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REVIEW ARTICLE

Diagnosis and management of acute variceal bleeding: Asian Pacific Association for Study of the Liver recommendations

Shiv Kumar Sarin · Ashish Kumar · Peter W. Angus · Sanjay Saran Baijal · Soon Koo Baik · Yusuf Bayraktar · Yogesh Kumar Chawla · Gourdas Choudhuri · Jin Wook Chung · Roberto de Franchis · H. Janaka de Silva · Hitendra Garg · Pramod Kumar Garg · Ahmed Helmy · Ming-Chih Hou · Wasim Jafri · Ji-Dong Jia · George K. Lau · Chang-Zheng Li · Hock Foong Lui · Hitoshi Maruyama · Chandra Mohan Pandey · Amrender S. Puri · Rungsun Rerknimitr · Peush Sahni · Anoop Saraya · Barjesh Chander Sharma · Praveen Sharma · Gamal Shiha · Jose D. Sollano · Justin Wu · Rui Yun Xu · Surender Kumar Yachha · Chunqing Zhang · Asian Pacific Association for the Study of the Liver (APASL) Working Party on Portal Hypertension

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Abstract
Background Acute variceal bleeding (AVB) is a medical emergency and associated with a mortality of 20% at 6 weeks. Significant advances have occurred in the recent past and hence there is a need to update the existing consensus guidelines. There is also a need to include the literature from the Eastern and Asian countries where majority of patients with portal hypertension (PHT) live.

Methods The expert working party, predominantly from the Asia–Pacific region, reviewed the existing literature and deliberated to develop consensus guidelines. The working party adopted the Oxford system for developing an evidence-based approach. Only those statements that were unanimously approved by the experts were accepted.

Results AVB is defined as a bleed in a known or suspected case of PHT, with the presence of hematemesis within 24 h of presentation, and/or ongoing melena, with last melanic stool within last 24 h. The time frame for the

S. K. Sarin (✉) · A. Kumar · H. Garg · P. Sharma
Department of Hepatology, Institute of Liver and Biliary Sciences (ILBS), New Delhi, India
e-mail: sksarin@nda.vsnl.net.in

P. W. Angus
Department of Gastroenterology, Austin Health, Studley Rd, Heidelberg 3084, Australia

S. S. Baijal
Department of Radiodiagnosis, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Road, Lucknow 226014, India

S. K. Baik
Division of Gastroenterology and Hepatology, Department of Internal Medicine, Wonju College of Medicine, Yonsei University, 162, Ilsan-dong, Wonju 220-701, South Korea

Y. Bayraktar
Department of Gastroenterology, Faculty of Medicine, Hacettepe University, 06100 Sihhiye, Ankara, Turkey

Y. K. Chawla
Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

G. Choudhuri
Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Raebareli Road, Lucknow 226 014, UP, India

J. W. Chung
Department of Radiology, Institute of Radiation Medicine, Seoul National University College of Medicine, Clinical Research Institute, 28 Yongon-Dong, Chongno-Gu, Seoul 110-774, South Korea

R. de Franchis
Department of Medical Sciences, University of Milan, Fondazione Ospedale IRCCS Maggiore Policlinico, Mangiagalli and Regina Elena, Milan, Italy

H. J. de Silva
Department of Medicine, Faculty of Medicine, University of Kelaniya, P.O. Box 6, Thalagolla Road, Ragama, Sri Lanka

P. K. Garg · A. Saraya
Department of Gastroenterology, All India Institute of Medical Sciences, New Delhi, India

AVB episode is 48 h. AVB is further classified as active or inactive at the time of endoscopy. Combination therapy with vasoactive drugs (<30 min of hospitalization) and endoscopic variceal ligation (door to scope time <6 h) is accepted as first-line therapy. Rebleeding (48 h of T_0) is further sub-classified as very early rebleeding (48 to 120 h from T_0), early rebleeding (6 to 42 days from T_0) and late rebleeding (after 42 days from T_0) to maintain uniformity in clinical trials. Emphasis should be to evaluate the role of adjusted blood requirement index (ABRI), assessment of associated comorbid conditions and poor predictors of non-response to combination therapy, and proposed APASL (Asian Pacific Association for Study of the Liver) Severity Score in assessing these patients. Role of hepatic venous pressure gradient in AVB is considered useful. Antibiotic (cephalosporins) prophylaxis is recommended and search for acute ischemic hepatic injury should be done. New guidelines have been developed for management of variceal bleed in patients with non-cirrhotic PHT and variceal bleed in pediatric patients.

Conclusion Management of acute variceal bleeding in Asia–Pacific region needs special attention for uniformity of treatment and future clinical trials.

Keywords Gastrointestinal hemorrhage · Cirrhosis · Portal hypertension · Vasoactive drugs · Endoscopy

Introduction

Acute variceal bleeding (AVB) is a medical emergency associated with a mortality that, in spite of recent progress, is still in the order of 20% at 6 weeks [1]. Design and conduct of good clinical trials for the evaluation of diagnostic modalties and assessment of treatment options for AVB have always been difficult. The Asian Pacific Association for the Study of the Liver (APASL) set up a w*orking party* on Portal Hypertension (PHT) in 2002, with a mandate to develop consensus guidelines on various clinical aspects of portal hypertension, relevant to disease patterns and clinical practice in the Asia–Pacific region. The present review summarizes the APASL consensus guidelines on AVB.

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

A. Helmy
Section of Gastroenterology, Department of Medicine MBC: 46, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Saudi Arabia

M.-C. Hou
Division of Gastroenterology, Department of Medicine, Taipei-Veterans General Hospital, No. 201 Sec. 2 Shih-Pai Road, Taipei 11217, Taiwan, ROC

W. Jafri
Section of Gastroenterology, Department of Medicine, The Aga Khan University Hospital, Karachi, Pakistan

J.-D. Jia
Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, People's Republic of China

G. K. Lau
Department of Medicine, 1838, Block K, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong SAR, People's Republic of China

C.-Z. Li
Department of Gastroenterology and Hepatology, Chinese PLA General Hospital, 28 Fuxing Road, Beijing 100853, People's Republic of China

H. F. Lui
Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore 169608, Singapore

H. Maruyama
Department of Medicine and Clinical Oncology, Chiba University Graduate School of Medicine, Chiba, Japan

C. M. Pandey
Department of Biostatistics, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Road, Lucknow 226014, India

A. S. Puri · B. C. Sharma
Department of Gastroenterology, GB Pant Hospital, New Delhi, India

R. Rerknimitr
Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10310, Thailand

P. Sahni
Department of Gastrointestinal Surgery, All India Institute of Medical Sciences, New Delhi, India

G. Shiha
GI and Liver Unit, Internal Medicine Department, Almansoura Faculty of Medicine, Almansoura 35516, Egypt

J. D. Sollano
Section of Gastroenterology, University of Santo Tomas, España, Manila, The Philippines

For the purpose of development of consensus guidelines, the APASL *working party* identified various contentious issues on various aspects of AVB. Experts predominantly from the Asia–Pacific region were requested by the *working party* to review the existing literature and develop consensus guidelines on each of these issues. A 2-day meeting was held on 31st January and 1st February, 2009, at New Delhi, India, to discuss, debate, and finalize the consensus statements. Only those statements that were unanimously approved by the experts were accepted. These statements were circulated to all the experts and were subsequently presented at the annual conference of the APASL at Hong Kong, China, in March 2009. The *working party* adopted the Oxford system [6] for developing an evidence-based approach. The group assessed the level of existing evidence and accordingly ranked the recommendations [i.e., level of evidence from 1 (highest) to 5 (lowest); grade of recommendation from A (strongest) to D (weakest)]. A summary of the most important conclusions is reported here.

Definitions of AVB and related states

Variceal bleeding constitutes 70% of all upper gastrointestinal bleeding episodes in patients with portal hypertension, and they result from esophageal varices (EVs), gastric varices (GVs), or ectopic varices. Remaining 30% is due to other causes, like portal hypertensive vasculopathies, Mallory Weiss lesions and ulcers [7, 8].

AVB needs a clear definition, especially in terms of time frame to differentiate it from recent bleeding and rebleeding. This is especially important because treatment modalities and prognosis may differ in each of these situations. Due to lack of a commonly used definition, comparison between studies and/or interpretation of outcomes research is difficult. It is important that the defined criteria should be easy and convenient with wide applicability to use for practice and should accurately identify and sufficiently discriminate patients with poorer outcomes. Till now there has been no homogeneity in definitions relating to AVB. This may be a result of different approaches of studies; for example, studies relating to vasoactive agents have used a time frame of 3–5 days, those relating to 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 and even months. Hence, consensus on a fixed time frame-based definition of AVB has been lacking.

The experts discussed on the time frame-based definition and arrived at the following consensus: AVB is defined as hematemesis within last 24 h of presentation, and/or ongoing melena, with last melanic stool within last 24 h in a known or suspected case of PHT. The time of presentation is considered as T_0. This definition clearly discriminates patients who at presentation would be categorized as having AVB or those having recent bleed. The treatment would differ in the two situations. Thus, a patient who has had hematemesis more than 24 h prior to presentation and is currently passing non-melanic stools will not be considered having AVB but will be considered as having had a recent bleed. Recent bleed refers to a clinically significant bleed which occurred within 6 weeks of presentation. A clinically significant bleed which occurred more than 6 weeks of presentation would be considered as a past bleed.

The time frame of AVB is 48 h. Hence, any subsequent bout of hematemesis from T_0 to 48 h of T_0 will be considered as part of the same episode of AVB and any bleeding occurring after 48 h will be considered as rebleeding. The time frame as defined in Baveno II [9, 10] and Baveno III [11, 12] was 48 h. However, it was increased to 120 h in Baveno IV [1]. However, the experts felt that a time frame longer than 48 h will make it difficult to differentiate between early rebleeding and failure to control bleeding.

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. This discrimination between active and inactive bleeding is important because the prognosis differs between the two. Significance of active bleeding (spurting or oozing) at endoscopy has evolved from Baveno I [13] where no consensus could be reached. In Baveno II [9], it was stated that its significance was unclear while in Baveno III [11], the consensus was that active bleeding at endoscopy is a predictor of failure to control bleeding, while its prognostic

J. Wu
Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, 30-32 Ngan Shing Street Shatin, Hong Kong, People's Republic of China

R. Y. Xu
Department of Hepatobiliary Surgery, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou 510630, Guangdong, People's Republic of China

S. K. Yachha
Department of Pediatric Gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Road, Lucknow 226014, India

C. Zhang
Department of Gastroenterology, Shandong Provincial Hospital, Jinan 250021, Shandong, People's Republic of China

Table 1 Time-dependent definitions of acute variceal bleeding and rebleeding

State	Time frame from T_0	Sub-types	Time frame from T_0
Acute variceal bleeding	48 h	Active (based on endoscopy)	48 h
		Inactive (based on endoscopy)	48 h
Rebleeding	After 48 h	Very early rebleed	48–120 h
		Early rebleed	6–42 days
		Late rebleed	After 42 days

Table 2 American College Criteria for amount of blood loss

	Class 1	Class 2	Class 3	Class 4
Blood loss (mL)	<750	750–1,500	1,500–2,000	>2,000
Blood loss (%)	0–15	15–30	30–40	>40
Systolic BP	No change	Normal	Reduced	Very reduced
Diastolic BP	No change	Raised	Reduced	Very reduced
PR (min)	Slight tachycardia	100–120	120 (thready)	>120 (very thready)
RR (min)	Normal	Normal	>20	>20
Mental state	Alert, thirsty	Anxious, aggressive	Anxious, aggressive, or drowsy	Drowsy, confused, or unconscious

value for mortality is unclear. The presence of active bleeding at endoscopy predicts early rebleeding [7].

Definitions and criteria to evaluate failure to control bleeding and failure to prevent rebleeding were introduced at Baveno II [9, 10]. They were again reviewed at Baveno III [11, 12] and further new definitions and criteria were proposed at Baveno IV [1]. These definitions and criteria have been extensively applied in trials, but it has been found that some of them are rather difficult to apply and do not reflect adequately the situation in clinical practice. Moreover, many investigators have used their own criteria and definitions resulting in a lot of heterogeneity in various reported trials.

The experts felt that prior to defining failure to control bleeding it was important to define "control" of AVB. The following definition was proposed: Control of AVB refers to cessation of bleeding with hemodynamic stability for 24 h after therapy. In patients with active bleeding on endoscopy, cessation of bleeding should be confirmed at the end of the procedure.

Failure to control AVB is defined by any of the following events, whichever occurs first, within 48 h from time of presentation to the hospital (T_0): development of fresh hematemesis after 2 h of combination [drugs + endoscopic variceal ligation (EVL)] therapy; or >2 g drop in Hb (6% drop in hematocrit) if no transfusion is administered; or death. The first two criteria would require modification of therapy (Table 1).

Box 1

1. Definitions of acute variceal bleeding and related states	Level	Grade
1.1. Variceal bleeding constitutes 70% of all upper gastrointestinal bleeding episodes in patients with portal hypertension, and they result from esophageal varices, gastric varices, or ectopic varices. The remaining 30% is due to other causes, like portal hypertensive vasculopathies, Mallory Weiss lesions, and ulcers	1b	A
1.2. Acute variceal bleeding is defined as	5	D
1.2.1. In a known or suspected case of PHT presence of		
1.2.1.1. Hematemesis within last 24 h of presentation, and/or		
1.2.1.2. Ongoing melena, with last melanic stool within last 24 h		
1.2.2. The time frame for the acute variceal bleeding episode is 48 h (Table 1)		
1.2.3. The acute variceal bleeding may be active or inactive at the time of presentation		
1.2.3.1. Active bleeding is a state which is defined endoscopically, when spurting or oozing is seen from the varix		
1.3. Control of acute variceal bleeding refers to cessation of bleeding with hemodynamic stability for 24 h after therapy	2a	B
1.3.1. In patients with active bleeding at endoscopy, cessation of bleeding should be confirmed at the end of the procedure		

Box 1 continued

1. Definitions of acute variceal bleeding and related states	Level	Grade
1.4. Failure to control acute variceal bleeding refers to failure of the combination therapy given and is defined by any of the following events, whichever occurs first, within 48 h from time combination (drugs + EVL) therapy is instituted	3	C
1.4.1. Development of fresh hematemesis after 2 h of combination (drugs + EVL) therapy		
1.4.2. >2 g drop in Hb (6% drop in Hct) if no transfusion is administered		
1.4.3. Continuous increase in heart rate and decrease of systolic blood pressure with adequate infusion		
1.4.4. Death (note: the first three criteria would require modification of therapy)		
1.5. Rebleeding is defined as any new hematemesis (or new melena) after 48 h of T_0 and after a period of 24 h of hemodynamic stability (Table 1)	5	D
1.5.1. Subtypes of rebleeding are		
1.5.1.1. Very early rebleeding—which occurs between 48 h and 120 h from T_0		
1.5.1.2. Early rebleeding—which occurs between 6 days and 42 days from T_0.		
1.5.1.3. Late rebleeding—which occurs after 42 days from T_0		
1.5.2. Clinically significant rebleeding is defined as rebleeding associated with any of the following		
1.5.2.1. Decrease of 2 g of Hb if no BT is given		
1.5.2.2. ABRI (adjusted blood requirement index) $\geq$0.5 at any time point		
1.6. Index bleed is defined as the first episode of bleeding with which the patient presents to the hospital	5	D
1.7. Recent bleed refers to a clinically significant bleed which occurred within 6 weeks of presentation	5	D
1.8. Past bleed refers to a clinically significant bleed which occurred more than 6 weeks of presentation	5	D
1.9. The following terms should no longer be used	5	D
1.9.1. Trivial bleed		
1.9.2. Spontaneous cessation of bleed		

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

Patients who have upper gastro-intestinal bleeding must be promptly and clinically assessed to provide a rational basis for key early decisions on management. The history, physical examination, and initial laboratory values are important in assessing resuscitation requirements, triage, endoscopy timing, consultation requirements, and prognostication [14].

The history should be focused on the gastrointestinal tract and significant comorbid conditions. If jaundice, ascites, signs of hepatic encephalopathy, splenomegaly, palpable firm left hepatic lobe, presence of abdominal wall collaterals, pedal edema, gynecomastia, testicular atrophy, parotid enlargement, vascular spiders, leukonychia, and palmar erythema are present, suspect the cause of bleeding to be portal hypertension. In cirrhotics, about 60% of initial upper gastro-intestinal bleeding is from EVs [15].

The physical examination, while complete, is directed at findings relevant to gastrointestinal bleeding. The severity of blood loss is roughly estimated by the hemodynamic status and other key signs (Table 2). Resting tachycardia, in the absence of another cause, suggests mild to moderate hypovolemia. Orthostatic hypotension is 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. Orthostatic hypotension suggests a loss of 15% or more of the blood volume. Hypotension is associated with a 40% loss of blood volume [16]. Patients in shock typically have a thready, weak pulse, and cold, clammy extremities. The abdomen is carefully examined. Hyperactive bowel sounds are consistent with a upper gastrointestinal bleeding because blood in the proximal gut is an irritant that stimulates peristalsis, whereas normoactive bowel sounds are more consistent with lower gastrointestinal bleeding.

Variceal hemorrhage is defined as bleeding from an EV or GV confirmed by endoscopy. Varices are accepted as the bleeding source, when blood is seen arising from an EV—usually spurting; or actively oozing; or when there is presence of a sign of recent bleed on a varix (white nipple sign or overlying clot); or when there is presence of EVs with red signs (risk factors for bleed) and presence of blood in the stomach in the absence of another source of bleed; or when there is presence of EVs with red signs and clinical signs of upper GI bleed, without blood in the stomach.

The expert panel proposed an APASL Severity Score for AVB to be used for severity assessment (Tables 3, 4). However, since this score is largely based on expert opinion, it needs prospective validation.

Table 3 Predictors of severity of acute variceal bleeding, treatment failure, early rebleeding, and mortality

Predictor	Severity of variceal bleed	Treatment failure	Early rebleeding	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/Hb 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
Urea			Yes	Yes
Hematemesis			Yes	
Creatinine				Yes
Albumin				Yes
Age				Yes
Early rebleeding				Yes
Prothrombin time				Yes
Treatment failure				Yes
Bilirubin				Yes

Box 2

2. Diagnosis, evaluation, and severity assessment of patients with acute variceal bleed	Level	Grade
2.1. In a patient with upper gastrointestinal bleeding, if the following are present, suspect the cause to be portal hypertension		
2.1.1. Previous history of hepatitis B, hepatitis C, or alcohol abuse	2a	B
2.1.2. Jaundice		
2.1.3. Ascites		
2.1.4. Signs of hepatic encephalopathy		
2.1.5. Splenomegaly		
2.1.6. Palpable firm left hepatic lobe		
2.1.7. Presence of abdominal wall collaterals		
2.1.8. Pedal edema		
2.1.9. Gynaecomastia		
2.1.10. Testicular atrophy		
2.1.11. Parotid enlargement		
2.1.12. Vascular spiders		
2.1.13. Leuconykia		
2.1.14. Palmar erythema		

Box 2 continued

2. Diagnosis, evaluation, and severity assessment of patients with acute variceal bleed	Level	Grade
2.2. The gold standard for diagnosis of acute variceal bleeding is upper gastrointestinal endoscopy.	2a	B
2.3. On endoscopy, one of the following is indicative of acute esophageal variceal bleed	1b	A
2.3.1. Direct visualization of blood arising from an esophageal varix—usually spurting or oozing		
2.3.2. Presence of a sign of recent bleed on a varix (white nipple sign or overlying clot)		
2.3.3. Presence of esophageal varices with red signs (risk factors for bleeding) and presence of blood in the stomach in the absence of another source of bleeding		
2.3.4. Presence of esophageal varices with red signs and clinical signs of upper GI bleeding, without blood in the stomach		
2.4 For the evaluation of amount of blood loss, the following may be used		
2.4.1. Change of vital signs (heart rate, blood pressure)	5	D
2.4.2. Hematocrit/hemoglobin		
2.4.3. Transfusion requirement		
2.4.4. ABRI (however, it is of limited value)		

Box 2 continued

2. Diagnosis, evaluation, and severity assessment of patients with acute variceal bleed	Level	Grade
2.4.5. American College Criteria (Table 2), however, targets specifically for acute variceal bleeding but need to be defined to plan management strategies		
2.5. All patients presenting for the first time should have a thorough work-up to assess for PHT and its cause and potential precipitating agents for the bleed, such as infections, drugs, etc.	5	D
2.6. Known cases of chronic liver disease presenting with acute variceal bleeding should have an updated assessment looking for potential precipitating causes such as	5	D
2.6.1. Causes which increase portal hypertension		
2.6.1.1. Portal vein thrombosis		
2.6.1.2. Hepatocellular carcinoma		
2.6.2. Sepsis/infection especially spontaneous bacterial peritonitis		
2.6.3. Acute-on-chronic liver failure		
2.6.4. Drug ingestion especially recent ingestion of non-steroidal anti-inflammatory drugs (NSAIDs)		
2.6.5. Alcohol abuse		
2.7. Assessment of co-morbidities should include		
2.7.1. Complications related to cirrhosis	5	D
2.7.1.1. Hepatorenal syndrome		
2.7.1.2. Ascites		
2.7.1.3. Hepatic encephalopathy		
2.7.1.4. Hepatocellular carcinoma		
2.7.2. Comorbidities unrelated to cirrhosis		
2.7.2.1. Infection		
2.7.2.2. Renal disease		
2.7.2.3. Cardio-respiratory disease		
2.8. Predictors of severe acute variceal bleeding should be carefully assessed (Table 3).	1b	A
2.9. The following categories of patients are difficult to treat patients and require higher expertise or facilities for management		
2.9.1. Esophageal variceal (EV) bleeding with large gastric varices (GV)	5	D
2.9.2. EV bleeding with difficult overtube insertion or difficult multiband ligator insertion		
2.9.3. EV bleeding with severe fibrosis or extensive ulceration		
2.9.4. Massive EV bleeding without identified site		
2.9.5. Isolated gastric variceal bleeding		
2.9.6. Active bleeding from PHG		
2.9.7. Ectopic variceal bleeding		
2.9.8. Bleeding refractory to drug, endoscopic, and shunting therapy		
2.10. Proposed APASL severity score for acute variceal bleeding (Table 4).	5	D

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

The management of AVB includes hemodynamic resuscitation, general treatment, prevention of complications, and achievement of hemostasis. Intravenous access must be promptly secured. Airway intubation is indicated in patients who are bleeding severely or who have mental status changes that preclude their ability to protect their airway. Intravascular volume loss is estimated and replaced with crystalloids and packed red cells. The systolic blood pressure should be maintained at least at 90–100 mmHg, and the heart rate should be maintained below 100 beats/min, with a 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 rebleeding [17, 18]. Fresh frozen plasma and platelets (particularly for a platelet count <50,000 mL^{-1}) have often been used to correct coagulopathy. They do not adequately correct the coagulopathy and can induce volume overload and rebound PHT [19]. The use of recombinant factor VII has been shown to improve hemostasis rates, but it does not improve survival [20].

Table 4 Proposed APASL severity score for acute variceal bleeding; it needs prospective validation

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

Currently, it is recommended that short-term antibiotic prophylaxis, a measure that reduces bacterial infections [21], variceal rebleeding [22], and death [21] be used in every patient with cirrhosis admitted with gastrointestinal hemorrhage [1, 2]. Different antibiotics have been used in different trials, and given different local antibiotic susceptibility patterns and different availability, it is unlikely that a definitive trial in this area will be performed.

Specific therapy is based on the combination of pharmacological and endoscopic therapy, which is better than either treatment alone [23–25], particularly with early administration of pharmacological therapy [26, 27]. In no randomized controlled trials (RCTs) different combinations of endoscopic/pharmacological therapy were compared.

RCTs comparing different pharmacological agents (vasopressin, somatostatin, terlipressin, and octreotide)

demonstrate no differences among them regarding control of hemorrhage and early rebleeding, although vasopressin is associated with more adverse events [24]. The clinical efficacy of terlipressin versus placebo has been assessed in seven RCTs, and a meta-analysis showed that terlipressin significantly reduced failure to control bleeding and mortality [28]. It is important to note that terlipressin is the only pharmacologic agent that has been shown to reduce mortality (a 34% reduction). Hence, terlipressin was considered by the experts as the first-line choice. In practice, the choice of pharmacological agent is usually based on availability and cost. The optimal duration of pharmacological therapy has not been well established. In RCTs, the duration of vasoactive treatment has varied between 8 h and 6 days. Trials aimed at determining the best duration of therapy are impractical and costly. There was majority agreement that an appropriate length of therapy would be anywhere between 2 and 5 days [2], depending on control of hemorrhage and the presence or absence of predictors of rebleeding (for example, CTP class and hepatic venous pressure gradient (HVPG)).

Box 3

3. Resuscitation, initial management, and monitoring of patients with acute variceal bleed	Level	Grade
3.1. Initial resuscitative measures include protection of airway, breathing, and circulation (ABC)	1a	A
3.1.1. For protection of the airway elective intubation is recommended in patients with	2b	B
3.1.1.1. Severe uncontrolled variceal bleeding		
3.1.1.2. Hepatic encephalopathy (grade III and IV)		
3.1.1.3. Aspiration pneumonia		
3.1.1.4. With difficulty maintaining oxygen saturation above 90%		
3.1.2. Fluid volume replacement	2b	C
3.1.2.1. Fluid replacement should be used very conservatively and cautiously		
3.1.2.2. Colloids are preferred and crystalloids should be avoided, particularly saline, maintenance fluids is by dextrose infusion	2a	C
3.1.2.3. The volume of fluids to administer should be aimed to maintain	2b	B
3.1.2.3.1. Systolic blood pressure of 90–100 mmHg		
3.1.2.3.2. Heart rate below 100 beats per minute		
3.1.2.3.3. CVP 1–5 mmHg		
3.1.2.3.4. Diuresis of 40 mL/h		
3.1.3. Blood volume restitution	5	D
3.1.3.1. Blood transfusion requirement is determined by estimating blood loss (Table 2).		
3.1.3.2. Blood volume replacement should be done cautiously and conservatively to maintain	1b	A
3.1.3.2.1. A hemoglobin level of approximately 7–8 g/dL		
3.1.3.2.2. A hematocrit value of 21–24%, depending on other factors, such as Patient's co-morbidities, age, haemodynamic status, and presence of ongoing bleeding		
3.1.3.3. Packed red blood cells (PRBC) is the preferred blood component	5	D
3.2. Administration of a short course of antibiotic prophylaxis (5–7 days) with intravenous ceftriaxone (2–4 g/day) decreases the rate of bacterial infections and increases survival in patients with variceal hemorrhage	1a	A
3.3. Specific management of coagulopathy or thrombocytopenia needs to be studied further for its relevance in acute variceal bleeding management	5	D
3.4. The use of recombinant activated factor VII (rFVIIa) in cirrhotic patients with acute variceal bleeding is not currently recommended	1b	A
3.5. Pharmacological therapy	1a	A
3.5.1. Pharmacological therapy using vasoactive drugs should be initiated as soon as variceal hemorrhage is suspected		
3.5.2. Door to needle time should be <30 min and once variceal bleed is confirmed, combination therapy should be started	5	D
3.5.3. Terlipressin should be the first choice for pharmacological therapy when available, and there is no contraindication. However, where terlipressin is not available, somatostatin, octreotide, and vapreotide could be used	5	D
3.5.3.1. Use of terlipressin requires baseline ECG		
3.5.3.2. Dose of terlipressin: 2 mg every 4 h		
3.5.4. In patients with esophageal variceal bleeding, pharmacological therapy should be maintained for 2–5 days. The latter duration should be used in difficulty to treat patients or those with high severity score	5	D
3.6. ICU care—following groups of patients should be managed in ICU	4	C
3.6.1. Presence of active bleeding		
3.6.2. Patients with elevated PT		
3.6.3. Patients with predictors of high mortality		
3.6.4. Difficulty to treat patients		
3.7. Monitoring	5	D
3.7.1. Naso-gastric (NG) tube monitoring: routine use of NG tube is not recommended but it may be used in cases of hepatic encephalopathy		

Box 3 continued

3. Resuscitation, initial management, and monitoring of patients with acute variceal bleed	Level	Grade
3.7.2. CVP monitoring	2a	B
3.7.2.1. CVP is helpful to optimize the decisions concerning volume of fluid replacement in selected patients		
3.7.2.1.1. Elderly		
3.7.2.1.2. Patients with cardiovascular co-morbidity		
3.7.2.1.3. Active bleeding at endoscopy		
3.7.2.1.4. Patients with severe bleeding		
3.7.2.1.5. Presence of shock		
3.7.2.1.6. Renal failure (impending or present)		
3.7.2.2. For CVP monitoring jugular approach is better but must be undertaken in expert hands	5	D
3.7.2.3. CVP alone may not accurately predict fluid responsiveness	2a	B
3.7.3. Pulmonary capillary wedge pressure monitoring: routine use of a pulmonary artery catheter in the management of patients of acute variceal bleeding with or without shock is not recommended	1a	A

Role of endoscopy in AVB

Endoscopic variceal ligation is more effective than endoscopic variceal sclerotherapy (EVS) with greater control of hemorrhage, lower rebleeding, and lower adverse events but without differences in mortality [29, 30]. No further trials are necessary to determine the best endoscopic therapy.

Since endoscopic therapy and medical therapy with vasoactive drugs each have been reported to control bleeding in up to 80–85% of patients and their mode of action is completely different, a synergistic effect of the two treatments can be anticipated. A meta-analysis of Banares and co-workers [23], who compared endoscopic therapy with combined endoscopic and pharmacologic treatment, showed that control of acute bleeding 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). To ensure smooth conduct of endoscopy in these patients a check-list should be maintained in the endoscopy theater (Table 5).

Table 5 Check-list to be maintained in the endoscopy theatre

Patient
Vital signs
Two intravenous lines
Fluid resuscitation
Supplemental oxygen
Informed consent
Endoscopy theatre
Check endoscope (air–water channel, suction, knobs, etc.)
Suction device
Patient resuscitation cart
Patient monitor
Accessories
Availability of alternate therapy
Interventional radiologist
GI surgeon
Sengstaken Blakemore tube

Box 4

4. Role of endoscopy in acute variceal bleeding	Level	Grade
4.1. All upper gastro-intestinal endoscopy (UGIE) in patient with acute upper gastro-intestinal bleed should undergo endoscopy with the intent to provide endotherapy	5	D
4.2. Combination of a vasoactive drug and endoscopic therapy is the first-line therapy for variceal bleed	1a	A
4.3. Timing of endoscopy (the door to scope time): in patients with acute variceal bleeding endotherapy should be done as soon as possible under resuscitation, preferably within 6 h of admission (T_0)	5	D
4.4. Following preparations should be done prior to endoscopy	2a	B
4.4.1. Blood pressure: systolic BP > 70 mmHg		
4.4.2. Unconscious patients should be intubated prior to endoscopy	5	D
4.4.3. Drugs	1a	A
4.4.3.1. A vasoactive drug should be initiated prior to endoscopy		
4.4.3.2. An injectible proton pump inhibitor should be given if there is doubt of diagnosis	1a	A
4.4.3.3. Third-generation cephalosporins should be given	1a	A
4.4.4 Sedation	5	D
4.4.4.1. Routine use of sedation is not recommended		

Box 4 continued

4. Role of endoscopy in acute variceal bleeding	Level	Grade
4.4.4.2. Sedation may be indicated in selected situations with back up of intubation	5	D
4.4.4.3. Drugs to be used (based on user ease)	5	D
4.4.4.3.1. Midazolam + pethidine/Fortwin		
4.4.4.3.2. Propofol		
4.4.4.3.3. Propofol + midazolam		
4.4.4.4. Special care should be taken in sedating patients with early encephalopathy or hemodynamic instability	5	D
4.4.5. To obtain better field of vision	2b	B
4.4.5.1. Injection erythromycin can be given		
4.4.5.2. Use of double or large channel endoscope to be preferred	5	D
4.4.5.3. Gastric lavage prior to endoscopy is not needed	2b	B
4.4.6. The posture of the patient should be left lateral, and to evaluate the fundus a right lateral posture should be preferred	5	D
4.4.7. Preferably a check-list should be maintained in the endoscopy theater (Table 5)	5	D
4.5. Endoscopic treatment	1a	A
4.5.1. EVL with multiband ligator is the treatment of choice for acute esophageal variceal bleeding		
4.5.2. Ideal EVL technique	2b	B
4.5.2.1. Use a multiband ligator		
4.5.2.2. Banding to be done starting from just above GE junction (5–10 mm) in a sequential manner up to 5 cm		
4.5.2.3. Up to 6 bands may be applied		
4.5.2.4. In case of active variceal bleed	5	D
4.5.2.4.1. First band to be applied on culprit vessel		
4.5.2.4.2. Try to catch the bleeding point or just below the ooze		
4.5.2.4.3. Clean field of view using flush catheter		
4.5.2.4.4. Go into the stomach and wait for varix to collapse over the endoscope		
4.5.3. Injection sclerotherapy (EST)	5	D
4.5.3.1. EST is indicated in setting of acute variceal bleed only when		
4.5.3.1.1. EVL is not available		
4.5.3.1.2. EVL is not technically feasible		
4.5.3.2. Intra-variceal injection with a free-hand technique is commonly used	1b	A
4.5.3.3. There is considerable variation in choice and volume of sclerosants	5	D
4.6. EVL-induced ulcer bleed	2	C
4.6.1. Diagnosis is based on endoscopy with finding of EVL-induced ulcer with		
4.6.1.1. Ooze or spurt or clot		
4.6.2.2. No evidence of other source of bleed		

Box 4 continued

4. Role of endoscopy in acute variceal bleeding	Level	Grade
4.6.2. Treatment	5	D
4.6.2.1. Indirect measures		
4.6.2.1.1. Correct coagulopathy		
4.6.2.1.2. PPI for two weeks		
4.6.2.1.3. Sucralfate		
4.6.2.2. Direct measures		
4.6.2.2.1. Banding, directly over the ulcer or below it		
4.6.2.2.2. Fibrin glue		
4.6.2.2.3. Cyanoacrylate injection		
4.7. Role of repeat endoscopy	5	D
4.7.1. In case of failure to control bleed, second attempt at UGIE is recommended to		
4.7.1.1. Re-evaluate the cause of bleed		
4.7.1.2. Have one more attempt at endotherapy		
4.7.2. Repeat UGIE in this situation may need more expertise	5	D
4.7.3. Patients with recently placed bands can be scoped but need caution and more expertise	5	D
4.7.4. Repeat endoscopy should be carefully planned with risk stratification, and a rescue therapy plan should be initialized simultaneously	5	D
4.7.5. A second endoscopic treatment is not needed always and the patient can be shifted to radiologic treatment when poor prognostic markers, such as high HVPG are present	4	C

Role of rescue therapies in AVB

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 rebleeding, balloon tamponade is not used routinely as the first-line treatment for control of AVB.

Transjugular intrahepatic portosystemic shunt (TIPS) is a reasonable alternative in the face of failure of combined pharmacologic plus endoscopic therapy. In the Baveno conference, it was considered that a second attempt at endoscopic therapy was one possibility and one could perform TIPS after failure of the second endoscopic therapy [1]. A small study suggests that early TIPS placement (within 24 h of hemorrhage) is associated with a significant improvement in survival in patients with HVPG greater than 20 mmHg [31]. Therefore, HVPG can provide useful

information that allows for risk stratification and more aggressive treatment in high-risk patients.

Box 5

5. Role of rescue therapies in acute variceal bleeding	Level	Grade
5.1. Role of balloon tamponade	1b	B
5.1.1. Balloon tamponade should only be used in uncontrolled bleeding as a temporary "bridge" until definitive treatment can be instituted for a maximum of 12 h		
5.1.2. If hemostasis is not achieved with tamponade within 2 h, other therapeutic options should be tried	5	D
5.2. Role of TIPS	2a	B
5.2.1. TIPS is indicated in patients in whom bleeding from esophageal varices cannot be controlled or who rebleed despite combined pharmacological and endoscopic therapy		
5.2.2. Early TIPS placement (within 24 h of hemorrhage) can be considered in "high-risk" patients (defined as those with an HVPG $>$ 20 mmHg) with acute variceal bleeding	1b	A
5.2.3. In centres where the expertise is available, surgical shunt can be considered in Child A patients. The performance of both shunt surgery and TIPS are dependent on local expertise	1b	A
5.2.4. TIPS stent may cause technical difficulties in subsequent liver transplantation without significant influence on patient and graft survival	3b	C
5.2.5. TIPS dysfunction is significantly reduced using covered stents	1b	A
5.3 Role of surgery	1b	A
5.3.1. Indication of surgery is persistent variceal bleeding despite non-operative treatment		
5.3.2. Contraindications to surgery are	1b	A
5.3.2.1. Patients with advanced hepatic functional deterioration including severe hepatitis, uncorrectable coagulopathy, or deep hepatic coma		
5.3.2.2. Child class C categorization, which includes a wide spectrum of patients, in itself is not a contraindication to emergency surgery and some Patients can be considered for emergency surgery		
5.3.3. Surgery for acute control of variceal bleeding can be placed into one of four categories	3a	C
5.3.3.1. Non-selective portosystemic shunts		
5.3.3.2. Selective portosystemic shunts		
5.3.3.3. Devascularization procedures		
5.3.3.4. Liver transplantation		
5.3.4. The procedure selected depends on many factors, including expertise of available personnel, activity of bleeding, hepatic functional reserve, patency status of splanchnic veins, and transplant candidacy	5	D
5.3.5. There is a paucity of controlled data comparing these procedures to one another or to non-operative therapies	5	D
5.3.6. The major factor determining survival is the status of the liver disease at the time of surgery rather than the procedure selected	2a	B
5.4. Role of newer therapies	4	C
5.4.1. Endoesophageal stent therapy of acute variceal bleed is still in early stage and needs further evaluation		
5.4.2. Vapreotide is an alternative in control of acute variceal bleed	1b	A

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 rebleeding and higher mortality, likely secondary to a further increase in PHT, further splanchnic arteriolar dilatation, and increased coagulopathy [32, 33]. 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 [34]. 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 rebleeding and mortality [29–31, 35, 36]. A more recent study performed in the era of combined vasoactive drug plus endoscopic therapy confirms this HVPG cut-off and shows that an index including CTP score and blood pressure at admission has similar prognostic value [37]. Furthermore, a drug-induced HVPG reduction of less than 10% predicts 5-day failure. This response may improve by doubling the dose of somatostatin or switching to another agent (such as terlipressin) [38].

Box 6

6. Special topics in acute variceal bleeding	Level	Grade
6.1. Infections in acute variceal bleeding and role of antibiotics	1a	A
6.1.1. Chances of developing infection in AVB is		
6.1.2. Significant and gram negative bacteria especially, *E. coli,* are commonly detected in cultures		

Box 6 continued

6. Special topics in acute variceal bleeding	Level	Grade
6.1.3. Various tubes (NG, CVP, ET, SB) insertion may cause infection and colonizing organisms in stomach and skin play a role as etiology, consider changing the tubes regularly	2b	B
6.1.4. Standard work-up for infection when suspected includes CBC, CXR, urine, and blood culture	1b	A
6.1.5. The preferred agents for prevention of infection in AVB is at least 5 days of intravenous third-generation cephalosporin	1b	A
6.2. Prevention, assessment, and management of hepatic ischemia	3a	C
6.2.1. Ischemic hepatic injury can occur in up to 10% cirrhotic patients with acute variceal bleed.		
6.2.2. Hepatic ischemic injury should be anticipated and prevented in high-risk groups of patients with bleeding varices	5	D
6.2.3. The following groups of patients have high risk of hepatic ischemic injury	5	D
6.2.3.1. Patients with severe haematemesis and melena		
6.2.3.2. Bleeding leading to significant hypotension and/or shock		
6.2.3.3. Recurrent bouts of bleeding: at home, during transfer, at the casualty department, in the ward, and before or during emergency endoscopy even if there is no shock		
6.2.3.4. Repeated vomiting of fresh bright red blood not altered by the acidity of the stomach		
6.2.3.5. Rebleeding in a known patient with history of variceal bleeding		
6.2.3.6. Significant drop of hemoglobin and more specifically hematocrit values		
6.2.3.7 Patients with obstruction to hepatic blood flow		
6.2.3.7.1. Portal vein thrombosis		
6.2.3.7.2. Veno-occlusive disease		
6.2.3.8. Patients with decompensated cirrhosis even if hypotension is not severe		
6.2.3.9. Elderly patients		
6.2.3.10. Patients with diabetes mellitus		
6.2.3.11. Cirrhotic patients with hepatocellular carcinoma		
6.2.4. Prevention of hepatic ischemic injury should be done as follows	5	D
6.2.4.1. Resuscitation and adequate correction of hypovolemia, hypotension, and shock		
6.2.4.2. Correction of severe anemia by blood transfusion when necessary		
6.2.4.3. Rapid control of active bleeding by endoscopy		
6.2.4.4. Prophylactic antibiotics to guard against sepsis		
6.2.5. Hepatic ischemic injury could lead to rises in serum total bilirubin and/or aminotransferases and LDH within 24 h and it may adversely affect outcomes	5	D
6.2.6. Patients should be carefully observed even if hemorrhage from varices is controlled	5	D
6.2.7. Daily monitoring of ALT, S. Bilirubin, S. Creatinine, serum LDH, and ALT/LDH ratio should be done when ischemic hepatic injury is suspected	5	D
6.2.8. There is a need for prospective studies to further investigate the prevalence, severity, and treatment of hepatic ischemia in cirrhotic patients with variceal bleeding	5	D
6.2.9. No definite therapy has been found for the treatment of ischemic hepatic injury, but *N*-acetylcysteine may be tried	5	D
6.3 Acute variceal bleeding in patients with liver failure	5	D
6.3.1. Patients with cirrhosis and liver failure have high propensity for bleeding from gastro-esophageal varices		
6.3.2. Attempt at endoscopy procedure to control variceal bleeding may be done with extra caution with or without endotracheal intubation	5	D
6.3.3. Coagulopathy should be corrected with FFP and platelets	5	D
6.3.4. Role of factor rVIIa in this setting needs evaluation	5	D
6.4 Role of HVPG in management of acute variceal bleeding	1a	A
6.4.1. Cirrhotic patients who experience variceal bleeding almost universally have an HVPG of $\geq$ 12 mmHg		
6.4.2. Portal pressure is an independent predictor of outcomes in patients with acute variceal bleeding. HVPG $\geq$ 20 mmHg predicts failure to control bleeding and poor outcome	1a	A
6.4.3. HVPG measurement within 24 h is useful in patients of AVB, since it gives important prognostic information and also helps in making treatment decision	2b	B
6.4.4. Vasoactive drugs reduce portal pressure, but all patients with AVB may not be HVPG responders and the level of clinically useful response is also not well established	2b	B
6.4.5. More data are needed to recommend a repeat HVPG measurement in identifying non-responders, and altering treatment decisions	5	D

Diagnosis and treatment of acute gastric variceal bleeding

Gastric varices occur in approximately 20% of patients with portal hypertension. The treatment modalities depend to a large extent on an accurate categorization of GVs (Fig. 1). The most widely used classification system is Sarin's classification and this has been recommended for use by the expert panel. This classification categorizes GVs on the basis of their location in the stomach and their relationship with EVs. Gastroesophageal varices (GOVs) are associated with varices along the lesser curve [type 1 (GOV1)], or along the fundus [type 2 (GOV2)]; isolated gastric varices (IGVs) are present in isolation in the fundus (IGV1) or at ectopic sites in the stomach, or the first part of the duodenum (IGV2). GOV1 are responsible for 70% of GVs, and can be managed as EVs. It is for the other types that the clinician is faced with several choices.

Bleeding from GVs is generally more severe than bleeding from EVs, but is thought to occur less frequently. Fundal varices are the subtype of GVs with highest bleeding and rebleeding rates [39]. Remarkably, large fundal varices may occasionally bleed despite HVPG values less than 12 mmHg [40, 41]. Because the blood flow in the GVs is relatively large and the bleeding is rapid and often profuse, endoscopic (EVL, glue, and thrombin) means of treating bleeding GVs are the treatments of choice. The choice of endoscopic therapy used often depends on local availability and expertise. Other therapies to control hemorrhage include radiological options (TIPS, balloon-occluded retrograde transvenous obliteration (BRTO)). Uncontrolled data comparing these therapies in bleeding fundal varices show that the best control of initial hemorrhage (90–100%) is achieved with glue, TIPS, or balloon-occluded retrograde transvenous obliteration [42]. In three small single-center RCTs, endoscopic variceal obturation (EVO) with glue versus EVS [43] or EVL in bleeding gastric varices were compared [44, 45]. All three RCTs are favorable for EVO in the control of acute hemorrhage [43, 44], rebleeding [45], or complication rate [44]. Unfortunately, less than 50% of the patients included in these studies had fundal varices, and a separate analysis was not performed. It is recommended that TIPS be used in acute bleeding from fundal varices when EVO is unavailable or if rebleeding 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 fundal varices [46].

Box 7

7. Diagnosis and treatment of acute gastric variceal bleeding	Level	Grade
7.1. On endoscopy, one of the following findings constitutes acute gastric variceal bleeding	1b	A
7.1.1. Direct visualization of blood issuing from a gastric varix—spurting or oozing		
7.1.2. Presence of a sign of recent bleed over a gastric varix—overlying clot or white nipple sign		
7.1.3. Presence of gastric varices with red signs (risk factors for bleed) and presence of blood in the stomach in the absence of another source of bleed/or stigmata of recent bleed on esophageal varices		
7.1.4. Presence of gastric varices with red signs and clinical signs of upper GI bleed—melaena or haematemesis—without blood in the stomach		
7.2. For describing location of acute gastric variceal bleeding Sarin's classification of gastric varices should be used	5	D
7.3. There is rationale to use combination of vasoactive drugs and endoscopic therapy despite lack of specific data at present	5	D
7.4. In patients with acute bleeding from gastric varices, endoscopic variceal obturation using tissue adhesives is the treatment of choice	1b	A
7.5. In patients with acute bleeding from GOV1 type of varices, treatment should be similar to that of esophageal varices or glue injection	2b	B
7.6. Rescue therapies in acute gastric variceal bleeding	2b	B
7.6.1. Role of TIPS		
7.6.1.1. TIPS should be considered in patients with uncontrolled bleeding from gastric varices or if bleeding recurs despite combined pharmacological and endoscopic treatment		
7.6.2. Role of balloon occluded retrograde transvenous obliteration (BRTO)	2b	B
7.6.2.1. BRTO is a good alternative to TIPS in patients with gastrorenal/gastrocaval shunt after achieving initial hemostasis		
7.6.2.2. BRTO is indicated in gastric varices with gastrorenal shunt when endoscopic cyanoacrylate injection is unavailable or failed	2b	B
7.6.2.3. Before BRTO, the patient should achieve hemostasis using balloon tamponade/endoscopic therapy/pharmacologic measures	2b	B
7.6.2.4. BRTO of gastric varices shows high rate (>90%) of complete eradication of gastric varices and low rate (<10%) of gastric variceal recurrence during long-term follow-up	2b	B
7.6.2.5. BRTO complications: BRTO	2a	B
7.6.2.5.1 May induce or aggravate esophageal varices in a substantial proportion of patients during long-term follow-up		
7.6.2.6. More data is needed for	5	D
7.6.2.6.1. Recommending BRTO in Child C patients		
7.6.2.6.2. Any stratification of patients for TIPS versus BRTO		
7.6.3. A second attempt at endoscopic therapy may be tried if other rescue therapies, like TIPS/BRTO are not available or are contraindicated	5	D
7.6.4. Role of surgery: the indications, contraindications, and choice of surgical procedure for uncontrolled acute gastric variceal bleeding remain the same as uncontrolled acute esophageal variceal bleeding	5	D

Diagnosis and treatment of acute ectopic variceal bleeding

Ectopic varices comprise large portosystemic venous collaterals located anywhere other than the gastro-esophageal region [47]. No large series or RCTs address this subject, and therefore its 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 [48].

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 panendoscopy, enteroscopy, endoscopic ultrasound, wireless capsule endoscopy, diagnostic angiography, multislice helical computed tomography, magnetic resonance angiography, color Doppler-flow imaging, laparotomy, laparoscopy, and occasionally during autopsy [47].

Patients with suspected ectopic varices bleeding need immediate assessment, resuscitation, hemodynamic stabilization, and referral to specialist centers. Endoscopy can diagnose most of the cases, but in inaccessible sites, RBC scan would 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 patients' condition, site of varices, available expertise and patients' 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 NCPHT. Duodenal variceal bleeding inaccessible by endoscopy can also have an option of BRTO if vascular anatomy permits [47, 49, 50].

Box 8

8. Diagnosis and treatment of acute ectopic variceal bleeding	Level	Grade
8.1 Bleeding ectopic varices are a rare cause of variceal bleeding and are common in non-cirrhotics	3b	C
8.2. Site	3b	C
8.2.1. Ectopic varices occur in anorectum, antrum (IGV2), and duodenum, small intestine, colon, and peristomal		
8.2.2. Ectopic variceal bleeding may be from varices located in the following sites: duodenum, choledochus, omentum, stoma, and rectum		
8.2.3. Bleeding is more frequent in peristomal varices		
8.3. Endoscopy can diagnose most of the cases, but in inaccessible sites, RBC scan would identify the site of bleed and could be confirmed by angiography or CT angiography	3b	C
8.4 One of the following endoscopic findings constitutes acute ectopic variceal bleeding	3b	C
8.4.1. Direct visualization of blood issuing from varix—usually spurting		
8.4.2. Presence of a sign of recent bleed: white nipple sign or overlying clot		
8.5. Pharmacotherapy and endotherapy should be the first line of therapy if a bleeding ectopic varix is accessible, but in inaccessible cases, TIPS or PTVE should be done in patients with patent portal vein in cirrhosis and NCPHT	4	C
8.6. Duodenal variceal bleeding inaccessible by endoscopy can also have an option of BRTO if vascular anatomy permits	4	C

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

Variceal bleeding is a common and life-threatening complication of PHT due to NCPHT. There is paucity of data on the management of AVB in NCPHT; 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, 2]. Bacterial infections are more common in patients with cirrhosis having variceal bleeding (35–66%) than in non-cirrhotic patients (5–7%) [51]. It has been shown that infected cirrhotic patients have a higher rate of variceal rebleeding (43%) than non-infected patients (10%) [32]. In patients with cirrhosis and variceal bleeding, prophylactic antibiotics reduce variceal rebleeding and improve survival [21, 22]. In NCPHT, 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 [24–26]. However, there are no data on the efficacy of vasoactive drugs in patients with NCPHT with AVB.

Endoscopic sclerotherapy and band ligation are effective in 80–90% of patients in controlling acute bleeding from EVs and preventing rebleeding. 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 (88 vs. 76%) and preventing rebleeding for 5 days (77 vs. 58%), while there is no difference in mortality [1, 2]. There is, however, paucity of data for NCPHT. 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 rebleeding in 8–12% of patients, who should be treated by alternative modes of treatment, like surgery or TIPS.

Box 9

9. Acute variceal bleed in NCPHT	Level	Grade
9.1. Absence of ascites, jaundice, and hepatic encephalopathy, and presence of large splenomegaly are the clinical clues in differentiating NCPHT from cirrhotic portal hypertension (CPHT)	2b	B
9.2. Natural history of acute variceal bleeding in NCPHT has not been well studied, but mortality is low	2b	B
9.3. Definitions and time frames for acute variceal bleeding as for cirrhotics can be adapted for NCPHT as well	5	D
9.4. First-line treatment options are essentially the same as in cirrhotics	5	D
9.5. Gastric varices are more common in NCPHT and may be refractory to obturation by tissue adhesives	5	D
9.6. Coagulopathy is generally not a feature of NCPHT, and so, correction is not required	5	D
9.7. Antibiotics are generally not needed, unless absolute neutrophil count is $<1{,}000\ mm^{-3}$	5	D
9.8. Rescue therapies remain the same as in cirrhotics	4	C
9.9. Radiological treatment options as rescue therapy in NCPHT: though no randomized control trials have been conducted to investigate the potential of these techniques, case reports and series suggest efficacy for controlling variceal bleeding	4	C
9.10. Factors influencing choice of radiological procedure are	5	D
9.10.1. Etiological considerations		
9.10.2. Anatomical considerations		
9.10.3. Clinical status of the patient		
9.10.4. Affordability and available expertise		
9.11. No published data is available on the rate of complications of TIPS in patients with NCPF; however, owing to the good hepatic function, it might be logical to conclude that such complications would be uncommon in NCPF	5	D
9.12. Patients with failed first-line therapy for variceal bleeding should be considered for surgery	3a	C
9.13. Portal decompressive procedures are better than non-shunt procedures	5	D
9.13.1. Non-shunt procedures are preferred in patients who do not have suitable veins		

Pediatric perspectives of AVB

Evidence-based approaches to the management of adults with AVB exist and have been comprehensively reviewed. 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. Approaches to the management of AVB in children are anecdotal and there are few, if any, generally agreed upon approaches. 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.

Box 10

10. Pediatric perspectives of acute variceal bleeding	Level	Grade
10.1. The pediatric age-group is defined as age up to 18 years	5	D
10.2. The majority of upper gastro-intestinal bleed in children is variceal in origin	2a	B
10.3. 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	2a	B
10.4. Diagnosis and management is broadly similar to that in adults	5	D
10.5. Dosage and safety profile of octreotide in children has been established, however, for terlipressin or somtostatin the dose and safety need to be established in children	5	D
10.6. Choice of endoscopic procedure	5	D
10.6.1. Band ligation is preferred over EST for acute variceal bleeding		
10.6.2. EST is technically more feasible in younger children and those with smaller varices		
10.7. Rescue therapies	4	C
10.7.1. Radiological: though no randomized control trials have been conducted to investigate the potential of radiological techniques in children, case reports and case series suggest efficacy for controlling variceal bleeding		
10.7.2. Since, the etiological profile of acute variceal bleeding in children is different from that in adults, the threshold for surgery as first-line rescue therapy is low	5	D

Conclusions

The 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. However, still many questions on important issues concerning variceal bleeding remain to be answered. As new diagnostic tools and new treatments appear, they will have to be assessed in comparison with these consensus definitions and then these consensus statements need to be updated. The consensus definitions are intended

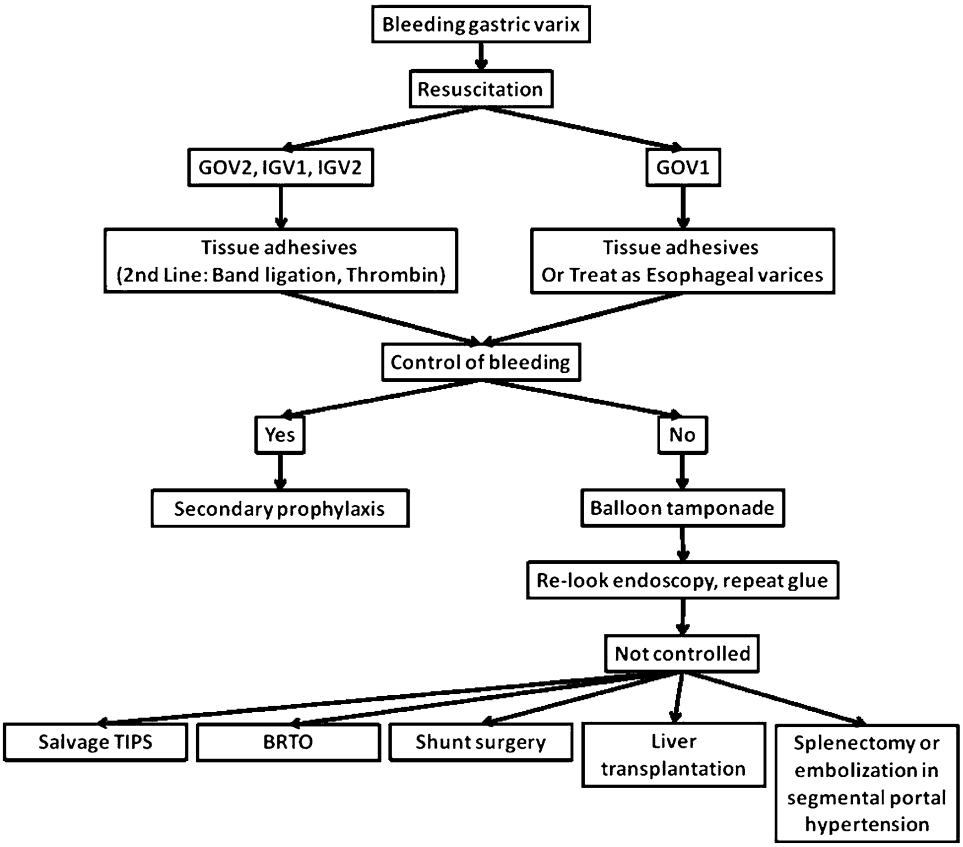

Fig. 1 Algorithm of management in patients with acute gastric variceal bleeding

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 end-points, meta-analyses will be based on more homogeneous studies, which is an essential prerequisite of this methodology. Change or refinement can then take place to ensure that the consensus definitions have clinical relevance and are easily applied in practice

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