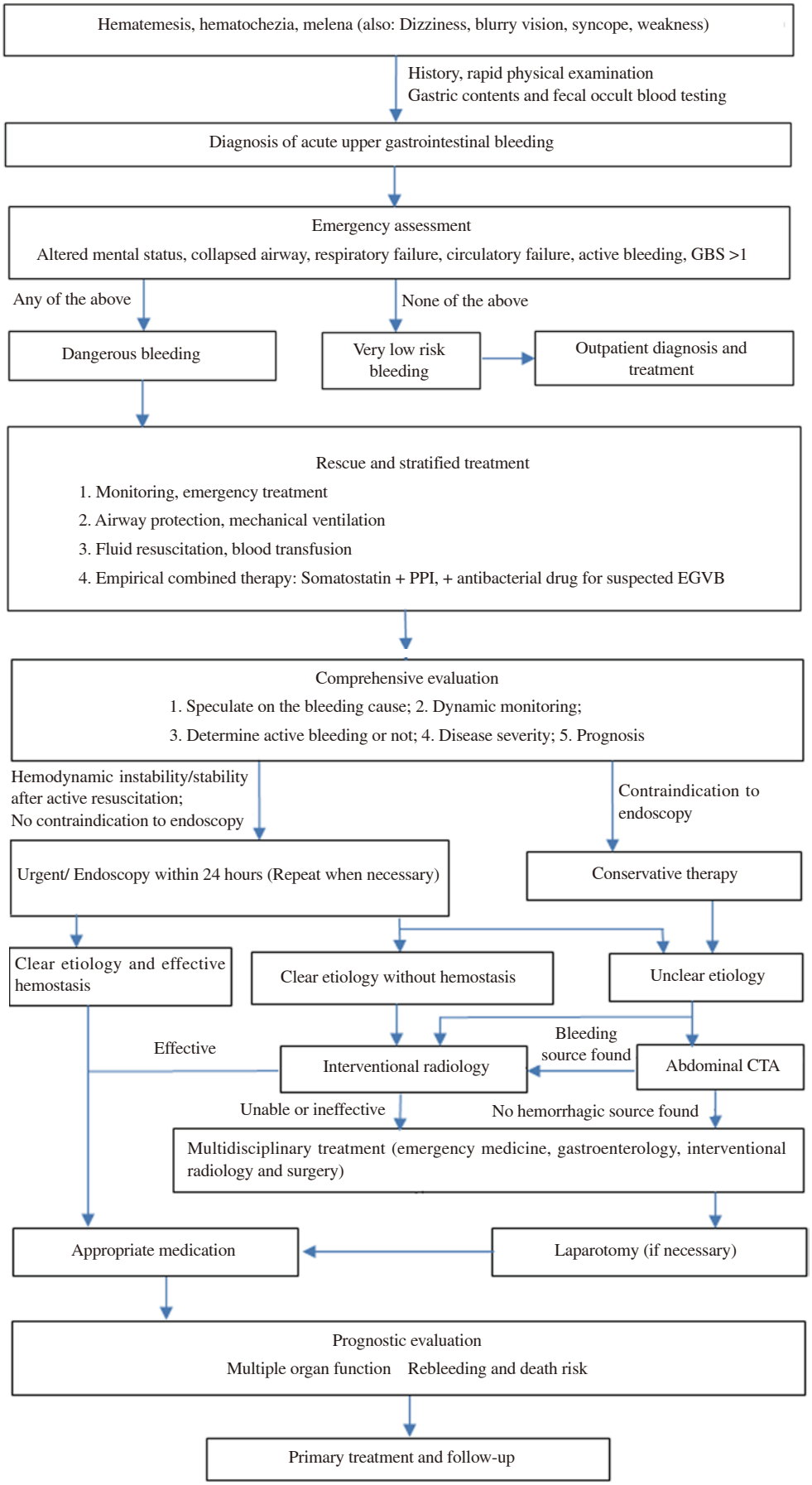

Figure 1. Emergency diagnosis and treatment procedures for acute upper gastrointestinal bleeding. GBS: Glasgow Blatchford Score; PPI: Proton pump inhibitor; EGVB: Esophageal-gastric variceal bleeding; CTA: Computed tomography angiography.

Table 2. Risk stratification of acute upper gastrointestinal bleeding.

Grade	Symptom and sign	Shock index*	Treatment	Medical area
Very high risk	Heart rate>120 beats/min, systolic blood pressure <70 mmHg or acute decrease of blood pressure (decrease of basal systolic blood pressure of 30-60 mmHg), cardiac, respiratory arrest or unstable rhythm, inability to maintain the airway	>1.5	Immediate resuscitation	Resuscitation area
High risk	Heart rate of 100-120 beats/min, systolic blood pressure of 70-90 mmHg, syncope, oliguria, confusion, cold and diaphoretic extremities, persistent hematemesis or hematochezia	1.0-1.5	Immediate monitoring of vital signs; active treatment within 10 min	Resuscitation area
Medium risk	Relatively normal blood pressure, heart rate, and hemoglobin, currently stable vital signs, advanced age or serious underlying disease, presence of potential life threat	0.5-1.0	Priority diagnosis and treatment, consulted within 30 min, re-assessment needed if the waiting time is >30 min	General diagnosis and treatment area
Low risk	Stable vital signs	0.5	Sequential consultation, consulted within 60 min, re-assessment needed if the waiting time is >60 min	General diagnosis and treatment area
Very low risk	Stable condition, GBS≤1	0.5	Follow up	Outpatient

While prioritizing patient safety, the above can be adjusted based on the regional- and hospital-specific medical environment and available resources. *Shock index=heart rate/systolic blood pressure; 0.5 represents normal blood volume; 1 represents mild shock, 20%-30% blood loss; >1 represents shock; >1.5 represents serious shock, 30%-50% blood loss; >2 represents severe shock, >50% blood loss.

3.3. Emergency treatment

Statement 3: Emergency treatment should be given for patients with high risk (evidence level: high, agreement: 100%).

Routine measures include "O.M.I.", *i.e.* oxygen, monitoring, and intravenous fluid[1,26]. In addition, ECG, blood pressure, and blood oxygen saturation should be monitored continuously. An indwelling urinary catheter may be placed to record urine output of patients with altered mental status or shock. Two large-bore, intravenous access points should be established for patients with serious hemorrhage (at least 18-gauge), and central venous catheterization should be performed if necessary. For patients with altered mental status, respiratory failure, or circulatory failure, attention should be paid to airway protection and prevention of aspiration. Oxygen therapy or artificial ventilation support can be given if necessary, and resuscitation therapy should be initiated. Resuscitation therapy includes volume resuscitation, blood transfusion(s), and the use of vasoactive drugs. Patients at high risk of acute upper gastrointestinal bleeding need strict bed rest. Gastric tubes were previously used to assist in the evaluation of hemorrhage, however current evidence does not support the benefit of gastric tube placement. Hence caution should be exercised in placing gastric tubes, particularly in patients with a history of liver cirrhosis, esophageal-gastric variceal bleeding (EGVB) or poor cooperation, so as to avoid exacerbation of hemorrhage or patient discomfort[1,27].

3.3.1. Volume resuscitation

Statement 4: Volume resuscitation should be performed immediately for acute upper gastrointestinal bleeding with hemodynamic instability, in order to recover and maintain vital organ perfusion (evidence level: high, agreement: 100%).

Volume resuscitation should be actively performed for acute upper gastrointestinal bleeding with hemodynamic instability. However, the evidence is lacking as far as a recommended specific resuscitation strategy. Referring to resuscitation in trauma with major hemorrhage, limited fluid resuscitation, and permissive hypotension resuscitation strategies should be used when the hemorrhage is not well-controlled. For example, it is recommended to maintain the systolic blood pressure around 80-90 mmHg[28]. Active resuscitation should be applied based on the baseline blood pressure level when hemorrhage has been controlled. For patients with acute massive hemorrhage, invasive hemodynamic monitoring should be implemented if the situation permits. Clinical manifestations, ultrasonography, and laboratory examinations should be comprehensively analyzed to guide volume resuscitation. In addition, attention should be paid to preventing hypothermia, acidosis, coagulopathy, and any deterioration of underlying diseases.

In terms of the volume and type of intravenous infusion, currently, no consensus has been reached. For volume resuscitation during hemorrhagic shock, massive crystalloid fluid infusions should be avoided, instead, such infusions should be reduced as much as possible (<3 L in the first 6 hours)[29]. Isotonic crystalloid fluid is not beneficial, except as a temporary expansion of intravascular volume. The risk of complications such as respiratory failure, compartment syndrome (abdominal or limb), and coagulopathy are likely to be elevated by a large infusion of isotonic crystalloid fluid. Artificial colloid or hypertonic solutions do not lead to any clear benefit when used as early treatments for severe hemorrhage[29]. Manifestations

of sufficient volume resuscitation include blood pressure returning to baseline, pulse rate<100 beats/min, urine volume output>0.5 mL/(kg·h), a clear consciousness, no obvious dehydration signs on physical exam, and normalized arterial lactate. Additionally, fluid infusions for variceal bleeding require caution as excessive fluid infusions may aggravate such bleeding[1]. For patients with cardiac, pulmonary, or renal diseases, excessive fluid infusions may lead to heart failure or pulmonary edema.

3.3.2. Blood transfusion

Statement 5: Balance risks and benefits of blood transfusion, and adopt the best possible blood transfusion strategy (evidence level: high, agreement: 97.7%).

Appropriate transfusion of blood products is required for patients with massive blood loss, in order to ensure enough oxygen supply to organs and maintain normal coagulation function. Blood transfusions should be considered in the following circumstances: (1) Systolic blood pressure<90 mmHg; (2) Heart rate>110 beats/min; (3) Hb<70 g/L; (4) Hematocrit<25%; (5) Hemorrhagic shock[13,30]. For acute massive hemorrhage, a massive blood transfusion protocol should be initiated immediately. Blood products with preset proportions (*e.g.* ratio of red blood cells, plasma, and platelets in a 1:1:1 ratio) as well as adjuvant drugs, *e.g.* calcium, may provide a survival benefit[29], although the best ratio of red blood cells to plasma to platelets has not yet been determined[31-33]. No platelet transfusion is required for cases of non-active bleeding and hemodynamic stability. In contrast, platelets should be transfused for patients with active bleeding and low platelet counts of $<50\times10^9$/L[9].

Risks and benefits of blood transfusion should be balanced individually. A restrictive transfusion strategy should be adopted generally, with a recommended Hb target value of 70-90 g/L[13,34-36]. Except for those with a Child grade C hepatic function, blood transfusions need to be strictly limited to Hb<70 g/L for variceal bleeding, otherwise mortality may be increased[37,38]. However, it is inappropriate to adopt a restrictive transfusion strategy in patients with advanced age, underlying cardiovascular or cerebrovascular diseases (*e.g.* acute coronary syndromes, myocardial infarction, stroke, or transient ischemic attack), hemodynamic instability, and persistent massive hemorrhage. For these patients, in order to avoid potential exacerbation of underlying disease(s) due to massive blood loss[8,38-41], the blood transfusion threshold could be extended to Hb<90 g/L or above.

For patients with coagulation disorders, changes in coagulation parameters or a thromboelastogram need to be dynamically observed to evaluate their real-time coagulation status. For patients with active bleeding, fresh frozen plasma (FFP) should be transfused if the prothrombin time (or international normalized ratio) or activated partial thromboplastin time is more than 1.5 times normal. Fibrinogen or a cryoprecipitate transfusion is recommended if the fibrinogen level is still lower than 1.5 g/L after initial FFP transfusion[9]. If fibrinogen<1 g/L, FFP should be transfused for active variceal bleeding in patients with liver cirrhosis[6].

Massive blood transfusions may cause known complications, including hypocalcemia and coagulation disorders. Calcium should be given empirically (*e.g.* by supplementing 1 g of calcium chloride after transfusing 4 units of a blood product), and calcium ion levels should be closely monitored[29]. During massive blood transfusions, it is important to attend to potential hypothermia, acidosis, or hyperkalemia[13].

3.3.3. Use of vasopressors

Statement 6: If continuous hypotension still exists after active volume resuscitation, vasopressors can be used to ensure the minimum effective perfusion of important organs (evidence level: moderate, agreement: 100%).

Vasopressors can be used in cases of serious persistent hypotension due to hemorrhagic shock[13,42,43]. However, there is currently a lack of high-level evidence to support this recommendation.

3.3.4. Initial drug therapy

Statement 7: Intravenous proton pump inhibitors (PPIs) and somatostatin can be combined when the cause of dangerous acute upper gastrointestinal bleeding is unknown, and the drugs should be adjusted once the etiology is identified (evidence level: low, agreement: 98.9%).

For cases with dangerous acute upper gastrointestinal bleeding of unknown cause, in order to minimize hemorrhage, serious complications, or death, and to create the optimal conditions for endoscopy or other subsequent therapies, “empirical combined therapy” could be used, when emergency endoscopy may be delayed, despite a lack of sufficient supporting evidence[1].

The most common cause of acute upper gastrointestinal bleeding is non-variceal bleeding, so it is recommended that a PPI should be administrated before endoscopy when the cause is unclear. In addition, a PPI should also be used before endoscopy for patients with a history of liver disease or cirrhosis who cannot exclude ulcerative bleeding.

Patients with a history of liver cirrhosis, chronic hepatic disease, or signs of portal hypertension are likely to have variceal bleeding. Such patients are also likely to have a massive hemorrhage and high early mortality, thus they need to be given drugs, including vasoactive drugs before endoscopy[5,6,11].

Somatostatin is suitable for the treatment of severe acute esophageal variceal bleeding, severe acute gastric or duodenal ulcer bleeding, and acute erosive gastritis or hemorrhagic gastritis. Therefore, a PPI and somatostatin can be combined when the cause of dangerous acute upper gastrointestinal bleeding is unclear, and once the etiology is identified it should be adjusted.

Statement 8: Prophylactic use of antibiotics is recommended when variceal bleeding is highly suspected (evidence level: high, agreement: 83%).

As prognosis can be greatly improved by the prophylactic use of antibiotics for variceal bleeding[44,45], prophylactic use of antibiotics should be implemented when variceal bleeding is highly suspected[6].

3.4. Comprehensive evaluation

3.4.1. Speculation about the cause of hemorrhage

Statement 9: The cause of hemorrhage should be comprehensively evaluated and assessed after initial treatments (evidence level: high, agreement: 100%).

The cause and site of hemorrhage should be comprehensively evaluated and identified after when the active bleeding or life-threatening massive hemorrhage is temporarily controlled, fluid resuscitation and drug therapy are initiated or when the condition is more mild and vital signs are stable. Attention needs to be paid to the early recognition of suspected variceal bleeding, which could be evaluated according to physical signs and risk factors of portal hypertension.

With respect to etiology, acute upper gastrointestinal bleeding can be divided into acute non-variceal bleeding and variceal bleeding. Acute non-variceal bleeding has the highest prevalence and its most common causes include gastroduodenal peptic ulcer, upper gastrointestinal tumor, stress ulcers, and acute or chronic upper gastrointestinal mucosal inflammation. Other causes include esophageal mucosal laceration (*i.e.* Mallory-Weiss) syndrome, upper gastrointestinal arteriovenous malformation, Dieulafoy's disease, and others[4]. Iatrogenic factors include the use of non-steroidal anti-inflammatory drugs, especially anti-platelet drugs (*e.g.* aspirin), and endoscopic mucosal resection/endoscopic submucosal dissection.

3.4.2. Dynamic monitoring

Statement 10: The condition should be dynamically monitored, and the presence of active bleeding should be assessed (evidence level: high, agreement: 100%).

Vital signs, complete blood cell count, coagulation function, and blood urea nitrogen should be dynamically monitored. Additionally, serum lactate levels should be dynamically monitored as well, in order to assess the efficacy of fluid resuscitation, improvements in tissue perfusion, and to guide further fluid resuscitation[13,46]. Active bleeding needs to be considered in the following conditions: (1) Increased frequency of hematemesis or melena, change in vomitus from coffee-brown to bright red, change in excreted feces from black dry stool to dark-red loose stool, or existence of active bowel sounds; (2) A large amount of fresh blood in the gastric drainage system; (3) Even though a rapid fluid infusion or blood transfusion was given, no significant improvement in peripheral circulatory perfusion or unstable central venous pressure is noted, or a transient improvement is seen followed by an acute exacerbation; (4) A continuous decrease in red blood cell count, hemoglobin and hematocrit, or a persistent increase in reticulocyte count; (5) A persistent abnormality or new elevation of blood urea nitrogen in cases with adequate fluid infusion and urine volume[47,48].

3.4.3. Evaluation of condition severity, clinical intervention requirements, and prognosis

Statement 11: Clinically evaluate condition severity, therapeutic intervention requirement(s), and prognosis (GBS may be used) (evidence level: moderate, agreement: 98.9%).

The severity of the disease, therapeutic intervention requirement(s), and prognosis should be comprehensively evaluated according to hemorrhagic manifestations, vital signs, hemoglobin change, and high-risk factors. The high-risk factors include age>60 years, advanced tumor(s), liver cirrhosis or other significant comorbidities, previous history of serious upper gastrointestinal bleeding or device implantation, hematemesis, coagulation disorders [international normalized ratio (INR)>1.5], and the absence of hepatic or renal disease accompanied by a continuous elevation of blood urea nitrogen[47,49].

Risk assessment scores can be generally divided into two types. The first type is used prior to endoscopy, for evaluating the risk for needing a clinical intervention or the risk of death without receiving a clinical intervention based on early clinical manifestations. The other risk assessment scores are mainly used for prognosis and some of these also include endoscopic findings. Some risk assessment scores are universal. Applying risk assessment scores prior to endoscopy could help subsequent clinical decision-making, and thus this type is more commonly used.

The most commonly used risk assessment scores prior to endoscopy include GBS, (pre-endoscopy) Rockall and AIMS65 (albumin, INR, mental status, systolic blood pressure, age>65 years)[50]. Unfortunately, one prospective, international, multi-center study with a large sample size demonstrated most risk assessment scores for acute upper gastrointestinal bleeding had low accuracy[24]. This study showed GBS was the best score for the early prediction of patients requiring a clinical intervention (such as a blood transfusion, endoscopy, or surgery) or mortality, and GBS scores$\geqslant$7 were best for predicting endoscopic therapy. However, its clinical application value is still limited. Unfortunately, risk assessment scores, including GBS, cannot identify high-risk patients with enough precision yet. Nevertheless, a GBS score$\leqslant$1 is valuable clinically as it can accurately predict those patients at a very low risk of mortality, who do not need any emergent clinical interventions[19,24,49].

3.5. Further diagnosis and treatment

After the comprehensive evaluation, emergency physicians should choose further diagnostic and therapeutic methods reasonably according to the results of the prior evaluations.

3.5.1. Medication management

3.5.1.1. Acid-suppression drugs

Statement 12: PPIs should be considered for acute non-variceal upper gastrointestinal bleeding before and after endoscopy (evidence level: moderate, agreement: 97.7%).

Acid inhibition therapy is often needed for acute non-variceal upper gastrointestinal bleeding. The commonly used acid-suppression drugs in clinical use include PPIs and H_2-receptor antagonists. PPIs are the first choice for acid-suppression drugs. Although several studies have shown that the use of PPIs before endoscopy does not

affect the rate of rebleeding, surgery, or mortality, the use of PPIs before endoscopy has been shown to reduce findings of high-risk hemorrhage on endoscopy and the overall need for endoscopy[51]. Considering that emergency endoscopy may be delayed or impossible to perform, it is still recommended to use a PPI prior to endoscopy.

PPIs should be given as appropriate after endoscopy. PPIs should be used for non-variceal upper gastrointestinal bleeding of which the causes related to gastric acid (such as peptic ulcer, erosive esophagitis, gastritis, duodenitis) or esophageal mucosal laceration syndrome. The usual course of PPI is between 4 and 8 weeks for peptic ulcers[26]. Peptic ulcers with a low risk of rebleeding (*e.g.* Forrest Ⅱc-Ⅲ: those with a flat and clean base) should be given an oral PPI daily[52]. For patients with high-risk peptic ulcers (*i.e.* those with active bleeding, visible blood vessels or adherent clots), a meta-analysis showed that a high-dose proton pump inhibitor given for 72 hours (bolus 80 mg intravenously initially, followed by constant infusion 8 mg/hour for the next 72 hours) after successful endoscopy reduced the re-bleeding rate and mortality[53]. A randomized controlled trial (RCT) showed that oral administration of PPI twice per day following high-dose PPI could significantly reduce re-bleeding risks in high-risk patients compared with treatment of PPI only once a day for two weeks after bleeding[54]. Current Chinese guidelines recommend that following high-dose PPI, patients with high risk should be switched to a standard-dose intravenous PPI twice a day, and then about 3-5 days later changed to an oral PPI at a standard dose until ulcer is healed[4].

3.5.1.2. Drugs for reducing portal pressure

Statement 13: For acute variceal upper gastrointestinal bleeding, it is recommended to use somatostatin (or its analogue octreotide) or vasopressin (or its analogue terlipressin) for up to 5 days (evidence level: high, agreement: 95.5%).

Early mortality is high in patients with EGVB. For patients with variceal bleeding, drug therapy is the first priority to reduce portal pressure and active bleeding[11]. Therapeutic drugs include somatostatin and its analogues (octreotide) as well as vasopressin and its analogues (terlipressin). Somatostatin is a cyclic active tetradecapeptide composed of multiple amino acids, with a half-life of about 3 min. Octreotide is a synthetic octapeptide somatostatin analogue, with a half-life of about 100 min. Somatostatin and octreotide decrease portal pressure mainly by reducing portal blood flow. Vasopressin and terlipressin can lead to visceral vasoconstriction. By activating the vascular smooth muscle V1 receptor, vasopressin can increase the resistance of mesenteric vessels and restrain portal vein blood flow, thus reduce portal vein pressure. Vasopressin has a strong vasoconstrictor effect, which can cause side effects of cardiac and peripheral blood vessel ischemia, therefore, its clinical application is limited. Terlipressin is a synthetic vasopressin analogue, which can reduce portal pressure persistently and effectively, and has little effect on systemic hemodynamics. The most significant side effect of terlipressin is peripheral limb ischemia.

Somatostatin usage: initial intravenous bolus of 250 μg, followed by a continuous intravenous infusion of 250 μg/h. Octreotide usage: initial intravenous injection of 50 μg, then a continuous intravenous infusion of 50 μg/h. Terlipressin usage: initial dose of terlipressin is 1 mg every 4 hours, and the first dose may be doubled. After the bleeding stops, terlipressin may be decreased to 1 mg every 12 hours. The duration of the above three drugs is generally 2-5 days. Several studies have shown that somatostatin (octreotide) or vasopressin (terlipressin) was able to improve endoscopic hemostasis rate and reduce recent re-bleeding rate after endoscopy[55,56]. Octreotide-assisted endoscopy (for 2-5 days) can prevent early re-bleeding in EGVB[57]. There was no difference in the efficacy of reducing bleeding across somatostatin, octreotide, and terlipressin[58,59]. If somatostatin or octreotide fails to control bleeding, combination with terlipressin can be considered, but its efficacy needs to be further verified.

3.5.1.3. Hemostatics

Statement 14: Cautious use of hemostatics in acute upper gastrointestinal bleeding (evidence level: low, agreement: 92%).

One RCT reported that the use of tranexamic acid helped reduce the application of emergency endoscopy. However, no improvement was seen in mortality or rebleeding rate[60]. As tranexamic acid carries a risk of thromboembolism[61], it is recommended to use it with caution before safety confirmation by larger RCTs[62,63]. The clinical efficacy of systemic and local uses of hemocoagulase, the oral or transgastric use of thrombin, Yunnan Baiyao (a hemostatic traditional Chinese medicine), sucralfate, or iced norepinephrine saline are all not yet confirmed. The use of vitamin K1 for treating acute upper gastrointestinal bleeding in patients with acute or chronic hepatic diseases has also not been reported yet[64].

3.5.1.4. Antibacterial drugs

Statement 15: Prophylactic antibacterial therapy should be given for liver cirrhosis patients with acute upper gastrointestinal bleeding (evidence level: high, agreement: 83%).

The risk of infection in patients with cirrhosis and acute variceal bleeding can be assessed by Child-Pugh classification. The higher the grade of Child-Pugh classification, the higher the infection risk[65]. Patients with Child-Pugh grade A and drinking habits are also at a high risk of infection after variceal bleeding[66]. Prophylactic administration of antibiotics is beneficial to hemostasis and could reduce the incidence of rebleeding and infection for liver cirrhosis patients with acute upper gastrointestinal bleeding[44,67,68]. The 30-day mortality of patients who received prophylactic antibacterial therapy is also lower[69]. Antibiotics should be selected according to the local antibacterial resistance pattern. One RCT showed that intravenous ceftriaxone was superior to oral norfloxacin in the prophylaxis of bacterial infections in patients with advanced cirrhosis and hemorrhage[70], while another RCT found no difference in the effects of ceftriaxone when comparing 3-day with 7-day courses[71].

3.5.1.5. Antithrombotic drugs

Statement 16: Balance the risk of hemorrhage and ischemia, and manage antithrombotic drugs individually (evidence level: high, agreement: 97.7%).

Antithrombotic drugs include those with antiplatelet or anticoagulant effects. Whether or not to stop antithrombotic drugs in the case of acute upper gastrointestinal bleeding is a clinical challenge. Individualized assessment of the risk of hemorrhage *vs.* the risk of ischemia made with specialists is recommended. In general, it is not suitable to withdraw all antithrombotic drugs routinely. A retrospective study showed that discontinuation of antithrombotic drugs after bleeding was associated with increased thrombotic events and reduced survival rate[72]. A small RCT study showed that the mortality of patients who took aspirin as secondary prevention for upper gastrointestinal bleeding after 8 weeks of discontinuation was significantly higher than that of patients with consistent administration. The main cause of death was thrombotic events, and there was no significant difference in the re-bleeding rate regarding whether to take aspirin or not[73].

Antiplatelet therapy for acute upper gastrointestinal bleeding should be considered from two aspects: the necessity of drug use and the risk of bleeding. If deemed likely unnecessary, such as the use of aspirin for primary cardiovascular event prevention, the drug should be discontinued and re-evaluated when clinically appropriate. The individual strategy is needed when aspirin is used alone or as part of dual anti-platelet therapy for secondary prevention, such as being first discontinued and then resumed, not discontinued or else based on the endoscopic signs of bleeding[8,74]. For acute coronary syndrome patients receiving dual anti-platelet therapy, Chinese experts recommend that there is no need to discontinue drugs for mild hemorrhage but to discontinue aspirin first for cases of obvious hemorrhage, discontinue all anti-platelet drugs when life-threatening active bleeding occurs, and anti-platelet therapy should be resumed as early as possible after effective hemostasis and stabilization of the condition. Generally, clopidogrel can be resumed in 3-5 days and aspirin in 5-7 days after effective hemostasis[75]. PPI therapy needs to be used continuously for those with acute non-variceal upper gastrointestinal bleeding, who cannot discontinue anti-platelet therapy[8,75].

Warfarin should be discontinued in cases of active bleeding or hemodynamic instability, and prothrombin complex or vitamin K could be used to reverse any anticoagulation effect[9]. The anticoagulant effect of the new generation of oral anticoagulants (*e.g.* dabigatran, rivaroxaban, apixaban) can disappear in 1-2 days, therefore generally prothrombin complex is not needed, and other treatments for reversing anticoagulation effect are controversial. If the risk of thrombosis is high after hemostasis, anticoagulation therapy should be evaluated and restarted as soon as possible. Heparin or low molecular weight heparin could be considered as a bridging medication for patients with high-risk cardiovascular diseases during discontinuation of oral anticoagulants[12].

3.5.2. Balloon tamponade

Statement 17: Balloon tamponade is only an interim transitional measure for the treatment of EGVB refractory to endoscopy (evidence level: high, agreement: 95.5%).

For EGVB, if bleeding is massive and refractory to endoscopic treatment, a balloon tamponade could be used as a temporary measure for hemorrhage control in short term and as a transition to definite therapy. Notably, it is inappropriate to place a balloon tamponade for more than 3 days. The balloon should be deflated once every 8-24 hours based on the condition. The balloon tamponade should be removed 24 hours after successful hemostasis. Generally, the balloon is deflated and then observed for 24 hours, and it can be removed if there is no further bleeding. Since re-bleeding is common, and balloon tamponade therapy, in general, is associated with some serious complications, *e.g.* esophageal rupture and aspiration pneumonia, more cautions are needed.

3.5.3. Emergency endoscopy

Endoscopy is a primary and key examination for identifying the etiology of acute upper gastrointestinal bleeding, and it plays an important role in risk stratification and treatment. Emergency physicians should actively stabilize the circulatory status of patients, protect their airways, and create better endoscopic conditions before endoscopy. Bedside endoscopy can be performed under close monitoring in an emergency resuscitation room or intensive care unit when the patient is in critical condition or not fit for transport. If hemostasis is not completed during a first endoscopy, repeated endoscopies can be considered when necessary[76].

3.5.3.1. Timing of endoscopy

Statement 18: Endoscopy should be performed in dangerous acute upper gastrointestinal bleeding within 24 hours after hemorrhage. Urgent endoscopy should be performed if hemodynamic instability persists after active resuscitation. Endoscopy could be performed within 24 hours for patients with hemodynamic stability. Endoscopy should be performed within 12 hours for suspected variceal bleeding (evidence level: moderate, agreement: 98.9%).

For acute non-variceal upper gastrointestinal bleeding, the current guideline recommends that endoscopy should be performed within 24 hours after hemorrhage in cases without contraindications[18]. Delayed endoscopy beyond 24 hours is associated with increased mortality in patients with acute upper gastrointestinal bleeding[77]. Urgent endoscopy should be performed for patients with persistent hemodynamic instability after active resuscitation[6,26]. A recent RCT study showed that for patients with acute upper gastrointestinal bleeding, who were at high risk of further bleeding or death but with hemodynamic stability, endoscopy performed within 6-24 hours after consultation was not associated with higher 30-day mortality compared with those within 6 hours[78]. Variceal bleeding is often massive, and the speed of blood transfusion and fluid infusion is often far slower than the bleeding, thus endoscopy should be performed within 12 hours[5]. It should be noted that some studies have shown that the majority of deaths after acute upper gastrointestinal bleeding were caused by potential complications rather than blood loss, so early resuscitation and management of complications before endoscopy are also crucial[79,80].

3.5.3.2. Endoscopy notes

Statement 19: An intravenous infusion of 250 mg of erythromycin 30-120 min prior to endoscopy can be considered to improve endoscopic visualization (evidence level: high, agreement: 80.7%).

High level evidence showed that administration of erythromycin before endoscopy can reduce the volume of blood in the stomach, improve endoscopic visualization, and significantly reduce the rate of secondary endoscopy and endoscopic duration for acute upper gastrointestinal bleeding[81].

In addition, existing evidence does not support that drainage of retained blood from the stomach by a gastric tube prior to endoscopy can improve the endoscopic view[82]. For patients taking anticoagulants, INR should be corrected to less than 2.5 before endoscopy[83]. Moreover, a patient's airway should be protected to prevent reflux, aspiration, and aspiration pneumonia, especially for older patients who are on hemodialysis, have a history of stroke, and undergo a longer procedure[84].

3.5.4. Abdominal CTA and other examinations

If endoscopy is contraindicated or negative, patients should still be empirically treated, pending alternative diagnostic testing. According to patient conditions, abdominal contrast-enhanced computed tomography, CT angiography (CTA), traditional angiography, enteroscopy, radionuclide scanning, or exploratory laparotomy can also be chosen to help arrive at the diagnosis.

Statement 20: Abdominal CTA can be performed to find the potential source of hemorrhage if active bleeding persists in patients with either contraindications or negative findings of endoscopy (evidence level: moderate, agreement: 98.9%).

For massive or active bleeding, if endoscopy cannot be performed or the cause cannot be determined, abdominal CTA can be selected to help determine the source or cause of bleeding[85]. Abdominal CTA can normally detect bleeding at a rate of 0.3-0.5 mL/min, which makes it sensitive to detect both arterial and venous bleeding. It can also be used to observe intestinal wall diseases, such as vascular malformations or masses. However, it should be noted that even in massive bleeding, bleeding may rapidly stop, resulting in a negative examination. Therefore, in order to improve the positive detection rate of abdominal CTA, examination delays should be minimized. In addition, abdominal CTA is not a treatment, and the benefits of auxiliary diagnosis and the risks of further treatment delays need to be balanced. When the risk of delayed treatment is high, interventional radiology should be chosen instead of CTA. Moreover, allergy to contrast agent and contrast-induced nephropathy are concerns when using CTA.

3.5.5. Interventional radiology

Statement 21: Interventional radiology can be performed if there is still active bleeding in patients with contraindications or negative findings at endoscopy, failure of pharmaceutical or endoscopic therapy, or hemorrhage as shown by abdominal CTA (evidence level: moderate, agreement: 98.9%).

Selective angiography can be performed to determine the site and source of bleeding in patients with acute non-variceal bleeding. The left gastric artery, gastroduodenal artery, splenic artery, and pancreaticoduodenal artery are selected regularly for angiography. The treatment includes injection of vasoconstrictors into the bleeding vessels or direct transcatheter arterial embolization[7].

Transjugular intrahepatic portosystemic shunt could be considered if hemostasis fails using drug and endoscopy in patients with acute variceal bleeding. In order to reduce a recurrence of variceal bleeding, the early transjugular intrahepatic portosystemic shunt could be considered in those patients with severe re-bleeding, Child-Pugh class C (<14 points), or class B with active bleeding[5,6].

3.5.6. Multidisciplinary treatment and surgery

Statement 22: For patients with persistent bleeding refractory to pharmaceutical therapy, endoscopy and interventional radiology, multidisciplinary treatment should be initiated, and surgery may be necessary (evidence level: moderate, agreement: 97.7%).

Most patients with acute upper gastrointestinal bleeding are admitted through the emergency department. The diversity of etiologies and the urgency of the disease often call for collaboration between different specialists for acute upper gastrointestinal bleeding, however, effective collaboration and treatment are often difficult to achieve with the traditional single disciplinary treatment and consultation model, especially for massive bleeding refractory to routine treatment. A retrospective study showed that multidisciplinary treatment can improve diagnosis and treatment efficiency, and reduce mortality[86]. Surgical exploration could be considered if hemostasis fails using medications, endoscopy, and interventional therapy.

3.6. Prognostic assessment

Statement 23: Prognosis should be evaluated for acute upper gastrointestinal bleeding after patient's condition is stabilized, but the clinical value of risk assessment scores is limited (evidence level: moderate, agreement: 94.3%).

Prognosis needs to be evaluated for acute upper gastrointestinal bleeding after patient's condition is stabilized. Assessments include the function of vital organs, risk of re-bleeding or death. The function of vital organs can be evaluated according to clinical characteristics. The risk of re-bleeding is higher if patients with acute non-variceal upper gastrointestinal bleeding have any of the following conditions: over 65 years old, severe comorbidities, shock, low hemoglobin concentration, blood transfusion, and a blood clot with exposed vessels at the ulcer base under endoscopy[4]. Acute variceal upper gastrointestinal bleeding is prone to rebleeding and the incidence of rebleeding after first hemorrhage is 60%-70% within 1-2 years, with high mortality of 33%[3]. The risk of death is evaluated empirically based on the high-risk factors of patients, and the existence of the above high-risk factors in comprehensive evaluation often suggests a poor prognosis. The accuracy of risk assessment scores in predicting rebleeding, length of hospitalization, or risk of death is unfortunately low. A study showed although PNED (Progetto Nazionale Emorragia

Digestiva) scores≥4 and AIMS65 score≥2 are the best predictors of death, but their clinical value is limited due to their low accuracy[24]. After a prognostic assessment is completed, according to the etiology and assessment results, the patient would be given advice for further diagnosis and treatment in a specialized department or a follow-up plan after discharge.

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Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

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