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GUIDELINES

Management of acute variceal bleeding: updated APASL guidelines

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Abstract

Acute variceal bleeding (AVB) is a common life-threatening complication of portal hypertension (PHT), having a six-week mortality of 10%-20%. Major advances in the hemodynamic management, risk stratification, pharmacotherapy, endoscopy techniques, hemostatic devices and radiological interventions have led to improved management and outcome of AVB patients in the recent past. Therefore, the APASL Portal Hypertension Working Party, chose a panel of experts, primarily from the Asia–Pacific region, to identify important developments and controversial areas in the field of AVB. They discussed through a pre-defined and structured process, advances in the field and proposed updates to the previous APASL AVB guidelines. These included emphasis on safe transportation, defining time frames for AVB episodes and re-bleeding, reporting of clinical outcomes, optimizing early intervention strategies, pharmacotherapy, medical management, endoscopic therapies, and salvage modalities, including TIPS and self-expanding metal stents. The current updates also cover variceal bleeding in special populations and situations, the skill sets required for managing AVB patients, and the research priorities in the field. The updated guidelines are based on the latest evidence and incorporate emerging trends to provide a contemporary template for management of AVB in both patients with cirrhosis and non-cirrhotic portal hypertension.

Keywords Gastrointestinal hemorrhage · Cirrhosis · Portal hypertension · Vasoactive drugs · Endoscopy · Varices · Non-cirrhotic portal fibrosis · EHPVO · CTP score · MELD score · Hepatic encephalopathy · TIPS · Ella-Denis Stent · Shunt surgery

Introduction

Acute variceal bleeding (AVB) is a medical emergency and is associated with a mortality of 10–20% at 6 weeks [1, 2]. Over the past decade several advances have taken place in the diagnosis and management of AVB. Due to the rapid and often episodic nature of AVB, and geographical variations in the expertise and the availability of the requisite infrastructure, the design and conduct of good clinical trials for the assessment and management for AVB has remained challenging. To move the field forward keeping in mind all the above issues, the Working party of the APASL on Portal Hypertension undertook to update the management of AVB.

In developing these updated guidelines, the working party of APASL was fully aware of, and acknowledged the significant contributions made by the Baveno VII consensus conference on Portal Hypertension [1] and the recent guidelines published by the American Association for the Study of the Liver [2]. In the past, the APASL working party on portal hypertension has published guidelines on acute variceal bleeding, extra-hepatic portal vein obstruction [3], non-cirrhotic portal fibrosis [4], and primary prophylaxis of variceal bleeding [5].

For the development of the consensus update on AVB, the experts of the APASL working party identified contemporary and controversial issues and available evidence on various aspects of AVB. Experts, predominantly from the Asia–Pacific region, were requested by the working party to critically analyze the existing literature and develop evidence-based consensus statements and recommendations on each of these issues. Several on-line meetings to define and focus the issues using the Delphi method were

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undertaken. Each working group conducted its meetings and prepared its consensus statements. These were subsequently presented to the entire group of experts. Statements that were unanimously approved by all the experts were finalized, drafted and then circulated for review, and were subsequently presented at the APASL single theme conference on "Portal Hypertension" at Bali, Indonesia, on October 13, 2024. Level of evidence (LoE) and grade of recommendations were based on the GRADE system [6]. A summary of the most important consensus statements which form the guidelines along with the background literature are presented here.

Definitions of acute variceal bleeding (AVB)

Variceal bleeding constitutes 70% of all upper gastrointestinal bleeding episodes in patients with portal hypertension, and it can result from esophageal varices (EVs) and/or gastric varices (GVs) [7]. The remaining 30% could be due to portal hypertensive gastropathy, gastric antral vascular ectasia, peptic ulcer disease (PUD), ectopic varices, Mallory-Weiss lesions, etc.[8]

AVB needs to be differentiated from recent bleeding and re-bleeding, because the prognosis and management algorithms differ in these situations. It is important that the defined criteria should be easy, convenient, widely applicable for clinical practice and should be able to stratify patients accurately. Currently, there are differences in the definitions relating to AVB. For example, studies for the efficacy of vasoactive agents have used a time frame of 2 to 5 days to define AVB [9]. Those relating to the impact of infection following AVB have used a time frame of 5–7 days, and those relating to impact of endoscopic therapies have used a time frame of days to weeks.

We propose that AVB be defined as hematemesis within last 48 h of presentation, and/or ongoing melena, with last melanic stool within last 24 h in a known or suspected case of portal hypertension (PHT). The time of the first bleed (symptom onset) is considered as T_0. Recent bleed refers to a clinically significant bleed which occurs within 6 weeks of presentation after the episode of AVB. A variceal bleed which occurred more than 6 weeks of presentation should be considered as a past bleed.

Any bout of hematemesis from T_0 to 48 h of T_0 should be considered as part of the same episode of AVB. The time frame for AVB as defined in Baveno II[10, 11] and Baveno III[12, 13] was 48 h, but was increased to 120 h in Baveno IV [14]. However, the expert groups felt that a time frame longer than 48 h will make it difficult to differentiate between early re-bleeding and failure to control bleeding.

Definition of 'active' bleeding

The definition of 'active' bleeding was clarified in the APASL 2011 guidelines. Active bleeding is a state which is defined endoscopically, when spurting or oozing is seen from the varix. This discrimination between active and inactive 'acute' bleeding is important because the prognosis differs between the two. Significance of active bleeding at endoscopy has evolved overtime. It predicts early rebleeding [15].

Definition of control of AVB

Control of AVB is defined as the cessation of bleeding with hemodynamic stability (systolic blood pressure > 90 mmHg and MAP ≥ 60 mmHg) for at least 48 h post-therapy. This definition has remained acceptable over the years due to its clarity and utility in clinical settings.

Definitions of failure to control AVB and refractory bleeding

In cases of active bleeding confirmed by endoscopy, cessation of bleeding should be achieved by the end of the procedure. Failure to control AVB should be defined as persistent bleeding at the end of endoscopy or refractory bleeding despite appropriate therapy**,** irrespective of the time frame, if the clinical situation meets one or more of the following criteria:

1. *Persistence of bleeding* at the end of the initial endoscopic procedure, as defined by:
- Active bleeding from varices despite endoscopic intervention, or
- Inability to perform endoscopic variceal ligation (EVL) or other endoscopic interventions due to inadequate visualization caused by ongoing bleeding.
2. *Refractory bleeding* is bleeding which is continuing even after appropriate combined pharmacotherapy and endoscopic therapy and is defined as:
- fresh hematemesis after initiation of combination therapy (vasoactive drugs and endoscopic treatment), or
- Drop in hemoglobin of ≥ 2 g/dL or in hematocrit of ≥ 6%, not explained by hemodilution or transfusion adjustments, or
- development of hemodynamic instability requiring urgent resuscitation (SBP < 90 mmHg, HR > 110 bpm), or

- death due to uncontrolled variceal bleeding.

Re-bleeding and subtypes

Re-bleeding is defined as bleeding occurring after the control of AVB and is classified into three categories:

- Very early re-bleeding: Rebleeding within 48 to 120 h from endoscopic therapy.
- Early re-bleeding: Rebleeding between 120 h and 42 days from endoscopic therapy.
- Late re-bleeding: Rebleeding beyond 42 days from endoscopic therapy.

This categorization facilitates better prediction and management of bleeding recurrence based on the timing of the event (Tables 1, 2 and Fig. 1).

Clinically significant re-bleeding

Clinically significant re-bleeding is defined as a rebleeding with a decrease of at least 2 g/dL in hemoglobin without transfusion or an adjusted blood requirement index (ABRI) ≥ 0.5 at any time point [16]. This formula aims to provide a quantifiable measure that reflects the efficiency of blood transfusion in improving the patient's hematocrit. This definition is retained to guide therapeutic decisions based on the clinical impact of re-bleeding.

Index bleeding

Index bleeding refers to the very first episode of UGI bleeding.

Table 1 Time dependent definition of acute variceal bleeding and re-bleeding

State	Time frame to T_0	Sub-types	Time frame from T_0
Acute variceal bleeding	48 h	Active (based on endoscopy)	48 h
Re-bleeding	Beyond 48 h	Very early rebleed	48–120 h
		Early rebleed	120 h—42 days
		Late rebleed	After 42 days

Table 2 Comparison of time frames: Baveno VII vs. APASL 2025

Aspect	Baveno VII (2021)	APASL 2025
Duration of an AVB episode	120 h (5 days)	48 h
Definition of re-bleeding	Any bleeding after 5 days	Any bleeding after 48 h
-Very early re-bleeding	Not separately defined	48–120 h (2–5 days) after AVB control
-Early re-bleeding	Beyond 5 days to 6 weeks	Beyond 5 days to 6 weeks
-Late re-bleeding	Beyond 6 weeks	Beyond 6 weeks

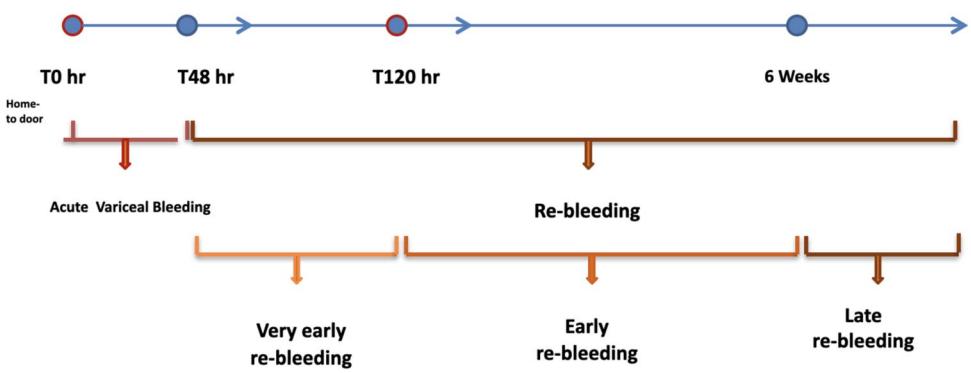

Fig. 1 Time frames of acute variceal bleeding

Outcomes in relation to AVB

To assess the prognosis and clinical outcome of AVB, we define outcome measures in two categories: conventional outcome measures (retained from APASL 2011) and newly introduced parameters that provide a more comprehensive assessment.

Mortality related to AVB includes all-cause mortality within 42 days of the AVB event.

New outcome measures introduced to assess clinical significance of AVB

The experts deliberated on the emergency management steps and protocols for AVB. They proposed to include the following additional outcome measures to be recorded and reported for standardization of protocols specially in relation to interventions. The objectives are to reduce the morbidity, minimize the complications, and improve survival of patients with AVB:

- *Duration of ICU stay*—indirectly captures the severity of AVB and likely clinical outcomes post-AVB.
- *Duration of hospital stay*—reflects bleed related events and healthcare resource utilization.
- *Quality of life*—this was evaluated using standardized assessment tools to gauge patient-reported outcomes post-AVB.
- *New decompensation events*—includes new-onset ascites, jaundice, hepatorenal syndrome (HRS), or hepatic encephalopathy (HE).
- *Delta-MELD Score at 42 Days*—change in the MELD score from baseline to 42 days post-AVB, indicating worsening of clinical condition or recovery.
- *Development of ACLF*—identification of acute-on-chronic liver failure (ACLF) triggered by AVB, as per the APASL criteria.
- *Further decompensation*—worsening of pre-existing decompensation status of liver disease with progression to new/additional organ failures beyond the initial bleeding event

These additional outcome measures were incorporated for reporting following AVB, to enhance the assessment of the long-term prognosis and recovery post-AVB, offering a more comprehensive patient-centered evaluation beyond conventional bleeding control and mortality endpoints.

Definition of time zero (T_0)

T_0 was previously defined as the time of hospital presentation. However, we propose redefining T_0 as the time of first bleed (symptom onset), as this approach captures the entire clinical course, including pre-hospital care (Fig. 1). This change aims to improve tracking and evaluation of early intervention strategies. Hematemesis was used as the reference point for symptom onset. Using the onset of melena as time zero in defining acute variceal bleeding is limited by its subjective nature, uncertain timing, limited patient knowledge and poor specificity. Melena may appear long after bleeding begins, persist despite hemostasis, and is not exclusive to variceal sources, potentially delaying diagnosis, and appropriate intervention. Objective indicators like hematemesis or endoscopic findings are more reliable for establishing the onset.

'Home-to-door' time

'Home-to-door' time is a novel concept and is defined as the time elapsed from the onset of bleeding at home to the time of arrival at the hospital. The ideal time for patients to reach to the hospital is proposed to be ideally two hours but may be acceptable for up to 4 h in mild cases. This aligns with the "golden hour" principle in emergency care . Delays beyond 4–6 h are likely to be associated with increased mortality due to uncontrolled bleeding, hepatic ischemia, and organ failure.

The updated definitions of AVB and its associated outcomes aim to reflect current knowledge base, clinical practices and incorporate insights from recent studies from different emergency scenarios from other branches of medicine.

Consensus statements

1. Definition of acute variceal bleeding and related states

1.1. Acute Variceal Bleeding (AVB) is defined as hematemesis within 24 hours of presentation and/or ongoing melena with the last melanic stool within the last 24 hours in a known or suspected case of portal hypertension. (LoE-High; Recommendation-Strong)

1.2. AVB episode is considered to last for 48 hours from the first episode of bleeding (T_0). Any subsequent bleeding within 48 hours is part of the same AVB episode. (LoE-Moderate; Recommendation-Strong)

1.3. Active bleeding in the context of AVB is defined as: (LoE-Moderate; Recommendation-Strong)

- Endoscopic Findings: Visible spurting or oozing of blood from a varix during endoscopy.
- Fresh blood in the nasogastric tube

- Hematemesis of fresh blood

1.4 Control of AVB is defined as: (LoE-Moderate; Recommendation-Strong)

- Cessation of bleeding with hemodynamic stability for 24 h after therapy.
- In patients with active bleeding on endoscopy, control of AVB indicates cessation of bleeding at the end of the procedure.

1.5. Failure to control AVB is defined by any of the following events within 48 hours: (LoE-Moderate; Recommendation-Strong)

- Fresh hematemesis despite adequate implementation of combination therapy (vasoactive drugs and endoscopic therapy).
- A drop of ≥ 2 g/dL in hemoglobin or 6% drop in hematocrit if no transfusion is administered.
- Death

1.6. Re-bleeding is classified into three categories: (LoE-Moderate; Recommendation-Strong)

- Very Early Re-bleeding: within 48 to 120 h from T_0.
- Early Re-bleeding: between 6 and 42 days from T_0
- Late Re-bleeding: after 42 days

1.7. Clinically significant re-bleeding is defined by: (LoE-Moderate; Recommendation-Strong)

- A decrease of 2 g/dL of hemoglobin if no transfusion is given, ABRI (adjusted blood requirement index) ≥ 0.5 at any time point.

1.8. Index bleeding is defined as the first episode of UGI bleeding (LoE-Moderate; Recommendation-Strong)

1.9. Outcomes of AVB should include: (LoE-Moderate; Recommendation-Strong)

- Control of AVB
- Failure to control AVB
- Re-bleeding events (categorized into very early, early, and late)
- Mortality related to AVB (within 42 days)
- Duration of ICU stay.
- Duration of hospital stay.
- Quality of life deterioration.
- New decompensation, such as ascites, new onset jaundice, acute kidney injury (AKI), HE, sepsis, ACLF, etc.
- Development of ACLF
- Further decompensation
- Development of Ischemic hepatitis
- Delta-MELD score at 42 days post-AVB compared to pre-AVB
- Requirement of alternative/rescue therapies; TIPS, PARTO (plug-assisted retrograde transvenous obliteration), etc.

1.10. Time zero (T_0) is defined as the time of first bleed (symptom onset). (LoE-Moderate; Recommendation-Weak)

1.11. Home-to-Door Time is defined as the time from symptom onset to hospital arrival. The ideal time is proposed to be 2 hours in most cases, but 4 hours may be acceptable in less severe cases. (LoE-Low; Recommendation-Weak)

Diagnosis, evaluation, and severity assessment of patients with AVB

Patients presenting with UGI bleeding (UGIB) must be promptly assessed to initiate appropriate management. This necessitates a more focused evaluation based on key high-yield indicators in the emergency department. Traditional detailed clinical examination with features like spider angiomas, testicular atrophy etc. may be deferred until urgent hemodynamic measures have been initiated. A quick and efficient history, physical examination, and initial laboratory values are important in assessing resuscitation requirements, triage, endoscopy timing, consultation requirements, and prognostication [17].

The initial evaluation of a patient with suspected UGIB begins with a history and physical examination. In particular patients should be asked about previous episodes of UGIB, a comprehensive review of recent and current

medications, and history of alcohol, tobacco, and substance use. All patients should specifically be asked about intake of non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulants, anti-platelet agents, and selective serotonin reuptake inhibitors because these medications increase the risk of bleeding. The goal of the patient history is to identify risk factors that may point to an underlying etiology of the UGIB. For example, a patient with NSAID use for osteoarthritis presenting with UGIB may have peptic ulcer disease related bleed, whereas a patient with alcohol abuse and cirrhosis may have esophageal varices.

The history should also include significant co-morbid conditions, and whether there is a past history of hepatitis B or C infection, metabolic dysfunction associated fatty liver disease (MAFLD) [18], portal hypertension or cirrhosis. On examination, important features include jaundice, ascites, hepatic encephalopathy, splenomegaly, palpable firm liver, enlarged left hepatic lobe and presence of dilated abdominal wall veins. The aforementioned signs indicate that the bleeding is likely to be associated with portal hypertension. In cirrhosis, about 60% of initial UGIB is from EVs [19].

Laboratory assessments focus on assessing liver function and coagulation status [20, 21]. The Child-Turcotte-Pugh (CTP) and Model for End-Stage Liver Disease (MELD) scores are utilized to assess the severity of liver dysfunction in cirrhosis [20]. Among laboratory markers, thrombocytopenia, elevated INR and bilirubin and low albumin should alert the provider to the possibility of cirrhosis and portal hypertension [21–24]. Ultrasound imaging may reveal features of cirrhosis or portal hypertension like an irregular liver margin or coarse liver echotexture, ascites, splenomegaly, dilated portal vein, portosystemic collaterals, or recanalized paraumbilical vein. Evidence from a retrospective study involving 1729 patients with cirrhosis demonstrated that approximately 60% had spontaneous porto-systemic shunts. The prevalence of these shunts increased with worsening liver function [25]. Development of spontaneous portal shunts is a marker of the progression of portal hypertension [26–28]. A retrospective study found that cirrhosis patients typically exhibit wider paraumbilical veins and a greater number of portosystemic collateral channels [26, 27]. Another study identified the diameters of the left gastric vein and its originating vessels as independent risk factors for the presence of varices [29]. Several studies have demonstrated that splenomegaly is a key indicator of portal hypertension [30–36]. Splenorenal shunts, dilated left and short gastric veins, and umbilical vein recanalization may also be seen in computed tomography (CT) and magnetic resonance imaging (MRI) [37]. Imaging signs for hepatic fibrosis and cirrhosis have been provided in Table 3.

CT scan is recommended as a non-invasive diagnostic tool for assessing esophageal varices. A systematic review of cohort studies concluded that CECT imaging is superior to liver stiffness measurement (LSM) and MRI in diagnosing esophageal varices and predicting cirrhosis patients at high-risk of bleeding [38].

Table 3 Imaging signs for cirrhosis or portal hypertension [48, 49]

Morphologic imaging signs
Liver parenchyma heterogeneity: liver fibrosis
Size of the liver: enlargement and later reduction
Dysmorphic liver:
Hypertrophy of the left lobe—atrophy of the right lobe
Segment I hypertrophy
Segment IV atrophy
Enlargement of hilar periportal space
Right posterior hepatic notch sign
Nodularity of liver surface
Signs of portal hypertension
Portal vein diameter > 12 mm
Spleen length > 11.2 cm
Portal velocity max < 18 cm/s, mean velocity < 10 cm/s
Portosystemic collateral vessels
Other hemodynamics changes
Arterial hepatic flow changes
Increase in diameter
Resistive index (RI) > 0.7, Pulsatility index (PI) > 1.2
Demodulation of hepatic veins on Doppler spectrum
Other signs
Ascites
Gallbladder wall thickening
Peribiliary cyst

Non-variceal bleeding in patients with UGIB should be suspected if there is abdominal pain or history of NSAID use, anticoagulants, or antiplatelet agents, past history of peptic ulcers, Helicobacter pylori infection, as well as the history of peptic esophageal lesions, neoplastic lesions, Dieulafoy's lesions, angiodysplasia or esophagitis [39–42].

Additionally, symptoms such as retrosternal chest discomfort, epigastric pain, belching, nocturnal pain, nausea, and vomiting may further suggest non-variceal bleeding [43]. Endoscopic findings, including ulcers with spurting or oozing blood (Forrest 1a or 1b) or ulcers with non-bleeding visible vessels [44–47], provide further confirmation of non-variceal bleeding as the underlying cause.

Diagnosis of AVB at endoscopy

The gold standard test to diagnose AVB is upper gastrointestinal endoscopy and the endoscopic diagnostic criteria of AVB are outlined in the previous APASL Guidelines [15]. Variceal hemorrhage is defined as bleeding from an EV and/or GV confirmed by endoscopy. AVB may be active or inactive at the time of presentation. Active bleeding is a state which is defined endoscopically, when spurting or oozing is seen from the varix [15].

The European Society of Gastrointestinal Endoscopy (ESGE) guidelines in 2022 recommended that the diagnosis of AVB should be classified into esophageal variceal hemorrhage and gastric variceal hemorrhage, with a detailed description of the endoscopic diagnosis of each [50].

- Esophageal variceal hemorrhage

  The endoscopic diagnosis of acute esophageal variceal bleeding is made when there is active hemorrhage from a varix, or a sign of recent hemorrhage (nipple sign, platelet-fibrin plug). An esophageal variceal source of upper gastrointestinal hemorrhage can also be inferred when there is blood in the stomach with no other source of bleeding except for esophageal varices.
- Acute gastric variceal hemorrhage

Gastric varices are universally classified according to the Sarin classification, which defines: Type-1 Gastro-oesophageal varices (GOV1), which extend below the gastroesophageal junction along the lesser curvature of the stomach, Type-2 GOV (GOV2) extend below the gastroesophageal junction into the gastric fundus, Isolated gastric varices—Type I (IGV1), which are located only in the fundus and with no or small esophageal varices, and Type-2 IGV (IGV2) are located elsewhere in the body or antrum of stomach (figures 2, 3).

Bleeding is considered to have arisen from a gastric varix if (a) active bleeding or oozing of blood is seen from a gastric varix, (b) a clot or blackish ulcer is seen over the gastric varix, or, (c) in the presence of distinct large gastric varices

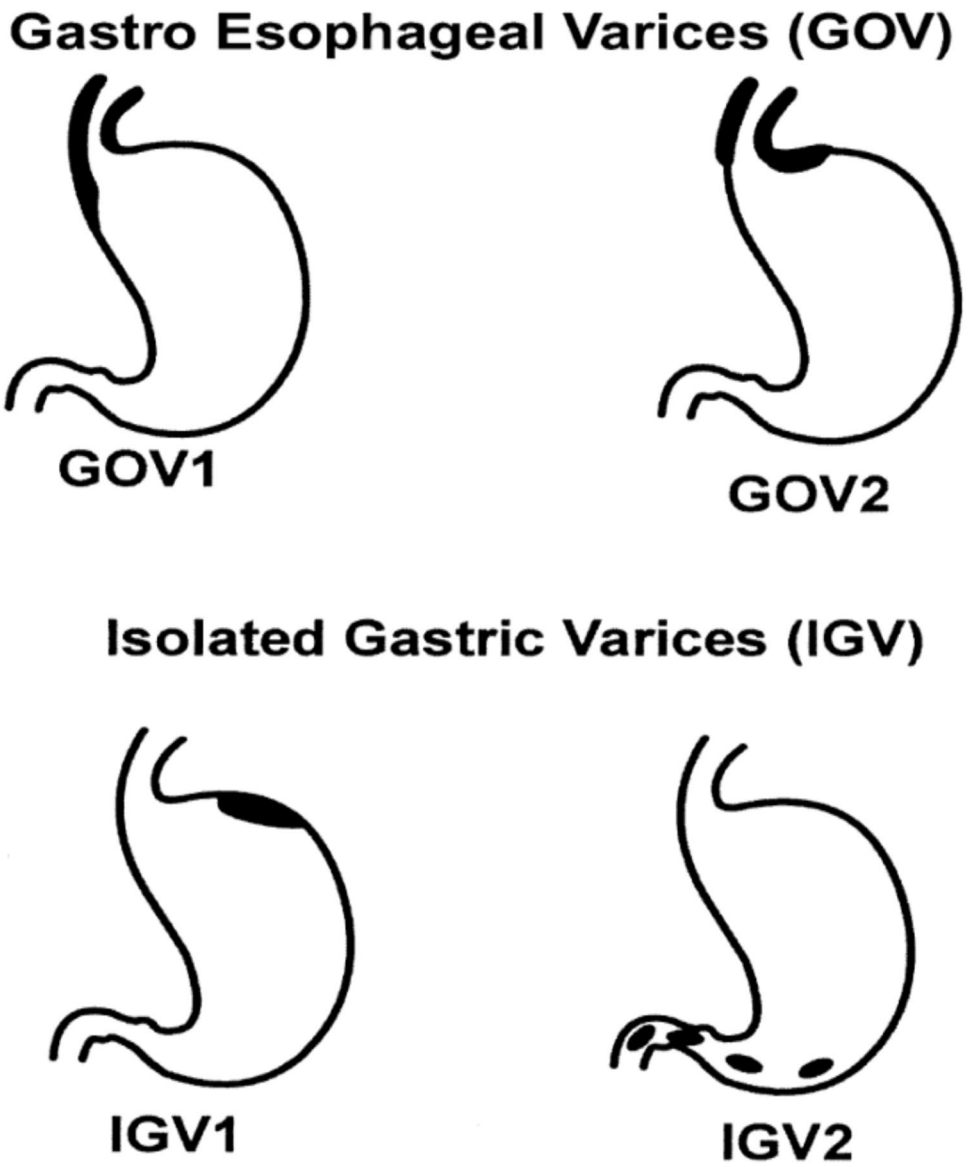

Fig. 2 Classification of gastric varices [51]

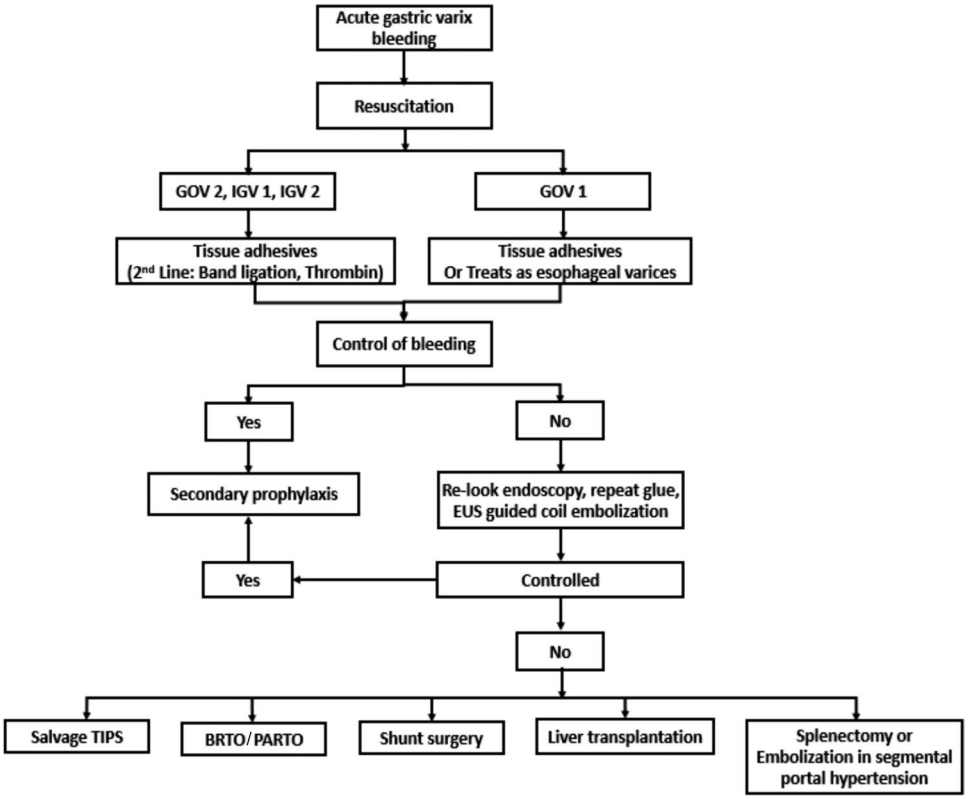

Fig. 3 Algorithm of management in patient with acute gastric variceal bleeding

and absence of esophageal varices and no other cause of upper gastrointestinal bleeding is detectable [51].

These endoscopic criteria play a critical role in the timely and accurate diagnosis of AVB, ensuring that appropriate treatments can be administered quickly. The presence of GV with red signs, accompanied by clinical signs of UGI bleeding such as melena or hematemesis, is also indicator of acute GV bleeding. Classification based on vascular anatomy is important to decide the type of radiological interventions in patients with GVs [51]. When both gastric and esophageal varices are present and the source of bleeding cannot be clearly identified; such cases may be classified under the category of 'variceal bleeding from uncertain source'. This terminology, however, needs to be assessed further.

Severity assessment and evaluation of patients of AVB

The severity of blood loss is roughly estimated by the hemodynamic status and other key signs. Visible blood loss can be estimated based on the patient's history and clinical observations. Resting tachycardia, in the absence of another cause and maintained blood pressure, suggests mild to moderate hypovolemia. Orthostatic hypotension, defined as a decrease in the systolic blood pressure of more than 20 mmHg or an increase in the pulse of more than 20 beats/min from recumbency to standing, suggests a loss of 15% or more of the blood volume. Hypotension is associated with loss of at least 40% blood volume [52]. Patients in shock typically have a thready, weak pulse, and cold, clammy extremities. Hyperactive bowel sounds are consistent with an UGIB because blood in the proximal gut is an irritant that stimulates peristalsis, whereas normal bowel sounds are more consistent with lower gastrointestinal bleeding.

The expert panel revisited the predictors of severity of AVB, treatment failure and early rebleeding including the APASL Severity Score for AVB assessment (Tables 4,5). Most early studies showed that alcoholic liver disease patients have more severe AVB, but recent studies have suggested better outcomes in alcohol-associated cirrhosis [53, 54]. Several factors, such as INR, encephalopathy, and Child–Pugh score overlap significantly. While these variables may not serve as independent predictors, they contribute to scoring systems (like, MELD, AIMS65, Neutrophil-to-Platelet Ratio, Platelet-Albumin-Bilirubin Index) that are instrumental in determining outcomes in AVB [55].

Consensus statements

2. Diagnosis, evaluation, and severity assessment of patients with acute variceal bleed

Table 4 Predictors of severity of acute variceal bleeding, treatment failure, early re-bleeding, and mortality

Predictor	Severity of variceal bleed	Treatment failure	Early re-bleeding	Mortality
HVPG	Yes	Yes	Yes	Yes
Alcoholic liver disease	Yes	Yes	Yes	Yes
Infection	Yes	Yes	Yes	Yes
CTP class/score	Yes	Yes	–	Yes
PRBC transfusion	Yes	Yes	–	Yes
Size and morphology of varices	Yes	Yes	–	–
Ascites	Yes	Yes	–	–
Portal vein thrombosis	Yes	Yes	–	–
Hematocrit/Hemoglobin at presentation	Yes	Yes	–	–
Platelet count	Yes	–	Yes	–
Degree of liver failure	Yes	–		–
Active bleeding at endoscopy	–	Yes	Yes	Yes
Shock	–	Yes	–	Yes
AST	–	Yes	–	–
First bleed	–	Yes	–	–
MELD > 18	–	–	Yes	Yes
Encephalopathy	–	–	Yes	Yes
Hepatocellular carcinoma	–	–	Yes	Yes
Short interval to admission	–	–	Yes	Yes
Blood urea	–	–	Yes	Yes
Hematemesis	–	–	Yes	
S. creatinine	–	–	–	Yes
S. albumin	–	–	–	Yes
Age	–	–	–	Yes
Early re-bleeding	–	–	–	Yes
Prothrombin time	–	–	–	Yes
Treatment failure	–	–	–	Yes
S. bilirubin	–	–	–	Yes

HVPG: hepatic vein pressure gradient; CTP: Child-Turcotte-Pugh; PRBC: packed red blood cell; AST: aspartate aminotransferase; MELD: Model for End Stage Liver Disease

Table 5 APASL bleed severity score for acute variceal bleeding*

Parameter	Value	Point
Systolic blood pressure	> 90 mmHg and no postural drop	0
	> 90 mmHg with postural drop	1
	< 90 mmHg	2
Child-Turcotte-Pugh class	A	0
	B	1
	C	2
Platelet count	≥ 100.000 mm-3	0
	< 100.000 mm-3	1
Infection	Absent	0
	Present	1
Active bleeding at endoscopy	Absent	0
	Present	1
	Total	Minimum 0, maximum 7

*Reproduced from 2011 APASL guidelines[15]

2.1 In a patient with UGI bleeding, if the following are present, suspect the cause to be variceal bleeding:

- Previous history of hepatitis B and C, or alcohol abuse, or metabolic-associated fatty liver disease [18], or exposure to hepatotoxic substances [56, 57], or long-term use of hepatotoxic medications [48, 58] (LoE-Moderate; Recommendation-Strong)
- *Physical findings:* jaundice, ascites, signs of hepatic encephalopathy, splenomegaly, firm hepatomegaly, abdominal wall collaterals or signs of hepatic failure. (LoE-Moderate; Recommendation-Strong)
- *Imaging signs*: spontaneous portosystemic shunts, dilated left and short gastric veins, umbilical vein recanalization, splenomegaly, nodular aspect of the liver, segmental dysmorphia, hypertrophy and hypotrophy of the liver, and enlargement of hilar periportal space. (LoE-Moderate; Recommendation-Strong)
- *Laboratory data:* thrombocytopenia, elevated INR, hepatic synthetic dysfunction, albumin and bilirubin abnormalities. (LoE-Moderate; Recommendation-Strong)
- *Endoscopy:* signs of variceal bleeding. (LoE-High; Recommendation-Strong)

2.2. The gold standard for diagnosis of acute variceal bleeding is UGI endoscopy. (LoE-Moderate; Recommendation-Strong)

2.3. Endoscopic diagnosis for variceal bleeding

2.3.1. Acute esophageal variceal bleeding (LoE-High; Recommendation-Strong)

- Direct visualization of blood arising from an esophageal varix—usually spurting or oozing.
- Presence of a sign of recent bleed on a varix (white nipple sign or overlying clot.
- Presence of esophageal varices with red signs (risk factor for bleeding) and presence of blood in the stomach in the absence of another source of bleeding.
- Presence of esophageal varices with red signs and clinical signs of UGIB without blood in the stomach.

2.3.2. Acute gastric variceal bleeding (LoE-High; Recommendation-Strong)

- Direct visualization of blood arising from a GV, spurting or oozing
- Presence of a sign of recent bleed over a GV (overlying clot or white nipple sign)
- Presence of GV with red signs (risk factor for bleeding) and presence of blood in the stomach in the absence of another source of bleed/or stigmata of recent bleed on esophageal varices

2.4. For describing site of acute GV bleeding, Sarin's classification of gastric varices should be used. (LoE-High; Recommendation-Strong)

2.5. For describing site of acute GV bleeding, Sarin's classification of gastric varices should be used. (LoE-High; Recommendation-Strong)

- Change of vital signs (heart rate, blood pressure)
- Hematocrit/hemoglobin
- Transfusion requirement
- Adjusted Blood Requirement Index

2.6. Predictors of severe acute variceal bleeding and rebleeding should be carefully assessed at presentation (Table 4). (LoE-High; Recommendation-Strong)

2.7. The APASL bleed severity score is a simple and reliable tool for assessing the severity of acute variceal bleeding and should be used to assess severity of AVB. (Table 5) (LoE-Moderate; Recommendation-Strong)

Resuscitation, initial management, and monitoring of patients with acute variceal bleeding

Management in pre-emergency period

The management of AVB includes protection and maintenance of airway, breathing, and circulation. Patients with AVB need urgent transport using specially equipped advanced life-care ambulance. It is very important that transport crew understands the underlying pathophysiology of variceal bleeding. A quick history and examination of patient by the transport team is useful to suspect PHT. A history of using direct oral anticoagulants or anti-thrombotic or anti-platelet medication need prioritization for transport because the high risk of persistent and severe bleeding.

Ultrasound by the transport crew can help discriminate possible variceal and non-variceal UGIB.

Airway intubation is indicated in patients who are bleeding severely, who have mental status changes, and difficult to maintain oxygen saturation above 90%. Hemodynamic condition should be monitored by using pulse oximeter and continuous cardiac monitoring during transportation. Vascular access needs to be placed for volume resuscitation and hemodynamic support. Two large bore (≥ 18 G) peripheral intravenous lines should preferably be placed. Ultrasound guided IV placement, or central venous access may be warranted in patients with difficult peripheral access. Transport crew, should preferably be trained for emergency balloon tamponade for hemodynamically unstable patients or those with clinical features of ongoing bleed. The systolic blood pressure should be maintained at least at 90–100 mmHg, and the heart rate should be maintained below 100 beats/ min. Terlipressin bolus of 2 mg, can be given in the ambulance or during transport of the patient (pre-ER).

Artificial intelligence (AI) can be used as a tool for patient risk assessment pre-endoscopy period. This can increase segregation of low-risk patients who can be safely discharged for after initial management at the hospital [59]. The AI can also be used for predicting the risk for re-bleeding. Study from Levi et al. showed that the machine learning algorithm can offer reliable guidance (AUC > 0.80) for predicting the need for transfusion in the next 24 h.[60]

Management in the emergency room

The principles to protect airway and breathing are the same between ER and pre-ER management. It is important to identify AVB patients at high risk for failure to control bleeding or requiring emergency intubation. Prophylactic endotracheal intubation in the setting of UGIB can be associated with higher rates of respiratory complications [61]. Circulation needs to be monitored, with a target hemoglobin level around 7–8 g/dL (hematocrit of 21–24), because equal or over transfusion can cause a rebound increase in portal pressure and precipitate early re-bleeding [62, 63]. Patients with co-morbidities, such as coronary artery disease need to maintain a higher hemoglobin to maintain cardiac perfusion. Empiric correction of coagulation parameters with fresh frozen plasma (FFP) and/or platelet transfusion is associated with worse outcomes in AVB due to the increased rebleeding [64, 65]. Thromboelastography (TEG) or Rotational Thromboelastometry (ROTEM) can be used for guiding correction of coagulation in patients with difficult to control bleed [66]. Echocardiography should be used to assess fluid status and cardiac function. Fluid replacement should be used very conservatively and cautiously. Crystalloids are preferred and colloids should be avoided, particularly dextran solution or albumin. The naso-gastric tube can be placed in the emergency room, if there is a strong suspicion of bleeding or associated hepatic encephalopathy [67].

Pharmacotherapy in AVB

Antibiotics must be promptly initiated in patients with AVB. Ceftriaxone is the preferred antibiotic due to its coverage of gram-negative bacteria, the commonest infection causing bacteria in this setting. Ceftriaxone was found to be superior to norfloxacin in preventing infections in patients with cirrhosis in a RCT [68]. In this trial of 111 patients with cirrhosis and GI bleeding, those receiving oral norfloxacin had higher infection rates (26% vs. 11%, p = 0.003) and spontaneous bacterial peritonitis (12% vs. 2%, p = 0.003) compared to those given intravenous ceftriaxone [69]. Key factors in selecting antibiotics include individual patient characteristics (e.g., prior antibiotic exposure or infection) and local antibiotic resistance pattern [69, 70].

Upper GI bleeding in a patient with chronic liver disease or cirrhosis should be deemed from GEVs and thus vasoactive treatment (terlipressin or somatostatin/octreotide) should be started at the earliest, preferably within 30 min of index bleed [71]. This should be followed by endoscopy and the appropriate treatment [72]. Terlipressin, somatostatin or octreotide are all vasoconstrictors which can be used in AVB. The choice among the vasoconstrictors may be difficult and often depends upon the availability, affordability and patient co-morbidities [73]. There are greater risks of arrhythmias with the use of terlipressin and therefore must be used with caution or avoided in patients who are at risk like IHD or atrial fibrillation. On the other hand, terlipressin should be preferred in the presence of AKI [74, 75]. The efficacy in the initial control of variceal bleeding is comparable amongst the three vasoactive agents [76]. Duration of pharmacological treatment should be kept for the optimal time with a minimum of 2 days, the duration for AVB [77–79]. Terlipressin infusion (4 mg/24 h) is preferred over the IV bolus injections, as the former modality achieves higher success rates in the control of AVB with lower dosages and fewer complications [80].

The use of PPIs in acute UGIB due to non-variceal etiology is a bit controversial. While, PPIs can reduce the incidence of post-EVL ulcers, they do not reduce the number of ulcers, severity of symptoms, and duration of hospital stay [81–84]. Some studies suggest that the duration of PPI use should be at least 10 days or one month after stopping the bleeding [80, 85]. A single study showed that a short course of vonoprazan 20 mg/day is safer and superior to pantoprazole 40 mg/day in the reduction of post-EVL ulcers and prevention of ulcer-related bleeding [86]. Acid suppression is superior to no acid suppression to prevent post-EVL complications [87]. However, the benefits of PPIs in reducing the variceal rebleeding, specially from the EVL ulcers,

is not established. Routine use of sucralfate in AVB should also not be recommended due to lack of data.

Tranexamic acid significantly reduces the failure to control bleeding post-EVL by day 5 and failure to prevent rebleeding after day 5 to week 6 in patients with advanced liver cirrhosis presenting with UGIB by reducing post-EVL ulcer bleeding. However, the use of tranexamic acid does not reduce mortality [88]. The use of tranexamic acid should be carefully considered due to the potential risk of portal vein thrombosis (PVT).

As MAFLD/MASLD and related cirrhosis become more prevalent, a growing number of patients on anticoagulation therapy are undergoing EVL for acute variceal bleeding. While coagulopathy may warrant correction, endoscopy can be safely performed at therapeutic levels of anticoagulation in selected cases, particularly for urgent/emergency procedures. Clinicians should emphasize individualized risk assessment for thromboembolism and bleeding when planning endoscopy [89].

Consensus statements

3. Resuscitation, initial management, and monitoring of patients with acute variceal bleed

3.1. Initial resuscitative measures include protection of airway, breathing, and circulation (ABC). (LoE-High; Recommendation-Strong):

3.1.1. For protection of the airway elective intubation is recommended in patients with: (LoE-Moderate; Recommendation-Strong)

- Massive hematemesis
- Altered mental status
- Known gastric varices
- Difficulty in maintaining oxygen saturation above 90%
- Massive ascites

3.1.2. Monitor hemodynamic condition preferably with cardiac monitor

3.1.3. Fluid volume replacement

- Fluid replacement should be used conservatively and cautiously. (LoE-Moderate; Recommendation-Weak)
- Crystalloids particularly saline is preferred and colloids should be avoided; maintenance fluids should be plasmalyte/ dextrose infusion. (LoE-Moderate; Recommendation-Weak)
- The volume of fluids should be aimed to maintain: (LoE-Moderate; Recommendation-Strong)
- Systolic blood pressure of 90–100 mmHg
- Heart rate below 100 beats per minute
- CVP 1–5 mmHg
- Diuresis of 40 mL/h

3.1.4. Blood volume restitution

3.1.4.1. Blood transfusion requirement is determined by estimating blood loss. (LoE-Low; Recommendation-Weak)

3.1.4.2. Blood volume replacement should be done cautiously and conservatively to maintain:

- A hemoglobin level of approximately 7–8 g/dL, depending on other factors, such as patient's co- morbidities, age, hemodynamic status, and presence of ongoing bleeding.
- Packed red blood cells (PRBC) is the preferred blood component. (LoE-Low; Recommendation-Weak)
- Fresh frozen plasma (FFP) and platelet transfusion should be given very cautiously due to its potential risk for higher rebleeding rate. (LoE-Moderate; Recommendation-Weak)
- Specific management of coagulopathy or thrombocytopenia needs to be studied further for its relevance in acute variceal bleeding management. (LoE-Low; Recommendation-Weak)

3.2. Pharmacological Therapy

3.2.1. Vasoactive treatment should be started at the earliest, preferably within 30 minutes of index bleed. (LoE-High; Recommendation-Strong)

3.2.2. Terlipressin, somatostatin, or octreotide can be used in the prescribed doses depending upon availability and patient comorbidities. (LoE-High; Recommendation-Strong)

3.2.3. Use of terlipressin requires baseline ECG. (LoE-Low; Recommendation-Weak)

3.2.4. Terlipressin infusion (4-6 mg/24 hours) is preferred over intravenous boluses (2 mg/4 hours). (LoE-High; Recommendation-Strong)

3.2.5. In patients where endoscopic therapy has successfully controlled AVB, the vasoactive drugs can be discontinued after 24 48 hours, and non-specific beta-blocker (NSBB) may be initiated, if there is no contraindication. (LoE-Moderate; Recommendation-Strong)

3.2.6. Tranexamic acid may reduce the risk of post-EVL rebleeding. (LoE-High; Recommendation-Strong)

3.2.7. For patients with cirrhosis with AVB, a broad-spectrum antibiotic like ceftriaxone (1-2 gram daily) is recommended for 5 days before endoscopic therapy. However, the duration could possibly be shortened to 2 days in patients with successful endoscopic therapy. (LoE- High ; Recommendation-Strong)

3.2.8. In patients with Child-Pugh A cirrhosis, benefit of antibiotics is not evident.[67, 90] (LoE-High; Recommendation-Weak)

3.2.9. The use of PPI in patients with acute UGIB due to non-variceal etiology is helpful. (LoE-High; Recommendation-Strong)

3.2.10. The use of factor VIIa is not routinely recommended. (LoE-High; Recommendation-Weak)

3.3. Patients with active variceal bleeding should be managed in ICU. (LoE-Low; Recommendation-Weak)

3.4. Monitoring

3.4.1. Naso-enteric tube can be used if there is a strong indication, such as hepatic encephalopathy. (LoE-Low; Recommendation-Weak)

3.4.2. Cardiac monitoring and IVC monitoring are helpful to optimize the decisions concerning fluid replacement, specially in: (LoE-Moderate; Recommendation-Strong)

- Elderly
- Patients with cardiovascular co- morbidity
- Active bleeding at endoscopy
- Patients with severe bleeding
- Presence of shock
- Renal failure (impending or present)

Role of endoscopy in AVB

Endoscopic variceal ligation (EVL) is more effective than endoscopic variceal sclerotherapy (EST) with greater control of hemorrhage, lower re-bleeding rate, and lower adverse events but without differences in mortality [91, 92]. Endoscopic therapy and medical therapy with vasoactive drugs have a synergistic effect as their modes of action are completely different. A meta-analysis by Banares and co-workers, who compared endoscopic therapy with combined endoscopic and pharmacologic treatment, showed that the control of AVB was more often achieved with combined treatment than after endoscopic treatment alone. Eight trials involving 939 patients were included in the meta-analysis. Combined treatment improved initial control of bleeding [relative risk (RR) 1.12, 95% confidence interval (CI) 1.02–1.23], and 5-day hemostasis (RR 1.28, 95% CI 1.18–1.39), with numbers of patients needed to treat (NNT) 8 and 5, respectively. The difference in favor of combined treatment remained significant when trials that used drugs other than octreotide or that included a low proportion of alcoholic patients (< 40%) or high-risk cirrhotic patients (< 35%) were excluded. Mortality was not significantly decreased by combined therapy (RR 0.73, 95% CI 0.45–1.18) [93]. To ensure smooth conduct of endoscopy in these patients a checklist should be maintained in the endoscopy room (Table 6).

Table 6 Checklist to be Maintained in the Endoscopy Room

Patient
Vital signs
Two intravenous lines
Judicious fluid/blood resuscitation
Supplemental oxygen
Child-Pugh status
Informed consent
Endoscopy room
Check endoscope (air–water channel, suction, knobs, etc.)
Suction device
Patient resuscitation chart
Patient monitor
Accessories
Intubation facility with anesthetist support and availability of alternate therapy
Sengstaken-Blakemore tube
Esophageal variceal self-expanding metal stent (SEMS)
Interventional radiology services
Gastrointestinal surgical team

Timing of endoscopy

Variceal bleed can precipitate decompensation and infections or even exsanguination or hemorrhagic shock. However, very early endoscopy does not appear to improve outcomes; However, the data is heterogenous and has provided conflicting results [89–93]. Endoscopy may be done as soon as the patient is stable enough for the procedure and logistics allow, preferably within 12 h and, at the latest, within 24 h. If the patient is hemodynamically unstable after resuscitation or is actively bleeding, endoscopy should be performed as soon as possible [94–97]. There are three proposed timelines that require further research: < 6 h as urgent, 6–12 h as early, and > 12 h as delayed.

Bedside vs endoscopic room

Endoscopy should preferably be performed in the well-equipped endoscopy room whenever possible, ensuring that all hemostatic accessories are available and the option to change scopes in case of channel blockage and the need of EUS is available. However, patients who are

hemodynamically unstable and/or require airway protection, should be scoped at the bedside in the ICU.

Expertise of endoscopists (attending or fellow)

There is no systemic data explaining who should perform the therapeutic endoscopic procedures in a patient with AVB. In most cases, band ligation of varices is a relatively low complexity procedure and can be performed by a fellow in a supervised setting. Glue injection for bleeding GV can be a challenging procedure with a steeper learning curve. It should preferably be done by an attending/consultant/faculty or a well-trained fellow under supervision. Endoscopy for patients who are hemodynamically unstable or those with major co-morbidities should be done by an attending/consultant/faculty to reduce the scope time. Longer scope time may increase pulmonary complications [98].

Type of scope and equipment needed

Normal UGI scope is generally adequate to manage most AVB patients. Rarely, if active bleeding continues, a therapeutic gastroscope is preferred due to a larger suction channel, and facility to pass desired accessories. One should have other accessories readily available, such as ligators, 21 and 23 G sclerotherapy needles, preferred type of tissue adhesive glue (N-butyl-cyanoacrylate or N-octyl-cyanoacrylate), hemostatic clips including over the scope clips, hemostatic powder, sclerosant and electrocautery setup with accessories—hemostatic cautery-enabled forceps, argon plasma coagulation catheters, snare for clot removal or spray coagulation should also be available.

Intubation / extubation

Patients with variceal bleed are at a high risk of pulmonary infections, possibly due to aspiration [99]. Routine intubation and nasogastric tube placement should be avoided due to the increased risk of pulmonary infections [100–102]. Intubation should be restricted to patients who are actively bleeding, and in patients with encephalopathy who are unlikely to tolerate endoscopy without sedation. If intubation is performed, extubation should be carried out as early as possible after successful completion of the procedure.

Sedation principles in AVB

Sedation with propofol and midazolam is generally safe and is associated with relatively lower procedure time. However, no impact on outcomes has been observed [103]. In patients requiring longer endoscopy procedures, (injecting glue or EUS), propofol should be preferred over midazolam as it is safer with low procedure and recovery time.

Prokinetics

The use of prokinetics prior to endoscopy improves mucosal visualization and reduces the need for second-look endoscopy. Erythromycin 250 mg or metoclopramide 10 mg can be administered 30–120 min prior to endoscopy [104, 105]. There is no data available regarding the use of simethicone prior to endoscopy.

If no bleeding source is visible and fundus is obscured by blood clots, the patient can be moved to a semi-recumbent position for better visualization of the fundus [106]. If stomach is clean and no varices are visible, then patient is managed as obscure overt GI bleeding. Colonoscopy and/or CT angiogram should be done to rule out other causes such as hemosuccus pancreaticus or telangiectasias. Varices may be decompressed after a bleed and hence a relook endoscopy could be done after 24–48 h in patients with index of suspicion.

Recommended endoscopic therapy for esophageal variceal bleeding

Endoscopic variceal band ligation (EVL) is the preferred modality of therapy for esophageal variceal bleed. Endoscopic sclerotherapy is discouraged due to higher rates of rebleed and adverse events. It may be considered in patients with variceal bleed in the setting of post-banding ulcer/fibrosis [107–109], or in children where passage of band ligator devise may not be possible. If both gastric and esophageal varices are present in a patient with variceal bleed, and esophageal banding is planned, it is advisable to obliterate GV first, even in the absence of stigmata of recent hemorrhage on GV.

Role of EUS

EUS can be used to assess esophageal variceal anatomy and predictors for variceal recurrence and is often used to directly inject glue into esophageal or gastric varices [110], and ectopic varices [111].

GAVE-related bleeding

Gastric antral vascular ectasia (GAVE) is an uncommon but important cause of upper gastrointestinal bleeding that is distinct from variceal bleeding. It is typically seen in patients with chronic liver disease, systemic sclerosis, diabetes, autoimmune disorders, or chronic renal failure. Unlike portal hypertensive gastropathy (PHG), GAVE-related bleeding occurs due to abnormal dilated capillaries in gastric mucosa and lamina propria in the gastric antrum, leading to persistent occult or overt bleeding. Management is primarily endoscopic, with APC being the first-line therapy, as it effectively coagulates superficial vascular ectasias. Alternative modalities include spray coagulation (hemostatic powders) for diffuse GAVE and endoscopic band ligation for focal nodular lesions, which may be preferable in cases of chronic or refractory bleeding. In severe or recurrent cases, radiofrequency ablation (RFA) and surgical antrectomy may be considered, though these are rarely required. Since GAVE-related bleeding is not related to portal hypertension, its management is distinct from acute variceal bleeding and should be approached separately in clinical decision-making.

Role of relook-endoscopy once successful hemostasis is achieved

Limited data suggests no benefit of relook-endoscopy once successful hemostasis is achieved, and therefore, it is not routinely recommended. Relook-endoscopy may be considered if endoscopist is not certain of complete hemostasis, clinical signs of rebleed (new onset of hematemesis, new drop in hemoglobin, and new onset hemodynamic instability) (Table 8) [112, 113]. Melena may persist for 3–5 days after hematemesis, and in isolation, should not be taken as indication for check endoscopy. Drop in hemoglobin is defined as progressive decrease in Hb for more than 1 g/dL or more.

Post-banding drugs

Vasoactive drugs may be continued for 48 h after successful endoscopic hemostasis for varices. Non-specific beta-blocker (NSBB) therapy may be introduced once vasoactive drugs are stopped or at day 6 after the control of acute bleed.

Endoscopic management of EVL-induced ulcer bleeding

Diagnosis of EVL-induced ulcer bleeding should be made based on endoscopy with ooze or spurt or clot and no evidence of other source of bleed. Severity assessment of EVL-induced ulcer bleeding can be done using Jamwal & Sarin classification. The post-EVL ulcer is classified based on their endoscopic appearance. In type A, there is active spurting from the ulcer. Type B is characterized as active oozing from the ulcer. In Type C, the ulcer appears with pigmented base, or a visible clot and the Type D ulcer has a clean base (white or yellow) [114].

There is no evidence demonstrating the superiority of one treatment technique over another. Treatment options include hemostatic agents, injection of glue or sclerosant, fully covered esophageal metallic stent, and EUS-guided vascular therapy. Combined therapy using one or more endoscopic techniques can be considered in difficult to control bleeding. TIPS is an effective rescue therapy [115].

Endoscopic therapy, recommendation for gastric variceal bleeding

Bleeding from GVs is generally more severe than bleeding from EVs but is thought to occur less frequently. Gastric varices in the fundus are GOV2 and IGV1, with the highest bleeding and re-bleeding rates [51]. Large IGV1 may bleed despite HVPG values less than 12 mmHg [116, 117]. Because the blood flow in the GVs is relatively large and the bleeding is rapid and often profuse, endoscopic means of treating bleeding GVs are the treatments of choice. The choice of endoscopic therapy used often depends on local availability and expertise. Endoscopic cyanoacrylate glue injection is the most preferred procedure for bleeding gastric varices [118]. Other therapies to control hemorrhage include radiological options (TIPS, balloon-occluded retrograde transvenous obliteration (BRTO). Uncontrolled data comparing these therapies in bleeding gastric varices show that the best control of initial hemorrhage (90–100%) is achieved with glue, TIPS, or balloon-occluded retrograde transvenous obliteration [119]. In three small single-center RCTs, endoscopic variceal obturation (EVO) with glue versus EVS[120] or EVL in bleeding gastric varices were compared [121, 122]. All three RCTs reported higher efficacy of EVO in the control of acute hemorrhage [120, 121], re-bleeding [122], or complication rate [121]. Unfortunately, less than 50% of the patients included in these studies had GOV2/IGV1 varices, and a separate analysis was not performed.

It is recommended that TIPS be used in acute bleeding from gastric varices when EVO is unavailable or if re-bleeding occurs after EVO; however, this has not been evaluated prospectively. A small single-center study comparing EVO versus TIPS in the prevention of recurrent hemorrhage in patients in whom acute gastric variceal

hemorrhage was controlled with EVO showed similar rebleeding rates, but again fewer than 50% of the patients were bleeding from GOV2/IGV1 varices [123].

Consensus statement

4. Role of endoscopy in acute variceal bleeding

4.1. All patients with acute UGI bleed should undergo endoscopy with the intent to provide endo therapy. (LoE-Low; Recommendation-Weak)

4.2 Combination of a vasoactive drug and endoscopic therapy is the first-line therapy for acute variceal bleed. (LoE-High; Recommendation-Strong)

4.3 Timing of endoscopy (the door -to-scope time):

4.3.1. In patients with AVB, endo therapy should be done as soon as possible under resuscitation, preferably within 6 hours of admission. (LoE-Low; Recommendation-Weak)

4.3.2. Endoscopy may be undertaken as soon as patient is stable (preferably within 12 hours, latest up to 24 hours). (LoE-Moderate; Recommendation-Weak)

4.4. Place to perform endoscopy

4.4.1. Endoscopy is preferably done in endoscopy room. Patients who are hemodynamically unstable and/or need of airway protection, should be scoped at bedside in the ICU. (LoE-Moderate; Recommendation-Weak)

4.5. Band ligation of varices can be done by a fellow in a supervised setting. (LoE-Low; Recommendation-Weak)

4.5.1. Skill level of endoscopist

4.5.2. Glue injection for gastric varices is preferably done by an attending or a well-trained fellow under supervision. (LoE-Low; Recommendation-Weak)

4.5.3. Endoscopy for patients who are in shock, intubated, or bedside in the ICU should be done by a consultant. (LoE-Low; Recommendation-Weak)

4.6. Following preparations should be done prior to endoscopy. (LoE-Moderate; Recommendation-Strong)

4.6.1. Blood pressure: systolic BP > 70 mmHg

4.6.2. Unconscious patients should be intubated prior to endoscopy. (LoE-Low; Recommendation-Weak)

4.6.3. Intubation / extubating (LoE-Moderate; Recommendation-Weak)

- Routine intubation and NGT placement should be avoided. (LoE-Moderate; Recommendation-Weak)
- Intubation should be restricted to patients who are actively bleeding, have encephalopathy, and are unlikely to tolerate endoscopy without sedation. (LoE-Moderate; Recommendation-Weak)
- Extubation needs to be performed as early as possible after control of bleeding. (LoE-Moderate; Recommendation-Weak)

4.6.4. Drugs (LoE-High; Recommendation-Strong)

- A vasoactive drug should be initiated prior to endoscopy.
- The use of prokinetics prior to endoscopy improves mucosal visualization and reduces the need for second-look endoscopy.
- Erythromycin 250 mg or metoclopramide 10 mg can be administered 30–120 min prior to endoscopy.
- There is no data available regarding the use of simethicone prior to endoscopy.

4.6.5. Sedation (LoE-Low; Recommendation-Weak)

- For patient comfort and better visualization, use of sedation is recommended
- Both propofol and midazolam are safe, though the former is preferred.
- A checklist of activities and required equipment and accessories should be maintained in the endoscopy theater (Table 6).

4.6.6. Endoscopic treatment (LoE-High; Recommendation-Strong):

Band ligation with multi-band ligator is the preferred modality of therapy for esophageal variceal bleed.

4.6.7. Role of relook- endoscopy is presented in Tables 7, 8. (LoE-Low; Recommendation-Weak)

4.7. Vasoactive drugs

4.7.1. Vasoactive drugs may be continued for 48 hours after successful endoscopic hemostasis for varices.

4.7.2. Non-selective beta-blocker (NSBB), like carvedilol may be initiated once vasoactive drugs are stopped or after 5 days of acutevariceal bleed.

4.8. Management of acute GV bleed

4.8.1. Following on the success in EV bleed, combination of vasoactive drugs and endoscopic therapy should be used for acute GV bleed, though specific data is lacking. (LoE-Low; Recommendation-Strong)

Table 7 Indications for Endotracheal Intubation in AVB

Massive hematemesis and active bleeding
Persistent hematemesis with hemodynamic instability (SBP < 90 mmHg, HR > 110 bpm, altered mentation)
Severe hypovolemic shock requiring aggressive resuscitation
High risk of aspiration
Severe hepatic encephalopathy (Grade III-IV) with an inability to protect the airway
Unresponsive or semi-conscious patients with AVB
Gastric retention (gastroparesis, gastric outlet obstruction, massive blood in the stomach) increases the aspiration risk
Planned therapeutic endoscopy procedures with high aspiration risk
EUS-guided gastric variceal therapy or procedures requiring prolonged sedation
Presence of significant blood in the stomach impairing visualization
Need for prolonged endoscopic intervention where airway protection is necessary
Severe respiratory compromise
Acute respiratory failure, ARDS, or worsening hypoxia
Severe metabolic acidosis (pH < 7.2) or hypercapnia requiring ventilatory support

Table 8 Indications of relook-endoscopy

1	Endoscopist not certain of complete hemostasis
2	Clinical sign of rebleed
	New onset of hematemesis
	New onset or continued Hb drop
	New onset of hemodynamic instability

4.8.2. Endoscopic cyanoacrylate injection (ECI) is the preferred procedure for bleeding GV. (LoE-Moderate; Recommendation-Strong)

4.8.3. In patients with acute bleeding from GOV1 type of varices, treatment should be similar to that of esophageal varices or glue injection. (LoE-Moderate; Recommendation-Strong)

4.8.4. Endoscopic ultrasound (EUS) based glue injection, with or without coil.

4.9. Management of portal hypertensive gastropathy related bleeding

4.9.1. Vasoactive agents are the first line of therapy for portal hypertensive gastropathy (PHG) related bleeding. (LoE-Moderate; Recommendation-Strong).

4.9.2. TIPS should be considered as a rescue therapy for refractory PHG related bleeding. (LoE-Moderate; Recommendation-Strong).

4.9.3. Endoscopic therapy, such as argon plasma coagulation (APC), radiofrequency ablation (RFA), or band ligation can be used for PHG and GAVE related bleeding. (LoE-Low; Recommendation-Strong).

Role of rescue therapies in AVB

Rescue therapy is indicated when endoscopic treatment or combination treatment has failed to control bleeding. Balloon tamponade using Sengstaken Blakemore tube enables temporary control of bleeding, by direct compression of varices at the esophagogastric junction, in 40–90% of cases. Owing to high rates of complications and re-bleeding [37, 124], balloon tamponade is not used routinely as the first-line treatment for control of AVB.

TIPS is a better alternative when available, in the presence of failure of combined pharmacologic plus endoscopic therapy. In the Baveno recommendations, it was considered that a second attempt at endoscopic therapy was also an option and one could perform TIPS after failure of the second endoscopic therapy [1]. There is data to suggest that TIPS placement is associated with a significant improvement in survival in patients with HVPG greater than 20 mmHg [125]. Therefore, HVPG can provide useful information that allows for risk stratification and more aggressive treatment in high-risk patients.

The role of interventional radiologist (IR) in AVB

Esophageal varices

Pre-emptive TIPS with PTFE covered stents within 72 h (ideally < 24 h) reduces re-bleeding and improves survival in carefully selected patients who met any of the following criteria: Child–Pugh class C < 14 points or Child–Pugh class B > 7 with active bleeding at initial endoscopy or

HVPG > 16 mmHg at the time of hemorrhage [126]. Patients fulfilling the criteria for pre-emptive TIPS should be referred to center with facility to perform TIPS within 72 h if interventional radiology facilities are not available. TIPS should be performed in patients having recurrent esophageal variceal bleed who could not get pre-emptive TIPS. Patients with uncontrolled variceal bleed should be considered for a rescue/salvage TIPS within 24 h, preferably < 8 h.

A combination of MELD score and serum lactate levels may provide an improved prediction of survival outcome after TIPS. Combined score using MELD > 30 and lactate > 12 mmol/L is associated with poor survival. Patients with acute variceal bleed and ACLF should be cautiously evaluated for TIPS based on CTP/MELD score and lactate levels. TIPS may be also considered in patients with HCC having acute variceal bleed, if it is technically feasible with Child Pugh score. Eight mm TIPS should be preferred over 10 mm TIPS for control of bleeding. Embolization of afferent veins feeding the varices and use of beta blockers may be utilized if post- TIPS portal pressure gradient of 12 mmHg is not achieved. TIPS stent of 6 mm may be considered in patients with small liver / poor hepatic reserve with uncontrolled variceal bleed as an emergent salvage pressure.

Rescue therapies for gastric varices

BRTO/PARTO should be considered as good alternatives for TIPS in patients with GOV2 and IGV1. Patients with active GV bleed should be considered for endoscopic obliteration followed by BRTO/PARTO or Salvage TIPS with antegrade embolization if feasible (presence of sizable gastro-renal, gastro-spleno-renal shunt) and local expertise is available. BRTO/PARTO should be performed with caution in patients with Child–Pugh score > 9. Suitable patients with high-risk GV and ascites may be considered for combination of BRTO/PARTO and TIPS, alternatively these patients may be considered for TIPS with antegrade embolization of all varices (LGV, SGV, PGV). Post BRTO/PARTO patients should be periodically evaluated with endoscopy to look for any enlargement of esophageal varices. Patients with bleeding from IGV2 can be considered for BRTO/PARTO with suitable venous anatomy. Alternatively, antegrade embolization/obliteration of IGV2 may be performed using percutaneous trans-hepatic or trans-splenic access. Radiological intervention with TIPS or BRTO can be used as secondary prophylaxis to reduce rebleeding and mortality from GVs. Coil-Assisted Retrograde Transvenous Obliteration (CARTO) serves as a valuable alternative to BRTO and TIPS in patients with GV bleeding. CARTO is a highly effective and durable treatment for GV bleeding, with minimal complications [127].

Consensus statement

5. Role of Rescue Therapies in Acute Variceal Bleeding

5.1. Role of balloon tamponade

5.1.1. Role of Rescue Therapies in Acute Variceal Bleeding

5.1.2. Balloon tamponade is effective in immediate and temporal control of AVB, but is associated with a high re-bleeding rate after balloon removal. (LoE-High; Recommendation-Strong)

5.1.3. Balloon tamponade should only be maintained for up to 24 hours to prevent severe adverse effects, such as esophageal rupture. (LoE-High; Recommendation-Strong)

5.1.4. Guidewire assistance may lead to a higher first-pass success, proper positioning and reduce the complication rate. (LoE-Moderate; Recommendation-Weak)

5.2. Role of Self-Expandable Metal Stents (SEMS)

5.2.1. SEMS is more effective and safer option than balloon tamponade for refractory variceal bleeding. (LoE-High; Recommendation-Strong)

5.2.2. SEMS is an effective bridge therapy for control of refractory variceal bleeding until a more definite treatment such as TIPS is undertaken. (LoE-High; Recommendation-Strong)

5.2.3. SEMS achieves immediate control of bleeding in up to 90% patients, though is infrequently associated with adverse events such as stent migration, esophageal ulcerations, and re-bleeding on removal of SEMS. (LoE-Moderate; Recommendation-Strong)

5.2.4. Esophageal stents are kept in place for up to 5-7 days, allowing for a longer bridge than balloon tamponade to definitive therapy. (LoE-Moderate; Recommendation-Strong)

5.3 Role of TIPS (LoE-Moderate; Recommendation-Strong)

5.3.1. Pre-emptive TIPS is recommended as the first-line treatment in high-risk patients with cirrhosis presenting with AVB, as it significantly improves survival outcomes. (LoE-High; Recommendation-Strong)

5.3.2. Failure to control variceal bleeding despite combined pharmacological and endoscopic therapy is best managed by salvage TIPS to decrease re-bleeding. An 8 mm TIPS should be preferred over 10 mm TIPS. (LoE-Moderate; Recommendation-Strong).

5.3.3. Rescue TIPS should be considered for patients with ACLF and variceal bleeding who do not have a contraindication for TIPS. (LoE-Moderate; Recommendation-Strong)

5.3.4. In patients with cirrhosis presenting with refractory AVB, very early TIPS (emergency TIPS) within 8 hours offers a better survival than TIPS beyond 8 hours. (LoE-Moderate; Recommendation-Strong)

5.3.5. Mean arterial pressure, active spurter at endoscopy and AKI independently predict post-TIPS mortality at 6 weeks and one-year. (LoE-Moderate; Recommendation-Strong)

5.3.6. TIPS may be futile in patients with Child-Pugh ≥ 14 cirrhosis, MELD score >30 and serum lactate >12mmol/L, unless liver transplantation is envisioned in the short term. (LoE-High; Recommendation-Strong)

5.4. Role of surgery

5.4.1. Indication of surgery is persistent variceal bleeding despite comprehensive medical and endoscopic and radiological interventions. (LoE-High; Recommendation-Strong)

5.4.2. Contraindications to surgery are

- Patients with advanced hepatic dysfunction, uncorrectable coagulopathy, or hepatic encephalopathy (LoE-High; Recommendation-Strong)
- Child class C categorization, which includes a wide spectrum of patients, in itself is not a contraindication to emergency surgery. (LoE- Low; Recommendation-Weak)

5.4.3. Surgery for acute control of variceal bleeding can be placed into one of four categories, non-selective portosystemic shunts, selective portosystemic shunts, devascularization procedures and liver transplantation. The procedure selected depends on many factors, including expertise of available personnel, severity of bleeding, hepatic functional reserve, patency of splanchnic veins, and transplant candidacy. (LoE-Low; Recommendation-Weak)

5.4.4. There is a paucity of controlled data comparing these procedures to one another or to non-operative therapies. (LoE-Low; Recommendation-Weak)

5.4.5. The major factor determining survival is the status of the liver disease at the time of surgery rather than the procedure selected. (LoE-Moderate; Recommendation-Strong)

5.5. Rescue therapy for gastric variceal bleeding

5.5.1. TIPS is an effective rescue therapy to control recurrent variceal bleeding from gastric or ectopic varices. (LoE-High; Recommendation-Strong)

5.5.2. Transvenous obliterative procedures like BRTO/PARTO are effective therapies to control recurrent or difficult to control gastric variceal bleeding in presence of appropriate anatomy. (LoE-High; Recommendation-Strong)

5.5.3. BRTO/PARTO and TIPS have comparable efficacy, but the former has lower re-bleeding rates and risk for hepatic encephalopathy. (LoE-High; Recommendation-Strong)

5.5.4. Combining TIPS and embolization of collaterals can reduce the risk of recurrent gastric variceal bleeding and is a preferred approach. (LoE-Moderate; Recommendation-Strong)

Special topics in AVB

Bacteremia is often present on admission for acute variceal hemorrhage. Common bacterial infections include spontaneous bacterial peritonitis, urinary tract infection, and pneumonia. Infections are associated with an increased risk of re-bleeding and higher mortality, likely secondary to a further increase in PHT, further splanchnic arteriolar dilatation, and increased coagulopathy [128, 129]. A complete microbiological work-up, including blood cultures and diagnostic paracentesis when appropriate, should be performed. Empiric therapy with a third-generation cephalosporin (e.g., ceftriaxone) should be uniformly instituted because several clinical trials have shown improvement in control of bleeding and in patient outcomes [130]. However, other broad-spectrum antibiotics including higher generation of quinolones are still acceptable agents.

Prospective cohort studies in which HVPG has been measured within 48 h of admission for hemorrhage show that levels greater than 20 mmHg are associated with increased re-bleeding and mortality [125, 131–134]. Another study confirms this HVPG cut-off and shows that an index including CTP score and blood pressure at admission has similar prognostic value [135]. Furthermore, a vasoactive drug-induced HVPG reduction of less than 10% predicts failure to control bleed. This response may

improve by doubling the dose of somatostatin or switching to terlipressin [136].

Consensus statement

6. Special Topics in Acute Variceal Bleeding

6.1 Infections in acute variceal bleeding and role of antibiotics. (LoE-High; Recommendation-Strong)

6.1.1. Chances of developing infection in AVB are high

6.1.2. Gram-negative bacteria, such as E. coli. are common agents

6.1.3. Placement of various tubes (NG, CVP, ET) predisposes to infections and colonizing organisms in stomach and skin play a role. Hence, consider changing these tubes regularly. (LoE-Moderate, Recommendation-Strong)

6.1.4. Standard work-up for infection includes CBC, chest x-ray, urine and blood culture and serum procalcitonin estimation. (LoE-High; Recommendation-Strong)

6.1.5. Third-generation cephalosporin is the preferred agent for prevention of infection in AVB and should be given intravenous

enously for 5 days.

6.2. Prevention, assessment, and management of hepatic ischemia. (LoE-High; Recommendation-Strong)

6.2.1. Ischemic hepatic injury can occur in up to 10% cirrhosis patients with AVB

6.2.2. Hepatic ischemic injury should be anticipated and prevented in high-risk groups of patients with bleeding varices. (LoE-Low; Recommendation-Weak)

6.2.3. The following groups of patients have high risk of hepatic ischemic injury:

- Patients with severe hematemesis and melena
- Bleeding leading to significant hypotension and/or shoc
- Recurrent bouts of bleeding at home, during transfer, at the casualty department, in the ward, and before or during emergency endoscopy
- Re-bleeding in a known patient with history of variceal bleeding
- Significant drop of hemoglobin and hematocrit values
- Patients with obstruction to hepatic blood flow (portal vein thrombosis, Budd-Chiari syndrome)
- Patients with decompensated cirrhosis
- Elderly patients
- Patients with diabetes mellitus or CKD
- Cirrhotic patients with hepatocellular carcinoma

6.2.4. Prevention of hepatic ischemic injury should be done as follows: (LoE-Low; Recommendation-Weak)

- Resuscitation and adequate correction of hypovolemia, hypotension, and shock
- Correction of blood loss by PRBC transfusion
- Rapid control of active bleeding by endoscopy
- Prophylactic antibiotics to guard against sepsis

6.2.5. Hepatic ischemic injury could lead to rise in serum total bilirubin and/or aminotransferases and LDH within 24 hours and this may adversely affect outcomes. (LoE-Low; Recommendation-Weak)

6.2.6. Patients should be carefully observed even if hemorrhage from varices is controlled. (LoE-Low; Recommendation-Weak)

6.2.7. Daily monitoring of ALT, serum bilirubin, creatinine, LDH, and ALT/LDH ratio should be done when ischemic hepatic injury is suspected. (LoE-Low; Recommendation-Weak)

6.2.8. No definite therapy has been found for the treatment of ischemic hepatic injury, but N-acetyl cysteine may be helpful. (LoE-Low; Recommendation-Weak)

6.2.9. There is a need for prospective studies to further investigate the prevalence, severity, and treatment of hepatic ischemia in cirrhosis patients with variceal bleeding.

6.3. Acute variceal bleeding in patients with liver failure

6.3.1. Patients with cirrhosis and liver failure have high propensity for bleeding from gastro-esophageal varices. (LoE-Low; Recommendation-Weak)

6.3.2. Endoscopic procedures to control variceal bleeding should be done with extra caution with or without endotracheal intubation. (LoE-Low; Recommendation-Strong)

6.3.3. Coagulopathy should be corrected with FFP and platelets. (LoE-Low; Recommendation-Weak)

6.3.4. Role of factor rVIIa in this setting needs evaluation. (LoE-Low; Recommendation-Weak)

Diagnosis and treatment of acute ectopic variceal bleeding

Ectopic varices comprise large portosystemic venous collaterals located anywhere other than the gastro-esophageal region [137]. No large series or RCTs address this subject, and therefore their management is based on available

expertise and facilities and may require a multidisciplinary team approach. Ectopic varices are common findings during endoscopy in portal hypertensive patients. Bleeding ectopic varices are a rare cause of variceal bleeding and accounts for only 1–5% of all variceal bleeding [138].

Ectopic varices occur in anorectum, antrum (IGV2), and duodenum, small intestine, colon, and peristomal. Ectopic variceal bleeding may be from varices located in the following sites: duodenum, choledochus, omentum, stoma, and rectum. Bleeding is more frequent in peristomal varices.

Ectopic varices develop secondary to portal hypertension, surgical procedures, anomalies in venous outflow, or abdominal vascular thrombosis and may be familiar in origin. Bleeding ectopic varices may present with anemia, shock, hematemesis, melena, or hematochezia and should be considered in patients with PHT and gastrointestinal bleeding or anemia of obscure origin. Ectopic varices may be discovered during pan-endoscopy, enteroscopy, endoscopic ultrasound, wireless capsule endoscopy, diagnostic angiography, multi slice helical computed tomography, magnetic resonance angiography, color Doppler-flow imaging, laparotomy, laparoscopy, and occasionally during autopsy [139].

Patients with suspected ectopic variceal bleeding need immediate assessment, resuscitation, hemodynamic stabilization, and referral to specialist centers. Endoscopy procedure able to diagnose most of the cases, but in inaccessible sites, red blood cell (RBC) evaluation can identify the site of bleed and could be confirmed by angiography or CT angiography. One of the following endoscopic findings constitutes acute ectopic variceal bleeding: direct visualization of blood issuing from varix—usually spurting; presence of a sign of recent bleed, white nipple sign, or overlying clot.

Management of ectopic varices involves medical, endoscopic, interventional radiological, and surgical modalities depending on the patient condition, site of varices, available expertise and patient's subsequent management plan. Pharmacotherapy and endotherapy should be the first line of therapy if a bleeding ectopic varix is accessible, but in inaccessible cases, TIPS or percutaneous transhepatic varices embolization (PTVE) should be done in patients with patent portal vein in cirrhosis and NCPH. Duodenal variceal bleeding inaccessible by endoscopy can also have an option of BRTO if vascular anatomy permits [137, 139, 140].

Consensus statement

7. Diagnosis and Treatment of Acute Ectopic Variceal Bleeding

7.1. Bleeding ectopic varices are a rare cause of variceal bleeding and are common in non-cirrhotic patients. (LoE-Moderate; Recommendation-Weak)

7.2. Site (LoE-Moderate; Recommendation-Weak)

7.2.1. Ectopic varices occur in anorectum, antrum (IGV2), and duodenum, small intestine, colon, and peristomal

7.2.2. Ectopic variceal bleeding may be from varices located in the following sites: duodenum, choledochal, omentum, stoma, and rectum

7.2.3. Bleeding is more frequent in peristomal varices

7.3. Endoscopy can diagnose most of the cases, but in inaccessible sites, RBC scan helps to identify the site of bleed, which is to be confirmed by CT angiography. (LoE-Moderate; Recommendation-Weak)

7.4. One of the following endoscopic findings constitutes acute ectopic variceal bleeding: (LoE-Moderate; Recommendation-Weak)

- Direct visualization of blood issuing from varix— usually spurting
- Presence of a sign of recent bleed: white nipple sign or overlying clot

7.5. Pharmacotherapy and endotherapy should be the first line of therapy if a bleeding ectopic varix is accessible. In inaccessible cases, TIPS or PTVE should be done with patent portal vein. (LoE-Low; Recommendation-Weak)

7.6. Duodenal variceal bleeding inaccessible by endoscopy can also have an option of BRTO (if vascular anatomy permits) and EUS guided embolization. (LoE-Low; Recommendation-Weak)

Acute variceal bleed in non-cirrhotic portal hypertension (NCPH)

Variceal bleeding is a common and life-threatening complication of PHT due to NCPH. There is paucity of data on the management of AVB in NCPH; however, the principles and modes of management remain the same as those for patients with cirrhosis. Blood transfusion, intravenous fluids, and standard ICU care are provided [1, 141]. Bacterial infections are more common in patients with cirrhosis having variceal bleeding (35–66%) than in non-cirrhotic patients (5–7%) [142]. It has been shown that infected cirrhotic patients have a higher rate of variceal re-bleeding (43%) than non-infected patients (10%) [128]. In patients with cirrhosis and variceal

bleeding, prophylactic antibiotics reduce variceal re-bleeding and improve survival [130]. In NCPH, however, there is no study on the use of prophylactic antibiotics.

Vasoactive drugs, such as somatostatin, octreotide, or terlipressin have been used in the treatment of AVB while endoscopic therapy is being arranged. The vasoactive drugs lead to reduction in portal pressure, which is associated with a better control of variceal bleeding [143–145]. However, there are no data on the efficacy of vasoactive drugs in patients with NCPH with AVB.

Endoscopic sclerotherapy and band ligation are effective in 80–90% of patients in controlling acute bleeding from EVs and preventing re-bleeding. At present, band ligation is preferred owing to lower complication rates. Combination treatment with drugs plus endoscopic therapy is more effective than endoscopic therapy or drug therapy alone in controlling acute bleeding and preventing re-bleeding for 5 days while there is no difference in mortality [1, 140]. There is, however, paucity of data in patients with NCPH. Failure of endoscopic therapy is defined, as further variceal bleeding after two endoscopic treatments during a single hospital admission for acute bleeding. The current therapies fail to control bleeding or prevent early re-bleeding in 8–12% of patients, who should be treated by alternative modes of treatment, like surgery or TIPS.

Consensus statement

8. Acute Variceal Bleed in NCPH

8.1. Absence of ascites, jaundice, and hepatic encephalopathy, and presence of large splenomegaly are the clinical clues in differentiating NCPH from cirrhotic portal hypertension (CPHT). (LoE-Moderate; Recommendation-Strong)
8.2. Natural history of acute variceal bleeding in NCPH has been well studied and shows low mortality. (LoE-Moderate; Recommendation-Strong)
8.3. Definitions and time frames for acute variceal bleeding as for cirrhosis can be adapted for NCPH patients as well. (LoE-Low; Recommendation-Weak)
8.4. First-line treatment options are essentially the same as in cirrhosis patients. (LoE-Low; Recommendation-Weak)
8.5. Gastric varices are more common in NCPH and may be refractory to obturation by tissue adhesives. (LoE-Low; Recommendation-Weak)
8.6. Coagulopathy is generally not a feature of NCPH, and so, correction is not required. (LoE-Low; Recommendation-Weak)
8.7. Antibiotics are not recommended in AVB in NCPF, unless absolute neutrophil count is $<1{,}000\ mm^{-3}$. (LoE-Low; Recommendation-Weak)
8.8. Rescue therapies remain the same as in cirrhosis patients. (LoE-Low; Recommendation-Weak)
8.9. Radiological interventions as rescue therapy in NCPH: though no randomized control trials have been conducted to investigate the potential of these techniques, case reports and series suggest their efficacy for controlling variceal bleeding. (LoE-Low; Recommendation-Weak)
8.10. Factors influencing choice of radiological procedure include etiological and anatomical considerations, clinical status of the patient and available expertise and affordability. (LoE-Low; Recommendation-Weak)
8.11. Though data is limited, it is likely that complications of TIPS would be uncommon in NCPF patients due to the relatively preserved liver functions in them. (LoE-Low; Recommendation-Weak)
8.12. Patients with failed first-line therapy for variceal bleeding and radiological interventional approaches should be considered for surgery. (LoE-Moderate; Recommendation-Weak)
8.13. Portal decompressive procedures are better than non-shunt procedures. Non-shunt procedures are preferred in patients who do not have suitable veins. (LoE-Low; Recommendation-Weak)

Pediatric perspectives of AVB

Evidence-based approaches to the management of adults with AVB exist and have been comprehensively reviewed [1]. Similar evidence-based approaches for the management of AVB in children do not exist and as such most international meetings on PHT have not focused on this problem in children [148]. Approaches to the management of AVB in children are few. Therefore, pediatricians typically have difficulty in deciding how to manage this important clinical problem in children. The statements presented here are mostly expert opinion with evidence being extrapolated from the studies done in adults.

Consensus statement

9. Pediatric Perspectives of Acute Variceal Bleeding

9.1. The pediatric age-group is defined as age up to 18 years. (LoE-Low; Recommendation-Weak)

9.2. The majority of upper gastro-intestinal bleed in children is variceal in origin. (LoE-Moderate; Recommendation-Strong)
9.3. The etiology of acute variceal bleeding in children varies in different geographical regions: in the West, cirrhosis is more common while in the East, EHPVO is more common. (LoE-Low; Recommendation-Strong
9.4. Diagnosis and management are broadly similar to that in adults [1], with some exceptions:

- Restrictive transfusion threshold (within the range of 7–8 g/dL) in pediatric variceal bleeding, as long as the child is hemodynamically stable, with slightly higher targets considered for specific cases, such as those with cyanotic heart disease or significant hypoxia [146]. (LoE-Low; Recommendation-Weak)
- Endoscopy performed within 12 to 24 h yields similar outcomes compared to more urgent procedures [147]. (LoE-Moderate; Recommendation-Strong)

9.5. Dosage and safety profile of octreotide in children has been established, however, for terlipressin or somatostatin, the dose and safety need to be established in children. (LoE-Low; Recommendation-Weak)
9.6. Choice of endoscopic procedure: (LoE-Low; Recommendation-Weak)

- Band ligation is preferred over EST for acute variceal bleeding
- EST is technically more feasible in younger children and those with smaller varices.

9.7. Rescue therapies
9.7.1. Radiological: though no randomized control trials have been conducted to investigate the potential of radiological techniques in children, case reports and case series suggest their efficacy for controlling variceal bleeding. (LoE-Low; Recommendation-Weak)
9.7.2. Radiological: though no randomized control trials have been conducted to investigate the potential of radiological techniques in children, case reports and case series suggest their efficacy for controlling variceal bleeding. (LoE-Low; Recommendation-Weak)

What's New in the APASL AVB Guidelines?

The APASL 2025 guidelines on AVB represent a major advancement over the 2011 recommendations, incorporating the latest evidence, refined definitions, and improved therapeutic strategies tailored to clinical practice in the Asia–Pacific region.

1. Refined Definitions and Risk Stratification
   The updated guidelines retain the core definitions of AVB and re-bleeding but now integrate home-to-door concept, management during patient transfer and in ER, validated risk prediction models, including the APASL Bleed Severity Score, HVPG-guided risk assessment, and AI-assisted prognostication. This ensures more precise risk stratification and individualized management.
2. Expanded Role of Early and Rescue Therapies
   While the 2011 guidelines recommended balloon tamponade and TIPS as rescue therapies, the 2025 guidelines redefine when and how to escalate therapy. The updated recommendations now incorporate:

- Use of self-expanded metal stents (SEMS) for control of AVB
- Early-TIPS strategy, particularly for patients with HVPG > 20 mmHg.
- EUS-guided glue and thrombin injection as alternatives for glue injection in acute gastric variceal bleeding.
- BRTO and CARTO/PARTO as key interventions in managing gastric varices, especially in patients with gastro-renal shunts.

3. Personalized Approach to Antibiotic Therapy and Pharmacologic Management
   The updated guidelines emphasize region-specific antibiotic choices, moving beyond a one-size-fits-all ceftriaxone approach. The selection of terlipressin, octreotide, or somatostatin has also been refined based on timing, severity, and patient comorbidities.
4. Standardization of Endoscopic Therapy and Anesthesia Protocols
   EVL remains the gold standard, but the new guidelines address anesthesia selection and peri-procedural risk assessment, ensuring greater safety in cirrhosis patients undergoing endoscopic interventions.
5. Greater Emphasis on Clinical Practice Implementation
   EVL remains the gold standard, but the new guidelines address anesthesia selection and peri-procedural risk assessment, ensuring greater safety in cirrhosis patients undergoing endoscopic interventions.

The updated APASL guidelines provide a more dynamic, evidence-based, and practical approach to managing AVB, ensuring earlier intervention, better risk stratification, and improved patient outcomes. These updates align with global

standards while addressing the unique epidemiology and healthcare challenges of the Asia–Pacific region.

Future research topics

Advancing the management of AVB will require multicentric studies to fill the current knowledge gaps. The priority areas include choice and efficacy of vasoactive drugs, portal pressure gradient measurement by EUS during AVB compared with HVPG compared and role of TIPS as a preemptive or a rescue therapy.

Conclusions

The new APASL consensus guidelines on AVB assimilate the latest evidence in the management of AVB and will contribute to a better care of patients suffering from this condition. The guidelines aimed to improve the quality of care and reduce the morbidity and mortality following an AVB. These guidelines have considered all available data and guidelines in the field to finalize the consensus statements, which were achieved with unanimity. These AVB guidelines are intended to provide the physicians and multi-disciplinary teams evidence-based clear roadmaps for patient stratification, strategizing timely interventions with judicious use of resources for the best possible outcomes of AVB patients. The experts have also highlighted the issues which could not be addressed due to lack of adequate evidence. The consensus definitions are intended to be used in trials and other studies on AVB, as well as in clinical practice. It is desirable that future studies be reported using these definitions as part of the evaluation. This should result in some measure of standardization and increased ease of interpretation among different studies. Equally important, if there are uniformly defined endpoints, meta-analyses will be based on more homogeneous studies, which is an essential prerequisite of this methodology. It is hoped that these guidelines will move the field of management of AVB to a much higher level.

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